North American Pediatric Renal Trials and Collaborative Studies

NAPRTCS

2011 Annual Dialysis Report

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III. DIALYSIS

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SECTION 1: DIALYSIS PATIENT CHARACTERISTICS

Maintenance dialysis initiation data have been submitted for 7,039 patients; selected characteristics of these patients are presented in Exhibit 1.1. The percentages of white, black, and Hispanic patients reported to the dialysis registry are 48.8%, 24.3%, and 20.2%, respectively, compared to 59.2%, 17.1%, and 17.0% reported in the 2010 transplant registry 2010 report. 13.2% of patients were less than 2 years old at initiation of the first registered (i.e., index) course of dialysis, compared to 5.3% who were less than 2 years old at index transplantation. (The index dialysis initiation or index transplant is defined as the first of each event reported since the start of the respective study component.) Patients 2-5, 6-12, 13-17, and ≥ 18 years of age at index initiation comprise 10.3%, 30.3%, 38.9%, and 7.3%, respectively, of the cohort. Whereas patients with focal segmental glomerulosclerosis (FSGS) comprise 11.7% of the transplant cohort (the 3rd most common primary renal disease), they comprise 14.4% of dialysis patients, the most prevalent group in the dialysis registry. FSGS cases comprise 23.7% of all black dialysis patients and 30.0% of black patients ≥ 13 years old. The next most prevalent diagnoses among all blacks are obstructive uropathy and renal dysplasia (both 11.5%), and among black patients ≥ 13 years old it is SLE nephritis (10.1%). FSGS accounts for 11.7% of all white dialysis patients, and 11.8% of white adolescents. Renal dysplasia (15.7%) remains most common for all whites, but obstructive uropathy (13.8%) is most prevalent among white patients ≥ 13 years old.

Also shown are distributions of selected characteristics, by cohort year. A total of 739 patients (10.5%) were already receiving maintenance dialysis as of the January 1, 1992 (start date for data collection); an additional 476 (6.8%) patients initiated dialysis that year. The distributions of age, race and gender, have remained fairly stable over the years of data collection. Dialysis modality shows a decrease in peritoneal dialysis (from 65.3 in 1992 to 55.7 (average of 2008, 2009 and 2010) and a corresponding increase in Hemodialysis from 34.7 in 1992 to 44.3 average in the last 3 years.

Race and age distributions, by dialysis modality, are shown in Exhibit 1.2 for all index courses of PD and HD. Among white patients, 41.9% are older than 12 years of age (34.1% of PD ≥ 13 years old, 59.0% of HD ≥13 years old), compared to 57.0% of blacks (46.4% PD, 68.6% HD). This phenomenon may, in part, be explained by the prevalence of FSGS among black adolescents already described.

Current concomitant drug therapy is described in Exhibits 1.3 for the 1-, 12-, 24- and 36-month follow-up visits of dialysis courses for dialysis sequences initiated in 2000-2010. Notable trends include the decreased use over time of anti-hypertensive medication among both PD and HD patients (63% and 68% at 1 month versus 50% and 54% at 36 months respectively) and calcium carbonate (59% and 56% at 1 month versus 51% and 37% at 36 months respectively). Use of sevelamer HCL increases in both PD and HD patients from 21% and 32% at 1 month to 38% and 54% at 36 months.

At baseline (30 days following index initiation), 4% of patients had completed their high school education and 23% were not of school age. Available education data for the remaining dialysis patients are presented in Exhibits 1.4 through 1.7. Among school-age patients maintained on peritoneal dialysis, 78% were attending school full-time and 9% part-time, compared to 53% and 28% of children on hemodialysis (Exhibit 1.4). Six percent of HD patients and 5% or PD patients were not attending school even though they were medically capable.

Education status is also shown according to race (Exhibit 1.5) and age (Exhibit 1.6). Patterns of school attendance are similar between black and white PD patients. Hispanic children have less full-time school attendance (64%) than black (84%) or white (81%) patients. The percentage of children not receiving any schooling is 7% (PD) and 9% (HD) for patients aged 6-12; 7% (PD) and 12% (HD) for patients older than 12. Full-time school attendance — through three years of maintenance dialysis therapy — is depicted in Exhibit 1.7, by dialysis modality, race, and age. Exhibit 1.7 shows that the percentage of Hispanic patients on PD who attend school full-time is less than that of black, white, or other patients at 6 and 12 months. There are 175 Mexican and Costa Rican Hispanics of school age. Full-time school attendance at entry is 69% in North American Hispanics versus 18% in "South of the Border" Hispanics.

To assess dialysis patient survival, we considered 2,995 patients on dialysis whose first reported course of dialysis appears to be the first ever with no history of prior renal transplantation (452 0-1 year-olds, 314 2-5 year-olds, 892 6-12 year-olds, and 1336 >12 year-olds). Deaths are counted only if the patient died while on dialysis (either the first course or subsequent courses, if patient switched modalities). The descending age groups have significantly worse survival experience relative to the >12 year old group (6-12 RH= 1.58 (95% CI= 0.97-2.55); 2-5 RH= 2.40 (95% CI= 1.33-4.32); 0-1 RH= 6.87 (95% CI= 4.54-10.39)).

Patient survival estimates at 12, 24, and 36 months following dialysis initiation, are provided in the table below.

PATIENT SURVIVAL WHILE ON DIALYSIS FROM FIRST DIALYSIS INITIATION, PATIENTS WITH NO HISTORY OF TRANSPLANT							
Age at dialysis initiation	N	12 Months		24 Months		36 Months	
		% survival	SE	% survival	SE	% survival	SE
0-1 year	452	88.9	1.6	80.7	2.4	75.1	3.2
2-5 years	314	95.0	1.4	93.0	2.0	89.6	3.0
6-12 years	892	97.5	0.6	95.3	1.0	94.3	1.5
> 12 years	1336	98.2	0.4	96.5	0.7	95.4	1.0

Exhibit 1.8 lists the causes of death according to age at time of first dialysis (for all dialysis patients and all patient deaths). Of the causes of death specified, cardiopulmonary was the reason cited most (21%), both overall and for each of the individual age groups. For those deaths from malignancy with a reported diagnosis (23 reported diagnoses in 34 malignancy deaths), 61% (14 deaths) were attributed to lymphoproliferative disorders.

Exhibit 1.9 shows patient survival while on dialysis for all index dialysis patients by age at dialysis initiation. Patient survival is measured from the time of dialysis initiation to death, with censoring for dialysis termination (due to transplant or returned function) or last follow-up visit. Younger patients have significantly worse survival. Exhibit 1.10 shows patient survival from dialysis initiation to last NAPRTCS follow-up. Patients are followed through registry changes until death or their last NAPRTCS visit. Survival rates by year of entry for all dialysis patients are shown below. Year of entry has had an impact on patient survival HR=0.95, $p<0.001$ after adjusting for patient's age in years.

PATIENT SURVIVAL BY ERA FROM FIRST DIALYSIS INITIATION TO LAST NAPRTCS FOLLOW-UP							
Year of dialysis initiation	N	12 Months		24 Months		36 Months	
		% survival	SE	% survival	SE	% survival	SE
1992 – 1994	1404	95.9	0.5	92.9	0.7	90.8	0.8
1995 – 1997	1444	95.7	0.6	92.9	0.7	90.8	0.8
1998 – 2000	1181	96.2	0.6	94.6	0.7	93.1	0.8
2001 – 2003	906	98.1	0.5	96.4	0.7	94.1	0.9
2004 – 2006	787	97.6	0.6	95.0	0.9	93.4	1.1
2007 – 2010	578	98.8	0.6	96.9	1.0	--	--

EXHIBIT 1.1
DIALYSIS PATIENT DEMOGRAPHICS

	N	%
All Dialysis Patients	7039	100.0
Gender		
Male	3948	56.1
Female	3090	43.9
Missing	1	0.0
Race /Ethnicity		
White	3420	48.6
Black	1712	24.3
Hispanic	1427	20.3
Other	480	6.8
Year of Initiation		
Before 1992	739	10.5
1992	476	6.8
1993	461	6.5
1994	467	6.6
1995	510	7.2
1996	468	6.6
1997	466	6.6
1998	400	5.7
1999	411	5.8
2000	370	5.3
2001	345	4.9
2002	293	4.2
2003	268	3.8
2004	287	4.1
2005	301	4.3
2006	199	2.8
2007	217	3.1
2008	209	3.0
2009	119	1.7
2010	33	0.5

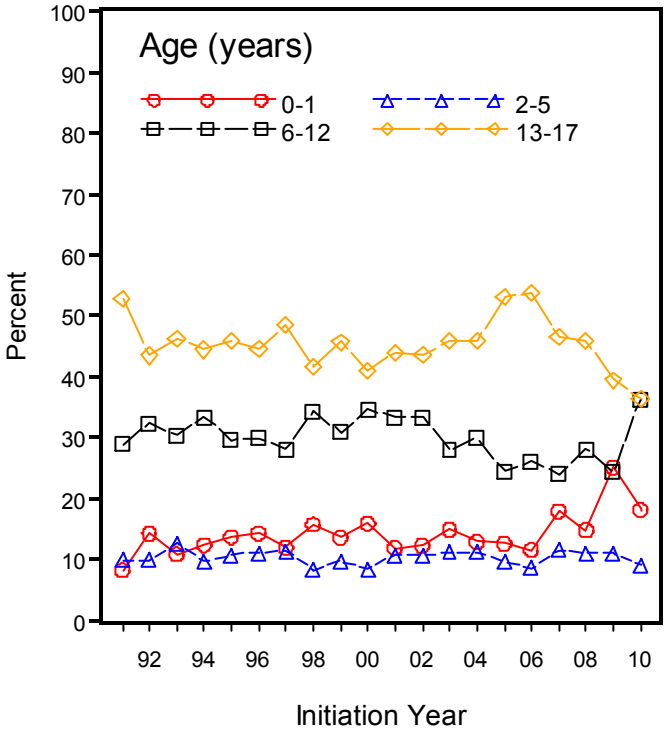
EXHIBIT 1.1 (continued)
DIALYSIS PATIENT DEMOGRAPHICS

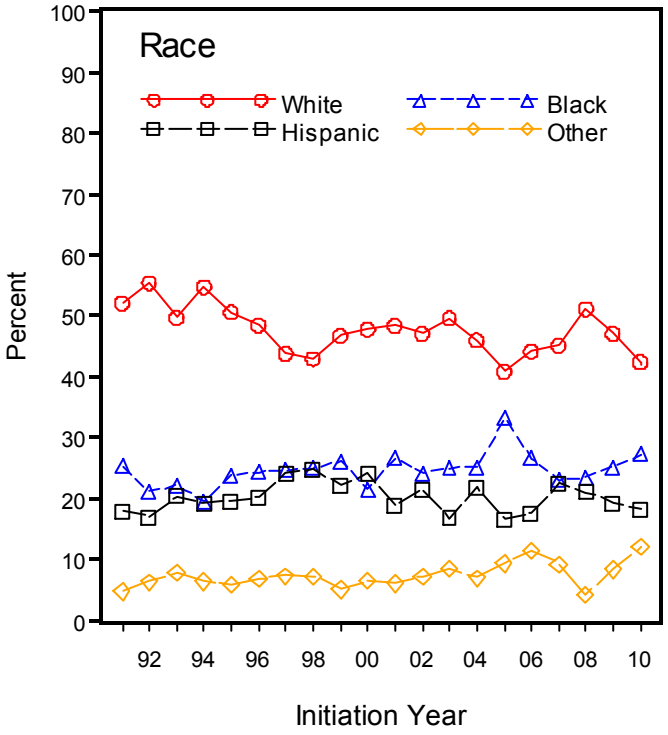
	N	%
All Dialysis Patients	7039	100.0
Primary Diagnosis		
FSGS	1016	14.4
A/hypo/dysplastic kidney	998	14.2
Obstructive uropathy	888	12.6
Reflux nephropathy	244	3.5
SLE nephritis	226	3.2
HUS	216	3.1
Chronic GN	214	3.0
Polycystic disease	201	2.9
Congenital nephrotic syndrome	182	2.6
Prune Belly	144	2.0
Medullary cystic disease	140	2.0
Idiopathic crescentic GN	130	1.8
Familial nephritis	130	1.8
MPGN - Type I	116	1.6
Pyelo/interstitial nephritis	101	1.4
Cystinosis	99	1.4
Renal infarct	90	1.3
Berger's (IgA) nephritis	86	1.2
Henoch-Schonlein nephritis	67	1.0
MPGN - Type II	64	0.9
Wilms tumor	55	0.8
Wegener's granulomatosis	49	0.7
Drash syndrome	39	0.6
Other systemic immunologic disease	37	0.5
OXALOSIS	32	0.5
Membranous nephropathy	29	0.4
Sickle cell nephropathy	21	0.3
Diabetic GN	10	0.1
Other	887	12.6
Unknown	528	7.5

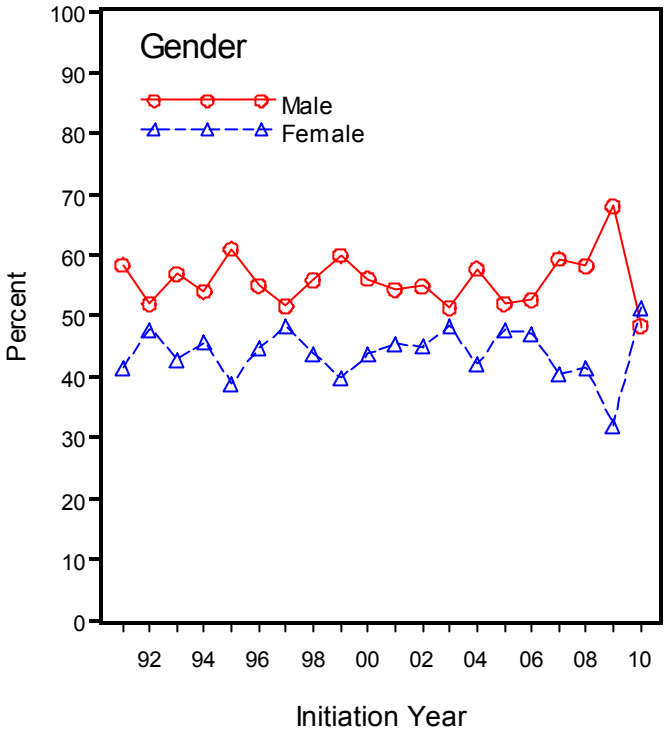
EXHIBIT 1.1 (continued)
DIALYSIS PATIENT DEMOGRAPHICS

	N	%
All Dialysis Patients	7039	100.0
Age at Index Initiation		
<1 year	661	9.4
1 year	267	3.8
2 years	199	2.8
3 years	138	2.0
4 years	194	2.8
5 years	196	2.8
6 years	182	2.6
7 years	232	3.3
8 years	270	3.8
9 years	271	3.8
10 years	359	5.1
11 years	392	5.6
12 years	424	6.0
13 years	529	7.5
14 years	576	8.2
15 years	631	9.0
16 years	555	7.9
17 years	445	6.3
≥ 18 years	517	7.3
Missing	1	0.0
Age Grouping		
0-1 years	928	13.2
2-5 years	727	10.3
6-12 years	2130	30.3
13-17 years	2736	38.9
≥ 18 years	517	7.3
Missing	1	0.0

EXHIBIT 1.1 (continued)
DIALYSIS PATIENT DEMOGRAPHICS







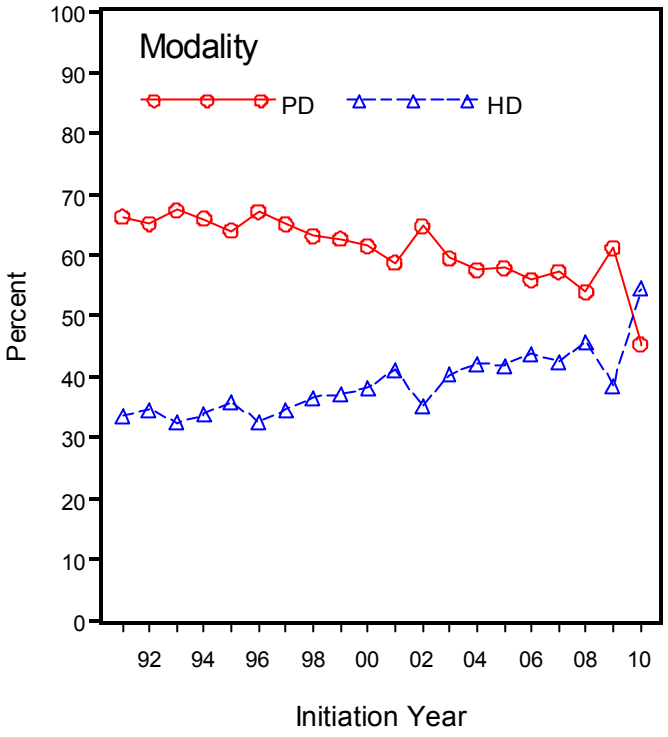


EXHIBIT 1.2
DIALYSIS MODALITY BY AGE AND RACE

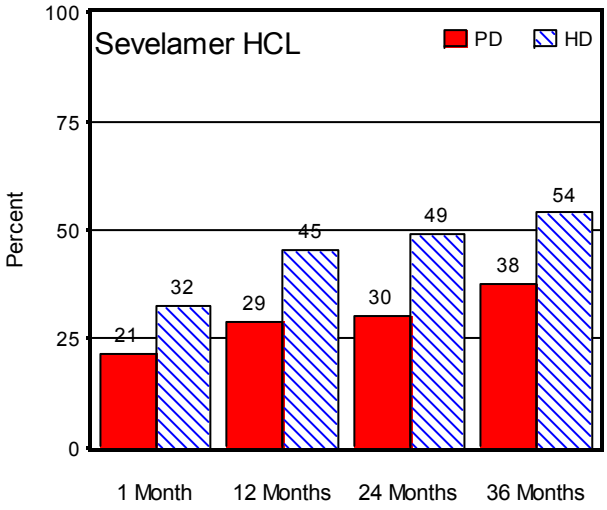
Peritoneal Dialysis

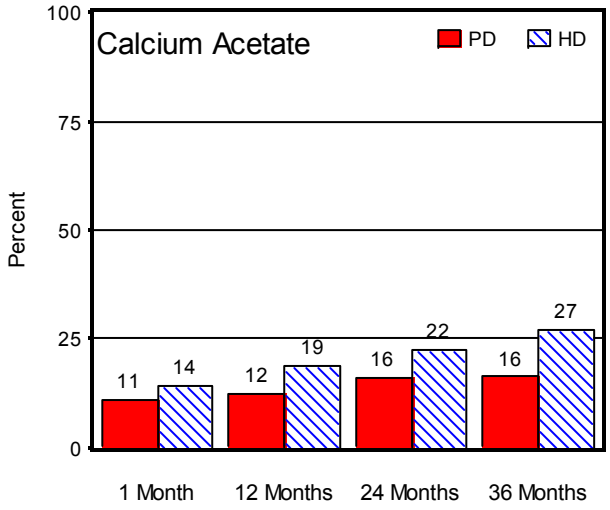
		Age at Index Dialysis Initiation							
		0-1 years		2-5 years		6-12 years		≥ 13 years	
	Total	N	%	N	%	N	%	N	%
All Races	4430	857	19.3	552	12.5	1373	31.0	1648	37.2
White	2355	546	23.2	313	13.3	693	29.4	803	34.1
Black	897	130	14.5	80	8.9	271	30.2	416	46.4
Hispanic	896	134	15.0	111	12.4	333	37.2	318	35.5
Other	282	47	16.7	48	17.0	76	27.0	111	39.4

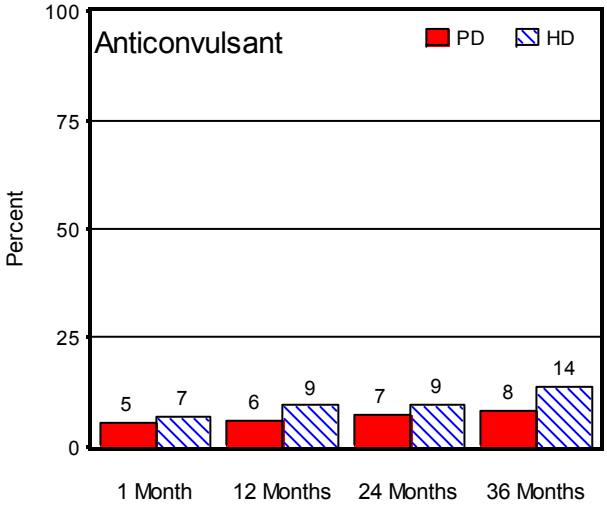
Hemodialysis

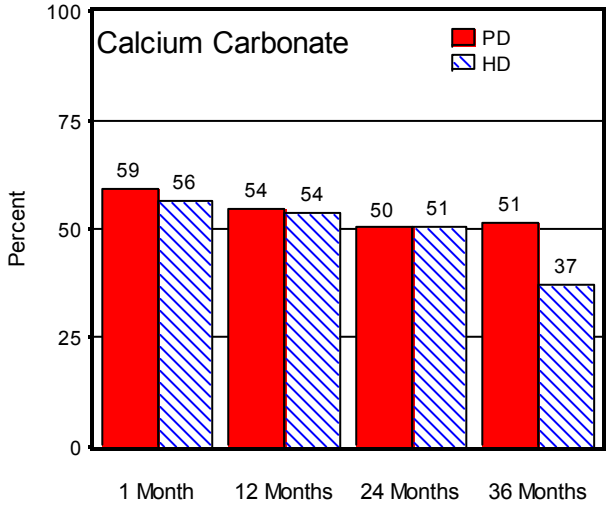
		Age at Index Dialysis Initiation							
		0-1 years		2-5 years		6-12 years		≥ 13 years	
	Total	N	%	N	%	N	%	N	%
All Races	2599	70	2.7	175	6.7	752	28.9	1602	61.6
White	1064	36	3.4	90	8.5	310	29.1	628	59.0
Black	813	13	1.6	36	4.4	206	25.3	558	68.6
Hispanic	527	16	3.0	33	6.3	168	31.9	310	58.8
Other	195	5	2.6	16	8.2	68	34.9	106	54.4

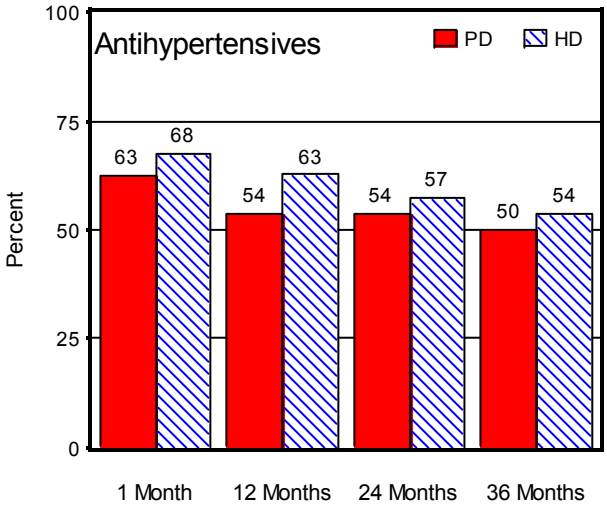
EXHIBIT 1.3
CONCOMITANT DRUG THERAPY
Dialysis Initiation 2000 – 2010

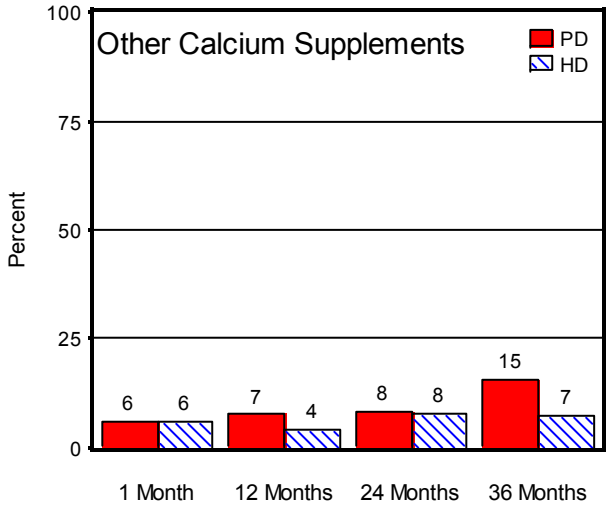












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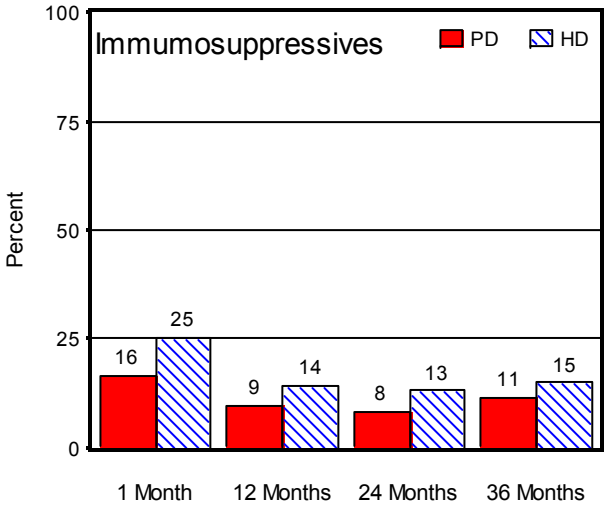
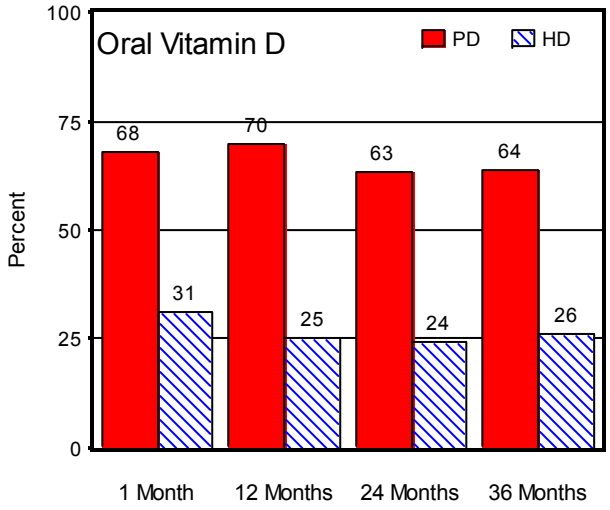
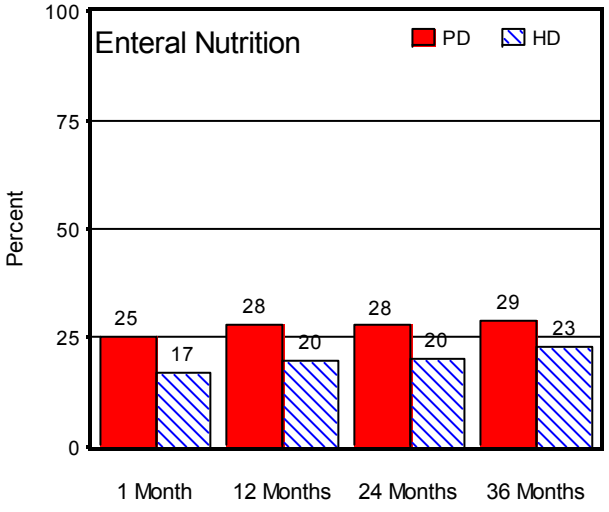
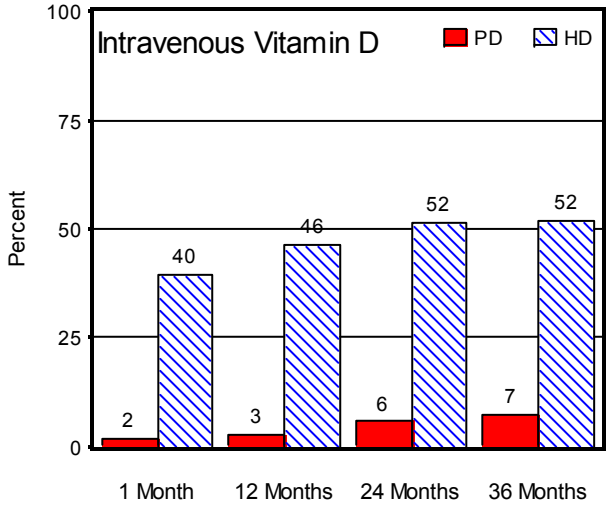
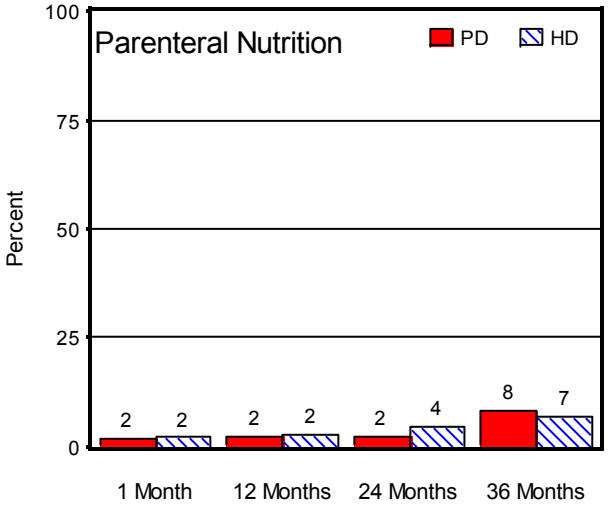
CONCOMITANT DRUG THERAPY
Dialysis Initiation 2000 - 2010











