The concept of FRAILTY in dialysis patients

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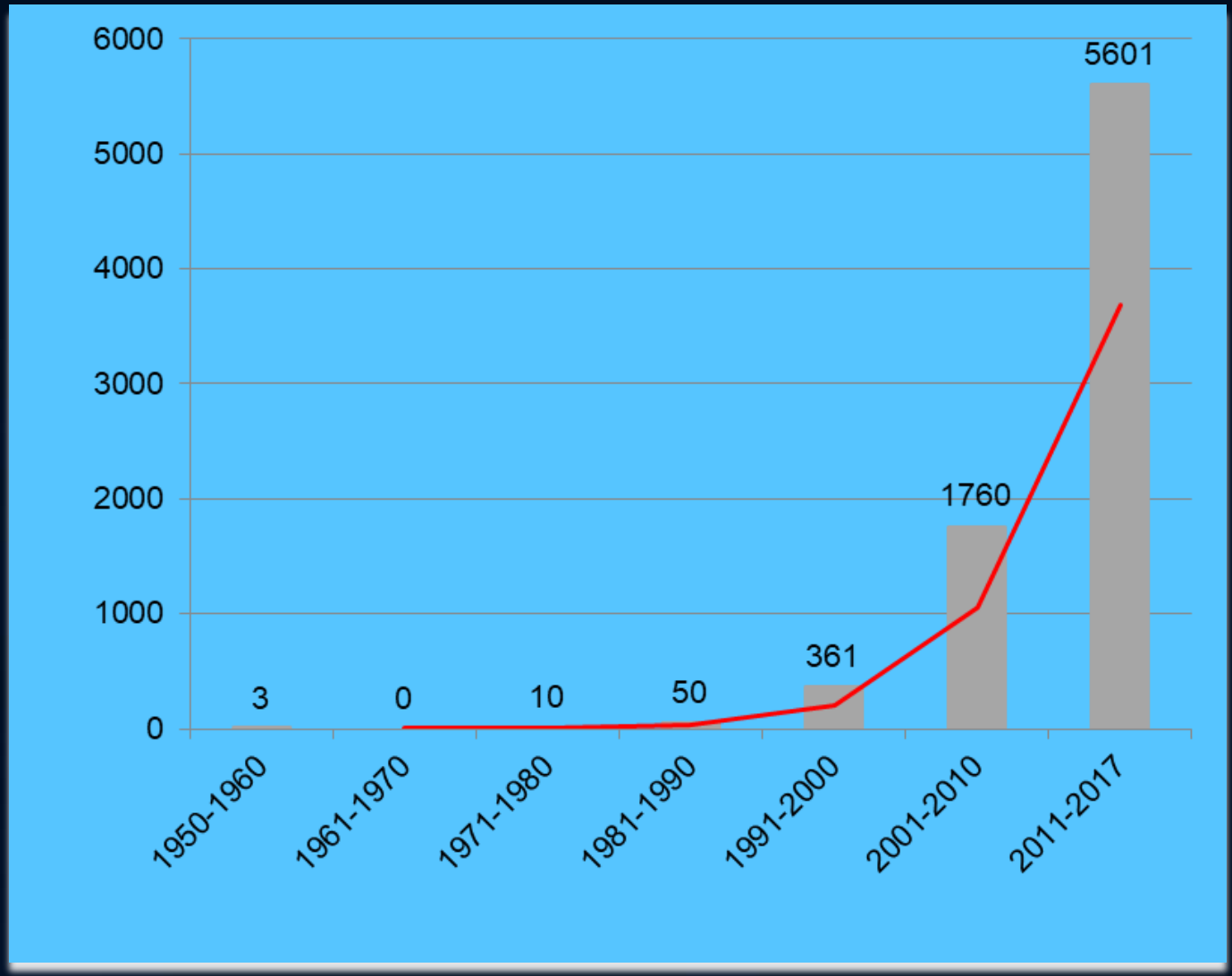


