* Risk factors or causes of frailty among CKD patients.

		Effect (descriptions)		Prevalence	CKD Severity	Frailty Assessment	Sample Size	Reference
Biological								
	Cardiovascular	Heart Failure		30% vs 12%	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
		Angina		34% vs. 22%	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
	Cerebrovascular	Cerebrovascular Disease Prevalence (%)		26.4 vs. 12.0	ESRD	Fried Phenotypes	324	(McAdams-Demarco, Tan, et al., 2015)
	Neurological	Brain Wave		F vs. NF	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	(Chao, Lai, Tsai, Yang, &Huang, 2017)
			Global DAR	283 ± 679 vs. 2971 ± 4859				
			DARs (left frontal)	135 ± 250 vs. 3073 ± 4702				
			DAR (left TO)	197 ± 318 vs. 3708 ± 6398				
			DAR (central)	55 ± 96 vs. 1773 ± 3262				
			DAR (right TO)	187 ± 261 vs.				

				4400 ± 7763				
			Global DTABR	191 ± 469 vs. 1781 ± 2793				
			DTABR (left frontal)	86 ± 158 vs. 1680 ± 2388				
			DTABR (left TO)	130 ± 210 vs. 1884 ± 2828				
			DTABR (central)	39 ± 65 vs. 1132 ± 1957				
			DTABR (right TO)	126 ± 178 vs. 2960 ± 5271				
	Cognitive	Mini-Mental State Examination (MMSE)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	(Fabrício-Wehbe et al., 2009)
			Spearman's correlation coefficient of EFS scores with gross MMSE scores	-0.607 ($p<0.01$)				
		Executive Function		F vs. NF at cohort entry				
			Trail Making Tests A (TMTA) scores	+12.08	ESRD	Fried Phenotypes	324	(McAdams-Demarco, Tan, et al., 2015)
			Trail Making Tests B	+33.15	ESRD	Fried	324	(McAdams-

			(TMTB) scores			Phenotypes		Demarco, Tan, et al., 2015)
	Microbiota	Gut Microbiota Composition		F vs. NF	Stage 3b-4, eGFR 15-45ml/min	Fried Phenotype score	64 (and 15 control subjects)	(Margiotta et al., 2018)
			Malnutrition-Inflammation-Score (MIS)	7.6 vs. 3.9				
			Abundance of unclassified Mogibacteriaceae and Oscillospira	Directly proportional to MIS				
			Abundance of Akkermansia, Ruminococcus, and Eubacterium	Inversely proportional to MIS				
			Bacterial Abundance of some genera (Mogibacteriacee, Coriobacteriacee, Eggerthella, Erwinia, Coprobacillus, Anaerotruncus, etc)	↑				
	Immunological	Inflammatory						

			CRP (ln CRP) (mg/dL)	1.12 vs 0.28	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	(Kamijo, Kanda, Ishibashi, &Yoshida, 2018)
			IL6 (ln IL6) (mg/dL)	2.45 vs. 1.58				
		Mycophenolate mofetil (MMF) dose reduction (MDR)		F vs. NF	CKD stage 5T	Fried Phenotypes	525	(McAdams-Demarco, Law, et al., 2015)
			1 year since KT (%)	44 vs 40				
			2 years since KT (%)	54 vs. 45				
			3 years since KT (%)	67 vs. 51				
		Viral infection		F vs. NF				
			HCV (n=37)	36 vs. 1	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	(Yadla, John, &Mummadi, 2017)
	Functional Status	Disability		F vs. NF	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
			At least one disability in activities of daily Living (ADLs)	15% vs. 5%				
			At least one disability in instrumental activities of daily living (IADLs)	60% vs. 28%				
			At least one disability in	40% vs. 18%				

			mobility tasks					
		Ability to perform basic activities of daily living		33.33% vs 76.4%	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	(Bancu et al., 2017)
		Ability to perform transfers		38.8% vs. 84.7%				
	Endocrinologic/ Metabolic	Diabetes		F vs. NF				
			Prevalence	64% vs. 49%	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
		Obesity		F vs. NF				
			Prevalence	64% vs. 50%	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
			Prevalence	51.8% vs. 23.9%	ESRD	Fried Phenotypes	324	(McAdams-Demarco, Tan, et al., 2015)
			BMI based on dry weight	31.5 vs. 27.6				
	Body Composition	Appendicular						
			Appendicular skeletal muscle mass index (ASMI)	6.8 vs. 7.7	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez, Senior, Field, Jindal, &Mager, 2018)

			Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively)	SFS scores				
			Left lower extremity	β = 0.34; t = 2.32; p = 0.03	ESRD	Simple FRAIL scale	44	(Chao, Chan, &Huang, 2017)
			Right lower extremity	β = 0.3; t = 2.05; p = 0.048				
			Left upper extremity	β = 0.37; t = 2.66; p = 0.01				
			Right upper extremity	β = 0.43; t = 3.09; p = <0.01				
			Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively)	Frail/Prefrail vs. Nonfrail				
			Left lower extremity	β = 0.33; t = 2.31; p = 0.03	ESRD	self- report instrument	44	(Chao, Chan, et al., 2017)

				Right lower extremity	β = 0.32; t = 2.28; p = 0.03		evaluating five dimensions of frailty (fatigue, resistance, ambulation, illnesses, and weight loss)		
				Right upper extremity	β = 0.33; t = 2.35; p = 0.03				
		Lower lean mass							
					F/PF vs. NF				
			Whole body (kg)		34.7 vs. 43.1	ESRD	Simple FRAIL scale	44	(Chao, Chan, et al., 2017)
			Cephalic area (g)		3059 vs. 3288				
			Trunk area (kg)		17.4 vs. 22.1				
			Right upper limb (g)		1831 vs. 2493				
			Left upper limb (g)		1869 vs. 2515				
			Right lower limb (g)		4920 vs. 6114				
			Left lower limb (g)		4650 vs. 6349				
					F vs. NF				
			lean body mass (i.e. sarcopenia) (in frail vs. nonfrail)		57.1% vs .14.7%	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)

		BMI	22.53 vs. 26.16	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	(Bancu et al., 2017)
	Laboratory Data	eGFR (mL/min/1.72m^2)	18 vs. 50	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
		eGFRcys <30	Frailty prevalence 2.8	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)*
		eGFRcys 30-44	Frailty prevalence 2.1				
		eGFRcys >60	Referent				
		Prealbumin (PRAB) (mg/dL)	28.9 vs. 38.3				
		Serum albumin (g/L)	38 vs. 41	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
			2.92 vs. 3.48	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	(Kamijo et al., 2018)
			3.61 vs. 3.85	CKD stage 5D	Fried	320	(Bancu et al.,

				(hemodialysis)	Phenotypes		2017)
			Frail with depression vs. Frail without depression vs. Nonfrail	32.9 vs. 34.9 vs. 35.8 (p=0.025)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	(Szeto et al., 2018)
		Calcium (mmol/L)		2.24 vs. 2.36	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
		Creatinine (umol/L)		299 vs. 115				
		Hemoglobin		10.35 vs. 10.97	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	(Bancu et al., 2017)
	Miscellaneous	Dialysis clearance rate		↑	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	(Chao, Lai, et al., 2017)
Psychological								
	Mood	Mood Change		Negative change	CKD stage 5D (hemodialysis)	Edmonton Frail Scale (EFS)	N/A	(DeSouza Orlandi &Gesualdo, 2014)
	Mental Health							
		Anxiety	Hospital Anxiety and Depression Scale (HADS)	Women: ↑ in global, psychological, social frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	(Sales et al., 2017)

				Men: ↑ in Physical frailty				
		Depression	Hospital Anxiety and Depression Scale (HADS)	Men ↑ in global, psychological, physical frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	(Sales et al., 2017)
			Incidence (%) (Self-reported Major Depression Inventory)	83 vs. 6	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
	Mental Function		Post-KT delirium	9.0% vs. 3.9%	CKD stage 5T	Fried Phenotypes	893	(Haugen et al., 2018)
Sociological								
	Isolation							
	Interaction		Interaction with family	Good				(Moffatt, Moorhouse, Mallery, Landry, &Tennankore, 2018)
Physical activity			Minnesota Leisure Time Activity (LTA)	95 vs. 735	CKD stage 5D	Fried	68	(Johansen,