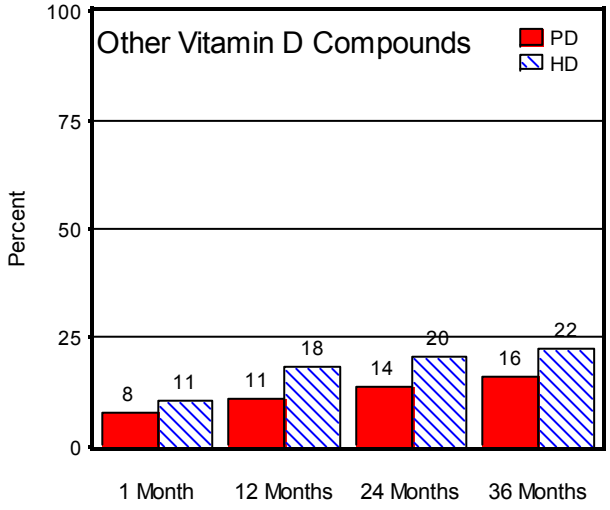
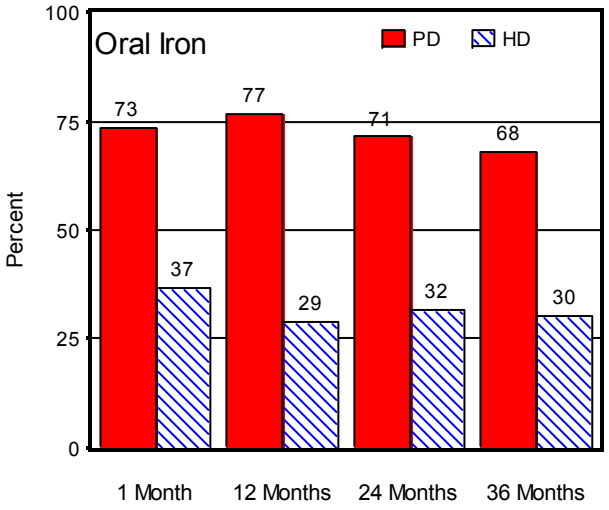
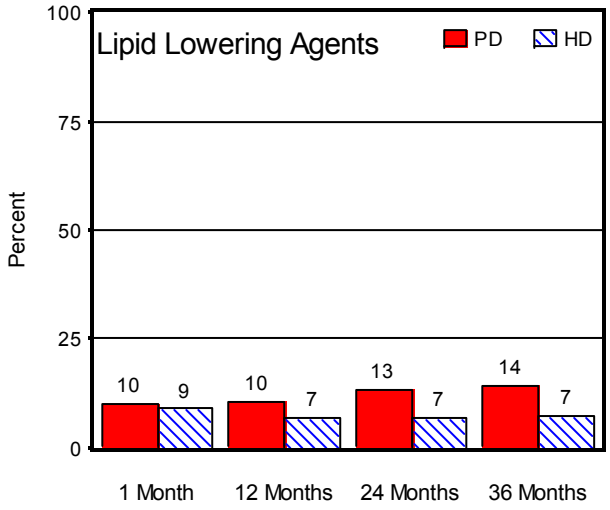
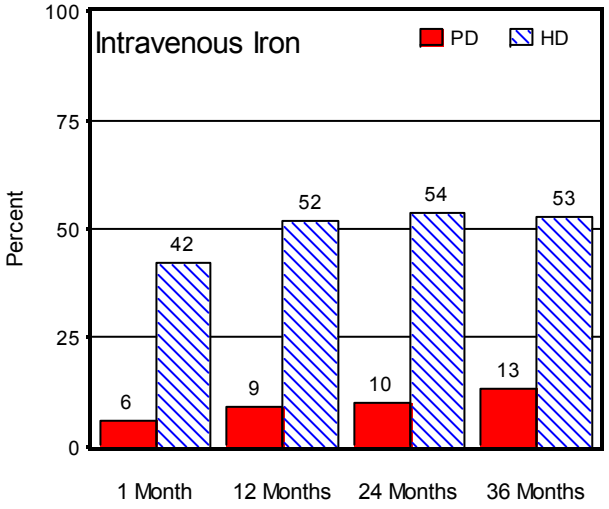
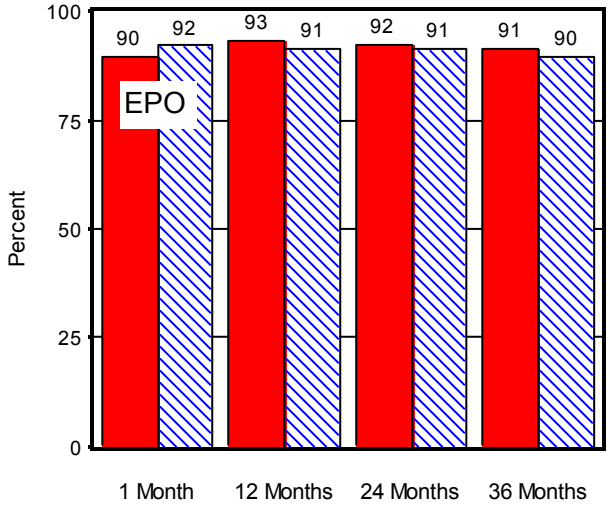


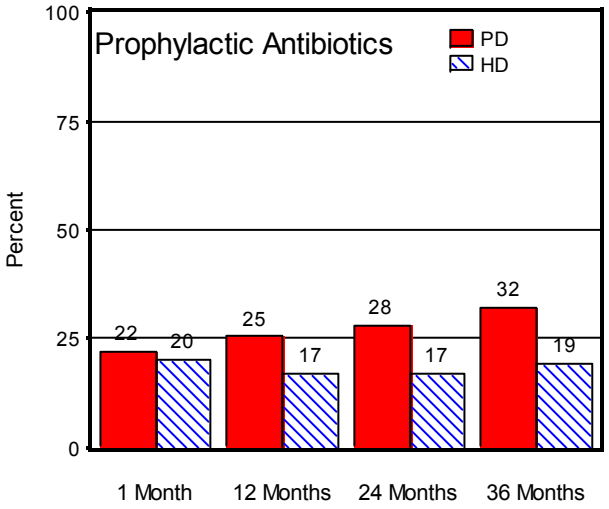
EXHIBIT 1.3 (continued)
CONCOMITANT DRUG THERAPY
Dialysis Initiation 2000 – 2007











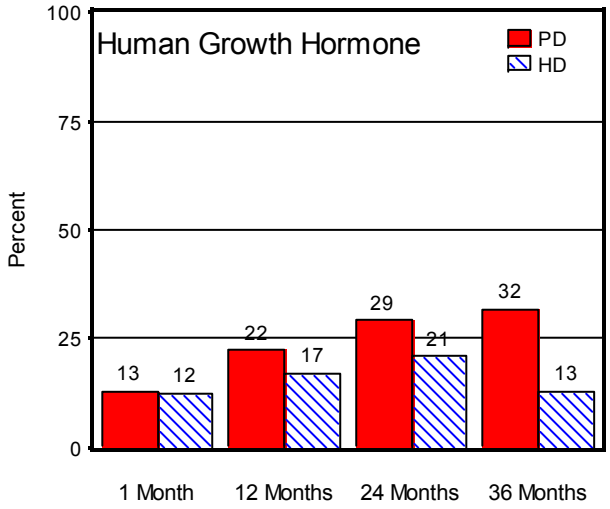
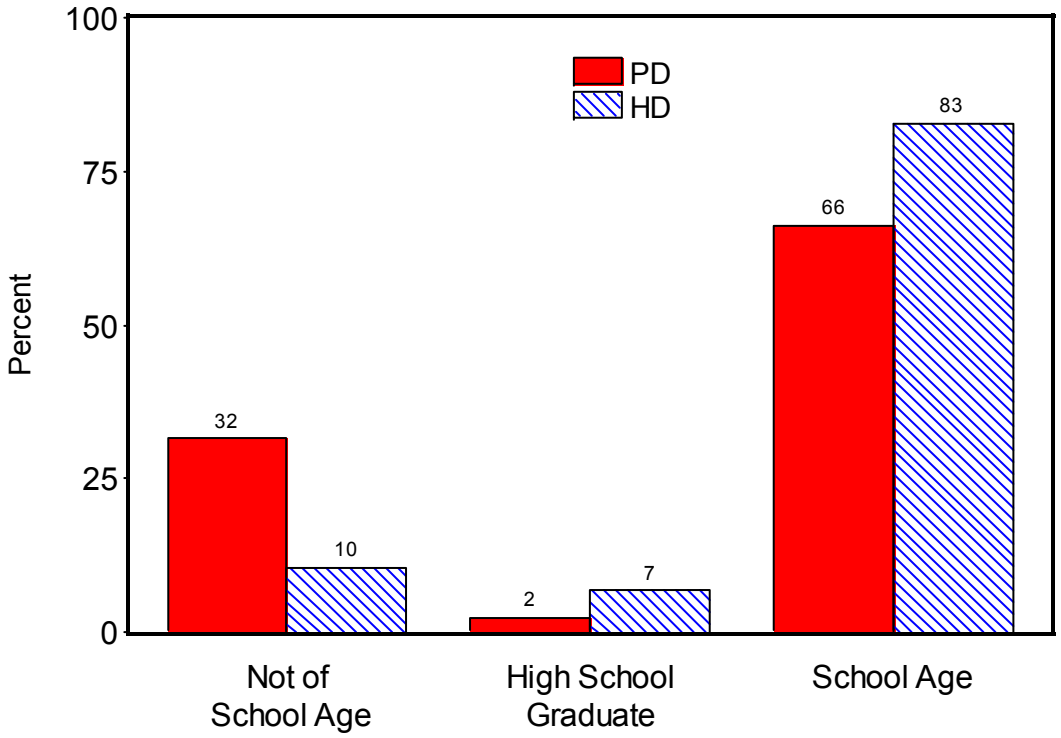


EXHIBIT 1.4
BASELINE EDUCATION STATUS

All Children



Children of School Age

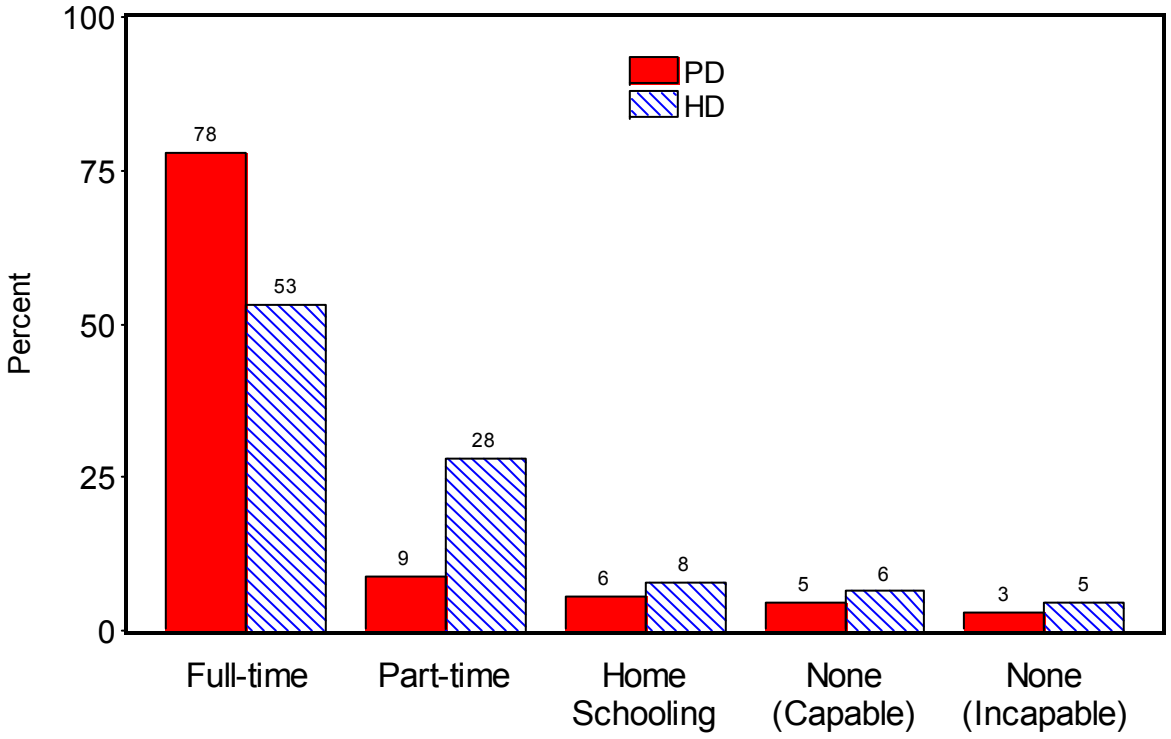
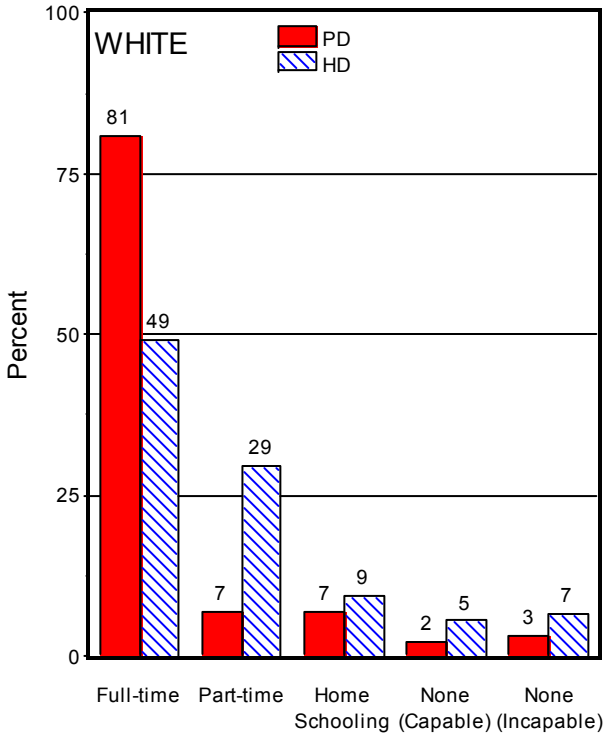
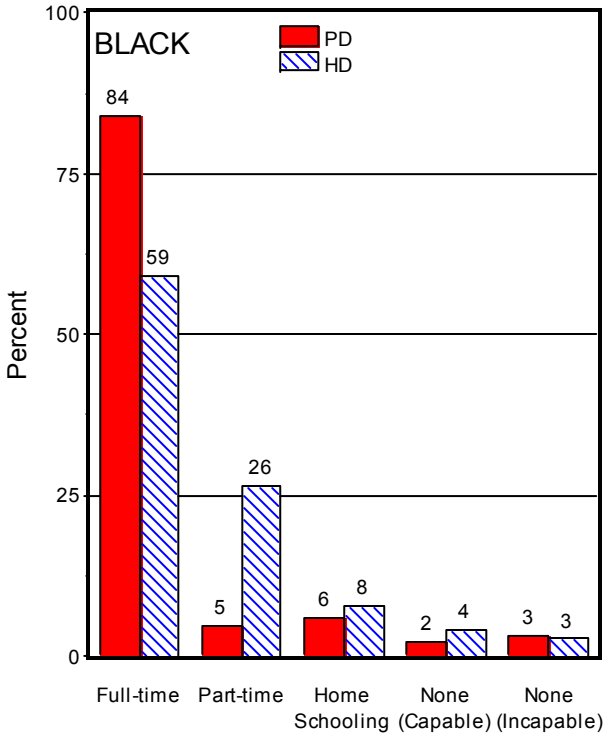
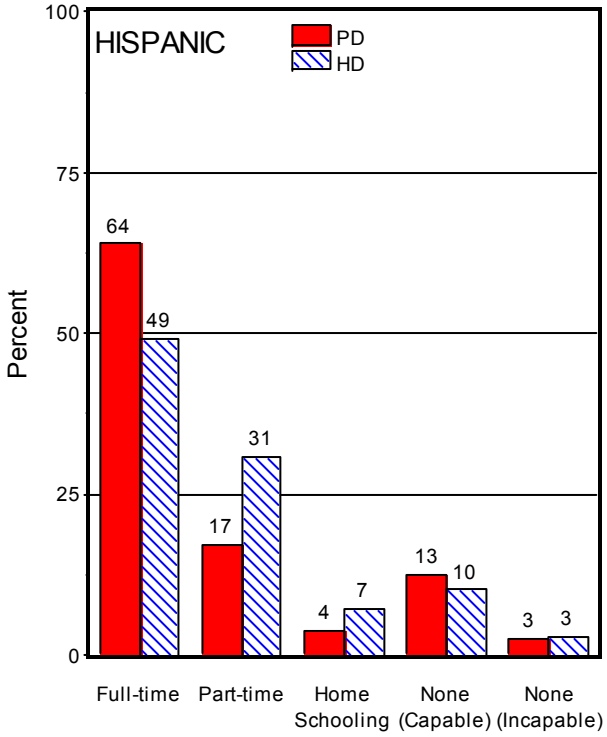


EXHIBIT 1.5
BASELINE EDUCATION STATUS BY RACE







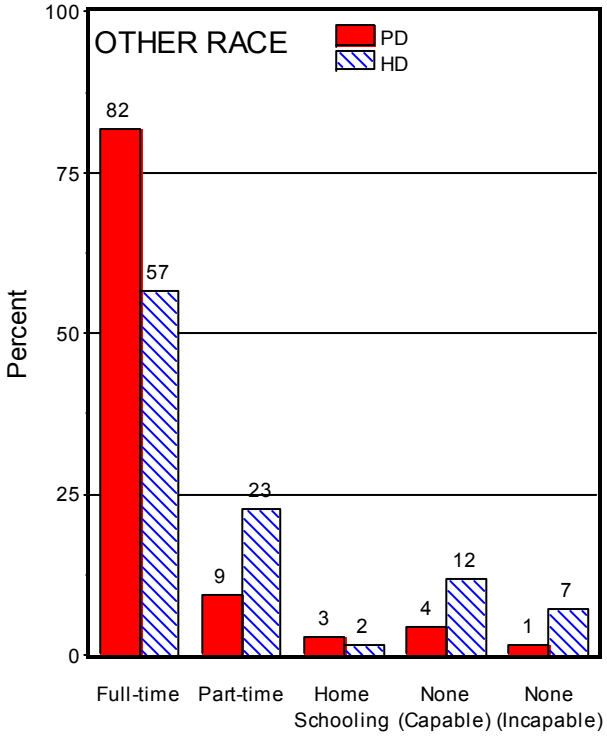
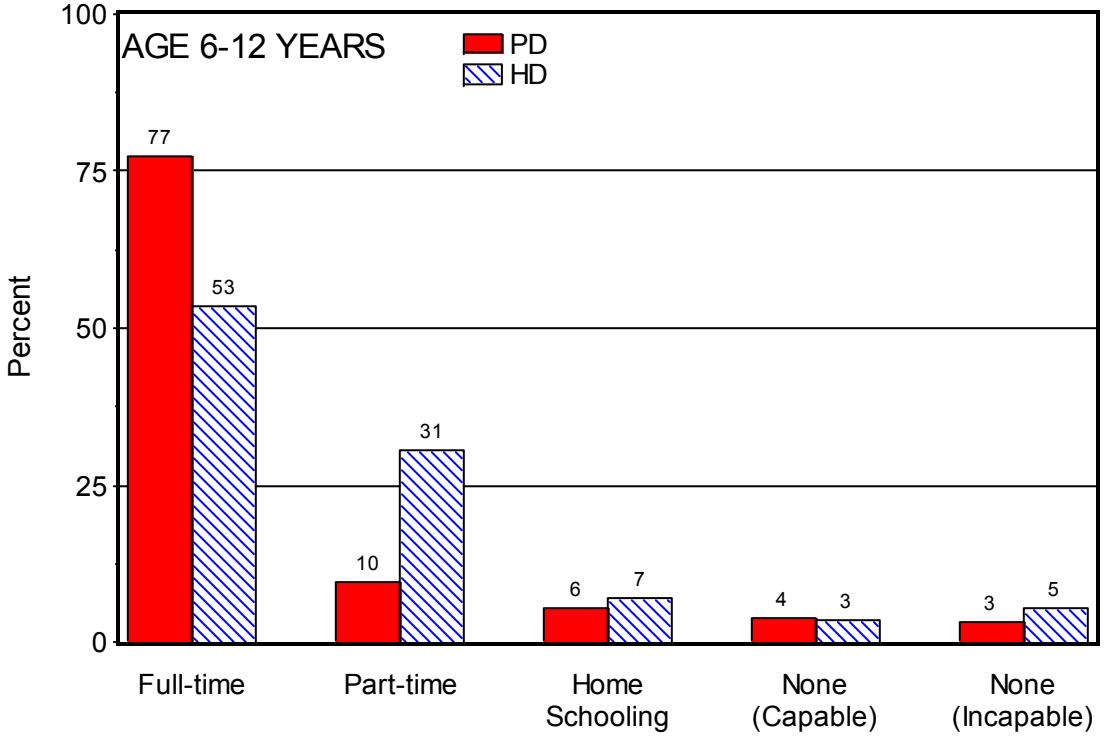


EXHIBIT 1.6
BASELINE EDUCATION STATUS BY AGE



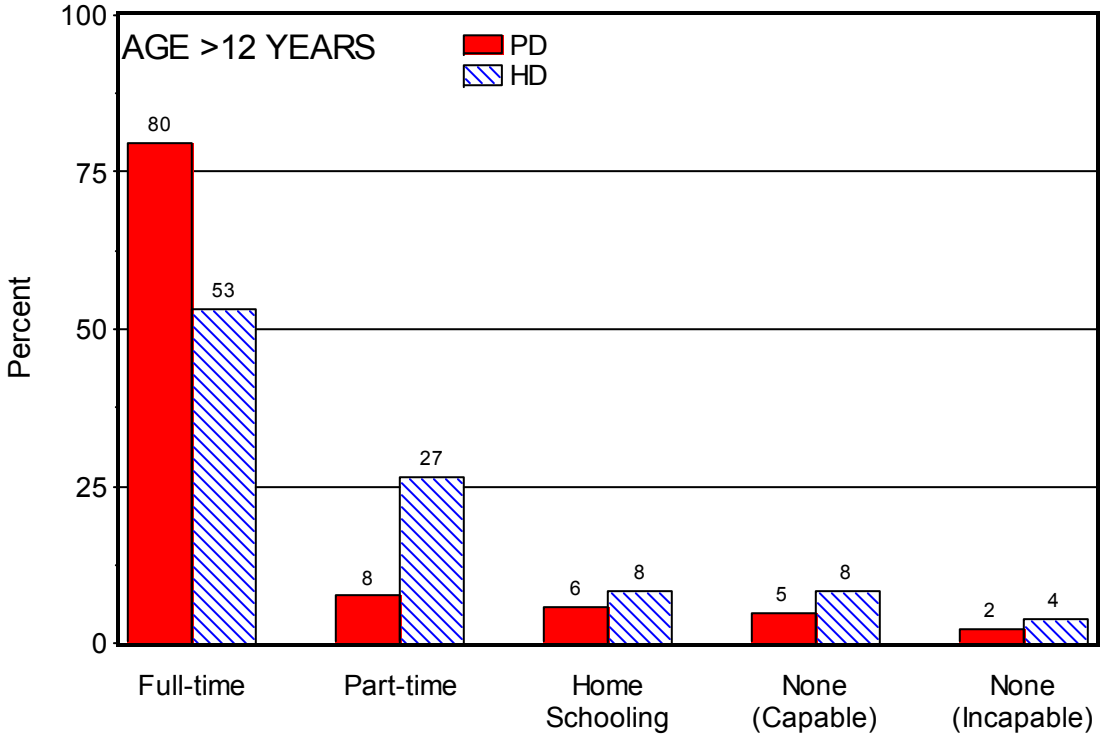
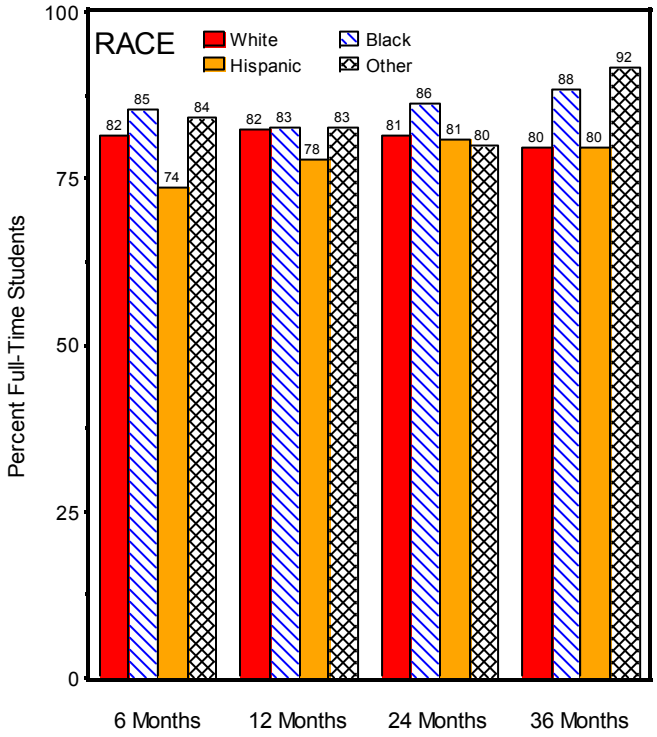
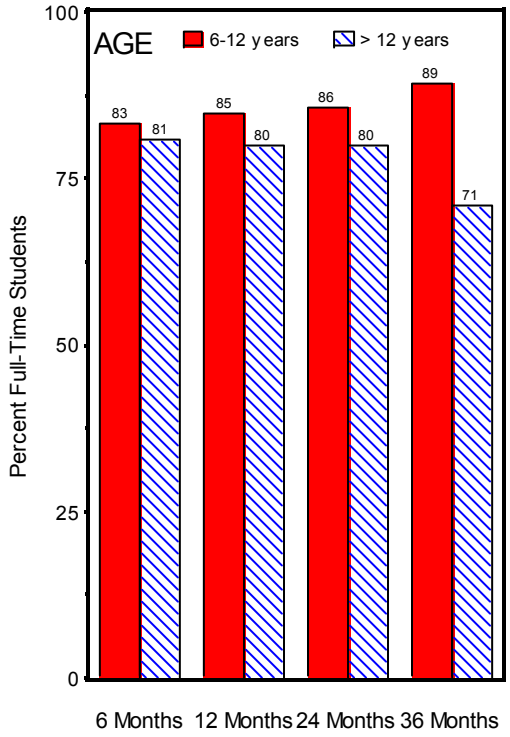