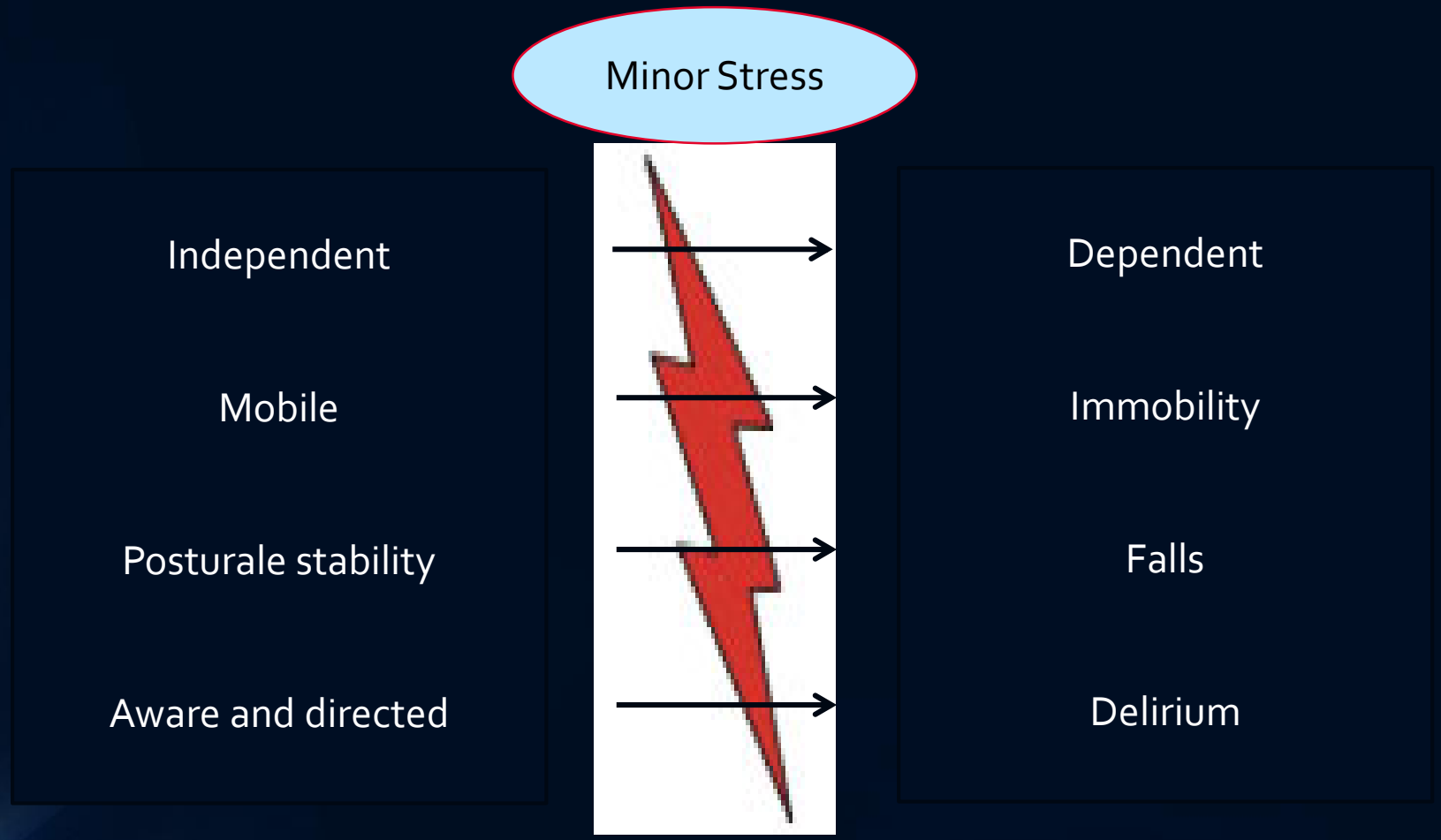
Updated from
Cesari et al.*The European Union Geriatric Medicine Society (EUGMS) Working Group on "Frailty in Older Persons".* J Frailty Aging, 2013. **2**(3): p. 118-20.

