

* Risk factors or causes of frailty among CKD patients.

	Effect (descriptions)	Risk Difference	Frailty Assessment	Sample Size	CKD Severity	Reference
Biological						
Cardiovascular	Hypertension*	RR 1.6 (1.26-2.04)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
	Peripheral vascular disease*	RR 1.58 (1.34-1.8)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
	Left ventricular dysfunction*	RR 1.18 (1.03-1.36)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
	Endothelial dysfunction	r= -0.367 (p= 0.004)	Fried Phenotypes	61	CKD stages 3-5	2
		OR 3.86 (1.00-14.88)				
Cerebrovascular	Cerebrovascular Accident	RR 1.34 (1.19-1.5)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
Pulmonary	COPD	OR 1.68 (1.16-2.45)	Fried Phenotypes	10256	CKD stages 1-5	3
Immunological	Inflammatory					
	IL-6*	Worse frailty	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	4*
	CRP	After	Fried	5888	Chronic kidney	5

		Fibrinogen	adjustment, OR 1.76 (1.28-2.41) to 1.50 (1.07- 2.09)	Phenotypes		insufficiency, serum creatinine ≥1.3mg/dL	
Endocrinologic/ Metabolic	Diabetes	Frailty scores +0.7 points per year	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	4*	
		OR 1.68 (1.16- 2.45)	Fried Phenotypes	10256	CKD stages 1-5	3	
		Obesity (IMC ≥ 30 kg/m ²)	OR 6.63 (1.16- 36.77)	Fried Phenotypes	61	CKD stages 3-5	2
		Higher parathyroid hormones (PTH)	r= 0.30 (p= 0.01)	Fried Phenotypes	61	CKD stages 3-5	2
Body Composition	Higher fat mass	r= 0.25 (p= 0.04)	Fried Phenotypes	61	CKD stages 3-5	2	
Cancer	Cancer	OR 1.89 (1.19- 2.99)	Fried Phenotypes	10256	CKD stages 1-5	3	
Arthritis	Arthritis	OR 3.34 (2.08- 5.38)	Fried Phenotypes	10256	CKD stages 1-5	3	
Laboratory Data	eGFR (mL/min/1.72m ²)						

		eGFRcys <30	Frailty prevalence 2.8	Fried Phenotypes	336	CKD stages 1-4	6*
		eGFRcys 30-44	Frailty prevalence 2.1				
		eGFRcys >60	Referent				
		Serum Albumin Concentrations (g/dL)	Frailty scores -1.1 points per g/dL	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	4*
		Serum Creatinine <4 mg/dL*	RR 1.46 (1.22-1.71)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
		Testosterone, per 50% lower free testosterone*		Fried Phenotypes	440	CKD stage 5D (hemodialysis), men	7*
		being frail	OR 1.40 (1.05-1.53)				
		becoming frail over 12 months	OR 1.40 (1.07-1.73)				
		Hemoglobin	Adjusted, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09)	Fried Phenotypes	5888	Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL	5
		LDL, HDL					
Lifestyle		Smoking*	RR 1.18 (1.04-	Fried	205	CKD stage 5D	1*

		1.34)	Phenotypes		(hemodialysis)	
Ethnicity	Hispanic*	Frailty scores +0.6 points per year	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	⁴ *

Bibliography

1. YadlaM, JohnJ, MummadiM. A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. *Saudi J Kidney Dis Transplant*. 2017. doi:10.4103/1319-2442.198102
2. MansurHN. Fragilidade na doença renal crônica: prevalência e fatores associados. 2012.
3. Wilhelm-LeenER, HallYN, MKT, ChertowGM. Frailty and chronic kidney disease: the Third National Health and Nutrition Evaluation Survey. *Am J Med*. 2009;122(7):664-71 e2. doi:10.1016/j.amjmed.2009.01.026
4. JohansenKL, DalrympleLS, DelgadoC, et al. Factors Associated with Frailty and Its Trajectory among Patients on Hemodialysis. *Clin J Am Soc Nephrol*. 2017;12(7):1100-1108. doi:10.2215/CJN.12131116
5. ShlipakMG, Stehman-BreenC, FriedLF, et al. The Presence of Frailty in Elderly Persons with Chronic Renal Insufficiency. *Am J Kidney Dis*. 2004;43(5):861-867. doi:10.1053/j.ajkd.2003.12.049
6. RoshanravanB, KhatriM, Robinson-CohenC, et al. A prospective study of frailty in nephrology-referred patients with CKD. *Am J Kidney Dis*. 2012;60(6):912-921. doi:10.1053/j.ajkd.2012.05.017
7. ChiangJM, KaysenGA, SegalM, ChertowGM, DelgadoC, JohansenKL. Low testosterone is associated with frailty, muscle wasting and physical dysfunction among men receiving hemodialysis: a longitudinal analysis. *Nephrol Dial Transplant*. 2018. doi:10.1093/ndt/gfy252