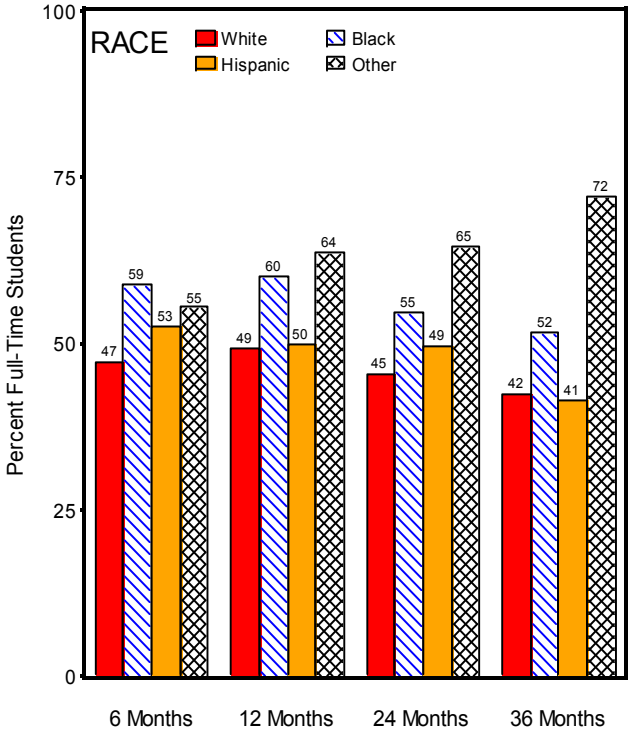
EXHIBIT 1.7
FULL-TIME SCHOOL ATTENDANCE

Peritoneal Dialysis





Hemodialysis



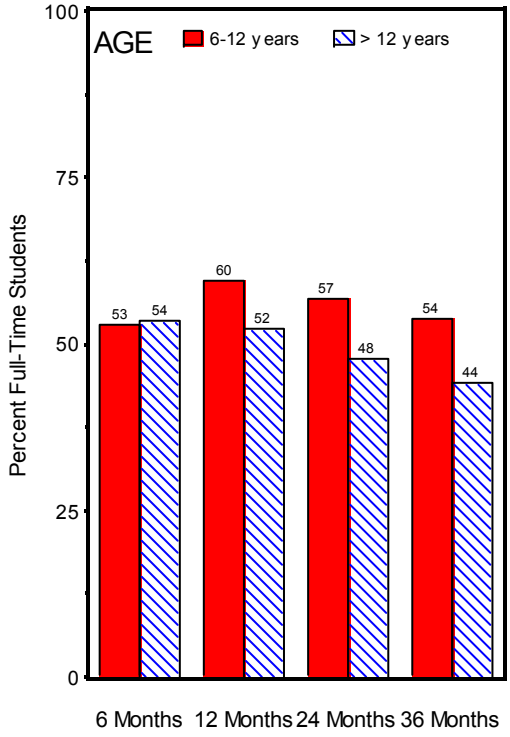


EXHIBIT 1.8
CAUSE OF DEATH BY AGE AT DIALYSIS INITIATION

	Total		Age at Index Dialysis Initiation							
			0-1 years		2-5 years		6-12 years		≥ 13 years	
	N	%	N	%	N	%	N	%	N	%
All Deceased Patients	523	100.0	171	100.0	71	100.0	141	100.0	140	100.0
Cause of Death										
Infection, viral	15	2.9	3	1.8	1	1.4	7	5.0	4	2.9
Infection, bacterial	58	11.1	25	14.6	7	9.9	8	5.7	18	12.9
Infection, not specified	34	6.5	12	7.0	4	5.6	8	5.7	10	7.1
Cancer/malignancy	34	6.5	5	2.9	9	12.7	12	8.5	8	5.7
Cardiopulmonary	110	21.0	39	22.8	13	18.3	27	19.1	31	22.1
Hemorrhage	21	4.0	4	2.3	1	1.4	9	6.4	7	5.0
Recurrence	7	1.3	2	1.2	1	1.4	2	1.4	2	1.4
Dialysis-related complications	18	3.4	3	1.8	3	4.2	6	4.3	6	4.3
Other	144	27.5	43	25.1	23	32.4	41	29.1	37	26.4
Unknown	82	15.7	35	20.5	9	12.7	21	14.9	17	12.1

EXHIBIT 1.9
PATIENT SURVIVAL WHILE ON DIALYSIS

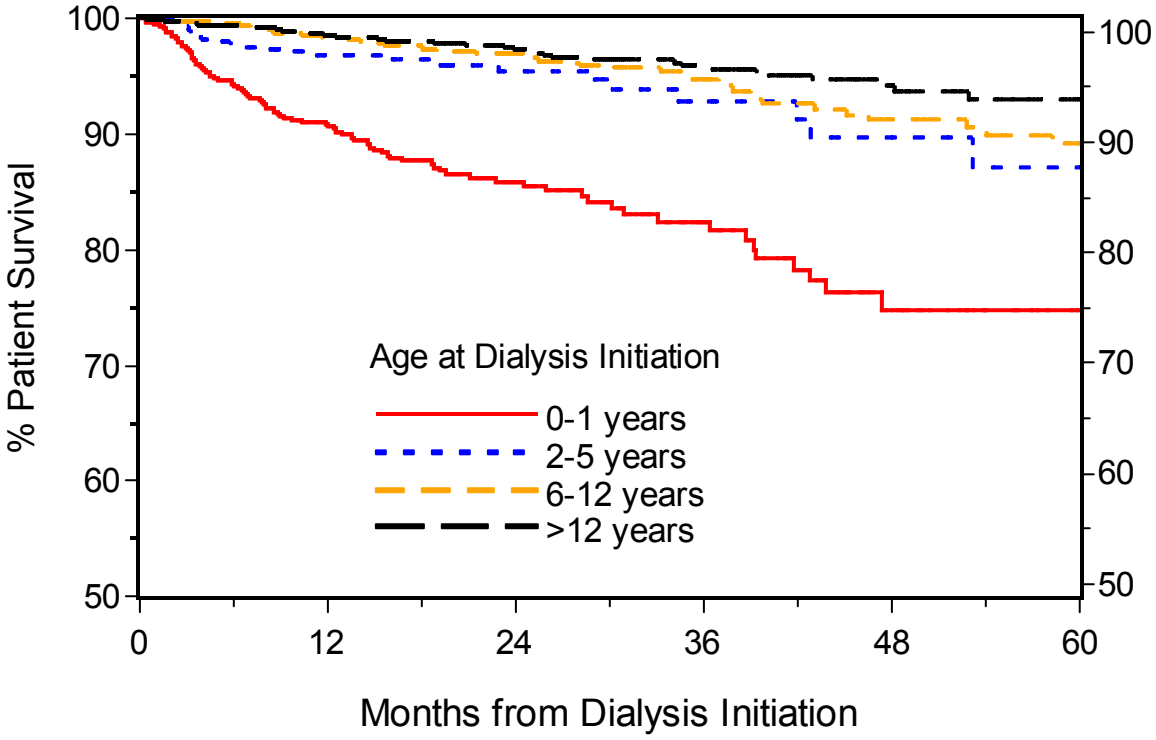
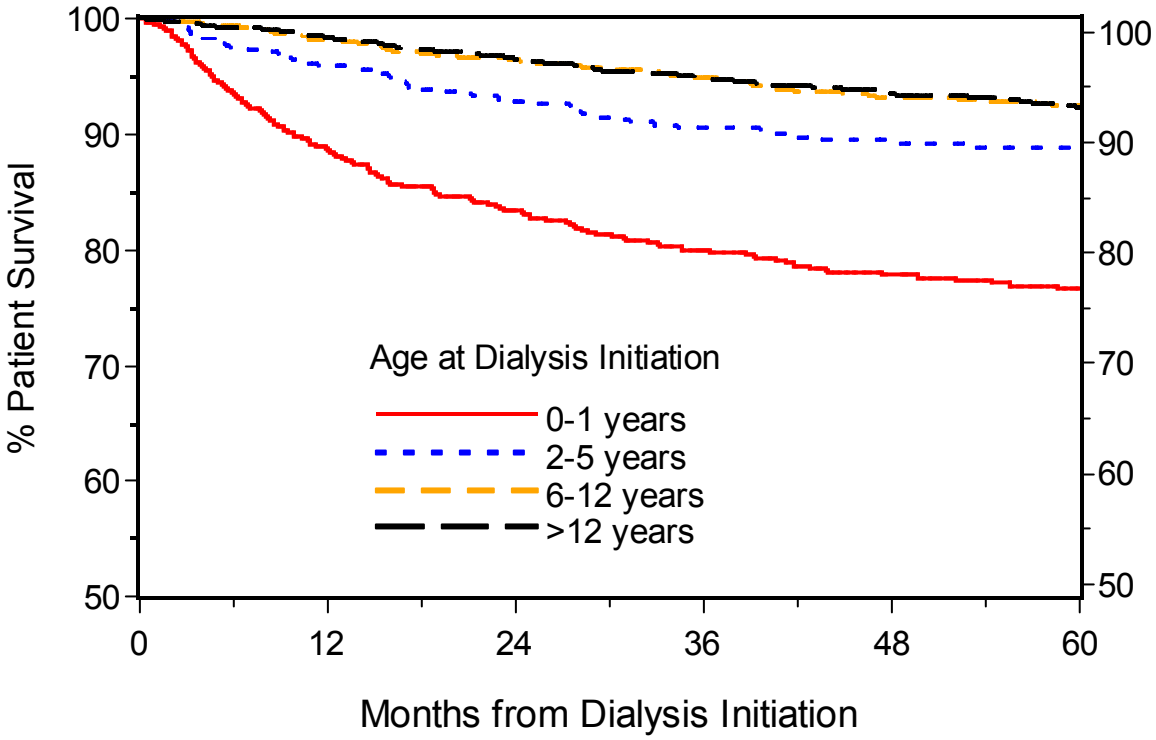


EXHIBIT 1.10
PATIENT OVERALL SURVIVAL



SECTION 2: DIALYSIS ACCESS DATA

This section reports on dialysis access data. A total of 9,108 courses have been recorded since the registry began in 1992; 739 courses began before January 1, 1992 and are not further analyzed. The focus of this section will be on the index cases after January 1, 1992 and their subsequent additional courses. This cohort represents 8,060 courses registered to 6,300 patients. 58% are peritoneal dialysis and 42% are hemodialysis courses (see Exhibit 2.1).

About 77% of the courses are terminated and the reasons are detailed in Exhibit 2.2. The majority of dialysis courses terminations are due to patient transplantation (66.4%), or to a change of modality (20.3%). When change of modality is the reason for termination, excessive infection and patient or family choice are the primary reasons. Access failure is the reason for change in 10.0% of such cases.

A summary of peritoneal dialysis access information is shown in Exhibit 2.3A. Most catheters were of the Tenckhoff curled (62.1%) or Tenckhoff straight (25.9%) configuration. About 50.7% of catheters had single cuffs, 61.8% had a straight tunnel, and 38.7% of the exit sites had a lateral orientation. Peritoneal dialysis access by year is shown in Exhibit 2.3B. The use of Tenckhoff curled catheter has increased from 55% in 1992 to 77% in 2010 with a corresponding decrease in Tenchhoff straight catheter use. The most prevalent combinations of PD access characteristics are shown in Exhibit 2.3C. The most frequently occurring combination (14.1%) consisted of a curled catheter with a single cuff, straight tunnel and a lateral exit site.

Data on 3,363 hemodialysis (HD) access locations and devices are shown in Exhibit 2.4A. HD access devices include external percutaneous catheters (2,645 or 78.7%), external arteriovenous shunts (10 or 0.3%), internal arteriovenous fistulae (398 or 11.8%), and internal arteriovenous grafts (225 or 6.7%). Most of the percutaneous catheter accesses were in the subclavian vein (51.1%), followed by the jugular (43.7%) and femoral (4.2%) veins. HD access approaches by year of initiation are shown in Exhibit 2.4B. The use of internal AV graft has decreased from 12% in the early 90s to about 1% recently, while use of a percutaneous catheter remains common and has increased from 73% in 1992 to >90% recently.

Exhibit 2.5 provides details of the current status of the 8,060 accesses, as of database closure for this report. Overall, there are 1,834 courses (22.8%) of ongoing dialysis therapy (i.e., not terminated) and 6,226 terminations. As a percent of all accesses, the terminations are due to patient transplant (4,131 or 51.3%), change of modality (1,263 or 15.7%), and other reasons (832 or 10.3%). The percent of patients terminated for transplant, by age, ranges from 45.9% for children >12 years to 58.9% for children between the ages of 6 and 12 years. Reasons for the 1,263 changes of modality include (Exhibit 2.6) excessive infection (28.3%), patient/family choice (22.8%), access failure (10.0%), other medical (23.9%), and other non-medical (15.0%). Whereas changes of modality due to excessive infection occur primarily with PD accesses (43% vs 7% in HD), changes due to patient or family choice occur primarily with HD accesses (43% vs 9% in PD). Modality change caused by access failure is more common in HD accesses (13%), black patients (14%) and patients 6-12 years of age at initiation (13%).

Patients are maintained on their index course of dialysis as follows: 10.9%±0.4% terminate by 3 months, 23.0%±0.5% by 6 months, 43.2%±0.7% by 12 months, 69.5%±0.6% by 24 months, and 83.4%±0.5% by 36 months. Exhibit 2.7 depicts time to index dialysis termination for all reasons, by modality. Although time to termination is shorter for HD (relative to PD) courses initially (30.0%±1.0% versus 18.9%±0.6% at 6 months), by 36 months of follow-up PD courses have a higher termination rate than HD (84.9%±0.6% PD versus 80.4%±1.0% HD). Time to dialysis termination, by age and race, are shown for each modality in Exhibit 2.8. Adolescents (age >12) tend to remain on dialysis longer than the younger children, and white patients tend to terminate dialysis sooner, particularly among HD.

Exhibit 2.9 shows time to dialysis termination for PD catheter characteristics; similar data for HD catheter access are shown in Exhibit 2.10. Dialysis courses for HD patients with an external percutaneous catheter terminate much sooner than for arteriovenous fistulae or grafts. By 3 months, 20.7%±1.0% of percutaneous catheter accesses have terminated, compared to 7.2%±1.6% for AV fistulae and 7.0%±2.0% for AV grafts. By 24 months, comparable percents are 71.9%±1.2%, 50.0%±3.2%, and 57.5%±4.3%.

Exhibit 2.11 shows time to termination, according to reason. If the reason for termination was that the patient was transplanted, then the relationship between PD and HD terminations is similar. However for patients who terminate their index dialysis to change modalities, HD

patients experience most of their terminations in the first 6 months while PD patients appear to have a slow and steady increase in terminations over time.

To compare experience of PD patients with different procedure types, 3,941 index peritoneal dialysis cases were selected. To capture the PD procedure information, we only include 3,501 patients who had submitted their Day 30 post dialysis forms where modality information was collected. Peritoneal dialysis modality included 743 (21.2%) patients with CAPD, 2,343 (66.9%) with APD, 226 (6.5%) with IPD, and 189 (5.4%) patients with unknown procedures. The 743 CAPD patients were 54% males, 42% white and 28% under 6 years of age while the 2,343 patients with APD were 56% male, 56% white and 33% under 6 years of age. Compared to patients who used APD, CAPD patients were significantly older when they initiated dialysis ($p<0.009$), were significantly more likely to have a minority ethnic background ($p<0.001$), and were registered in earlier years ($p<0.001$, Exhibit 2.12). Patient survival of these two groups did not differ.

A higher percentage of patients terminated dialysis due to transplantation in the CAPD group (crude rate 75.0%) than in APD group (crude rate 68.3%) ($p<0.008$) while terminations were more likely due to change of modality in APD group (18.9%) than in CAPD group (13.2%). In general, time to termination for all reasons in CAPD vs. APD patients was significantly different ($p=0.002$, Exhibit 2.13). Time to termination due to transplantation differed ($p<0.001$, Exhibit 2.14) while time to termination due to change of modality was not significantly different.

EXHIBIT 2.1
DIALYSIS INITIATION AND TERMINATION

	All Dialysis Courses		All Index Courses after 01/01/92		All Courses where Index course is after 01/01/92	
	N	**%**	**N**	**%**	**N**	**%**
Total courses	9108	100.0	6300	100.0	8060	100.0
Dialysis Course						
First	7039	77.3	6300	100.0	6300	78.2
Second	1474	16.2	0	0.0	1263	15.7
Third	412	4.5	0	0.0	342	4.2
Fourth	127	1.4	0	0.0	108	1.3
Fifth or more	56	0.6	0	0.0	47	0.6
Modality						
Peritoneal Dialysis	5293	58.1	3941	62.6	4687	58.2
Hemodialysis	3804	41.8	2351	37.3	3363	41.7
Missing	11	0.1	8	0.1	10	0.1
Terminated	7031	77.2	4929	78.2	6226	77.2

EXHIBIT 2.2
DIALYSIS TERMINATION

	All Index Courses after 01/01/92		All Courses where Index course is after 01/01/92	
	N	**%**	**N**	**%**
Terminated Dialysis Courses	4929	100.0	6226	100.0
Reason for Termination				
Patient Transplanted	3412	69.2	4131	66.4
Change of Modality	870	17.7	1263	20.3
Death	116	2.4	154	2.5
Kidney Function Returned	143	2.9	154	2.5
Other/Unknown	388	7.9	524	8.4
Courses Changing Modality	870	100.0	1263	100.0
Reason for Modality Change				
Excessive infection	265	30.5	358	28.3
Patient/family choice	178	20.5	288	22.8
Access failure	86	9.9	126	10.0
Inadequate ultrafiltration	45	5.2	62	4.9
Inadequate solute clearance	21	2.4	29	2.3
Excessive hospitalization (Dialysis-related)	17	2.0	27	2.1
Excessive hospitalization (Other)	4	0.5	5	0.4
Other (medical)	112	12.9	179	14.2
Other (non-medical)	40	4.6	47	3.7
Unknown	102	11.7	142	11.2

EXHIBIT 2.3A
PERITONEAL DIALYSIS ACCESS

	N	%
Peritoneal Dialysis Courses	4687	100.0
Catheter		
Tenckhoff straight	1213	25.9
Tenckhoff curled	2909	62.1
Toronto western	26	0.6
Presternal	272	5.8
Other	111	2.4
Unknown/missing	156	3.3
Cuffs		
One	2375	50.7
Two	2124	45.3
Unknown/missing	188	4.0
Tunnel		
Swan neck/curved	1590	33.9
Straight	2895	61.8
Unknown/missing	202	4.3
Exit Site Orientation		
Up	564	12.0
Down	1537	32.8
Lateral	1816	38.7
Unknown/missing	770	16.4

EXHIBIT 2.3B
PERITONEAL DIALYSIS CATHETER ACCESS TYPE BY INITIATION YEAR

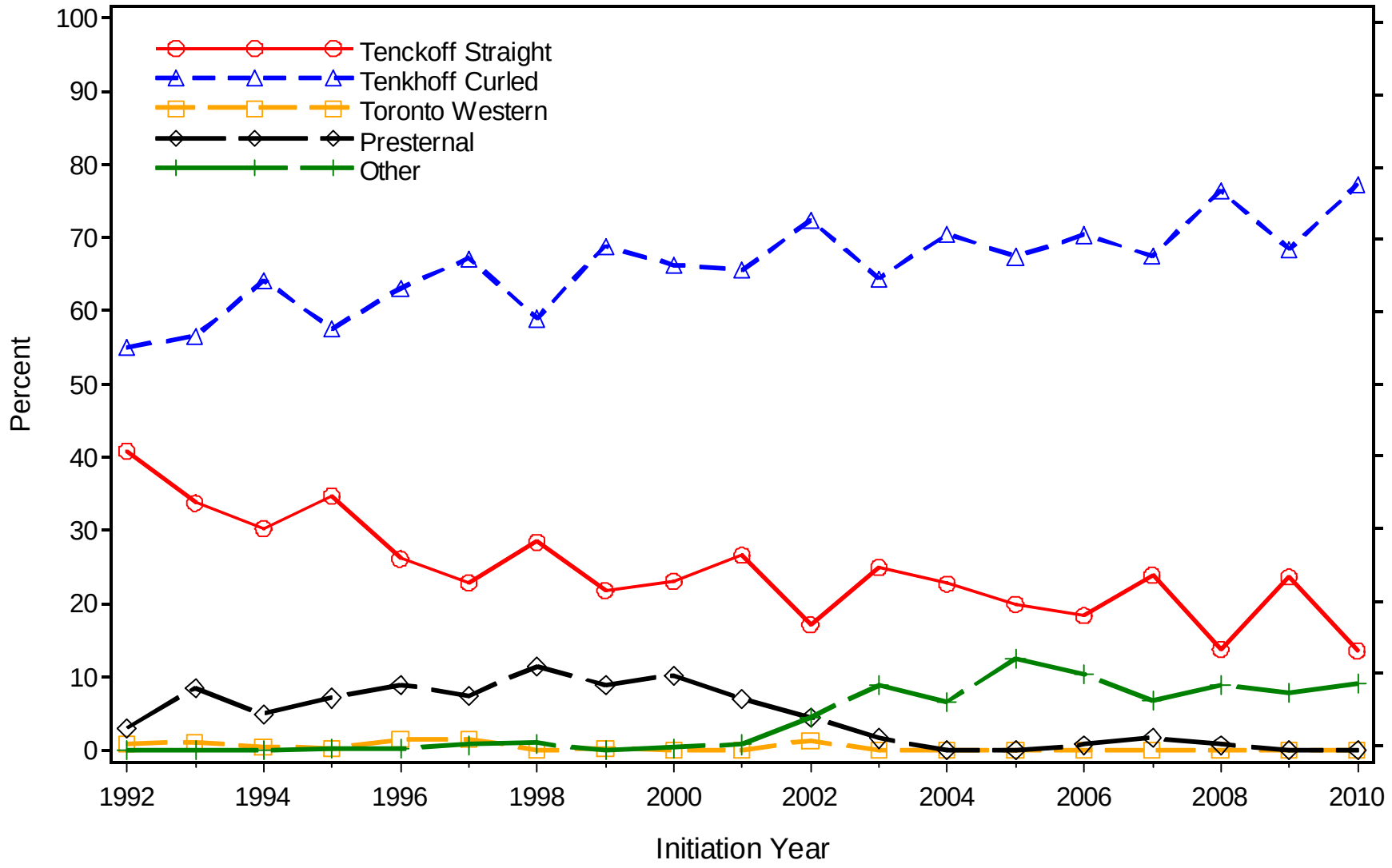


EXHIBIT 2.3C
PERITONEAL DIALYSIS ACCESS CHARACTERISTICS

Catheter	Cuffs	Tunnel	Exit Site	N (4391)*	% (100.0)
Curled	One	Straight	Lateral	619	14.1
Curled	Two	Swan necked/curved	Down	458	10.4
Curled	Two	Straight	Lateral	315	7.2
Straight	One	Straight	Lateral	313	7.1
Curled	Two	Straight	Down	277	6.3
Curled	One	Straight	Down	267	6.1
Curled	One	Straight	Up	209	4.8
Curled	Two	Swan necked/curved	Unknown	145	3.3
Straight	One	Straight	Up	136	3.1
Curled	Two	Swan necked/curved	Lateral	132	3.0
Presternal	Two	Swan necked/curved	Down	129	2.9
Straight	One	Straight	Unknown	123	2.8
Straight	One	Swan necked/curved	Lateral	105	2.4
Straight	One	Straight	Down	102	2.3
Straight	Two	Straight	Lateral	100	2.3
Curled	One	Swan necked/curved	Lateral	78	1.8
Curled	One	Swan necked/curved	Down	78	1.8
Curled	One	Straight	Unknown	76	1.7
Curled	Two	Straight	Unknown	57	1.3
Straight	Two	Straight	Up	54	1.2
All other combinations (<1% each)				618	14.1

*NOTE: Cases with missing elements are excluded.

EXHIBIT 2.4A
HEMODIALYSIS ACCESS

	N	%	N	%
Total			**3363**	**100.0**
External Percutaneous Catheter			**2645**	**78.7**
Subclavian vein	1351	51.1		
Jugular vein	1156	43.7		
Femoral vein	112	4.2		
Missing vein	26	1.0		
Single lumen	97	3.7		
Double lumen	2475	93.6		
Missing lumen	73	2.8		
External Arteriovenous Shunt			**10**	**0.3**
Upper arm	2	20.0		
Thigh	0	0.0		
Other location	1	10.0		
Location not reported/Missing	7	70.0		
Internal Arteriovenus Fistula			**398**	**11.8**
Upper arm	50	12.6		
Lower arm	53	13.3		
Thigh	1	0.3		
Other location	17	4.3		
Location not reported/Missing	277	69.6		
Internal Arteriovenus Graft			**225**	**6.7**
Autologous vein	9	4.0		
Bovine graft	1	0.4		
PTFE graft	204	90.7		
Other graft	7	3.1		
Missing graft	4	1.8		
Upper arm	6	2.7		
Lower arm	9	4.0		
Thigh	9	4.0		
Location not reported/Missing	201	89.3		
Hemodialysis access unknown			**85**	**2.5**

EXHIBIT 2.4B
HEMODIALYSIS ACCESS TYPE BY INITIATION YEAR

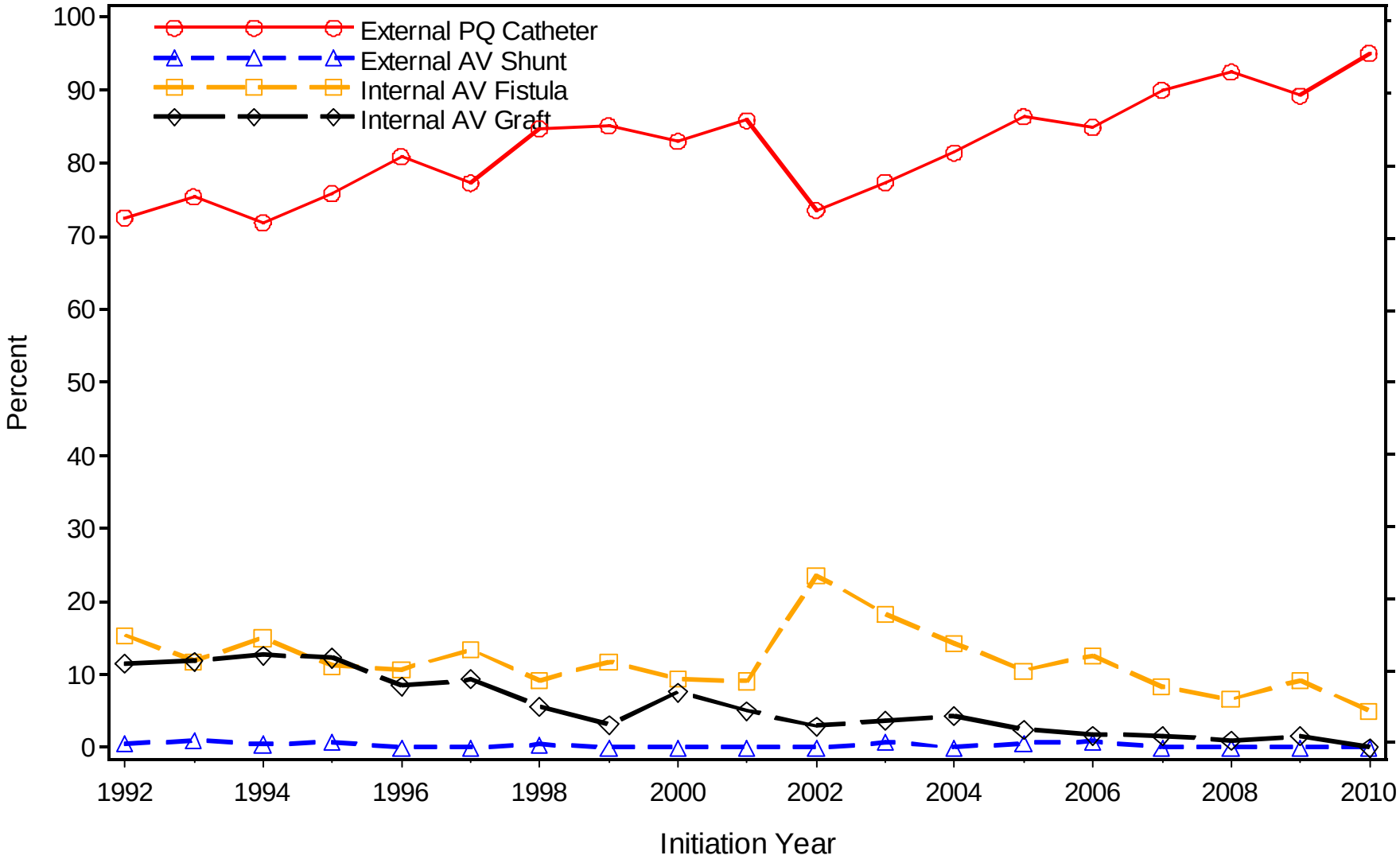


EXHIBIT 2.5
DIALYSIS ACCESS BY SELECTED CHARACTERISTICS

		Working Access		Transplanted		Change of Modality		Other	
	N	N	%	N	%	N	%	N	%
Total Courses	8060	1834	22.8	4131	51.3	1263	15.7	832	10.3
Modality									
PD	4687	907	19.4	2518	53.7	748	16.0	514	11.0
HD	3363	923	27.4	1609	47.8	514	15.3	317	9.4
Missing	10	4	40.0	4	40.0	1	10.0	1	10.0
Year initiated									
1992-1993	1082	130	12.0	590	54.5	221	20.4	141	13.0
1994-1995	1263	178	14.1	659	52.2	258	20.4	168	13.3
1996-1997	1328	263	19.8	669	50.4	249	18.8	147	11.1
1998-1999	1055	259	24.5	540	51.2	156	14.8	100	9.5
2000-2001	934	232	24.8	498	53.3	122	13.1	82	8.8
2002-2003	708	162	22.9	402	56.8	85	12.0	59	8.3
2004-2005	720	188	26.1	379	52.6	84	11.7	69	9.6
2006-2007	525	163	31.0	256	48.8	55	10.5	51	9.7
2008-2010	445	259	58.2	138	31.0	33	7.4	15	3.4
Age at initiation									
0-1 years	970	152	15.7	457	47.1	153	15.8	208	21.4
2-5 years	882	116	13.2	516	58.5	156	17.7	94	10.7
6-12 years	2388	392	16.4	1406	58.9	388	16.2	202	8.5
>12 years	3820	1174	30.7	1752	45.9	566	14.8	328	8.6
Gender									
Male	4420	987	22.3	2359	53.4	629	14.2	445	10.1
Female	3639	847	23.3	1772	48.7	634	17.4	386	10.6
Race/Ethnicity									
White	3834	705	18.4	2161	56.4	561	14.6	407	10.6
Black	2001	567	28.3	856	42.8	345	17.2	233	11.6
Hispanic	1657	433	26.1	824	49.7	259	15.6	141	8.5
Other	568	129	22.7	290	51.1	98	17.3	51	9.0