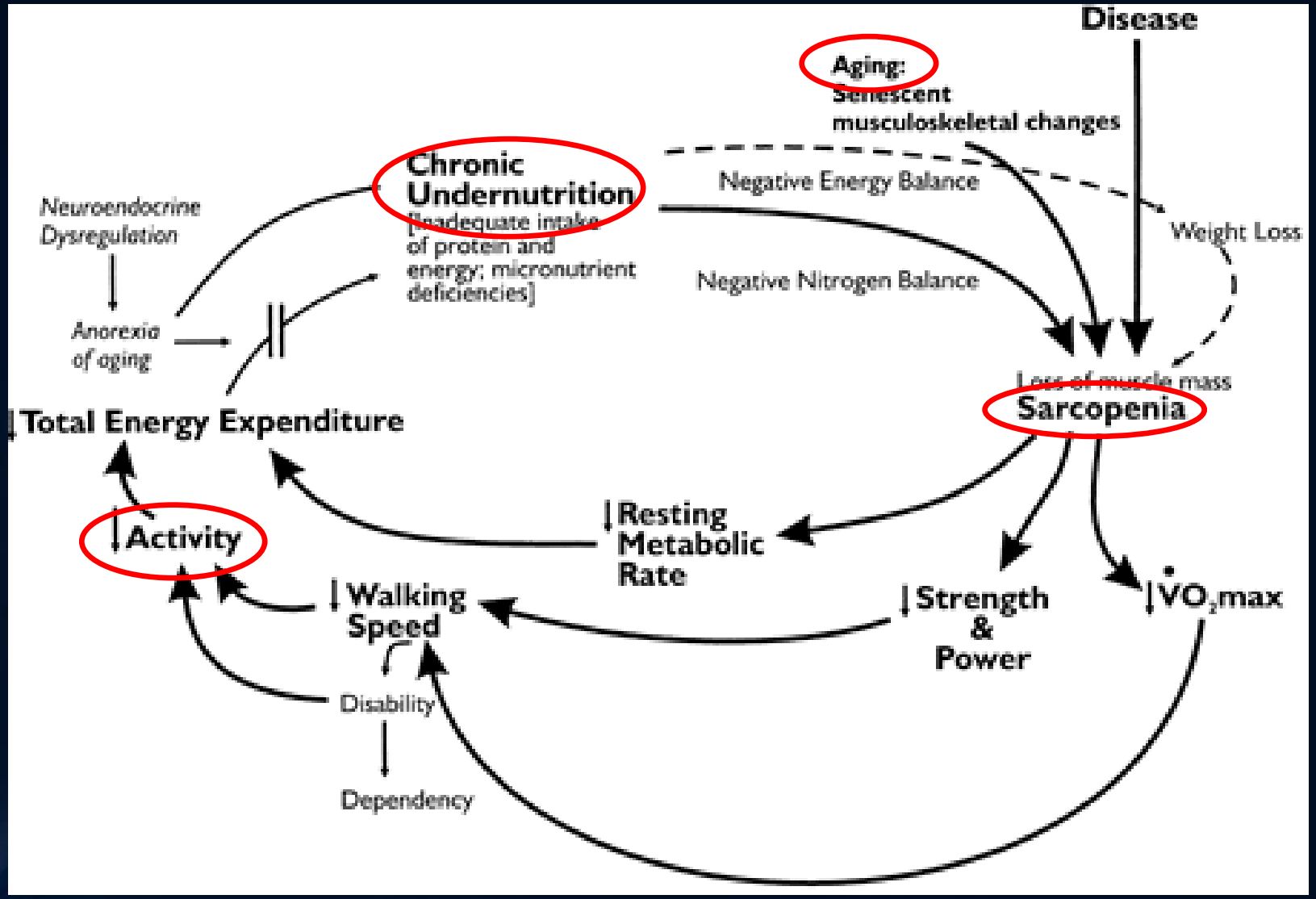
Definition of Frailty

« Frailty is a biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes »