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	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			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 (Mogibacteriaceae, Coriobacteriaceae, Eggerthella, Erwinia, Coprobacillus, Anaerotruncus, etc)	↑				
	Immunological	Mycophenolate mofetil (MMF) dose		F vs. NF	CKD stage 5T	Fried	525	(McAdams-

		reduction (MDR)				Phenotypes		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 mobility tasks	40% vs. 18%				
	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	$\beta = 0.34$; $t = 2.32$; $p = 0.03$	ESRD	Simple FRAIL scale	44	(Chao, Chan, & Huang,

			Right lower extremity	$\beta = 0.3$; $t = 2.05$; $p = 0.048$				2017)
			Left upper extremity	$\beta = 0.37$; $t = 2.66$; $p = 0.01$				
			Right upper extremity	$\beta = 0.43$; $t = 3.09$; $p = <0.01$				
			Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively)	Frail/Prefrail vs. Nonfrail				
			Left lower extremity	$\beta = 0.33$; $t = 2.31$; $p = 0.03$	ESRD	self- report instrument evaluating five dimensions of frailty (fatigue, resistance,	44	(Chao, Chan, et al., 2017)
			Right lower extremity	$\beta = 0.32$; $t = 2.28$; $p = 0.03$				
			Right upper extremity	$\beta = 0.33$; $t = 2.35$; $p = 0.03$				

						ambulation, illnesses, and weight loss)		
		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)
	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				
		Albumin (g/L)		38 vs. 41	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	(Adame Perez et al., 2018)
		Calcium (mmol/L)		2.24 vs. 2.36				
		Creatinine (umol/L)		299 vs. 115				
	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)		<u>Women</u> : ↑ in global, psychological, social frailty <u>Men</u> : ↑ in	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	(Sales et al., 2017)

				Physical frailty				
		Depression	Hospital Anxiety and Depression Scale (HADS)	<u>Men</u> ↑ 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 (p<0.001)	CKD stage 5D (hemodialysis)	Fried Phenotypes	68	(Johansen, 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 (hemodialysis)	Fried Frailty Phenotypes	205	(Yadla et al., 2017)
Independence	Functional Independence Measure			Elderly, ≥65y/o	Edmonton	137	(Fabrício-

	(FIM)				Frail Scale (EFS)		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				
	Early Hospital Readmission (EHR) (%)		45.8 vs. 28.0				

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
- 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.
- 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.
- Fabício-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.
- 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.
- 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). SP651 ANXIETY AND DEPRESSION IN END STAGE RENAL DISEASE PATIENTS AND ITS ASSOCIATION WITH CLINICAL AND LABORATORIAL DATA. *Nephrology Dialysis Transplantation*, 32, iii355-iii355.
- 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

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Biological						
Cardiovascular	Cerebrovascular Accident	OR 1.55 (1.05-2.99)	CKD stage 5D (hemodialysis)	Fried Phenotypes	2275	(Johansen, Chertow, Jin, & Kutner, 2007)
	Vascular Access failure	HR 2.63 (1.03-6.71)	ESRD (CKD stage 5D)	Self-reported simple FRAIL scale	51	(Chao, Chiang, Huang, & Hung, 2017)
	Permanent Vascular Access (fistula or graft)	CKD stage 5D (hemodialysis)		Fried Phenotypes	2275	(Johansen et al., 2007)
Renal Function Decline	Risk for death or dialysis therapy	2.5 (1.4-4.4)-fold greater	CKD stages 1-4	Fried Phenotypes	336	(Roshanravan et al., 2012)
Immunological	Mycophenolate mofetil (MMF) dose reduction (MDR)	HR 1.29 (1.01-1.66)	CKD stage 5T	Fried Phenotypes	525	(McAdams-Demarco, Law, et al., 2015)
Cognitive	Modified Mini-Mental State (3MS)	-2.37 to -2.80 (1 year) (p=0.03)	ESRD	Fried Phenotypes	324	(McAdams-Demarco, Tan, et al., 2015)
Diabetes	Diabetes	OR 1.35 (1.10-1.65)	CKD stage 5D	Fried Phenotypes	2275	(Johansen et al., 2007)