EXHIBIT 2.6
CHANGE OF DIALYSIS MODALITY BY SELECTED CHARACTERISTICS

	Total	Excessive Infection	Choice	Access Failure	Other Medical	Other/ None
	N	N	%	N	N	%
Total Changes of Modality	1263	28.3	22.8	10.0	23.9	15.0
Modality						
PD	748	43.0	8.8	8.2	26.7	13.2
HD	514	7.0	43.0	12.6	19.8	17.5
Year initiated						
1992-1993	221	29.9	21.3	10.9	21.3	16.7
1994-1995	258	33.3	19.4	8.1	23.6	15.5
1996-1997	249	25.3	24.9	9.6	25.3	14.9
1998-1999	156	28.2	23.1	7.7	25.6	15.4
2000-2001	122	31.1	21.3	18.0	23.0	6.6
2002-2003	85	22.4	25.9	9.4	25.9	16.5
2004-2005	84	26.2	25.0	10.7	22.6	15.5
2006-2007	55	20.0	27.3	5.5	29.1	18.2
2008-2010	33	27.3	27.3	9.1	18.2	18.2
Age at initiation						
0-1 years	153	37.9	9.2	10.5	24.2	18.3
2-5 years	156	35.3	25.0	6.4	21.2	12.2
6-12 years	388	32.5	18.8	12.6	20.4	15.7
>12 years	566	21.0	28.6	9.0	27.0	14.3
Gender						
Male	629	30.4	20.5	8.4	25.3	15.4
Female	634	26.3	25.1	11.5	22.6	14.5
Race/Ethnicity						
White	561	27.1	22.8	8.4	26.7	15.0
Black	345	24.6	24.9	13.6	20.6	16.2
Hispanic	259	37.1	19.7	6.9	22.8	13.5
Other	98	25.5	23.5	14.3	22.4	14.3

EXHIBIT 2.7
TIME TO DIALYSIS TERMINATION BY MODALITY
(Index Cases)

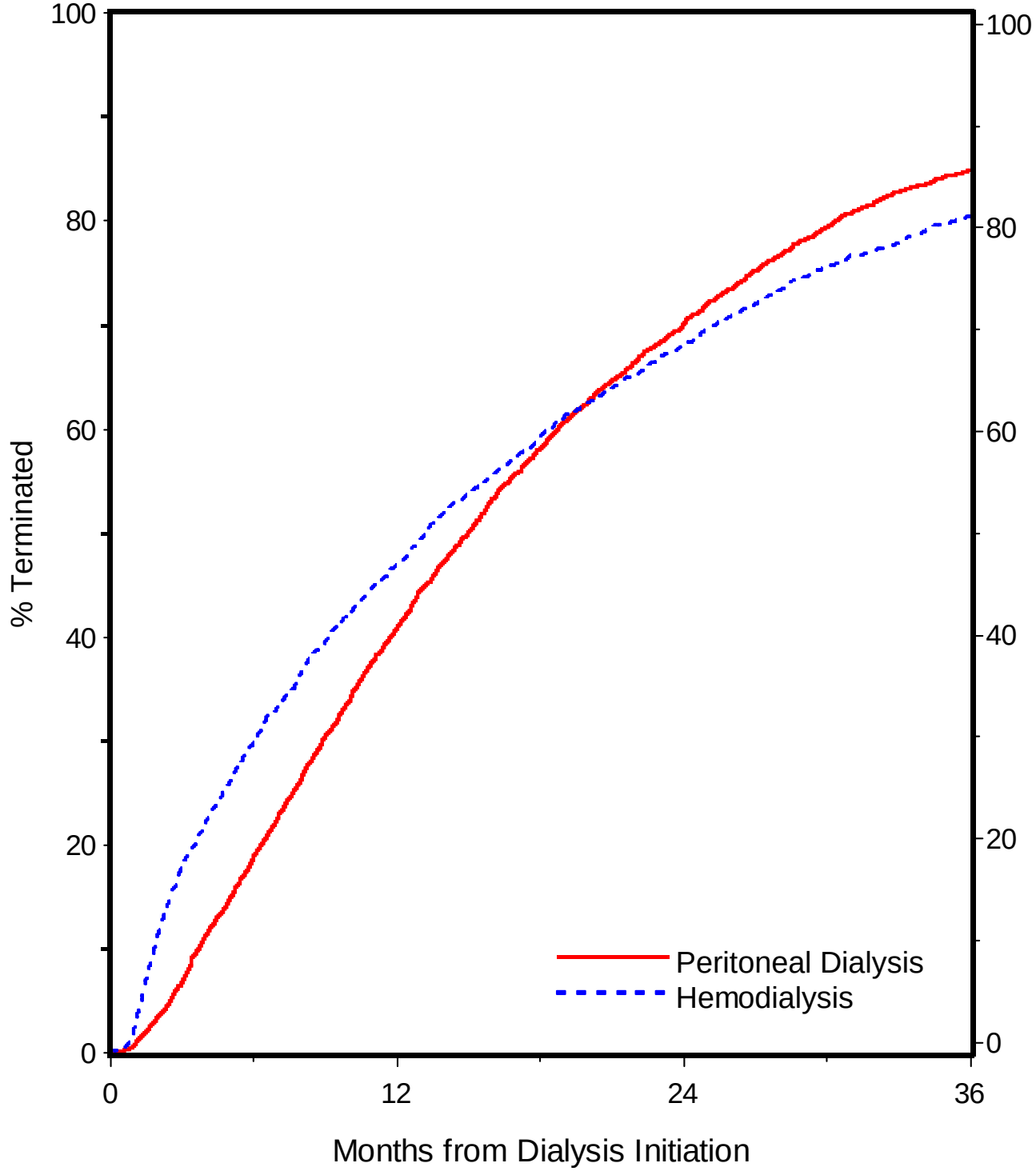
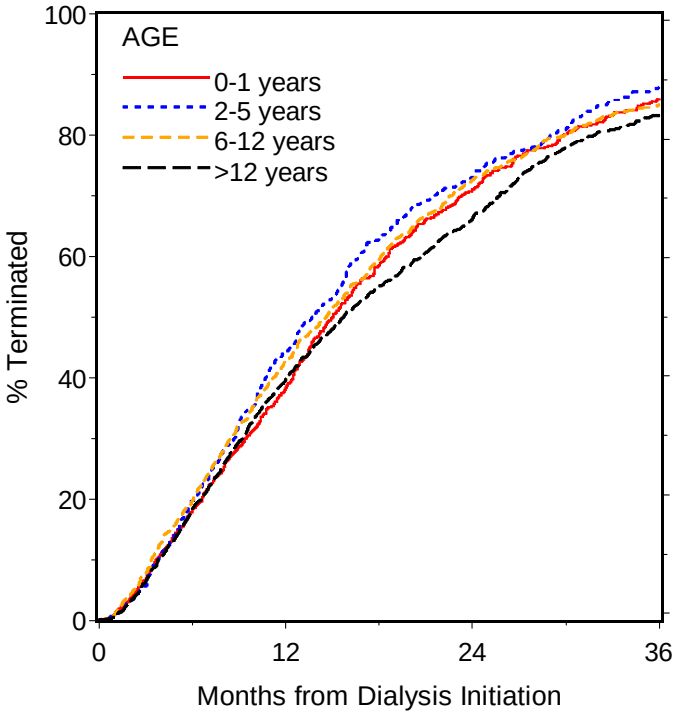
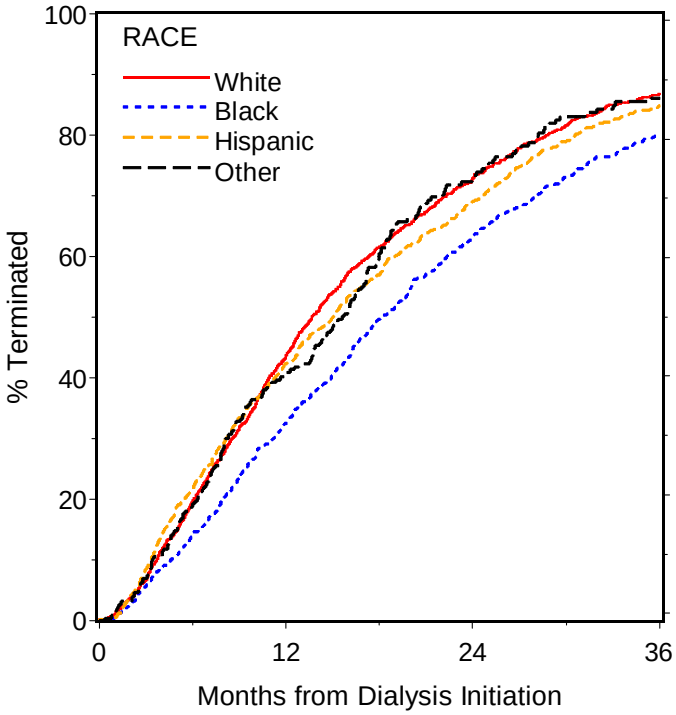


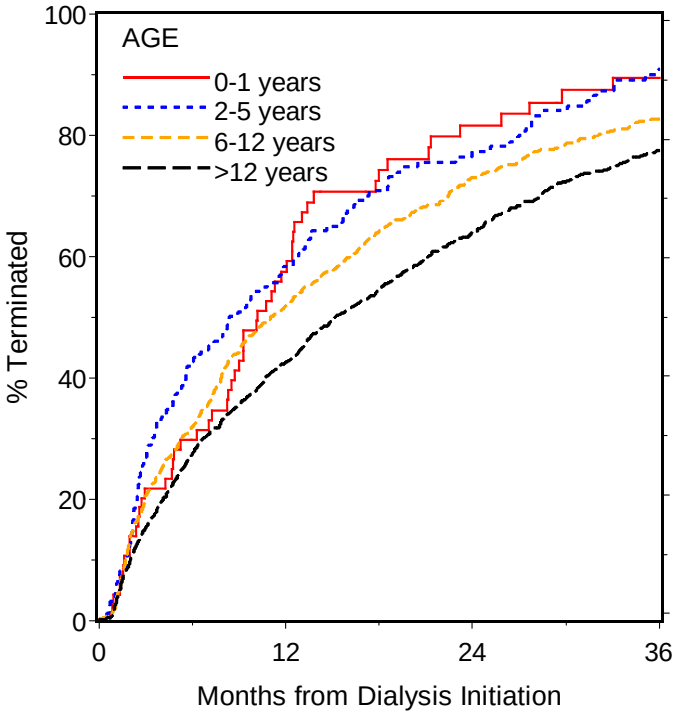
EXHIBIT 2.8
TIME TO DIALYSIS TERMINATION BY AGE AND RACE
(Index Cases)

Peritoneal Dialysis





Hemodialysis



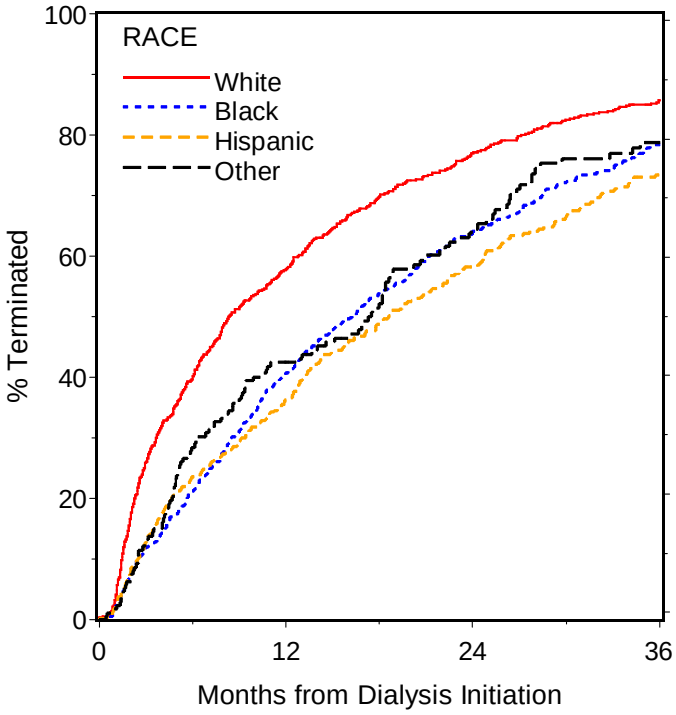
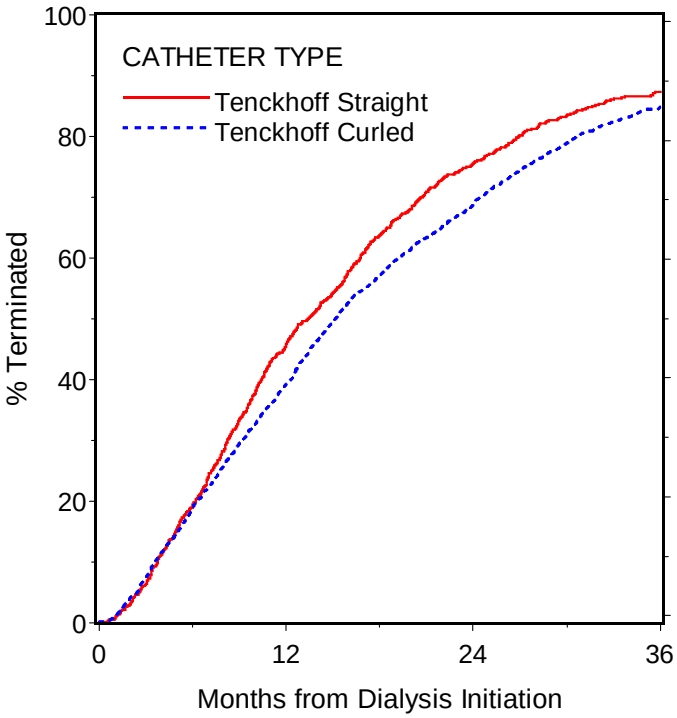
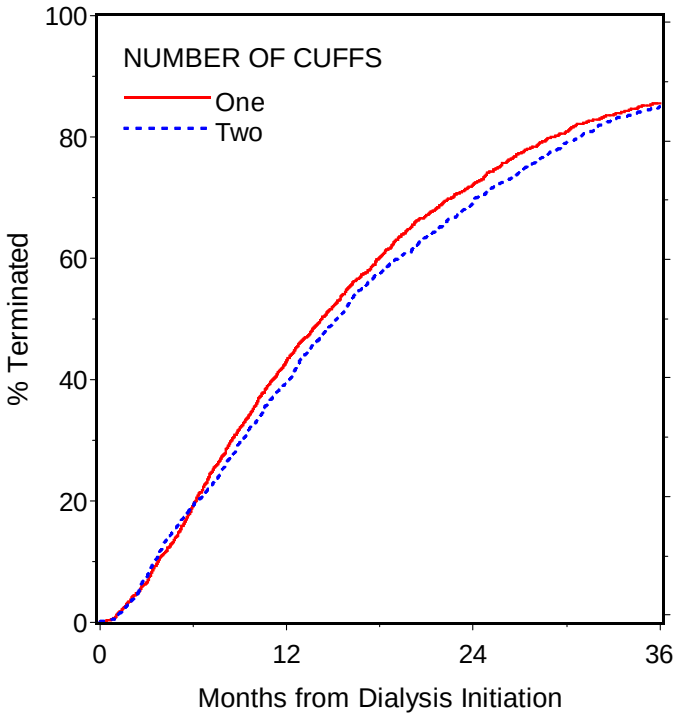
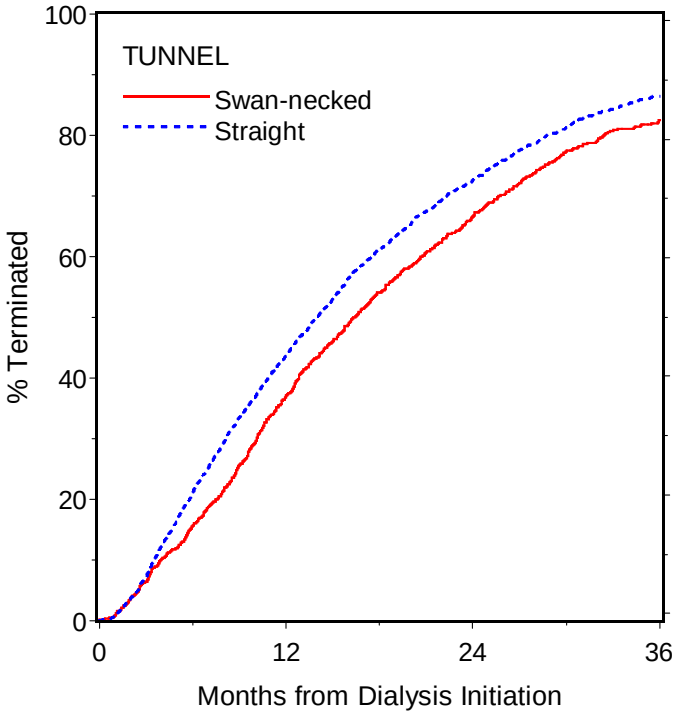


EXHIBIT 2.9
TIME TO DIALYSIS TERMINATION
BY PERITONEAL DIALYSIS ACCESS CHARACTERISTICS
(Index Cases)







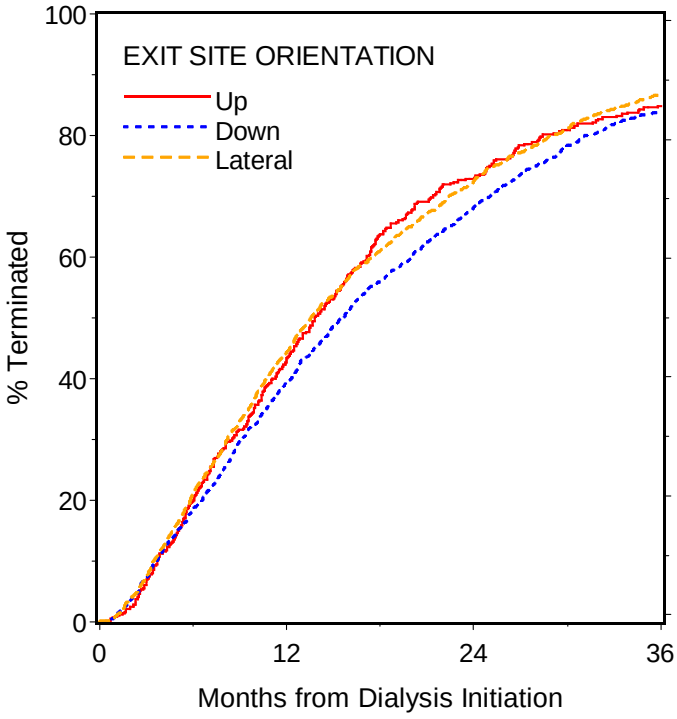


EXHIBIT 2.10
TIME TO DIALYSIS TERMINATION BY HEMODIALYSIS ACCESS
(Index Cases)

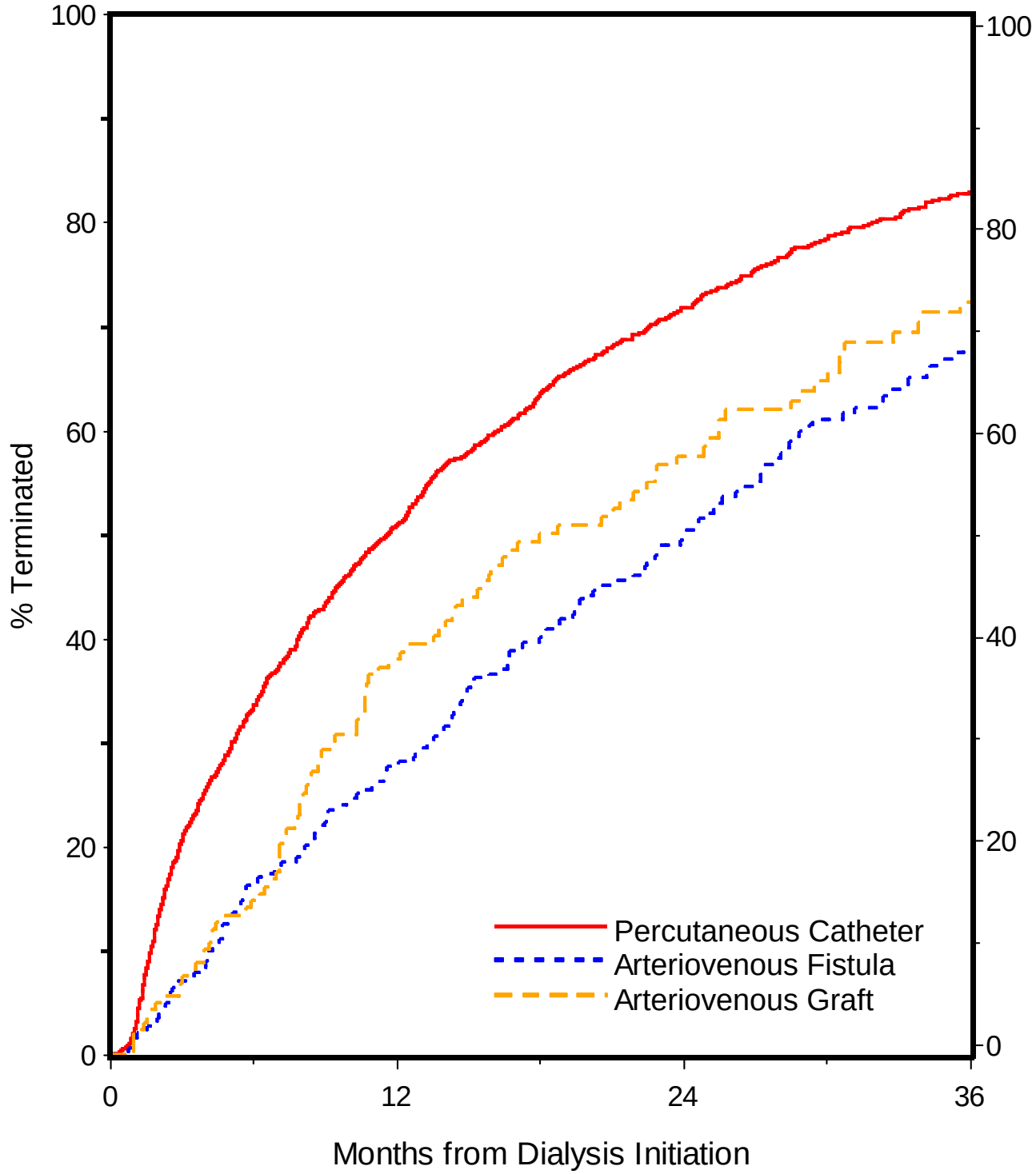
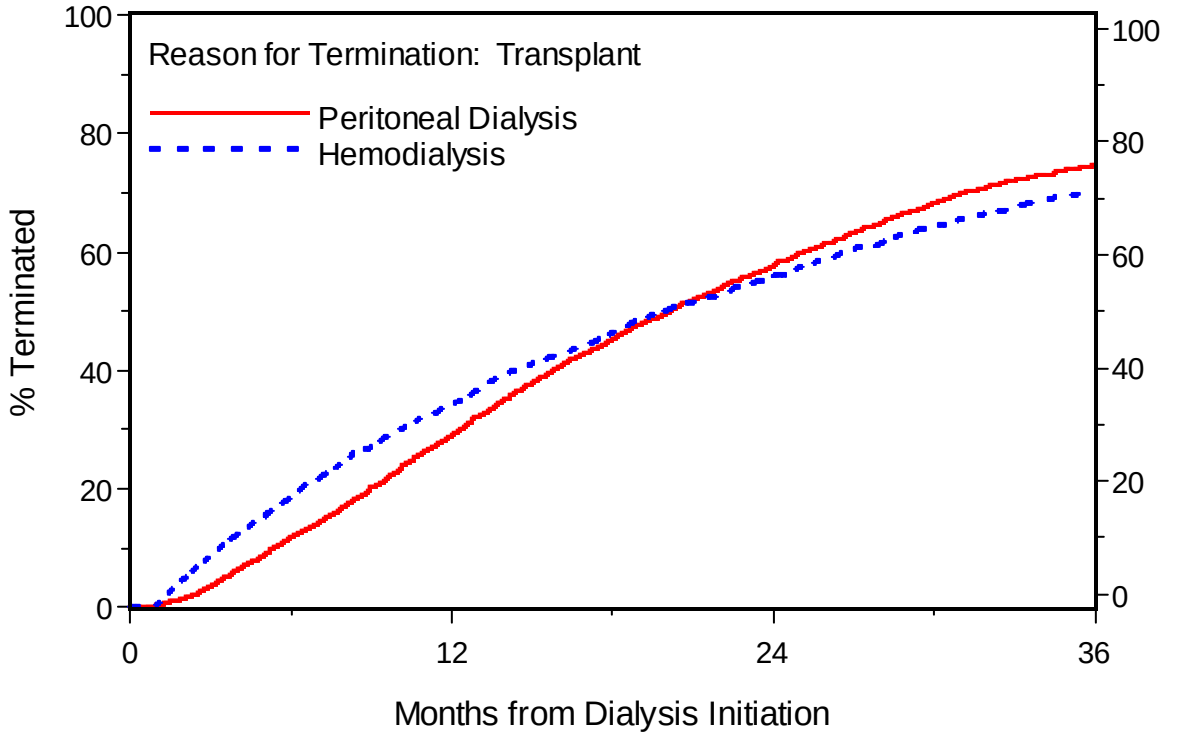