Fried LA, J Gerontol A Biol Sci Med Sci, 2001, 56, M146

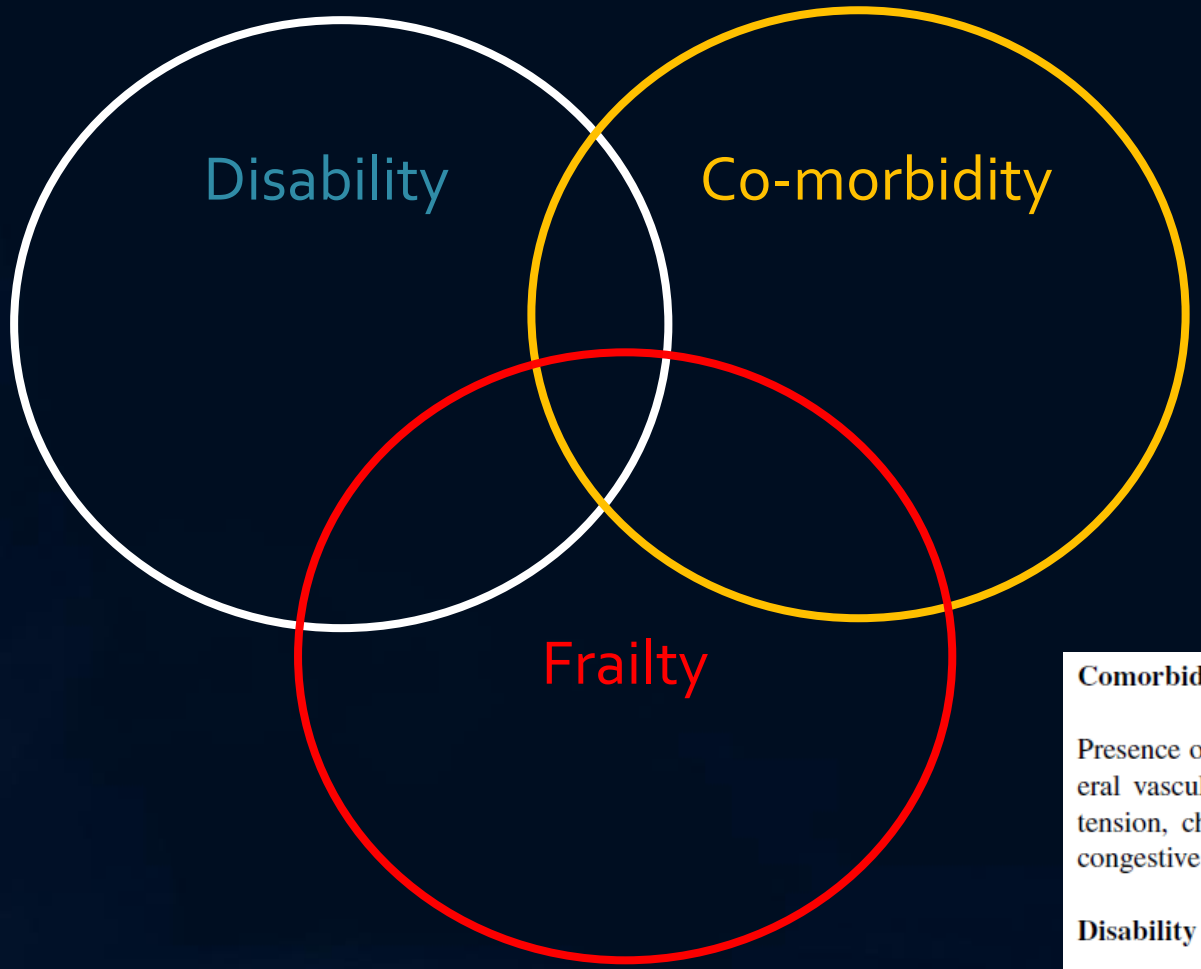
Definition of Frailty





Fried LA, J Gerontol A Biol Sci Med Sci, 2001, 56, M146

Definition of Frailty



Comorbidity Fried et al. [7]

Presence of 4 or more of the following conditions: peripheral vascular disease, rheumatoid arthritis, cancer, hypertension, chronic obstructive pulmonary disease, diabetes, congestive heart failure, angina, and myocardial infarction.