		(p<0.001)	(hemodialysis)	Phenotypes		Painter, Delgado, &Doyle, 2015)
	Low Physical Activity Questionnaire (LoPAQ)	280 vs. 798 (p=0.003)				
	Sitting (hours/day)	6.5 vs. 5 (p=0.04)				
Quality of Life	HRQoL					
	SF-36					
	Scores in physical functioning, blood pressure, role physical, and physical component summary domains	↓	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
	Kidney Disease Quality of Life (KDQoL)	F vs. NF				
	Physical health	33.7 vs. 40.7	ESRD CKD stage 5D (conventional hemodialysis)	Fried Phenotypes	151	(Noori, Sharma Parpia, Lakhani, Janes, &Goldstein, 2018)
	Kidney disease effects	51.6 vs. 66.8				
	Falls (times)	115 vs. 12	CKD stage 5D	Fried Frailty	205	(Yadla et al.,

				(hemodialysis)	Phenotypes		2017)
Independence	Functional Independence Measure (FIM)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	(Fabrício-Wehbe et al., 2009)
	Spearman's correlation coefficient	Frailty diagnosis with global FIM	-0.703 (p<0.001)				
		Frailty diagnosis with motor FIM	-0.714 (p<0.001)				
		Frailty diagnosis with cognitive FIM	-0.575 (p<0.001)				
		EFS scores with gross FIM	-0.53 (p<0.01)				
Health-care utilization	Hospitalization						
		Cumulative number of inpatient health-care visits	↑	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
		Cumulative number of emergency health-care visits					
		Cumulative number of total health-care visits					
		>3 times (n=141)	127 vs. 14	CKD stage 5D (hemodialysis)	Fried Frailty Phenotypes	205	(Yadla et al., 2017)
		1-2 times (n=64)	40 vs. 24				

		Admissions/year	0.77727 vs. 0.2838	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	(Bancu et al., 2017)
Composite	Overall subjective global assessment (SGA) (weight loss, anorexia, subcutaneous fat, muscle mass) (Frail with depression vs. Frail without depression vs. Nonfrail)		5.04 vs. 5.41 vs. 5.75 ($p<0.0001$)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	(Szeto et al., 2018)
	Malnutrition inflammation score (MIS) (frail with depression vs. frail without depression vs. nonfrail)		9.48 vs. 7.13 vs. 5.12 ($p<0.0001$)				
	Number of complications (complications identified at data collection: High Pressure Cramping, Anemia, Weight loss Pain, Weakness, Weight gain Constipation, Heart Arrhythmia, Headache, Itch, Recurrent infections, Arterial hypertension)		Spearman's correlation 0.666 ($p=0.000$ in table) ($p<0.05$ in text)	Elderly (≥ 60 yo), with diagnosis of CKD	Edmonton Frail Scale	35	(deSousa Meira et al., 2016)
	Charlson's comorbidity score		Spearman's rank correlation coefficient r = 0.40 (p <	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	(Ng et al., 2016)

		0.0001)				

Bibliography

Adame Perez, S. I., Senior, P. A., Field, C. J., Jindal, K., &Mager, D. R. (2018). Frailty, Health-Related Quality of Life, Cognition, Depression, Vitamin D and Health-Care Utilization in an Ambulatory Adult Population with Type 1 or Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Cross-Sectional Analysis. *Canadian Journal of Diabetes*. doi:10.1016/j.jcjd.2018.06.001

Bancu, I., Graterol, F., Bonal, J., Fernandez-Crespo, P., Garcia, J., Aguerrevere, S., …Bonet, J. (2017). Frail Patient in Hemodialysis: A New Challenge in Nephrology-Incidence in Our Area, Barcelones Nord and Maresme. *Journal of Aging Research*, *2017*, 7624139.

Chao, C.-T., Chan, D.-C., &Huang, J.-W. (2017, April). Frail Phenotype Might Be Associated With Higher Appendicular but Not Truncal Fat Among End-Stage Renal Disease Patients. *Journal of Pain and Symptom Management*. United States.

Chao, C.-T., Lai, H.-J., Tsai, H.-B., Yang, S.-Y., &Huang, J.-W. (2017). Frail phenotype is associated with distinct quantitative electroencephalographic findings among end-stage renal disease patients: an observational study. *BMC Geriatrics*, *17*, 277.

deSousa Meira, A., Aparecido Batista, M., dePina Pereira, R. M., Partezani Rodrigues, R. A., Silva Fhon, J. R., &Kusumota, L. (2016). Frailty in elderly patients with chronic kidney disease under conservative treatment. *Revista Da Rede de Enfermagem Do Nordeste*, *17*, 386–392.

DeSouza Orlandi, F., &Gesualdo, G. D. (2014). Assessment of the frailty level of elderly people with chronic kidney disease undergoing hemodialysis. *ACTA Paulista de Enfermagem*, *27*, 29–34.