EXHIBIT 2.11
TIME TO DIALYSIS TERMINATION BY DIALYSIS MODALITY
(Index Cases)



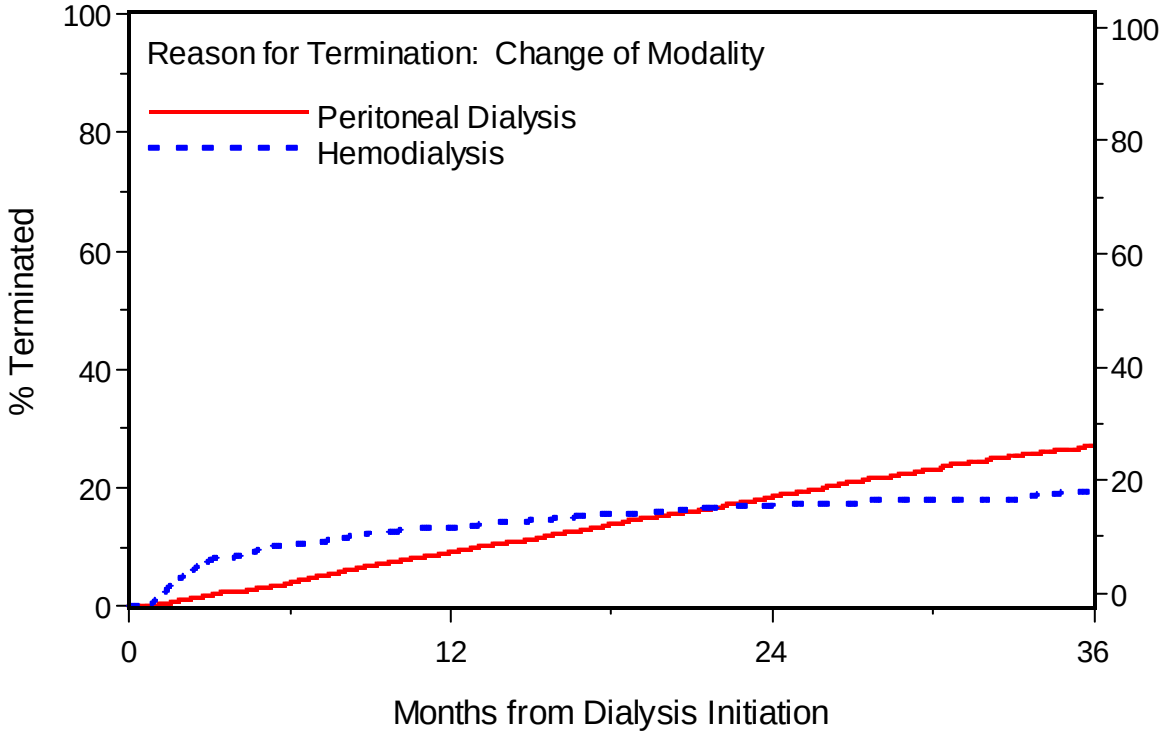


EXHIBIT 2.12
PERITONEAL DIALYSIS ACCESS BY SELECTED CHARACTERISTCS
(Index cases with 30 day data)

	CAPD		APD	
	N	%	N	%
Total	743	100.0	2343	100.0
Race/Ethnicity				
White	308	41.5	1319	56.3
Black	112	15.1	505	21.6
Hispanic	273	36.7	363	15.5
Other	50	6.7	156	6.7
Age at initiation				
0-1 years	112	15.1	483	20.6
2-5 years	94	12.7	293	12.5
6-12 years	245	33.0	695	29.7
>12 years	292	39.3	872	37.2
Gender				
Male	399	53.7	1304	55.7
Female	343	46.2	1039	44.3
Year initiated				
1992-1993	150	20.2	307	13.1
1994-1995	133	17.9	357	15.2
1996-1997	114	15.3	400	17.1
1998-1999	98	13.2	297	12.7
2000-2001	74	10.0	243	10.4
2002-2003	44	5.9	233	9.9
2004-2005	38	5.1	252	10.8
2006-2007	47	6.3	143	6.1
2008-2010	45	6.1	111	4.7

EXHIBIT 2.13
TIME TO DIALYSIS TERMINATION BY PERITONEAL DIALYSIS MODALITY
(Index cases with 30 day data)

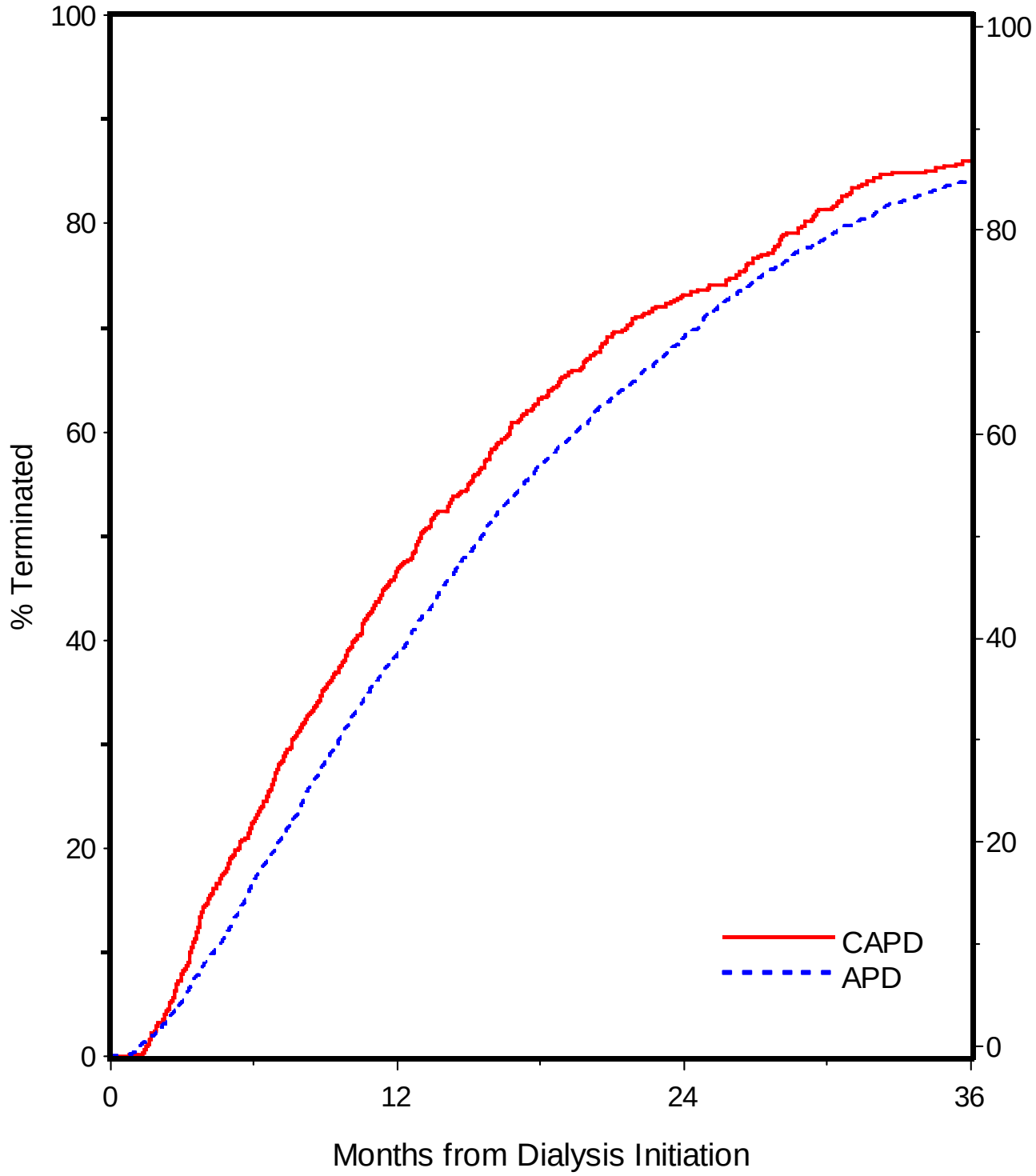
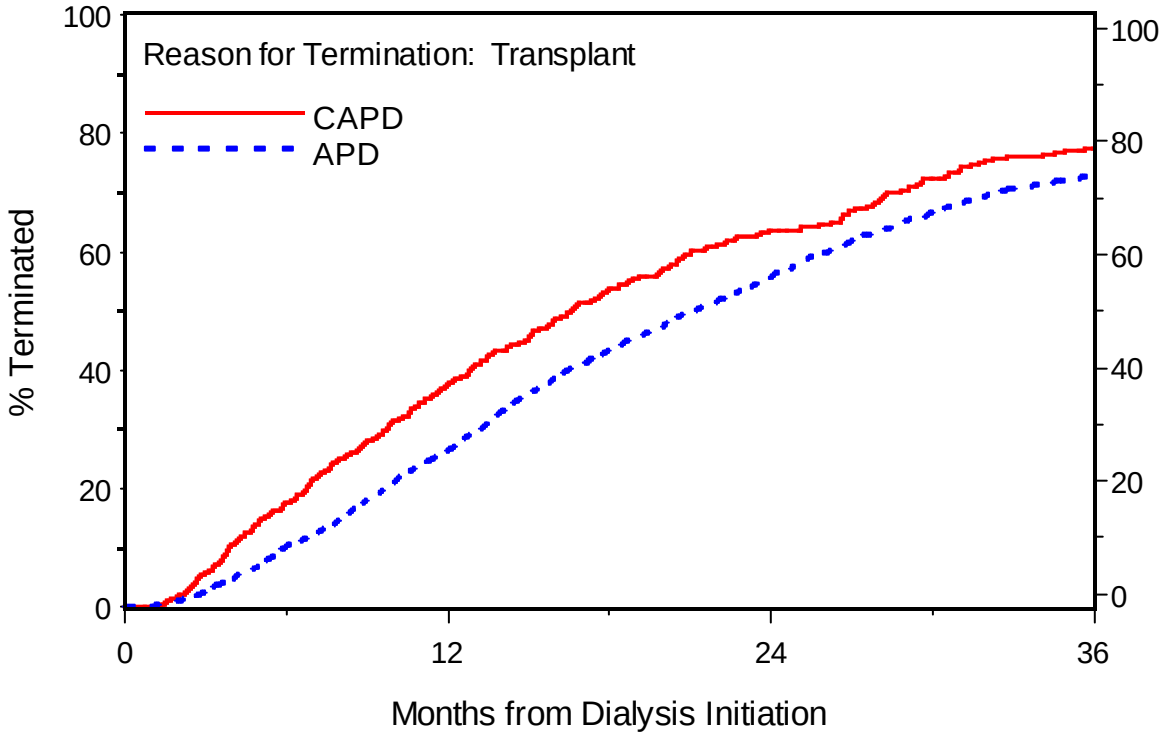
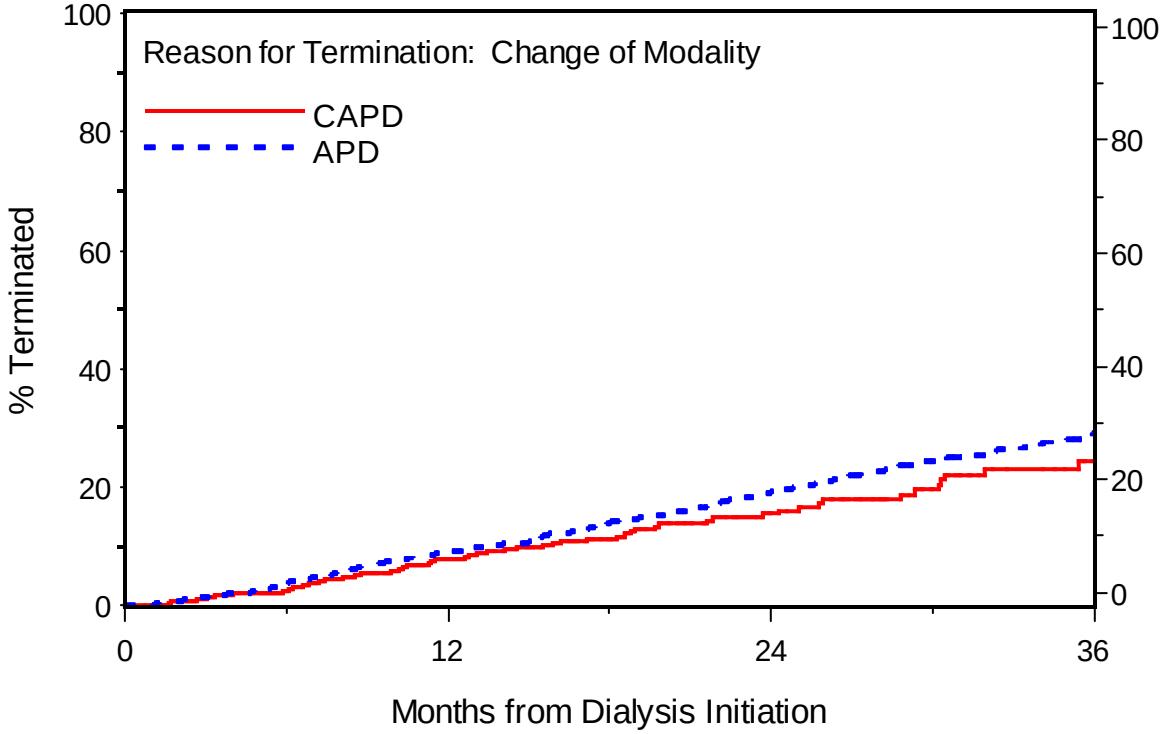


EXHIBIT 2.14
TIME TO DIALYSIS TERMINATION BY PERITONEAL DIALYSIS MODALITY
(Index cases with 30 day data)





SECTION 3: ERYTHROPOIETIN USE IN DIALYSIS PATIENTS

Data on the use of erythropoietin (EPO) are presented in this section. The cohort of interest is the 6,300 cases of maintenance dialysis, as described in the preceding section, for which the *index* course of dialysis was initiated after January 1, 1992. In particular, we evaluate herein the use of EPO following the reported index initiation of dialysis for these patients.

The percent use of EPO across time is described in Exhibit 3.1 for patients with non-missing data at the post dialysis initiation times shown. The use of EPO increases from 88.7% at baseline (Day 30) to 94.1% after two years of dialysis. While EPO use is lower initially for peritoneal dialysis (PD) patients (87.2%) compared to hemodialysis (HD) patients (91.5%), by two years of dialysis therapy, EPO use in similar (94.5% for PD and 93.4% for HD). EPO use at baseline, by patient age, gender, and race/ethnicity is depicted in Exhibit 3.2. Overall, EPO is used similarly among the age groups, with 89.1%, 89.7%, 89.5%, and 87.9% of patients, respectively, in age groups 0-1, 2-5, 6-12, and >12 receiving EPO therapy initially. Since over 90% of children <6 years old are treated with peritoneal dialysis, data are sparse regarding EPO usage patterns among HD patients in this age group. Among older children and adolescents, initial use of EPO is about 4-6 percentage points higher for HD relative to PD patients (Exhibit 3.2). EPO usage patterns, by gender, are similar within dialysis modality group. Hispanic PD patients receive EPO therapy less frequently than their HD counterparts (82.5% versus 92.2%).

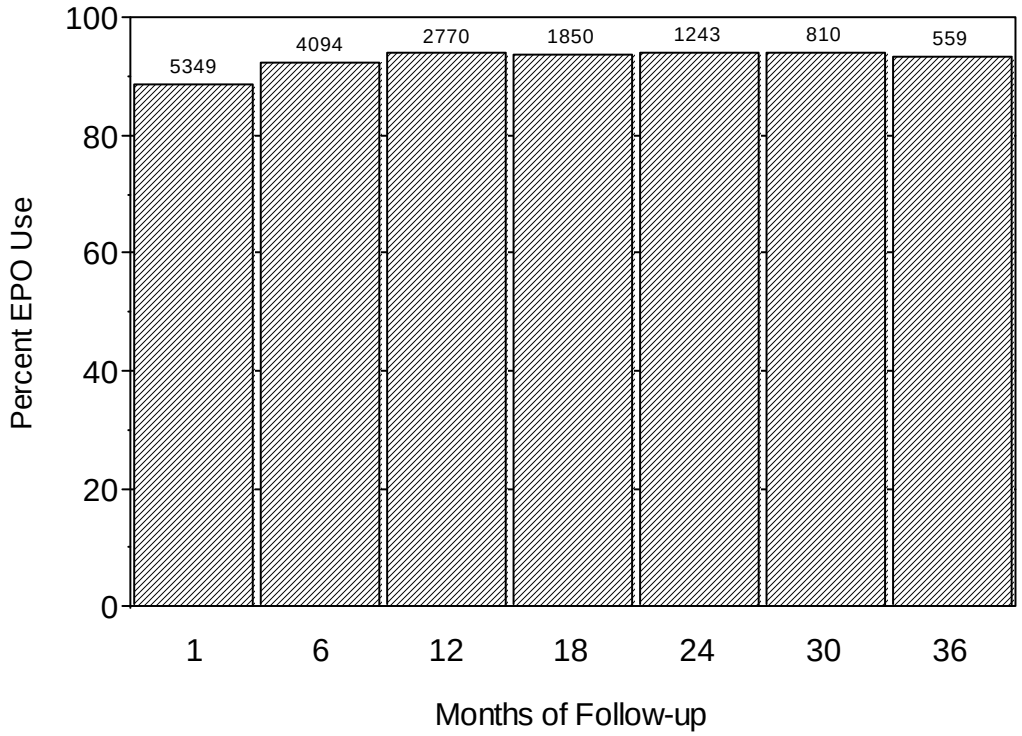
Of those treated with EPO therapy, data pertaining to route and frequency of use are described in Exhibit 3.3. As shown, most PD patients (95.2%) receive subcutaneous administration and 3.5% receive intravenous administration of EPO. Most HD patients are treated intravenously (84.5%) with 15% treated subcutaneously at day 30. Frequency of EPO administration is more varied among PD than HD. At 6 months, about 74% of PD patients are treated once or twice weekly, and about 17% are treated three times per week. The percentage of PD patients who are treated less frequently than once per week, increased from 4.8% initially to 8.5% at 12 months and remains stable afterwards. HD patients, however, are mostly treated three times per week (75%), presumably at the time of their dialysis therapy. Over the first 2 years time, 81% of the PD patients and 89% of the HD patients receive Epogen, with 6% of PD and 1% of HD receiving Procrit and 12% and 9% receiving Aranesp, respectively. Since 2004 the use of Aranesp has increased to 21% in PD patients and 19% in HD patients.

EPO dosing was examined in units per kilogram per week (Exhibit 3.4). The exhibit suggests, mean doses for the younger patients (<24 months, 2-5 years) are higher than mean doses for the older patients (6-12, >12) which remain stable over time. Moreover, mean doses for different gender, race, and dialysis modality groups are similar and remain stable overtime.

To assess more clearly the use and potential effect of EPO therapy on hematocrit, we considered 4,094 patients still maintained on their index course of dialysis at 6 months. By year of dialysis initiation, the percent use of EPO at Day 30 is increased from 73.3% in 1992 to 92.2% in 1995 where it remains stable. Frequency of EPO administration, by dialysis modality and patient age at initiation, is shown in Exhibit 3.5. Frequency of administration is slightly greater for infants receiving PD therapy, relative to older PD patients. Of these 4,094 patients, we have complete reporting on EPO use and hematocrit at the baseline and 6-month post dialysis initiation visits for 3,650. The percent distribution of hematocrit at 6 months, by EPO use, is shown in Exhibit 3.6. Of the 3,650 patients, 3,264 (89.4%) began EPO therapy by Day 30, 237 (6.5%) began EPO therapy after Day 30, and 149 (4.1%) had not received EPO through 6 months of dialysis therapy. Of patients who began EPO therapy by Day 30, 52% had a hematocrit level of 33% or above at 6 months. Forty-six percent of patients not treated by EPO during the first 6 months of dialysis had hematocrit levels of 33% or above at 6 months. Mean and median hematocrit levels at 6 months are shown in Exhibit 3.7 by EPO use.

EXHIBIT 3.1
ERYTHROPOIETIN USE BY FOLLOW-UP MONTH

All Patients



By Modality

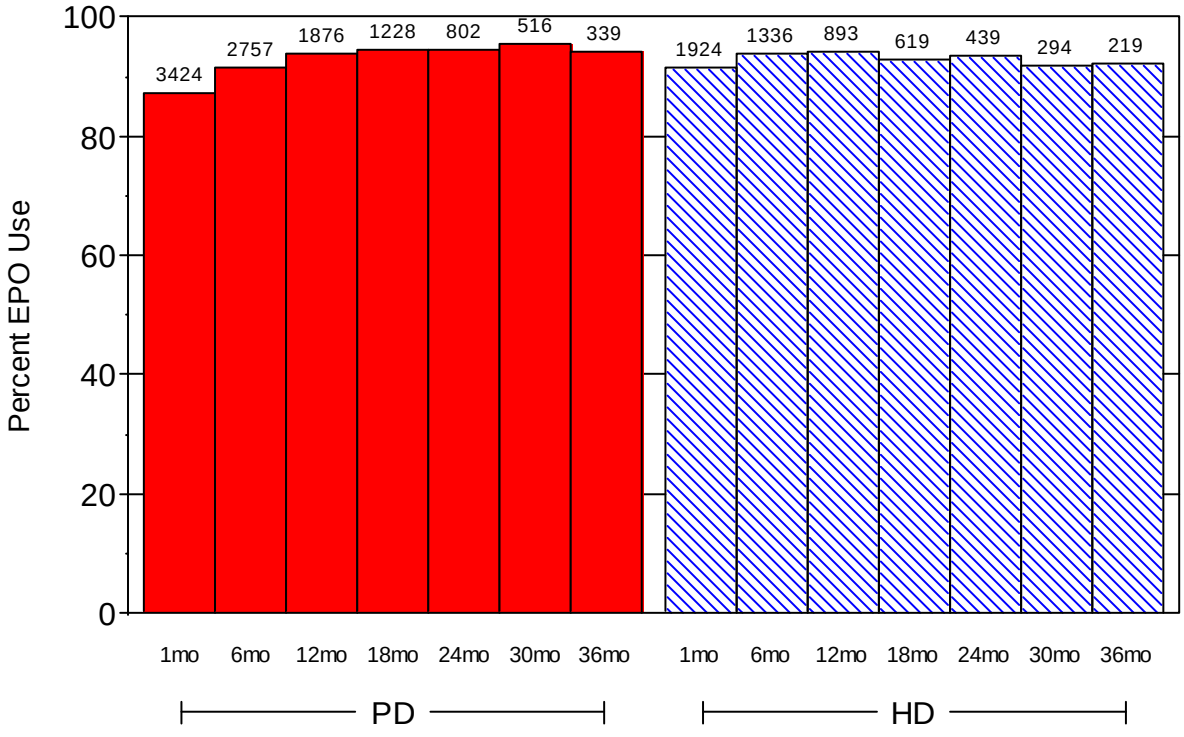
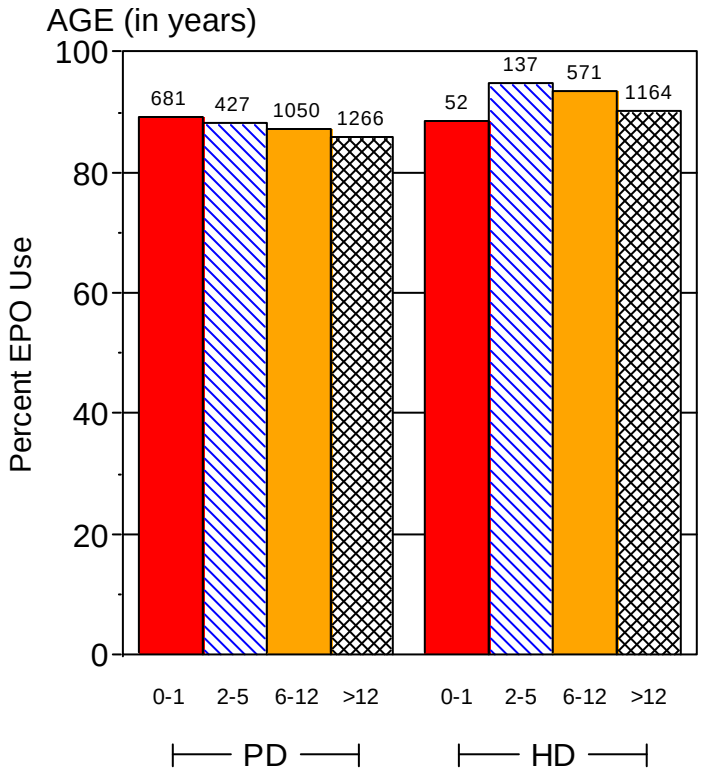
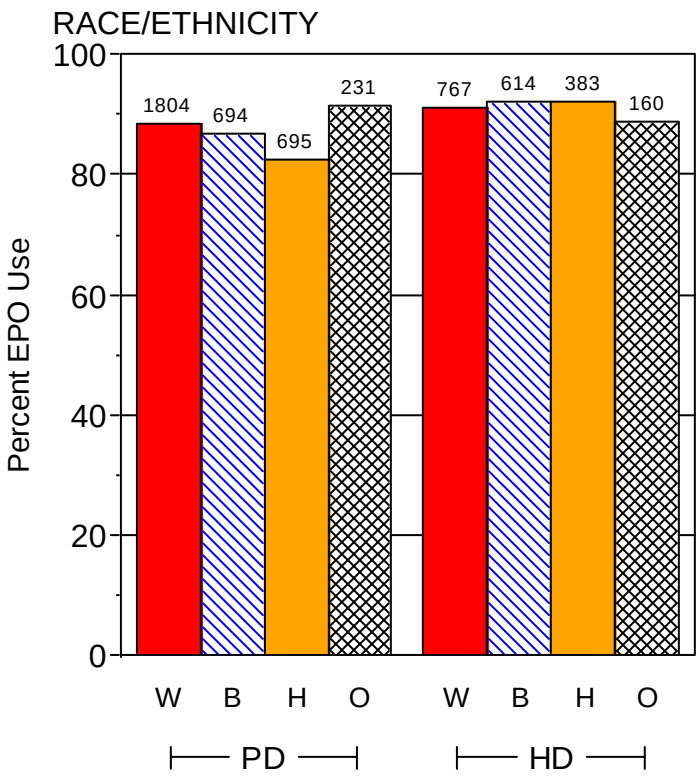