Disability Fried et al. [7, 47]

Inability to perform at least 2 of the following domains without assistance: feeding, dressing, ambulation, grooming, using a toilet, and bathing.

FRAILTY according to FRIED

5 CRITERIA
Scoring
0 criteria: robust
1-2 criteria: pre-frailty
≥ 3 criteria: frailty

Easy and inexpensive
Objective and subjective
Functional tests

Criteria	Threshold
Shrinking: Unintentional weight loss (self reported)	4.5 kg or 5% in the past year
Weakness: Hand Grip Strength	
Men	
BMI ≤ 24	≤ 29 kg
BMI 24.1-26	≤ 30 kg
BMI 26.1-28	≤ 30 kg
BMI > 28	≤ 32 kg
Women	
BMI ≤ 23	≤ 17 kg
BMI 23.1-26	≤ 17.3 kg
BMI 26.1-29	≤ 18 kg
BMI > 29	≤ 21 kg
Poor endurance and energy: Self reported exhaustion	two statements are read. (a) I felt that everything I did was an effort (b) I could not get going. Then "How often in the last week did you feel this way?" rarely or none of the time=0, some or a little of the time (1–2 days)=1, moderate amount of the time (3–4 days),=2, most of the time=3. Subjects answering "2" or "3" to either of these questions are categorized as frail
Slowness: Walking speed on 4,5 m	
Men	
Height ≤ 173 cm	≥ 7 seconds
Height > 173 cm	≥ 6 seconds
Women	
Height ≤ 159 cm	≥ 7 seconds
Height > 159 cm	≥ 6 seconds
Level of activity (kcal/week) (Minnesota Leisure Time Activity questionnaire)	
Men	< 383 Kcal/week
Women	< 270 Kcal/week

Fried LA, J Gerontol A Biol Sci Med Sci, 2001, 56, M146

Prevalence of Frailty

In general geriatric population

- 10.7 % in subjects older than 65 year (4 % to 59,1 % but 4 to 17% if Fried only)
- Prevalence higher in women
- Prevalence is increasing in old old

Collard RM, J Am Geriatr Soc, 2012, 60, p1487

In Nursing homes

- 52.3 % (19 % et 75.6 %) (46,9% if Fried only)
- 9 % if between 60 and 69 years, 45.5 % if between 70 and 79 years and 61.8 % if older than 80 years

Kojima G, J Am Med Dir Assoc, 2015, 16, p940

FRAILTY as a risk factor and prediction tool

In the general geriatric population, frailty people have an increased risk of

- Falls (OR = 2.06 ; IC 95 % = 1.28 – 3.34)
- Fractures (OR = 3.64 ; IC 95 % = 1.53 – 8.67)
- Physical Limitation (OR = 3.63 ; IC 95 % = 2.14 – 6.16)
- Dependency for basic activities of daily living (OR = 2.05 ; IC 95 % = 1.73 – 2.44) and instrumental ADL (OR = 2,52 ; IC 95 % = 2.08 – 3,06)
- Cognitive decline (HR = 1.47 ; IC 95 % = 1.23 – 1.76)
- Hospitalization (OR = 1.82 ; IC 95 % = 1.53 – 2.15)
- Mortality (OR = 2.34 ; IC 95% = 1.77 – 3.09)