Fabrício-Wehbe, S. C. C., Schiaveto, F. V., Vendrusculo, T. R. P., Haas, V. J., Dantas, R. A. S., &Rodrigues, R. A. P. (2009). Cross-cultural adaptation and validity of the “Edmonton Frail Scale - EFS” in a Brazilian elderly sample. *Revista Latino-Americana de Enfermagem*, *17*, 1043–1049.

Haugen, C. E., Mountford, A., Warsame, F., Berkowitz, R., Bae, S., Thomas, A., …McAdams-DeMarco, M. (2018). Incidence, Risk Factors, and Sequelae of Post-kidney Transplant Delirium. *Journal of the American Society of Nephrology : JASN*, *29*, 1752–1759.

Johansen, K. L., Painter, P., Delgado, C., &Doyle, J. (2015). Characterization of physical activity and sitting time among patients on hemodialysis using a new physical activity instrument. *Journal of Renal Nutrition : The Official Journal of the Council on Renal Nutrition of the National Kidney Foundation*, *25*, 25–30.

Kamijo, Y., Kanda, E., Ishibashi, Y., &Yoshida, M. (2018). Sarcopenia and Frailty in PD: Impact on Mortality, Malnutrition, and Inflammation.

Peritoneal Dialysis International : Journal of the International Society for Peritoneal Dialysis, *38*, 447–454.

Margiotta, E., Caldiroli, L., Vettoretti, S., Meneghini, M. A. E., Zanoni, F., Miragoli, F., …Messa, P. (2018). SuO004GUT MICROBIOTA COMPOSITION AND FRAILTY IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE. *Nephrology Dialysis Transplantation*, *33*, i618–i618.

McAdams-Demarco, M. A., Law, A., Tan, J., Delp, C., King, E. A., Orandi, B., …Segev, D. L. (2015). Frailty, mycophenolate reduction, and graft loss in kidney transplant recipients. *Transplantation*, *99*, 805–810.

McAdams-Demarco, M. A., Tan, J., Salter, M. L., Gross, A., Meoni, L. A., Jaar, B. G., …Sozio, S. M. (2015). Frailty and cognitive function in incident hemodialysis patients. *Clinical Journal of the American Society of Nephrology*, *10*, 2181–2189.

Moffatt, H., Moorhouse, P., Mallery, L., Landry, D., &Tennankore, K. (2018). Using the Frailty Assessment for Care Planning Tool (FACT) to screen elderly chronic kidney disease patients for frailty: the nurse experience. *Clinical Interventions in Aging*, *13*, 843.

Ng, J. K.-C., Kwan, B. C.-H., Chow, K.-M., Cheng, P. M.-S., Law, M.-C., Pang, W.-F., …Szeto, C.-C. (2016). Frailty in Chinese Peritoneal Dialysis Patients: Prevalence and Prognostic Significance. *Kidney & Blood Pressure Research*, *41*, 736–745.

Noori, N., Sharma Parpia, A., Lakhani, R., Janes, S., &Goldstein, M. B. (2018). Frailty and the Quality of Life in Hemodialysis Patients: The Importance of Waist Circumference. *Journal of Renal Nutrition : The Official Journal of the Council on Renal Nutrition of the National Kidney Foundation*, *28*, 101–109.

Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K.V, deBoer, I. H., …Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. *Am J Kidney Dis*, *60*, 912–921.

Sales, C., Tavares, R., Amado, L., Martins, P., Barros, J., Miranda, V., …Costa, E. (2017). SP651ANXIETY AND DEPRESSION IN END STAGE RENAL DISEASE PATIENTS AND ITS ASSOCIATION WITH CLINICAL AND LABORATORIAL DATA. *Nephrology Dialysis Transplantation*, *32*, iii355-iii355.

Szeto, C.-C., Chan, G. C.-K., Ng, J. K.-C., Chow, K.-M., Kwan, B. C.-H., Cheng, P. M.-S., …Li, P. K.-T. (2018). Depression and Physical Frailty Have Additive Effect on the Nutritional Status and Clinical Outcome of Chinese Peritoneal Dialysis. *Kidney & Blood Pressure Research*, *43*, 914–923.

Yadla, M., John, J., &Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by

cashless government scheme. *Saudi Journal of Kidney Diseases and Transplantation*. doi:10.4103/1319-2442.198102