EXHIBIT 3.2
ERYTHROPOIETIN USE AT BASELINE BY PATIENT CHARACTERISTICS





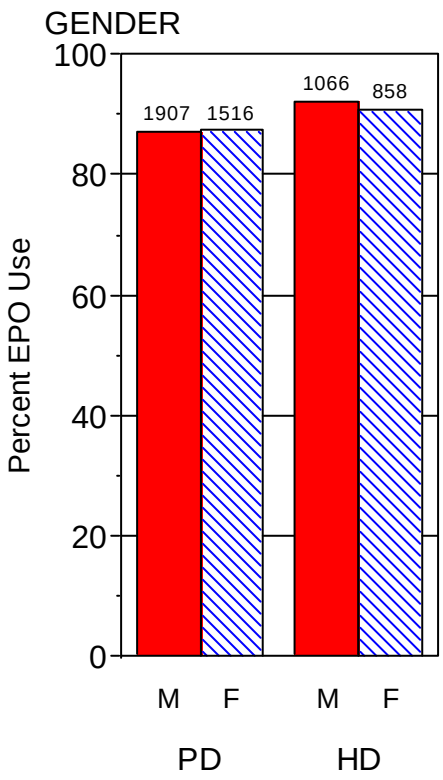
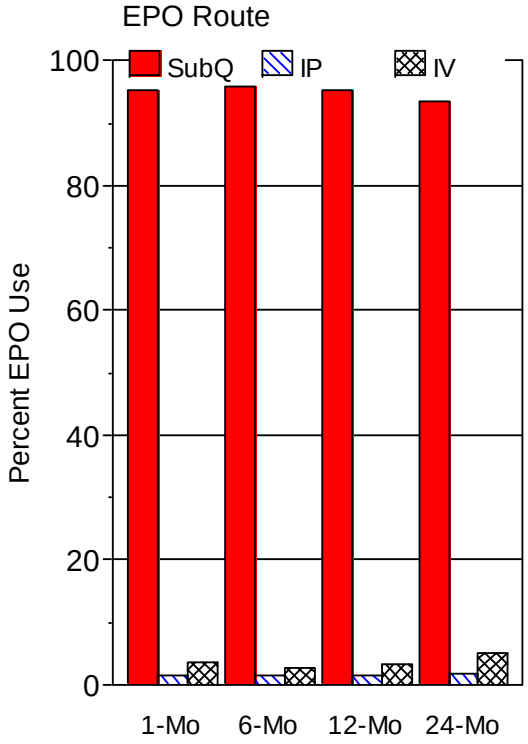
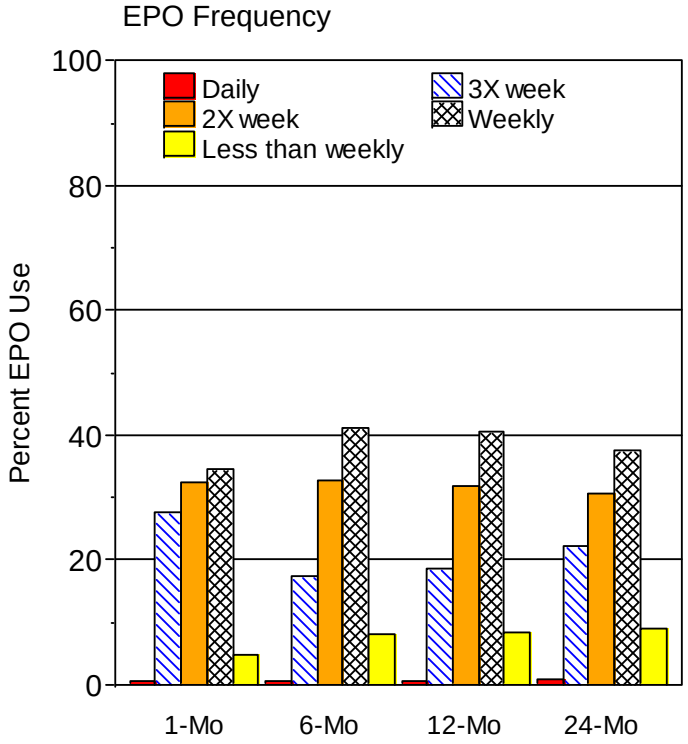


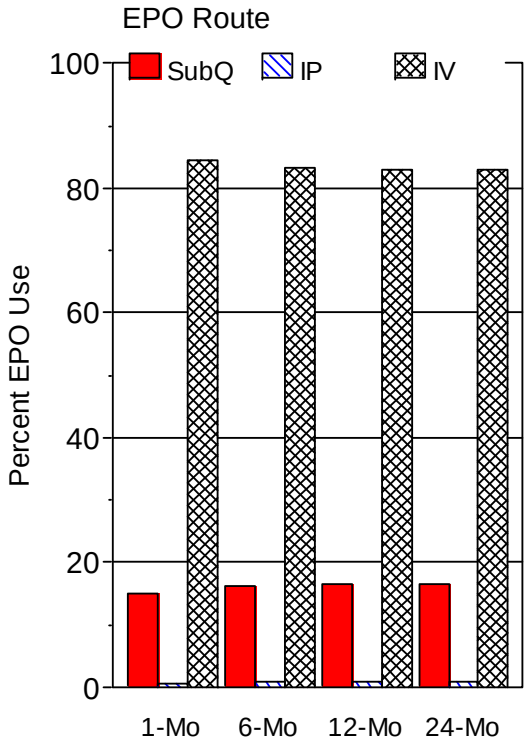
EXHIBIT 3.3
ERYTHROPOIETIN USE

Peritoneal Dialysis





Hemodialysis



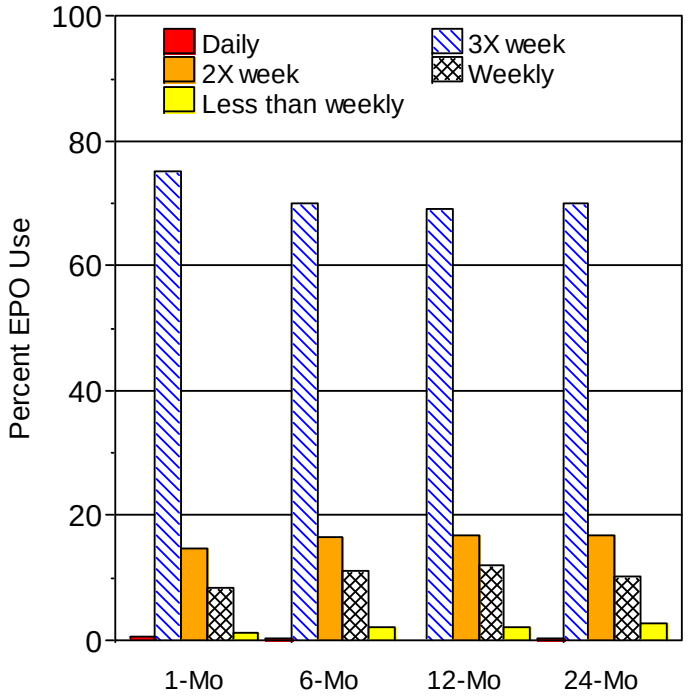
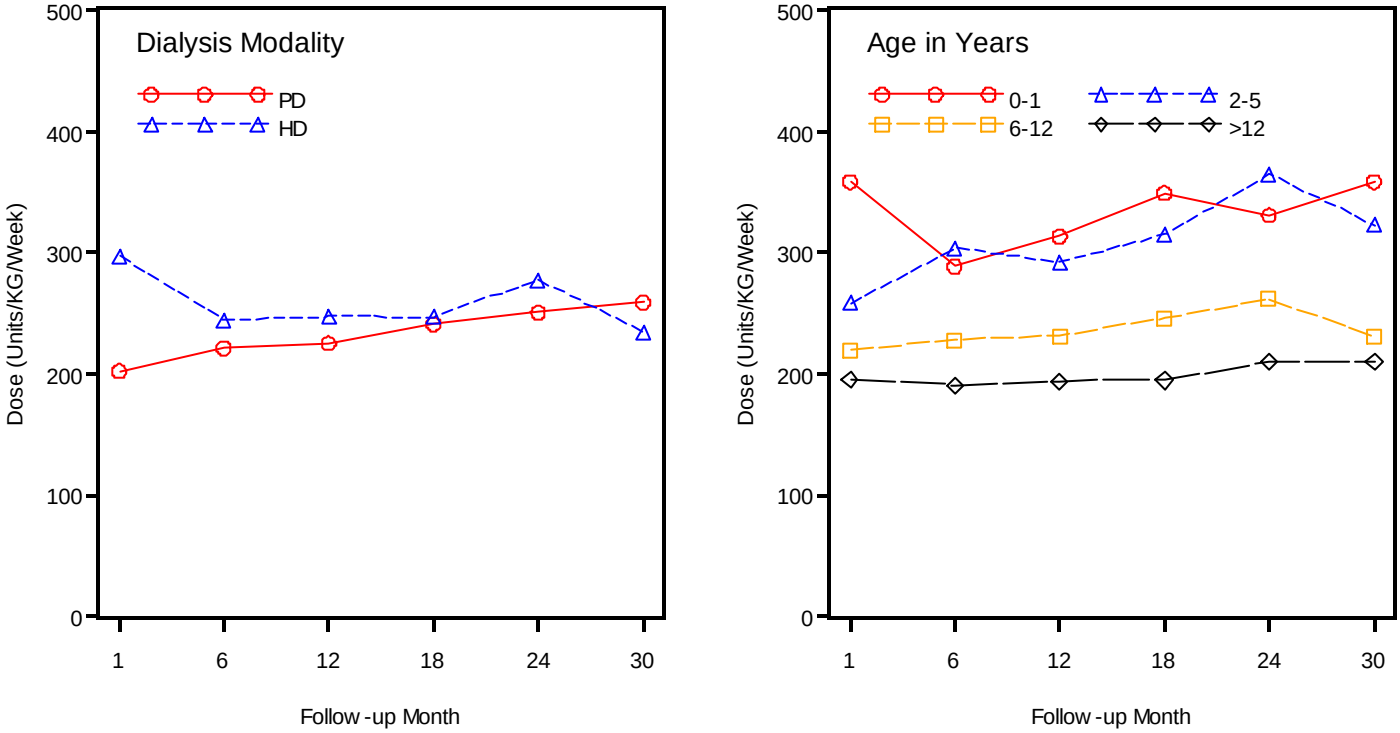
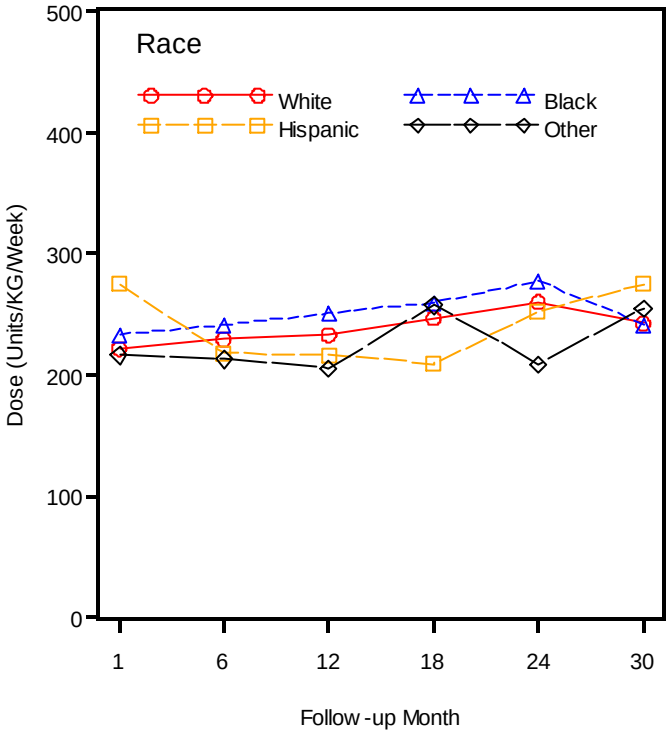


EXHIBIT 3.4
MEAN ERYTHROPOIETIN DOSE (UNITS/KG/WEEK)





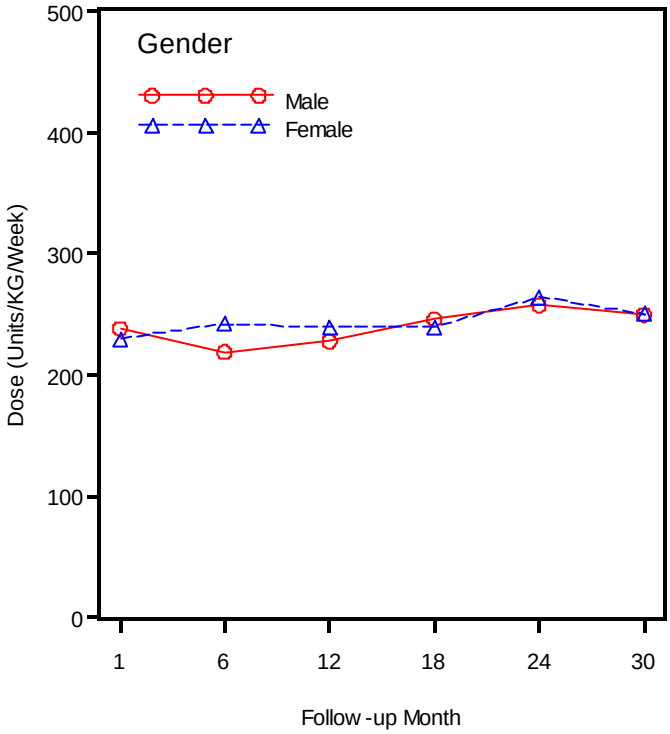


EXHIBIT 3.5
DISTRIBUTION (%) OF ERYTHROPOIETIN USE AT 6 MONTHS

	Peritoneal Dialysis				Hemodialysis			
	Age (years) at Index Initiation				Age (years) at Index Initiation			
EPO frequency	0-1	2-5	6-12	>12	0-1	2-5	6-12	>12
Daily	1.5	0	0.3	0.6	2.9	0	0.3	0.1
Three times/week	22.2	16.0	16.2	16.0	62.9	61.5	66.1	73.3
Two times/week	34.8	34.3	33.1	30.9	17.1	21.8	19.5	14.5
Weekly	35.2	42.6	41.8	43.9	14.3	15.4	11.7	9.9
<Weekly	6.3	7.1	8.6	8.6	2.9	1.3	2.3	2.1

EXHIBIT 3.6
DISTRIBUTION (%) OF HEMATOCRIT AT 6 MONTHS BY ERYTHROPOIETIN USE

		Hematocrit (%) at 6 Months				
EPO Use	Total	<25	27-30	31-33	33-35	> 35
Began EPO by day 30	3264	13.4	20.4	13.9	14.8	37.5
Began EPO after day 30	237	16.5	23.2	10.5	10.5	39.2
No EPO	149	21.5	18.1	14.8	8.1	37.6

EXHIBIT 3.7
HEMATOCRIT LEVELS AT 6 MONTHS BY ERYTHROPOIETIN USE

	Hematocrit (%) at 6 Months			
EPO Use	N	Mean	SE	Median
Began EPO by day 30	3264	32.9	0.1	33.0
Began EPO after day 30	237	32.6	0.4	32.7
No EPO	149	32.1	0.6	32.0

SECTION 4: DIALYSIS FOLLOW-UP

Follow-up data on peritoneal dialysis and hemodialysis initiations are presented in this section. We consider only those courses of dialysis for patients registered after January 1, 1992. This includes 4,687 courses of peritoneal dialysis with 3,941 being index courses and 3,363 courses of hemodialysis with 2,351 being index courses.

Exhibit 4.1 presents follow-up data at 1 month and at 6, 12, 24, and 36 months following PD initiation. Most patients used automated peritoneal dialysis (APD) [67.8% at 1 month, 70.0% at 36 months] rather than continuous ambulatory peritoneal dialysis (CAPD) or intermittent peritoneal dialysis (IPD). At one month post-initiation, 86.6% of patients were receiving erythropoietin (EPO) and 10.3% were receiving human growth hormone (rhGH); at 6 months, 90.7% were receiving EPO and 15.2% rhGH; at 36 months, 90.1% EPO and 24.2% rhGH. Exit site infections occurred in about 16-20% of cases between 6-month follow-up visits. Transplant status is also characterized: at 6 months post initiation, 22.9% of patients were on the deceased donor waiting list and 33.0% had a DD or LD work-up in progress. Of the 40.8% of patients who were not transplant candidates at 6 months 71.1% had a medical reason for remaining on dialysis and 21.3% were due to family or patient preference. By 12 months, 30.6% of patients were on the deceased donor list and 28.3% had a work-up in progress.

Also shown is the number of reported peritonitis episodes. During the first 30 days of PD, 436 (10.6%) patients had a peritonitis episode, and 50 patients had two episodes. Of the 536 reported infections that occurred within the first month, 16 (3.0%) were fungal, 239 (44.6%) were Gram-positive, 103 (19.2%) were Gram-negative, 21 (3.9%) were gram-positive and negative, 137 (25.6%) were cultured with no growth, and 20 (3.7%) were other or not cultured. Over the course of the study, 4,248 peritonitis infections have been reported in this cohort of PD patients: 877 patients have had only 1 infection, 432 patients have had two infections, 482 patients have had 3 to 7 infections, and 53 patients have had 8 or more infections. Infection rate is constant between age groups.

Peritonitis infection rates, by age and catheter characteristics, are presented in Exhibit 4.2. A total of 4,248 episodes of peritonitis have occurred in 6658 years of follow-up (4,687 PD courses), yielding an annualized rate of 0.64, or 1 episode every 18.8 months. The annualized rate decreases with age, and is better for double cuffs, swan neck tunnels, and downward

pointed exit sites. The percentage of patients using the double cuffs/swan neck/downward pointed exit site configuration increased from 5% in 1992-1995 to 15% in 1996-2001 to 24% since 2002. Significant improvement is seen since 2002 with the annualized rate of infection decreasing from 0.79 in 1992-1996 to 0.44 in recent years.

Time to first peritonitis infection is depicted in Exhibits 4.3, 4.4, 4.5 and 4.6; Exhibit 4.3 is for all patients, Exhibit 4.4 is by age at initiation, and Exhibit 4.5 is by catheter access characteristics. Overall, 37.5% of patients have had at least one infection by 12 months; 51.0% have had an infection by 24 months. Tenckhoff straight and Tenckhoff curled catheters have similar times to first peritonitis infection. Overall, the time to first peritonitis infection is longer for: two cuffs compared to one, for swan neck tunnels compared to straight tunnels, and for down exit sites compared to up & lateral (see Exhibit 4.5).

Time to first peritonitis episode was not different between CAPD patients and APD patients, as shown in Exhibit 4.6. 50% of the cases had their first peritonitis episode by 19.3 months compared in both groups. At 1 year post initiation, 42.1% of CAPD patients and 40.1% of APD patients had experienced at least one episode of peritonitis.

Data on PD catheter access revisions are shown in Exhibit 4.7. The revision access ratio (number of revisions / number of accesses) is 0.19. Accesses were revised due to catheter malfunction (40%), peritonitis (16%), exit site tunnel infections (14%), dialysate leaks (4%), and missing/other (26%). Percent distributions of reasons for access revisions are also shown according to catheter access characteristics. Recall that the most common access configuration is a Tenckhoff curled catheter with one cuff, a straight tunnel, and a lateral exit site orientation. The ideal access configuration (with respect to having an access revision) would be Tenckhoff curled (Toronto western is used very infrequently), two cuffs, swan/curved tunnel and a downward exit site orientation.

Follow-up data on HD patients and accesses are shown in Exhibit 4.8 and Exhibit 4.9. The use of EPO in HD patients exceeds that of PD patients for the first year of dialysis (90% versus 87%), but is about 90% at 24 months for both groups. On the other hand, the use of rhGH is less in HD than in PD (16% versus 25% at 24 months). The transplant status of HD patients is similar to that observed for the PD cohort with 13% and 14% respectively on the deceased donor list at 30 days. The revision access ratio for HD is 0.80. Accesses were revised because

of infection (15%), clotting (23%), malfunction (26%), to create a more permanent access (25%), and other/missing in 12%.

For the 601 index patients who were placed on the deceased donor waiting list at dialysis initiation, Exhibits 4.10 and 4.11 show the time to deceased donor transplantation by year listed and by age, respectively.

In 2003, NAPRTCS initiated collection of dialysis dose measurements with capture, at each reporting time point of most recent single pool Kt/V and Urea Reduction Ratio (URR) for hemodialysis patients and most recent weekly Kt/V for peritoneal dialysis patients. Exhibit 4.12 displays initial reported Kt/V by age grouping, race, visit timing since initiation and baseline BMI standardized score for 910 peritoneal dialysis and 770 hemodialysis patients. For peritoneal dialysis patients, dialysis dose is lower in ages > 12 years, black race, at 30 day visit and with higher BMI scores. The median Kt/V was 2.2, the lower quartile was 1.8 and the lowest decile was 1.4. Peritoneal dialysis strategies (CAPD versus APD versus IPD) did not differ significantly in Kt/V values. Hemodialysis patients Kt/V was lower for infants, blacks, earlier visit months, and higher BMI Z-scores. Kt/V percentiles (50^{th}, 25^{th} and 10^{th}) for hemodialysis patients are 1.5, 1.3 and 1.0. Mean URR values for selected hemodialysis patient subgroups are presented in Exhibit 4.13. Since Kt/V and URR values are highly correlated, similar differences in race, visit month and BMI Z-score are noted; however for age, the >12 year olds had the lowest URR value.

In addition, for patients with more than one Kt/V measurement, the mean of the first reported Kt/V was compared with the mean of their second Kt/V. This was performed separately for both hemodialysis and peritoneal dialysis patients. In an analysis of 502 HD patients, a mean difference of -0.052 was observed (p=0.011). There was no significant difference in mean values for the 596 PD patients (mean difference –0.001, p=0.986). Among 526 HD patients with more than one URR measurement, the mean of the first reported URR was compared with the mean of the second reported URR measurement. The average difference in values was –1.143 (p=0.015). Exhibit 4.14 shows box plots for the Kt/V values over time. The box represents the 25^{th} and 75^{th} percentiles with whiskers showing the 10^{th} and 90^{th} percentiles. The median value for PD patients at day 30 is 2.1, at 1 year is 2.2, and at 2 years post-initiation, the median Kt/V for PD patients is 2.3. For HD patients median values at day 30, 1 year and 2 years post-initiation are 1.5, 1.6 and 1.6 respectively.

EXHIBIT 4.1
PERITONEAL DIALYSIS AT FOLLOW-UP

	1 Month		6 Month		12 Month		24 Month		36 Month	
	N	%	N	%	N	%	N	%	N	%
Total Courses	4110	100.0	3307	100.0	2300	100.0	1011	100.0	434	100.0
Modality										
CAPD	851	20.7	623	18.8	419	18.2	155	15.3	64	14.7
APD	2787	67.8	2306	69.7	1595	69.3	699	69.1	304	70.0
IPD	261	6.4	191	5.8	114	5.0	39	3.9	17	3.9
Missing/Unknown	211	5.1	187	5.7	172	7.5	118	11.7	49	11.3
EPO Therapy										
Yes	3560	86.6	3000	90.7	2100	91.3	910	90.0	391	90.1
No	486	11.8	252	7.6	128	5.6	53	5.2	22	5.1
Missing/Unknown	64	1.6	55	1.7	72	3.1	48	4.7	21	4.8
hGH Therapy										
Yes	424	10.3	504	15.2	462	20.1	256	25.3	105	24.2
No	3616	88.0	2736	82.7	1761	76.6	706	69.8	310	71.4
Missing/Unknown	70	1.7	67	2.0	77	3.3	49	4.8	19	4.4
Seizures										
Yes	148	3.6	153	4.6	76	3.3	34	3.4	10	2.3
No	3804	92.6	3016	91.2	2083	90.6	889	87.9	383	88.2
Missing/Unknown	158	3.8	138	4.2	141	6.1	88	8.7	41	9.4
Exit Site Infections										
Yes	350	8.5	644	19.5	439	19.1	167	16.5	72	16.6
No	3623	88.2	2557	77.3	1748	76.0	785	77.6	338	77.9
Missing/Unknown	137	3.3	106	3.2	113	4.9	59	5.8	24	5.5
Transplant Status										
DD List	521	12.7	757	22.9	704	30.6	399	39.5	170	39.2
Work-up in progress	1531	37.3	1091	33.0	651	28.3	201	19.9	65	15.0
Medical Reasons	1576	38.3	1037	31.4	589	25.6	201	19.9	91	21.0
Choice	339	8.2	311	9.4	257	11.2	147	14.5	81	18.7
Missing/Unknown	143	3.5	111	3.4	99	4.3	63	6.2	27	6.2
# of Peritonitis Episodes (in period)										
0	3624	88.2	2444	73.9	1704	74.1	770	76.2	310	71.4
1	436	10.6	585	17.7	399	17.3	163	16.1	81	18.7
2	50	1.2	180	5.4	122	5.3	53	5.2	30	6.9
>2	0	0.0	98	3.0	75	3.3	25	2.5	13	3.0

EXHIBIT 4.2
PERITONEAL DIALYSIS PERITONITIS RATES

	N of episodes	Years of FU	Annualized Rate		Expected Months between infections	
			Rate	95% CI	Months	95% CI
Total	4248	6658	0.64	(0.62 - 0.66)	18.8	(18.3 - 19.4)
Age						
0-1 years	938	1193	0.79	(0.74 - 0.84)	15.3	(14.3 - 16.3)
2-5 years	552	821	0.67	(0.62 - 0.73)	17.9	(16.5 - 19.5)
6-12 years	1345	2145	0.63	(0.59 - 0.66)	19.1	(18.2 - 20.2)
>12 years	1413	2499	0.57	(0.54 - 0.59)	21.2	(20.2 - 22.4)
Catheter						
Straight	1180	1668	0.71	(0.67- 0.75)	17.0	(16.0 - 18.0)
Curled	2697	4137	0.65	(0.63 - 0.68)	18.4	(17.7 - 19.1)
Presternal	225	420	0.54	(0.47 - 0.61)	22.4	(19.8 - 25.8)
Cuff						
One	2553	3440	0.74	(0.71 - 0.77)	16.2	(15.6 - 16.8)
Two	1620	2912	0.56	(0.53 - 0.58)	21.6	(20.6 - 22.7)
Tunnel						
Swan necked/curved	1161	2317	0.50	(0.47 - 0.53)	23.9	(22.6 - 25.4)
Straight	2995	4032	0.74	(0.72 - 0.77)	16.2	(15.6 - 16.8)
Exit Site Orientation						
Up	702	850	0.83	(0.76 - 0.89)	14.5	(13.5 - 15.7)
Down	1181	2221	0.53	(0.50 - 0.56)	22.6	(21.4 - 23.9)
Lateral	1828	2466	0.74	(0.71 - 0.78)	16.2	(15.5 - 17.0)
Year of Dialysis Initiation						
1992-1996	2166	2752	0.79	(0.75 - 0.82)	15.2	(14.6 - 15.9)
1997-2001	1303	2095	0.62	(0.59 - 0.66)	19.3	(18.3 - 20.4)
2002-2006	610	1431	0.43	(0.39 - 0.46)	28.2	(26.1 - 30.6)
2007-2010	169	380	0.44	(0.38 - 0.51)	27.0	(23.5 - 31.8)

Note: Other/unknown/missing catheter, cuff, tunnel and exit site orientation not shown.