Body composition	Bones						
		Bone Mineral Density (BMD)	One year follow-up, with frailty	ESRD CKD stage 5D (chronic hemodialysis)	Simple FRAIL Scale (SFS)	43	(Chao, Huang, & Chan, 2017)
		L1	$\beta = -0.4$, $t = -2.18$, $p=0.04$				
		L4	$\beta = -0.39$, $t = -2.1$, $p=0.046$				
		Femur Neck (FN)	$\beta = -0.5$, $t = -2.96$, $p<0.01$				
		Total	$\beta = -0.53$, $t = -3.27$, $p<0.01$				
		Areas	One year follow-up, with frailty				
		Average L-spine areas	$\beta = -0.48$, $t = -2.84$, $p < 0.01$				
		Changes of average L-spine areas	$\beta = -0.5$, $t = -3.02$, $p<0.01$				
		Z-score	One year follow-up, with frailty				

			Percentage change of L1 Z-score	$\beta = -0.45$, $t = -2.11$, $p=0.049$				
	Laboratory data		Serum Albumin Concentrations (g/dL)					
			<3.2 vs. ≥ 3.9	OR 1.89 (1.30-2.59)	CKD stage 5D	Fried Phenotypes	2275	(Johansen et al., 2007)
	Psychological							
	Delirium		Post-KT delirium	OR 2.05 (1.02-4.13)	CKD stage 5T	Fried Phenotypes	893	(Haugen et al., 2018)
	Quality of Life		HRQoL					
			Fair/Poor HRQOL at follow-up (median 9.4 mo)	aOR 2.79 (1.32-5.90)	ESRD CKD stage 5T	Fried Phenotypes	233	(M AMcAdams-DeMarco et al., 2016)
			Worsening HRQOL at follow-up (median 9.4 mo)	aRR 2.91 (1.08-7.80)				
			SF-36					
			Hierarchical regression R^2 change (effects of frailty on HRQoL) in Physical Component Summary (PCS)	29% ($p<0.001$)	CKD stage 2-4	Fried Phenotypes	168	(S. J.Lee, Son, &Shin, 2015)

		Hierarchical regression R ² change (effects of frailty on HRQoL) in Mental Component Summary (MCS)	21.3% (p<0.001)				
		SF-12					
		MCS	Effect estimate 0.94 (0.91-0.97) (p<0.01)	CKD stage 5D (peritoneal dialysis, n=129; hemodialysis, n=122)	The Canadian Study of Health and Aging Clinical Frailty Scale (CFS)	251	(Iyasere et al., 2016)
		PCS	Effect estimate 0.88 (0.84-0.91) (p<0.01)				
		KDQOL-SF scores in physical and kidney disease-specific HRQoL					
		At KT	↓	CKD stage 5T	Fried Phenotypes	443	(Mara AMcAdams-DeMarco et al., 2018)
		Post-KT	Greater increase				
		Illness Intrusiveness Rating Scale	Effect estimate 1.14 (1.09-1.20)	CKD stage 5D (peritoneal dialysis, n=129;	The Canadian Study of Health and Aging Clinical Frailty Scale	251	(Iyasere et al., 2016)
		Barthel Index	Effect estimate				

		0.89 (0.86-.093)	hemodialysis, n=122)	(CFS)		
	Symptom score	Effect estimate 1.23 (1.13-1.34)				
	Hospital Anxiety and Depression Scale	Effect estimate 1.21 (1.11-1.31)				
	Falls	HR 2.1 (1.21- 3.92)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	(Yadla, John, &Mummadi, 2017)
	Time to first fall or fracture requiring medical attention	HR 1.60 (1.16- 2.20)	CKD stage 5D (maintenance hemodialysis)	Modified Fried Phenotypes by Bao Y (Bao, Dalrymple, Chertow, Kaysen, &Johansen, 2012).	1646	(Delgado et al., 2015)
Graft Loss	Death-censored graft loss					
	F vs. NF (in patients with depressive symptoms)	aHR 6.20 (1.67, 22.95) vs. 3.16 (0.90, 11.04)	CKD stage 5T	Fried Phenotypes	773	(Konel et al., 2018)
Health-care utilization	Hospitalization/Death	HR 1.56 (1.36- 1.79)	CKD stage 5D	Fried Phenotypes	2275	(Johansen et al., 2007)
	Hospitalization	HR 2.06 (1.18- 3.58)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	(Yadla et al., 2017)
		aHR 1.80 (1.4-	CKD stage 5D	Adopted	1658	(S.Lee &Kim,