Vermeiren S, J Am Med Dir Assoc, 2016, 17,p. 1163

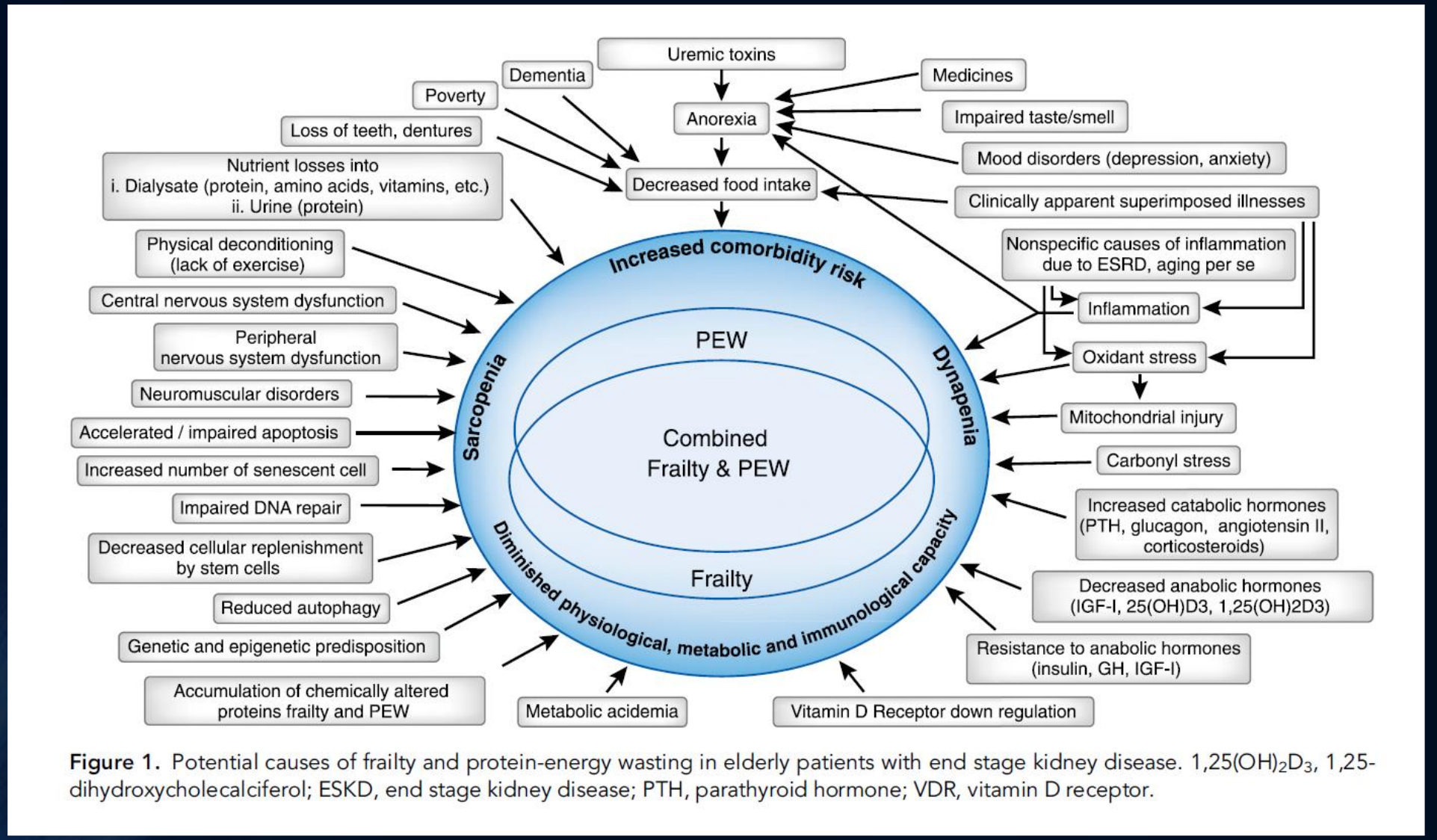


Figure 1. Potential causes of frailty and protein-energy wasting in elderly patients with end stage kidney disease. $1,25(OH)_2D_3$, 1,25-dihydroxycholecalciferol; ESKD, end stage kidney disease; PTH, parathyroid hormone; VDR, vitamin D receptor.