EXHIBIT 4.3
TIME TO FIRST PERITONITIS INFECTION (PD Index Cases)

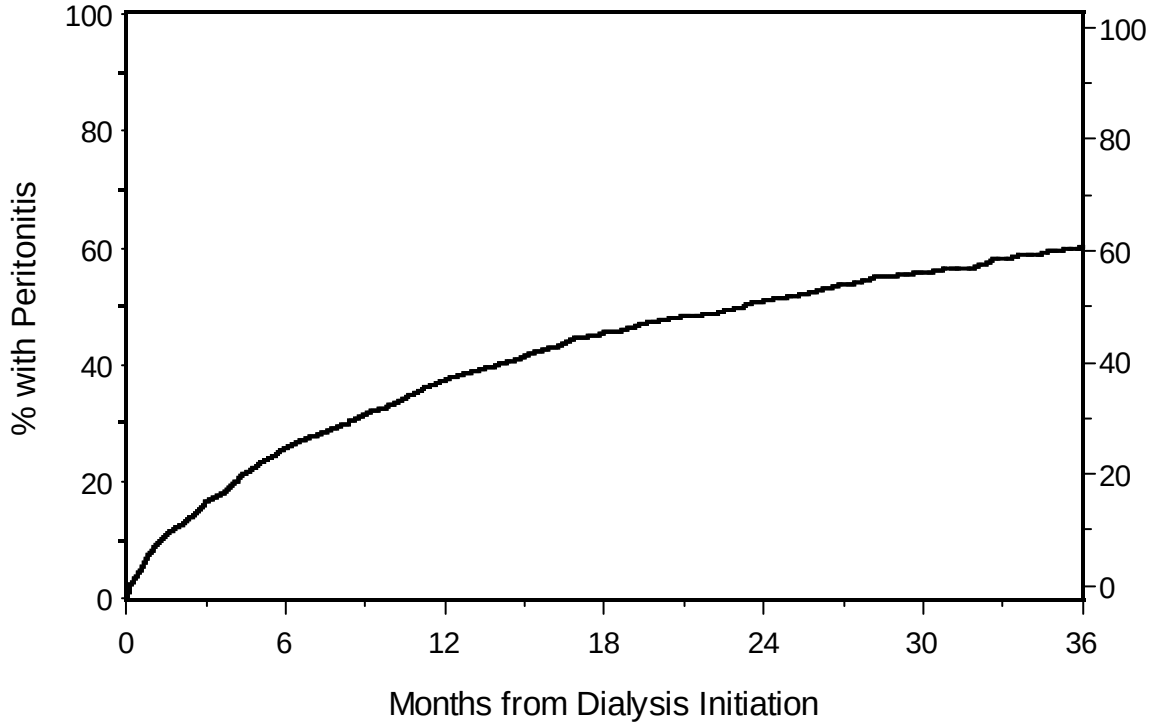


EXHIBIT 4.4
TIME TO FIRST PERITONITIS INFECTION BY AGE (PD Index Cases)

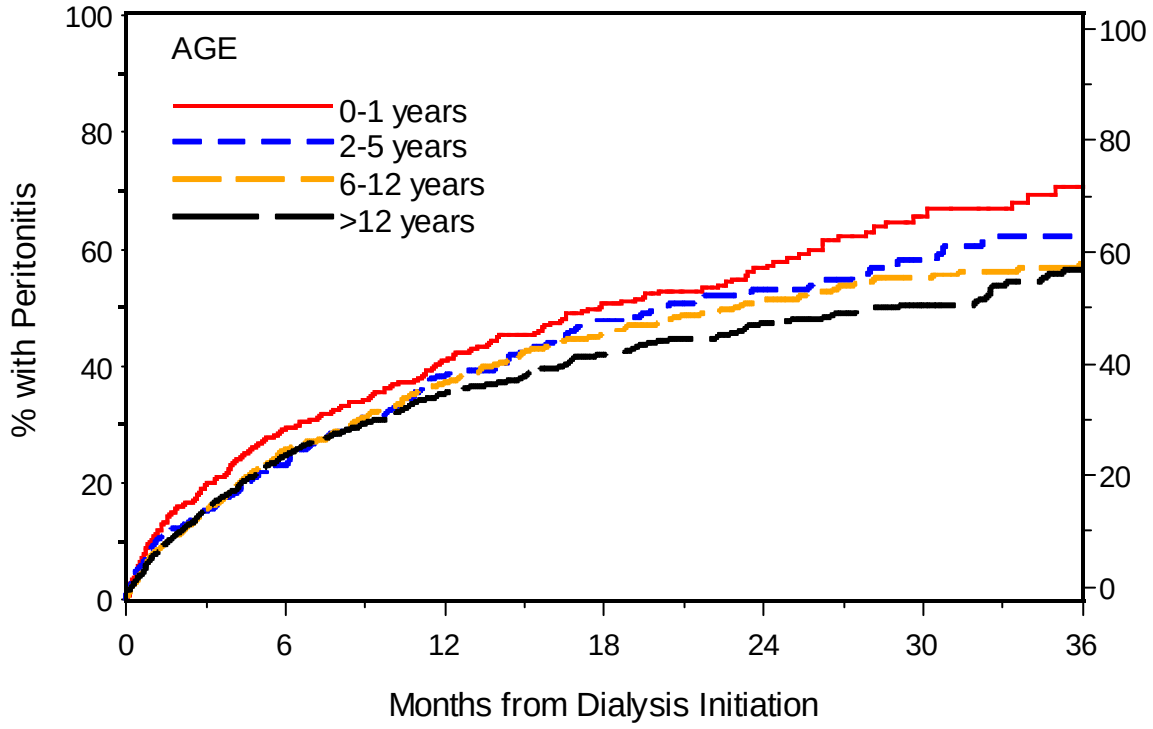
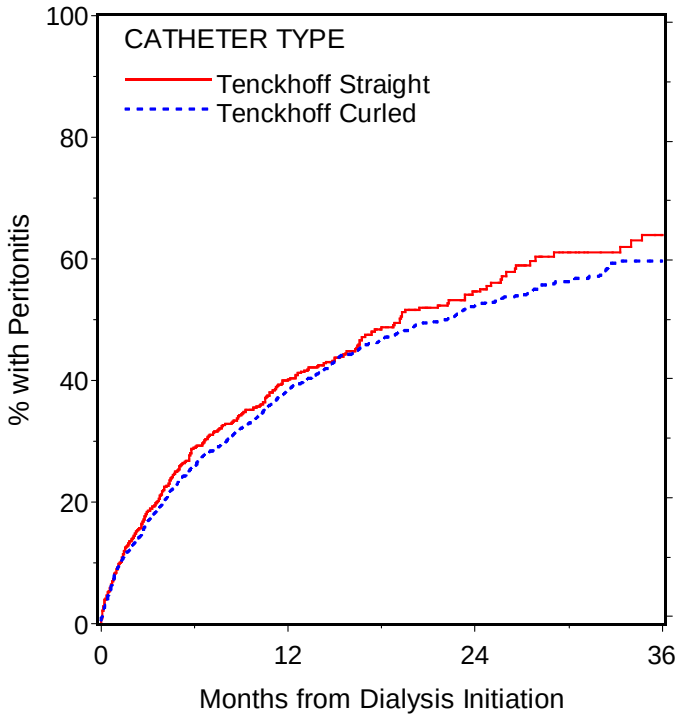
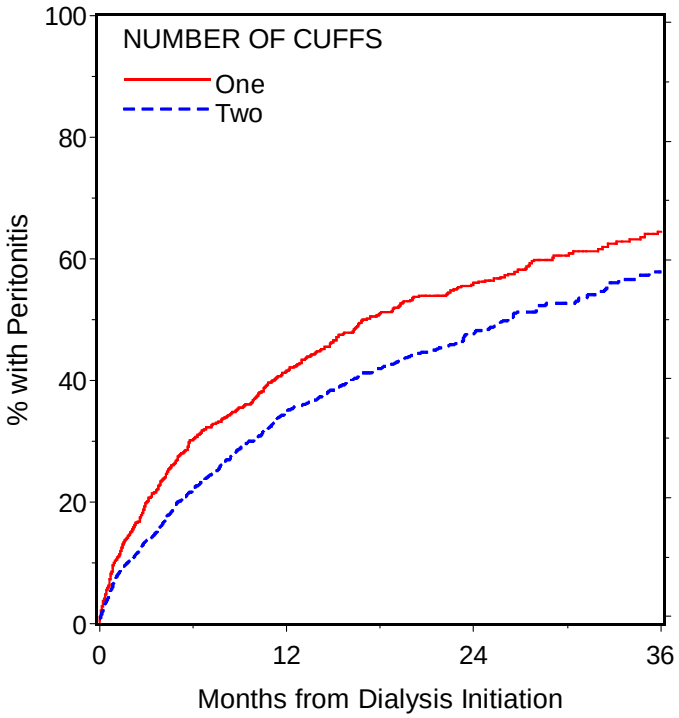
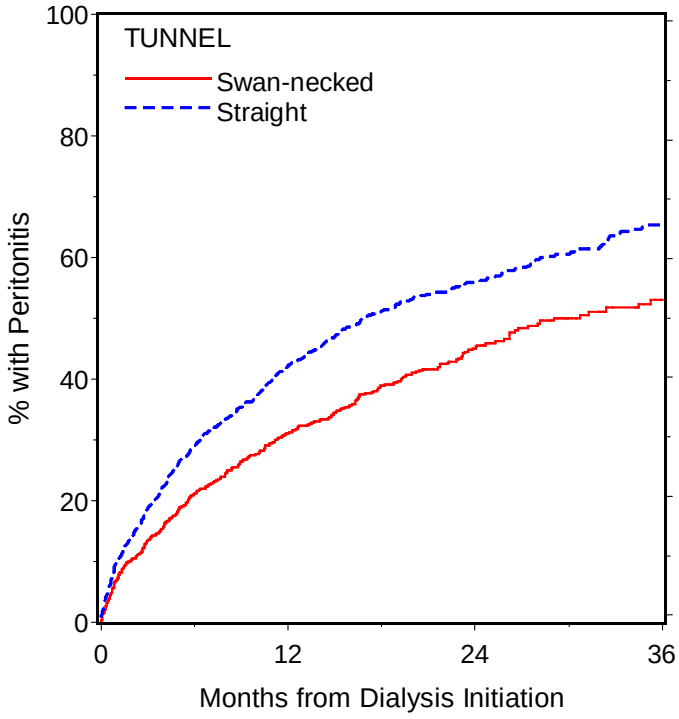


EXHIBIT 4.5
TIME TO FIRST PERITONITIS INFECTION
BY PERITONEAL DIALYSIS ACCESS CHARACTERISTICS
(PD Index Cases)







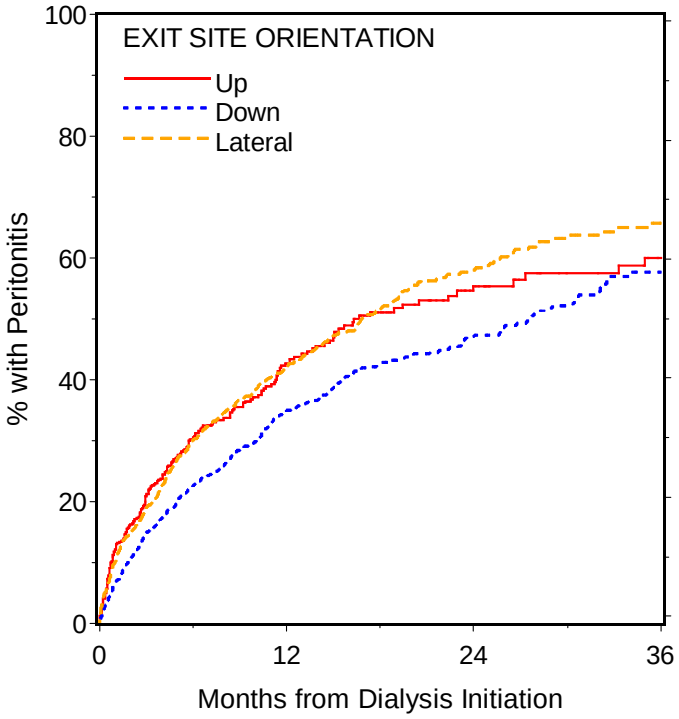


EXHIBIT 4.5 (continued)
TIME TO FIRST PERITONITIS INFECTION
BY PERITONEAL DIALYSIS ACCESS CHARACTERISTICS
(PD Index Cases)

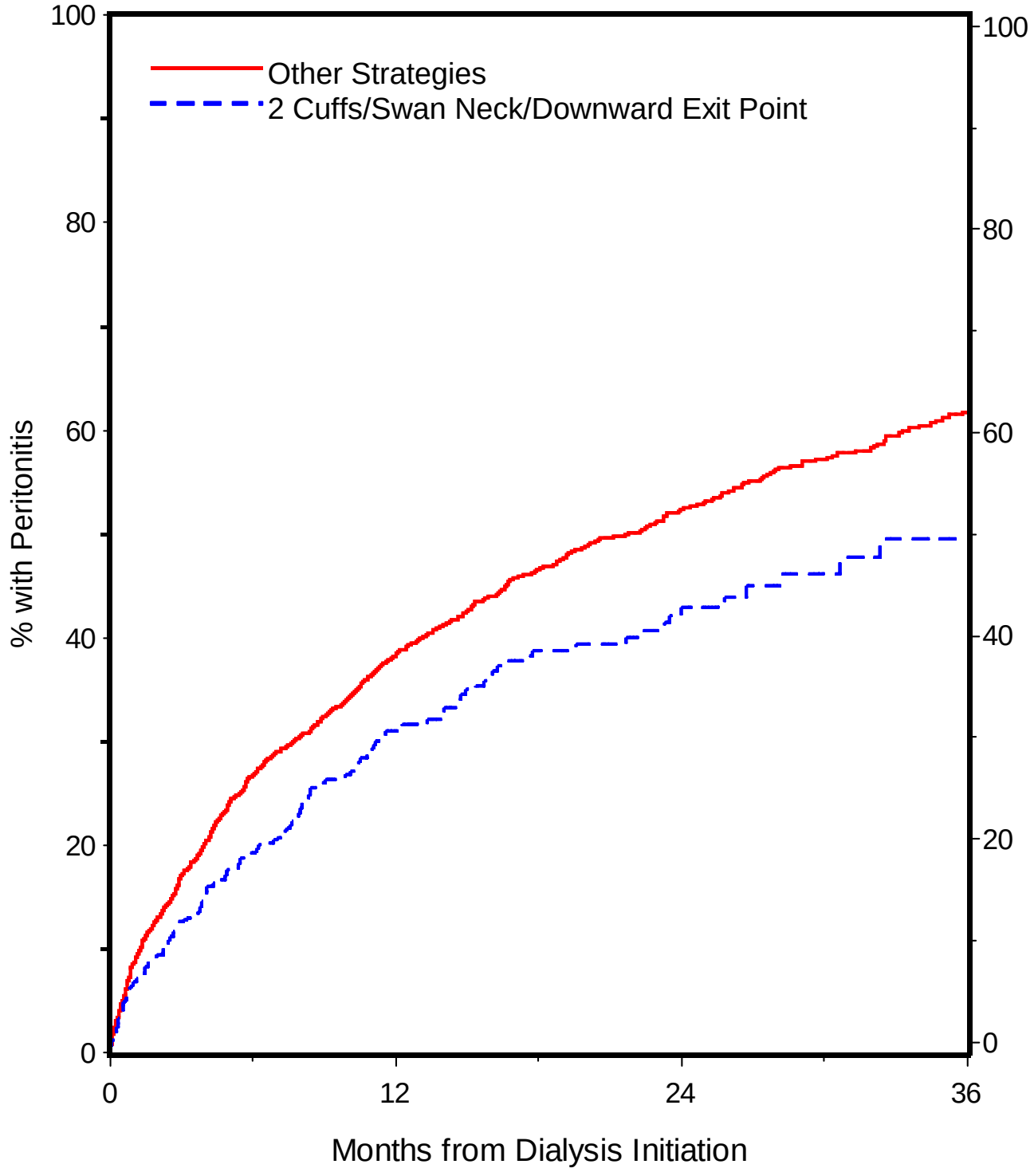


EXHIBIT 4.6
TIME TO FIRST PERITONITIS EPISODE BY PERITONEAL DIALYSIS MODALITY
(Index cases with 30 day data)

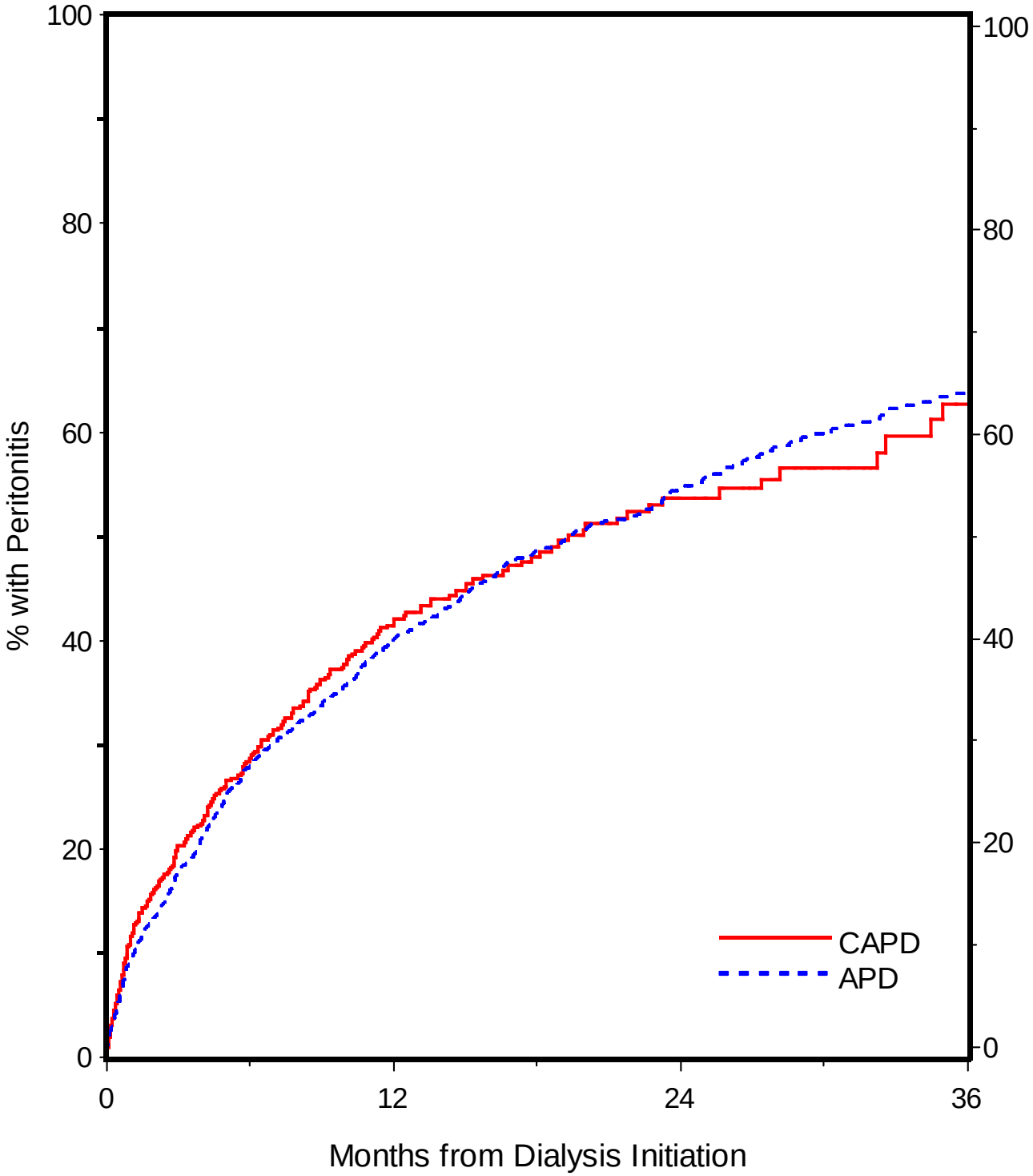


EXHIBIT 4.7
PERITONEAL DIALYSIS ACCESS REVISIONS

	Number of Accesses	Number of Revisions	Revision/ Access x 100	Reason For Access Revision											
				Infection		Leak		Malfunction		Peritonitis		Other		Missing	
				N	%	N	%	N	%	N	%	N	%	N	%
Total	4687	902	19.2	125	13.9	37	4.1	358	39.7	148	16.4	90	10.0	144	16.0
Catheter															
Tenckhoff Straight	1213	250	20.6	34	13.6	8	3.2	114	45.6	39	15.6	28	11.2	27	10.8
Tenckhoff Curled	2909	560	19.3	73	13.0	25	4.5	208	37.1	99	17.7	51	9.1	104	18.6
Toronto Western	26	5	19.2	0	0.0	0	0.0	4	80.0	1	20.0	0	0.0	0	0.0
Presternal	272	54	19.9	11	20.4	1	1.9	23	42.6	6	11.1	5	9.3	8	14.8
Other	111	9	8.1	2	22.2	2	22.2	2	22.2	1	11.1	1	11.1	1	11.1
Cuff															
One	2375	515	21.7	61	11.8	26	5.0	209	40.6	100	19.4	43	8.3	76	14.8
Two	2124	366	17.2	61	16.7	11	3.0	142	38.8	45	12.3	45	12.3	62	16.9
Tunnel															
Swan /curved	1590	267	16.8	43	16.1	11	4.1	97	36.3	41	15.4	29	10.9	46	17.2
Straight	2895	616	21.3	79	12.8	25	4.1	253	41.1	106	17.2	58	9.4	95	15.4
Exit Site Orientation															
Up	564	147	26.1	20	13.6	9	6.1	55	37.4	37	25.2	9	6.1	17	11.6
Down	1537	276	18.0	42	15.2	12	4.3	113	40.9	42	15.2	29	10.5	38	13.8
Lateral	1816	350	19.3	48	13.7	14	4.0	134	38.3	49	14.0	35	10.0	70	20.0

EXHIBIT 4.8
HEMODIALYSIS AT FOLLOW-UP

	1 Month		6 Month		12 Month		24 Month		36 Month	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Total Courses	2732	100.0	1948	100.0	1330	100.0	665	100.0	353	100.0
EPO Therapy										
Yes	2466	90.3	1769	90.8	1201	90.3	594	89.3	305	86.4
No	196	7.2	108	5.5	73	5.5	38	5.7	22	6.2
Missing/Unknown	70	2.6	71	3.6	56	4.2	33	5.0	26	7.4
hGH Therapy										
Yes	264	9.7	218	11.2	164	12.3	104	15.6	42	11.9
No	2391	87.5	1650	84.7	1102	82.9	527	79.2	281	79.6
Missing/Unknown	77	2.8	80	4.1	64	4.8	34	5.1	30	8.5
Seizures										
Yes	119	4.4	132	6.8	76	5.7	38	5.7	16	4.5
No	2500	91.5	1706	87.6	1156	86.9	579	87.1	295	83.6
Missing/Unknown	113	4.1	110	5.6	98	7.4	48	7.2	42	11.9
Exit Site Infections										
Yes	230	8.4	290	14.9	160	12.0	55	8.3	23	6.5
No	2354	86.2	1516	77.8	1066	80.2	552	83.0	287	81.3
Missing/Unknown	148	5.4	142	7.3	104	7.8	58	8.7	43	12.2
Transplant Status										
DD List	379	13.9	524	26.9	464	34.9	288	43.3	150	42.5
Work-up in progress	1032	37.8	549	28.2	296	22.3	102	15.3	48	13.6
Medical Reasons	968	35.4	571	29.3	359	27.0	147	22.1	76	21.5
Choice	211	7.7	177	9.1	124	9.3	78	11.7	41	11.6
Missing/Unknown	142	5.2	127	6.5	87	6.5	50	7.5	38	10.8

EXHIBIT 4.9
HEMODIALYSIS ACCESS REVISIONS

	Number of Accesses	Number of Revisions	Revision/ Access Ratio x 100	Reason For Access Revision											
				Infection		Clot		Malfunction		Re-access		Other		Missing	
				N	%	N	%	N	%	N	%	N	%	N	%
Total	3363	2696	80.2	390	14.5	612	22.7	691	25.6	681	25.3	245	9.1	77	2.9
HD Access															
External	2645	2307	87.2	350	15.2	422	18.3	633	27.4	629	27.3	207	9.0	66	2.9
Shunt	10	13	130.0	1	7.7	6	46.2	1	7.7	4	30.8	1	7.7	0	0.0
Fistula	398	139	34.9	10	7.2	63	45.3	26	18.7	22	15.8	15	10.8	3	2.2
Graft	225	211	93.8	24	11.4	117	55.5	23	10.9	24	11.4	20	9.5	3	1.4
Unk/Missing	85	26	30.6	5	19.2	4	15.4	8	30.8	2	7.7	2	7.7	5	19.2

EXHIBIT 4.10
TIME TO TRANSPLANT FOR PATIENTS ON DECEASED DONOR LIST (at 30 days)

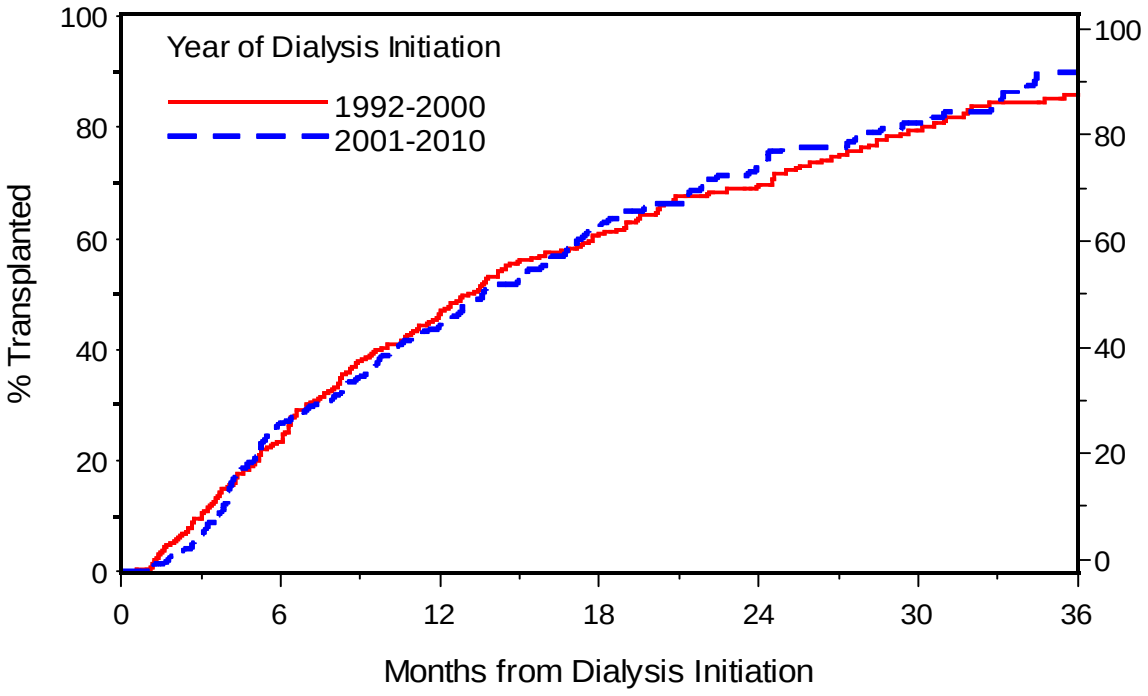


EXHIBIT 4.11
TIME TO TRANSPLANT FOR PATIENTS ON DECEASED DONOR LIST (at 30 days)

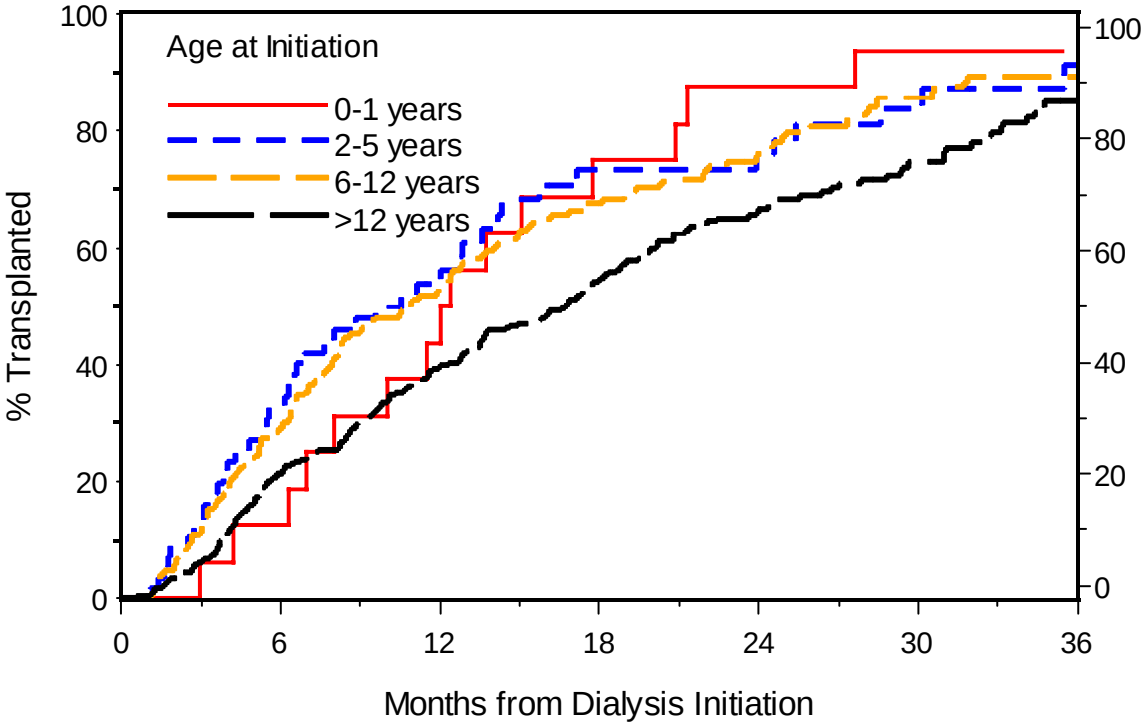


EXHIBIT 4.12
FIRST Kt/V MEASUREMENT

Peritoneal Dialysis

Kt/V	N	Mean	SE	Median
Total	910	2.40	0.04	2.20
Age				
0-1 years	183	2.46	0.07	2.30
2-5 years	120	2.48	0.09	2.30
6-12 years	272	2.53	0.07	2.30
>12 years	335	2.24	0.06	2.00
Race				
Non-Black	696	2.47	0.04	2.20
Black	214	2.18	0.06	2.00
Visit Month				
1 Month	447	2.31	0.05	2.10
6 Month	250	2.56	0.08	2.30
12 Month	87	2.41	0.12	2.20
>12 Month	126	2.41	0.09	2.20
BMI Z-score				
≤ 0	318	2.53	0.06	2.35
> 0	365	2.25	0.05	2.10
Missing	227	2.46	0.07	2.20