		2.3)	(maintenance hemodialysis & peritoneal dialysis)			2015)
	Early Hospital Readmission (EHR)	aRR 1.61 (1.81-2.19) (p=0.002)	CKD stage 5T	Fried Phenotypes	383	(M. A.McAdams-DeMarco et al., 2013)
	Longer Length of Stay (LOS)					
	with delayed graft function (DGF), LOS	Relative Risk 1.15 (1.03-1.29)	CKD stage 5T	Fried Phenotypes	589	(Mara AMcAdams-DeMarco et al., 2017)
	With DGF, LOS ≥2 weeks	OR 1.57 (1.06-2.33)				
	≥2 weeks		CKD stage 5 to 5T	Fried Phenotypes	569	(Chu et al., 2019)
	Change in 3 categories (more frail)	OR 2.02 (1.20-3.40)				
	Change in frailty scores (more frail)	OR 1.92 (1.13-3.25)				
	With depressive symptoms (aRR difference between F and NF)	aRR 1.88 (1.70-2.08) vs. 1.38 (1.27-1.52)				(Konel et al., 2018)
	CES-D score (10-point	aRR 1.23 (1.16-				

		increase) (aRR increase between F and NF)	1.31) vs. 1.17 (1.08-1.27)				
Mortality	Mortality		2.17 fold	CKD stage 5T	Fried Phenotypes	537	(M AMcAdams-DeMarco et al., 2015)
			HR 1.22 (1.04-1.43)	CKD stage 5D (incident chronic dialysis)	CFS	390	(Alfaadhel et al., 2015)
		F vs. NF (in patients with depressive symptoms)	aHR 2.62 (1.03, 6.70) vs. 1.92 (0.68, 5.38)	CKD stage 5T	Fried Phenotypes	773	(Konel et al., 2018)
	All-cause mortality						
		Adjusted	HR 1.66 (1.03-2.67)	CKD stage 5D (incident chronic dialysis)	Fried Phenotypes	370	(Fitzpatrick et al., 2019)
		Among BMI ≥ 30 kg/m ²	HR 3.77 (1.10-12.92)				
		Above median Waist-Hip Ratio (WHR)	HR 2.38 (1.17-4.82)				
	Post-KT mortality						
		Change in 3 categories (more frail)	HR 2.27 (1.11-4.65)	CKD stage 5 to 5T	Fried Phenotypes	569	(Chu et al., 2019)
		Change in frailty scores	HR 2.36 (1.12-				

	(more frail)	4.99)				
Composite Outcomes	Composite outcomes of all-cause death or cardiovascular hospitalization	HR 23.58 (1.61-346.03)	CKD stage 5D ESRD	Multidimensional frailty score based on comprehensive geriatric assessment (CGA) protocol	46	(S. W.Lee et al., 2017)