Hemodialysis

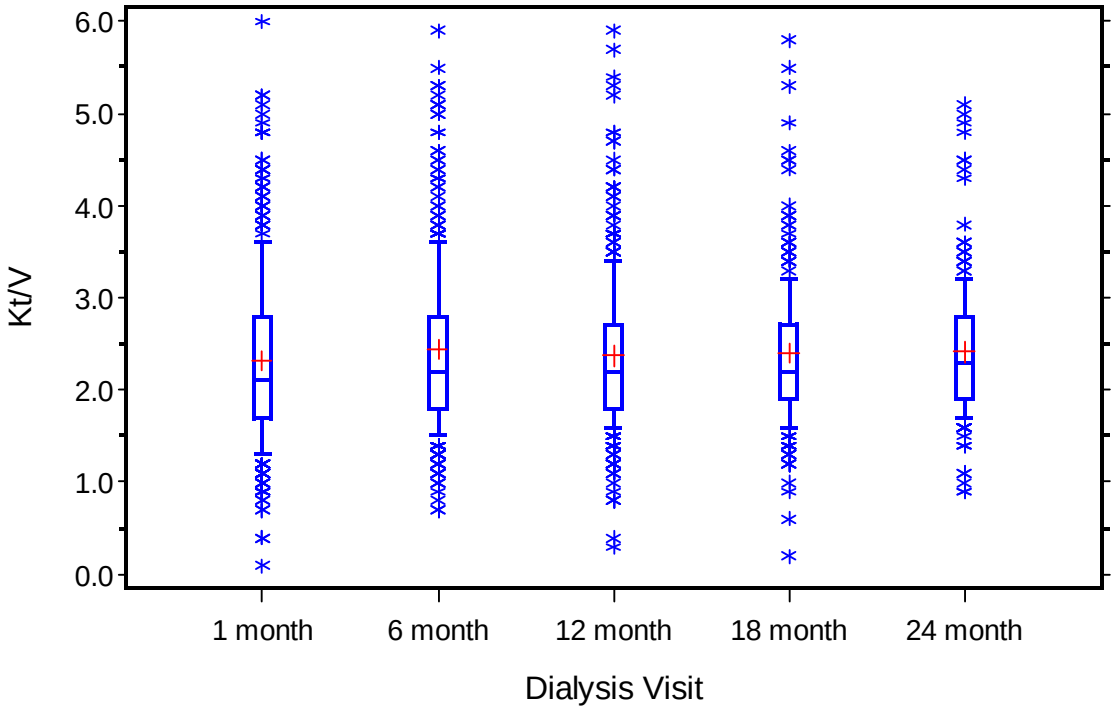
Kt/V	N	Mean	SE	Median
Total	770	1.58	0.02	1.50
Age				
0-1 years	21	1.42	0.09	1.40
2-5 years	56	1.72	0.06	1.60
6-12 years	214	1.64	0.03	1.60
>12 years	479	1.54	0.02	1.50
Race				
Non-Black	490	1.60	0.02	1.60
Black	280	1.54	0.03	1.50
Visit Month				
1 Month	529	1.54	0.02	1.50
6 Month	92	1.59	0.05	1.60
12 Month	57	1.68	0.05	1.70
>12 Month	92	1.72	0.05	1.60
BMI Z-score				
≤ 0	296	1.66	0.03	1.60
> 0	349	1.51	0.02	1.50
Missing	125	1.59	0.04	1.50

EXHIBIT 4.13
FIRST URR MEASUREMENT
Hemodialysis

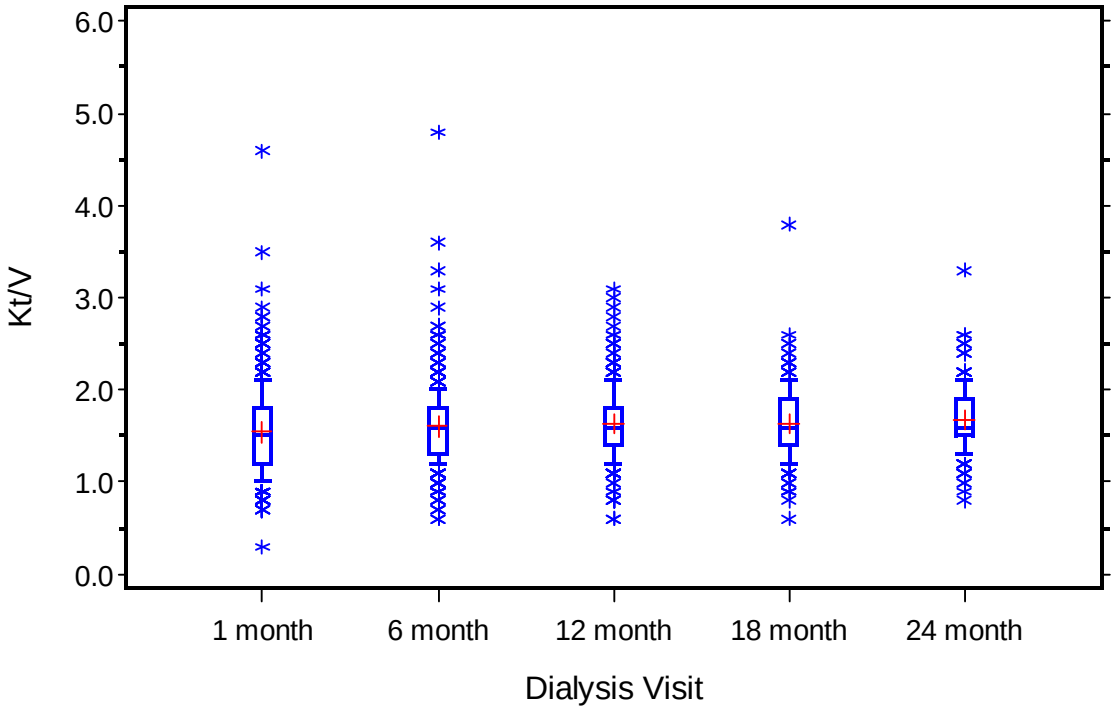
URR	**N**	**Mean**	**SE**	**Median**
Total	791	71.25	0.37	72.00
Age				
0-1 years	18	72.28	2.56	73.00
2-5 years	63	73.40	1.52	75.00
6-12 years	220	72.29	0.82	74.00
>12 years	490	70.46	0.42	72.00
Race				
Non-Black	508	71.93	0.48	73.00
Black	283	70.01	0.57	71.00
Visit Month				
1 Month	568	70.69	0.38	71.00
6 Month	77	71.14	1.59	73.00
12 Month	53	74.87	0.95	76.00
>12 Month	93	72.68	1.59	74.00
BMI Z-score				
$\leq$ 0	311	71.87	0.56	73.00
> 0	352	69.98	0.60	71.00

EXHIBIT 4.14
KT/V OVER TIME

Peritoneal Dialysis



Hemodialysis



NOTE: Box represents the 25th and 75th percentiles, whiskers the 10th and 90th percentiles,
'-' is the median value ,'+' is the mean value and '*' are values above and below the 10th and 90th percentiles

SECTION 5: GROWTH

Data on growth following dialysis initiation are presented in this section. The cases with the index course of dialysis starting after January 1, 1992 are used and this is the baseline measurement that provides the reference value from which changes in height are calculated. Patients are censored from the analysis at the time of dialysis termination and do not re-enter, even if a subsequent course of dialysis is initiated. Height and weight measurements are reported at each 6-month follow-up visit, and baseline measurements are obtained 30 days following initiation. Z-scores are calculated by using the appropriate gender-age specific mean, standard deviation and adjustment parameters for the national population derived from NHANES III study (2000) of the National Center of Health Statistics. Direct comparison with early registry reports is not possible because of the use of these new standards.

Exhibit 5.1 presents mean height scores, by selected characteristics and during the first two years after dialysis initiation. On average at baseline, patients are 1.60 standard deviations below the appropriate age- and sex-adjusted height levels. Height deficits are worse for males and for younger patients. Patients were also stratified according to baseline Z-score (<–1.88 vs. ≥–1.88 Z-score). Note that the third percentile of the normal population corresponds to –1.88 in the Z-score scale. Post-dialysis height deficits for children with worse deficit score at baseline improve slightly from -3.21±0.03 at 1 month to -2.90±0.06 at 24 months. Children who had less deficit at baseline, -0.54±0.02, experience worse deficit by 24 months (-0.87±0.04). Median change from baseline height is -0.11 (n=1,375) and -0.20 (n=594) at 12 and 24 months, respectively, for patients whose baseline Z-score is ≥–1.88. The comparison for patients with baseline Z-score <–1.88 is 0.09 (n=957) and 0.14 (n=442) at 12 and 24 months. Although the weight deficits of dialysis patients are not as severe as for height, patients are, on average, 1.13 standard deviations below normal in weight (Exhibit 5.2). Changes from baseline in height and weight Z-score are depicted graphically in Exhibit 5.3. Young patients (less than 6 years) increase their weight Z-score more than older children. In Exhibit 5.4, height changes for peritoneal dialysis and hemodialysis patients by age are shown.

Growth for rhGH-treated and untreated dialysis patients by age is shown in Exhibit 5.5. Treated patients are patients who had consistently reported rhGH use at baseline, 6 months, and one year. Similarly, untreated patients are patients who had consistently reported no rhGH use at baseline, 6

months, and one year. There are 2 control groups, all untreated patients and those untreated patients whose baseline height Z-score was worse than –1.88 (short control). Older cases without growth hormone show no increase in standardized height in either control group versus 0.26 increase in Z-score for the older growth hormone treated cases. The growth hormone treated 0-5 year olds had a 1-year increase in height Z score of 0.73 standard deviations vs. 0.56 in short controls and 0.05 in all controls. The 0-1 year old patients were examined separately with all groups experiencing some catch-up growth, 1.02 standard deviations for GH treated patients, 0.73 for short controls and 0.21 for all controls (data not shown).

EXHIBIT 5.1
HEIGHT Z SCORES
MEAN AND SE AT FOLLOW-UP

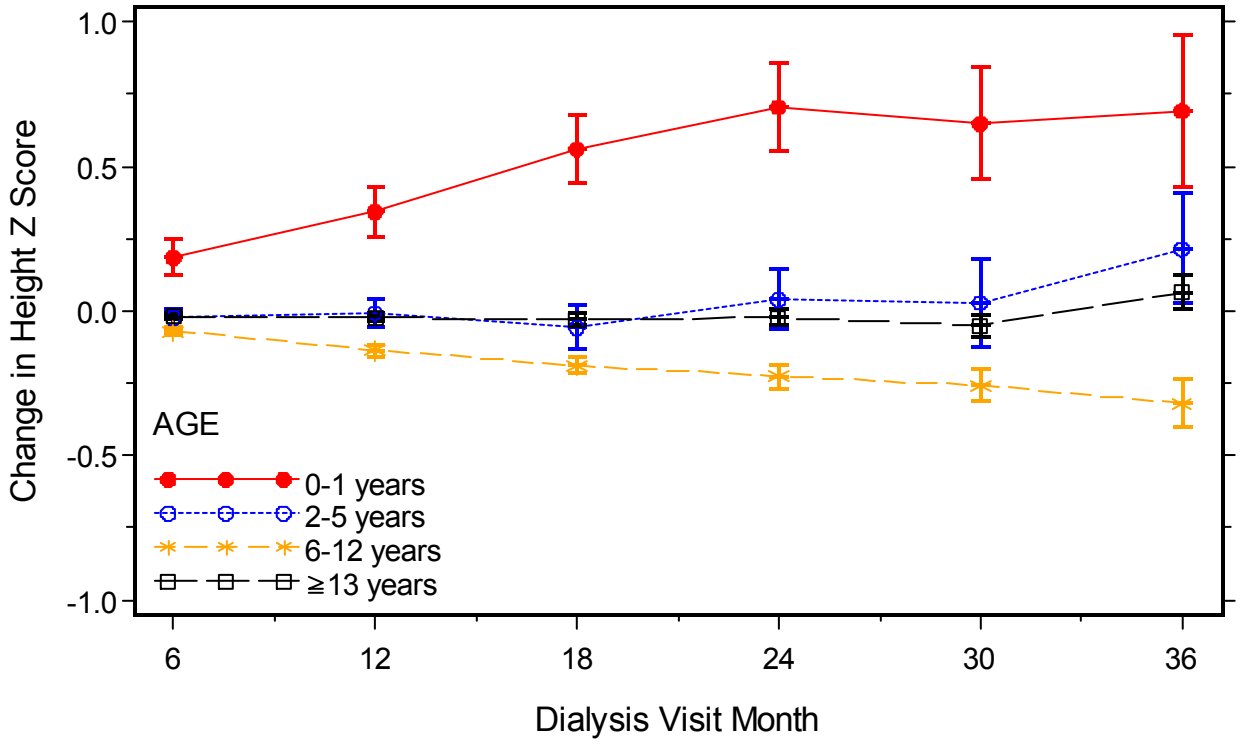
	Month 1			Month 6			Month 12			Month 24		
	N	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**
Total	5022	-1.60	0.02	3902	-1.65	0.03	2622	-1.70	0.03	1177	-1.75	0.04
Modality												
PD	3292	-1.71	0.03	2690	-1.75	0.03	1815	-1.76	0.04	781	-1.77	0.05
HD	1729	-1.40	0.04	1212	-1.45	0.05	805	-1.55	0.06	395	-1.70	0.08
Gender												
Male	2794	-1.71	0.03	2141	-1.75	0.03	1463	-1.79	0.04	667	-1.79	0.06
Female	2228	-1.47	0.03	1761	-1.53	0.04	1159	-1.58	0.05	510	-1.70	0.07
Age												
0-1 years	659	-2.59	0.07	581	-2.43	0.07	410	-2.31	0.08	171	-2.15	0.12
2-5 years	528	-1.95	0.06	413	-2.01	0.08	260	-2.05	0.09	110	-1.91	0.12
6-12 years	1567	-1.62	0.04	1188	-1.68	0.04	786	-1.72	0.05	359	-1.94	0.07
>12 years	2268	-1.22	0.03	1720	-1.29	0.04	1166	-1.39	0.05	537	-1.46	0.07
Baseline Height Deficit												
< 3%	1997	-3.21	0.03	1422	-3.06	0.03	958	-2.99	0.04	442	-2.90	0.06
≥ 3%	3021	-0.54	0.02	2097	-0.66	0.02	1376	-0.73	0.03	594	-0.87	0.04

EXHIBIT 5.2
WEIGHT Z SCORES
MEAN AND SE AT FOLLOW-UP

	Month 1			Month 6			Month 12			Month 24		
	N	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**
Total	5206	-1.13	0.02	3986	-1.06	0.03	2685	-1.03	0.03	1173	-1.06	0.05
Modality												
PD	3371	-1.24	0.03	2705	-1.11	0.03	1837	-1.03	0.04	775	-0.96	0.06
HD	1834	-0.91	0.04	1280	-0.97	0.05	846	-1.03	0.06	396	-1.26	0.09
Gender												
Male	2908	-1.19	0.03	2204	-1.13	0.04	1498	-1.10	0.05	669	-1.10	0.07
Female	2298	-1.05	0.04	1782	-0.99	0.04	1187	-0.93	0.05	504	-1.00	0.08
Age												
0-1 years	713	-2.26	0.06	596	-1.94	0.07	421	-1.67	0.09	175	-1.05	0.14
2-5 years	558	-1.14	0.07	424	-1.06	0.08	271	-0.97	0.09	114	-0.91	0.13
6-12 years	1611	-1.07	0.04	1217	-1.03	0.04	817	-1.01	0.06	375	-1.22	0.08
>12 years	2324	-0.81	0.04	1749	-0.79	0.04	1176	-0.82	0.05	509	-0.97	0.08
Baseline Weight Deficit												
< 3%	1630	-3.15	0.03	1159	-2.84	0.04	776	-2.61	0.05	344	-2.46	0.09
≥ 3%	3572	-0.20	0.02	2529	-0.22	0.02	1683	-0.25	0.03	718	-0.38	0.05

EXHIBIT 5.3
MEAN CHANGE FROM BASELINE (30 day) IN STANDARDIZED SCORE

Change in Height Z Score



Change in Weight Z Score

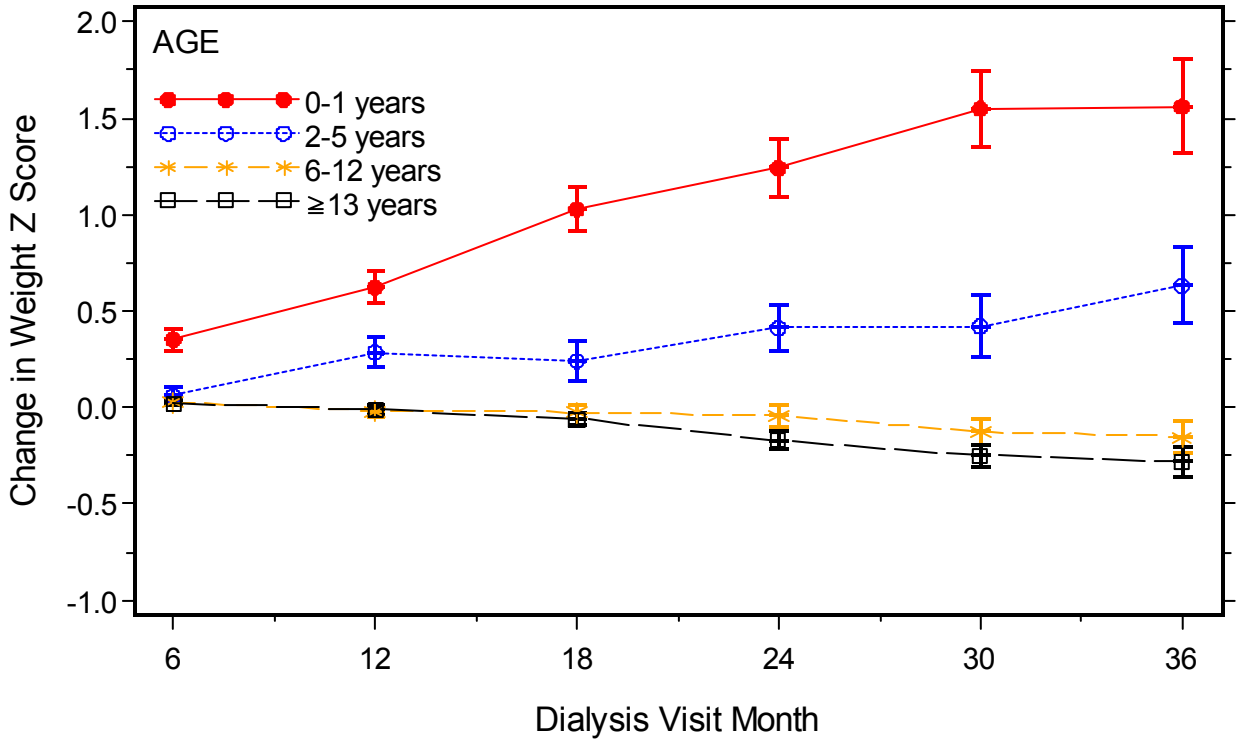
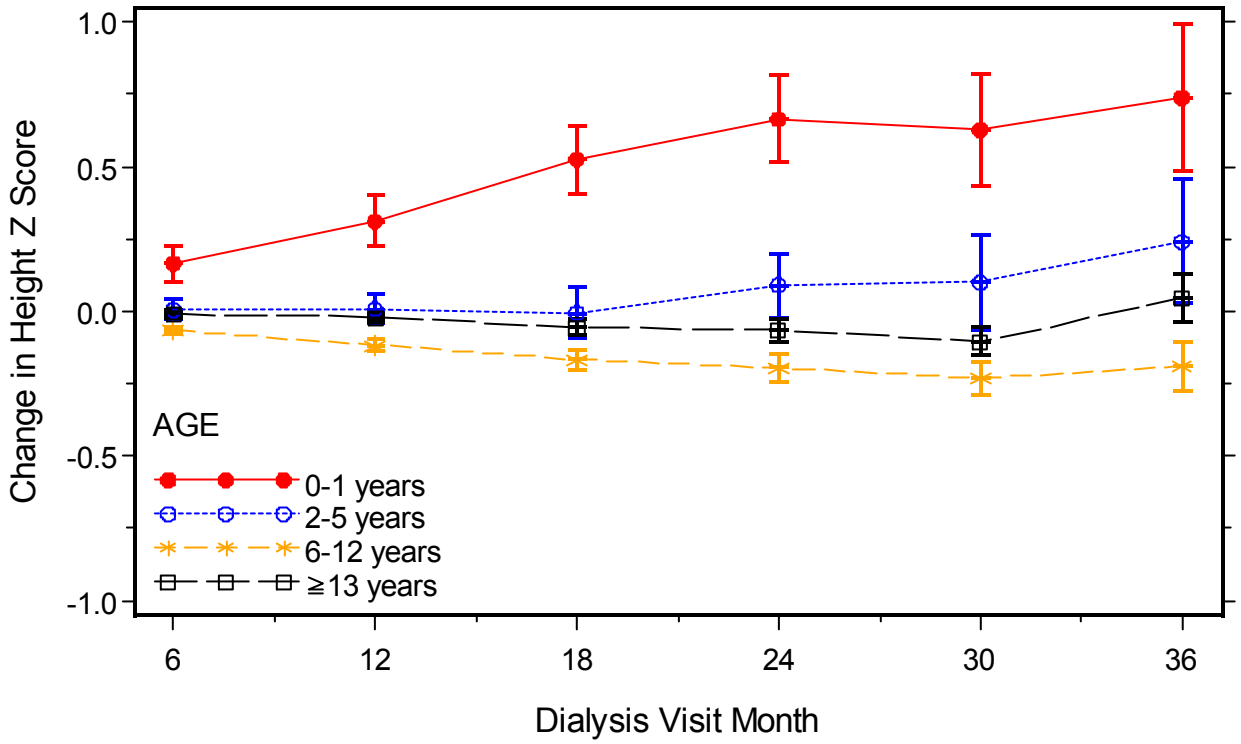


EXHIBIT 5.4
MEAN CHANGE FROM BASELINE (30 day) IN STANDARDIZED HEIGHT SCORE

Peritoneal Dialysis: Change in Height Z Score



Hemodialysis: Change in Height Z Score

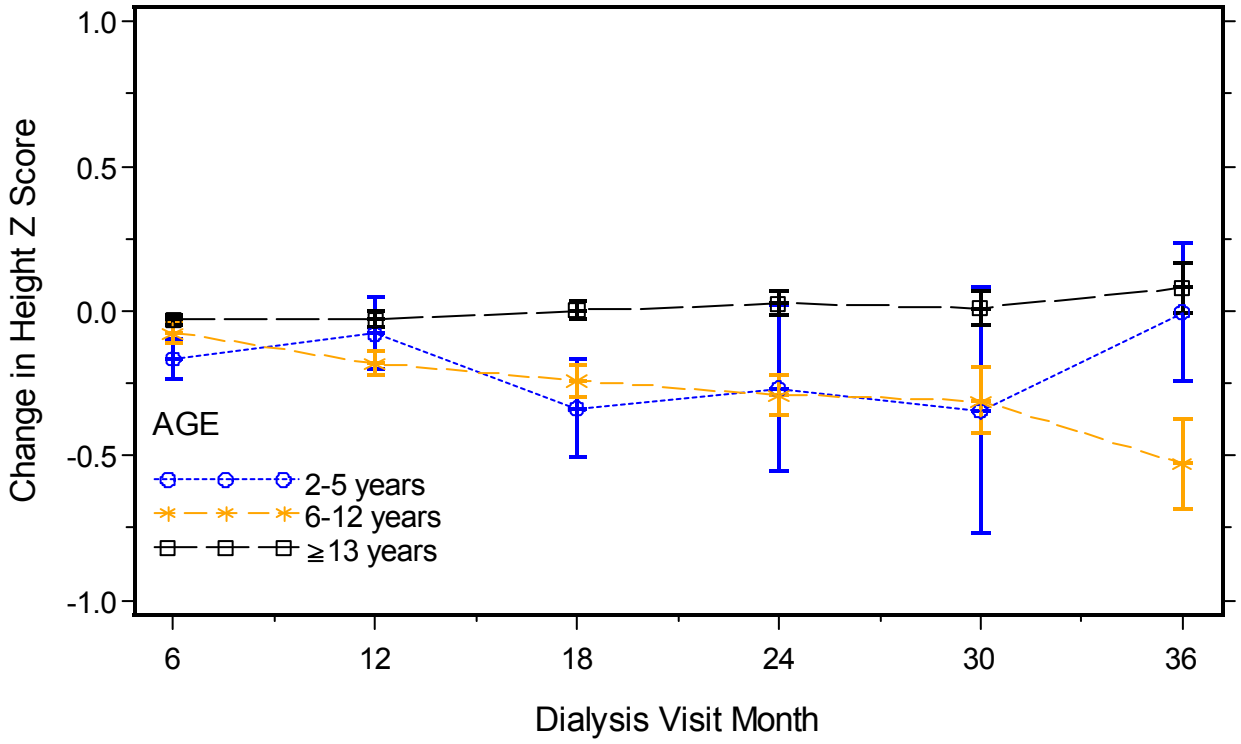


EXHIBIT 5.5
12 MONTH GROWTH DATA BY AGE

	rhGH (n=163)				Short Controls (n=616)				All Untreated Patients (1797)			
	N	Mean	SE	Median	N	Mean	SE	Median	N	Mean	SE	Median
0-5 years old at Baseline	57				193				366			
Baseline Height Z score	57	-2.62	0.20	-2.79	193	-3.54	0.09	-3.25	366	-2.20	0.10	-1.99
12 Month Height Z score	57	-1.89	0.21	-1.89	193	-2.97	0.10	-2.79	366	-2.14	0.08	-2.07
Change in Height Z score	57	0.73	0.13	0.63	192	0.56	0.09	0.44	365	0.05	0.07	-0.01
Baseline BMI Z score	38	1.08	0.18	1.10	61	0.20	0.20	0.59	153	0.31	0.12	0.59
12 Month BMI Z score	52	1.13	0.19	1.15	82	0.67	0.17	0.91	193	0.56	0.10	0.79
Change in BMI Z score	38	0.13	0.20	-0.04	61	0.40	0.19	0.25	153	0.19	0.11	0.11
>6 years old at Baseline	106				423				1431			
Baseline Height Z score	106	-2.36	0.13	-2.52	423	-3.16	0.06	-2.84	1431	-1.26	0.04	-1.12
12 Month Height Z score	106	-2.10	0.14	-1.98	423	-3.17	0.06	-2.92	1431	-1.37	0.04	-1.21
Change in Height Z score	106	0.26	0.03	0.26	422	-0.01	0.03	-0.02	1428	-0.10	0.01	-0.08
Baseline BMI Z score	106	-0.13	0.13	-0.19	412	-0.35	0.07	-0.32	1407	-0.07	0.04	-0.08
12 Month BMI Z score	106	0.01	0.13	0.00	399	-0.32	0.07	-0.24	1387	-0.07	0.04	-0.06
Change in BMI Z score	106	0.13	0.06	0.19	397	0.03	0.05	0.02	1379	0.00	0.02	-0.02