Bibliography

- Alfaadhel, T. A., Soroka, S. D., Kiberd, B. A., Landry, D., Moorhouse, P., & Tennankore, K. K. (2015). Frailty and mortality in dialysis: evaluation of a clinical frailty scale. *Clinical Journal of the American Society of Nephrology : CJASN*, 10, 832–840.
- Bao, Y., Dalrymple, L., Chertow, G. M., Kaysen, G. A., & Johansen, K. L. (2012). Frailty, dialysis initiation, and mortality in end-stage renal disease. *Arch Intern Med*, 172, 1071–1077.
- Chao, C.-T., Chiang, C.-K., Huang, J.-W., & Hung, K.-Y. (2017, April). Self-reported frailty among end-stage renal disease patients: A potential predictor of dialysis access outcomes. *Nephrology (Carlton, Vic.)*. Australia.
- Chao, C.-T., Huang, J.-W., & Chan, D.-C. (2017). Frail phenotype might herald bone health worsening among end-stage renal disease patients. *PeerJ*, 5, e3542.
- Chu, N. M., Deng, A., Ying, H., Haugen, C. E., Garonzik Wang, J. M., Segev, D. L., & McAdams-DeMarco, M. A. (2019). Dynamic Frailty Before Kidney Transplantation-Time of Measurement Matters. *Transplantation*. doi:10.1097/TP.0000000000002563
- Delgado, C., Shieh, S., Grimes, B., Chertow, G. M., Dalrymple, L. S., Kaysen, G. A., ...Johansen, K. L. (2015). Association of Self-Reported Frailty with Falls and Fractures among Patients New to Dialysis. *American Journal of Nephrology*, 42, 134–140.
- Fitzpatrick, J., Sozio, S. M., Jaar, B. G., Estrella, M. M., Segev, D. L., Parekh, R. S., & McAdams-DeMarco, M. A. (2019). Frailty, body composition and the risk of mortality in incident hemodialysis patients: the Predictors of Arrhythmic and Cardiovascular Risk in End Stage Renal Disease study. *Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association*, 34, 346–354.
- 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.
- Iyasere, O. U., Brown, E. A., Johansson, L., Huson, L., Smee, J., Maxwell, A. P., ...Davenport, A. (2016). Quality of Life and Physical Function in Older Patients on Dialysis: A Comparison of Assisted Peritoneal Dialysis with Hemodialysis. *Clinical Journal of the American Society of Nephrology : CJASN*, 11, 423–430.
- Johansen, K. L., Chertow, G. M., Jin, C., & Kutner, N. G. (2007). Significance of frailty among dialysis patients. *Journal of the American Society of*

Nephrology : JASN, 18, 2960–7.

- Konel, J. M., Warsame, F., Ying, H., Haugen, C. E., Mountford, A., Chu, N. M., ...McAdams-DeMarco, M. A. (2018). Depressive symptoms, frailty, and adverse outcomes among kidney transplant recipients. *Clinical Transplantation*, 32, e13391.
- Lee, S. J., Son, H., &Shin, S. K. (2015). Influence of frailty on health-related quality of life in pre-dialysis patients with chronic kidney disease in Korea: a cross-sectional study. *Health Qual Life Outcomes*, 13, 70.
- Lee, S., &Kim, J. C. (2015). Frailty as an independent predictor for hospitalization-free survival even in relatively healthy patients receiving chronic dialysis. *Nephrology Dialysis Transplantation.*, 30, iii316.
- Lee, S. W., Lee, A., Yu, M. Y., Kim, S. W., Kim, K.II, Na, K. Y., ...Chin, H. J. (2017). Is Frailty a Modifiable Risk Factor of Future Adverse Outcomes in Elderly Patients with Incident End-Stage Renal Disease? *Journal of Korean Medical Science*, 32, 1800–1806.
- McAdams-DeMarco, M. A., King, E. A., Luo, X., Haugen, C., DiBrito, S., Shaffer, A., ...Segev, D. L. (2017). Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients: A National Registry and Prospective Cohort Study. *Annals of Surgery*, 266, 1084–1090.
- McAdams-DeMarco, M. A., Law, A., King, E., Orandi, B., Salter, M., Gupta, N., ...Segev, D. L. (2015). Frailty and mortality in kidney transplant recipients. *American Journal of Transplantation : Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, 15, 149–154.
- McAdams-DeMarco, M. A., Law, A., Salter, M. L., Chow, E., Grams, M., Walston, J., &Segev, D. L. (2013). Frailty and Early Hospital Readmission After Kidney Transplantation. *American Journal of Transplantation*, 13, 2091–2095.
- 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., Olorundare, I. O., Ying, H., Warsame, F., Haugen, C. E., Hall, R., ...Segev, D. L. (2018). Frailty and Postkidney Transplant Health-Related Quality of Life. *Transplantation*, 102, 291–299.
- 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.
- McAdams-DeMarco, M. A., Ying, H., Olorundare, I., King, E. A., Desai, N., Dagher, N., ...Segev, D. L. (2016). Frailty and Health-Related Quality of

Life in End Stage Renal Disease Patients of All Ages. *The Journal of Frailty & Aging*, 5, 174–179.

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.

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