Kim, JC, J Am Soc Nephrol, 2013, 24, p337

FRAILTY IN DIALYSIS PATIENTS

CLINICAL EPIDEMIOLOGY www.jasn.org

Significance of Frailty among Dialysis Patients

Kirsten L. Johansen,*†‡ Glenn M. Chertow,†‡ Chengshi Jin,‡ and Nancy G. Kutner§

*Nephrology Section, San Francisco VA Medical Center, †Division of Nephrology, University of California, San Francisco, and ‡Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California; and §Department of Rehabilitation Medicine, Emory University, Atlanta, Georgia

J Am Soc Nephrol 18: 2960–2967, 2007.

Dialysis Morbidity and Mortality Study (DMMS) Wave 2, 1996-1997
Incident dialysis representative of US dialysis population
PD over-represented
One-year follow-up

Table 1. Baseline characteristics by availability of frailty criteria

Variable	Complete Data (n = 2275)
Age (yr; mean ± SD)	58.2 ± 15.5
Gender (% male)	53.4
Race (%)	
white	65.4
black	26.5
Asian	2.3
other	5.8
Serum albumin (mg/dl; mean ± SD)[b]	3.5 ± 0.6
BMI (kg/m^2; mean ± SD)	25.8 ± 5.8
Peritoneal dialysis (%)	48.1
Comorbidity (%)	
diabetes	47.6
CAD	31.4
cerebrovascular disease	8.7
peripheral vascular disease	15.3
cancer	8.4
Current smoker (%)	13.9
Married (%)	56.4
Employed (%)	13.8
High school graduate (%)	69.8
Medicaid (%)	26.8

[a]BMI, body mass index; CAD, coronary artery disease.
[b]To convert mg/dl to g/L, multiply by 10.

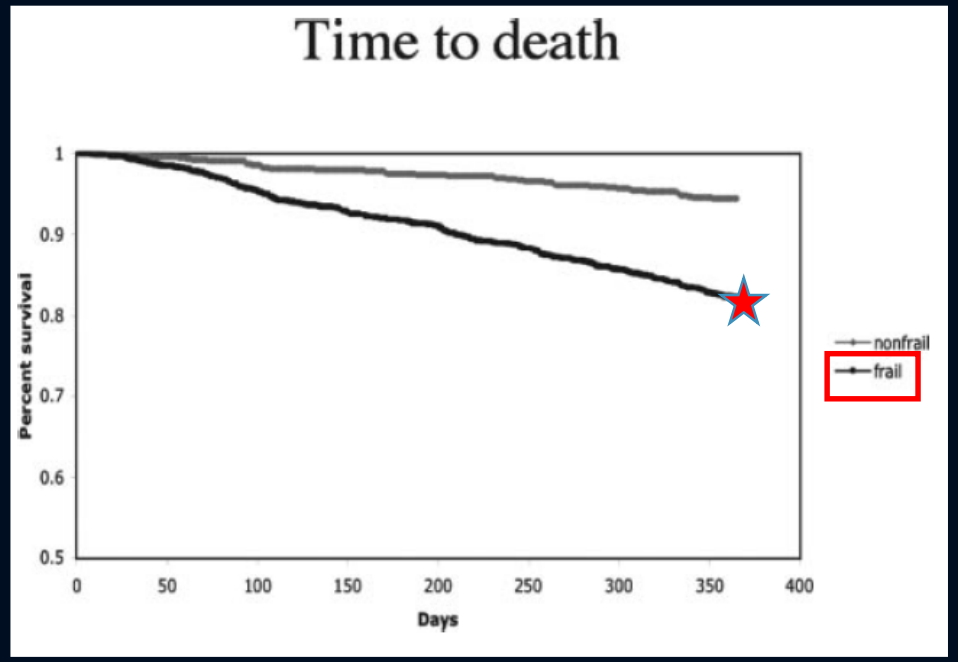
Table 2. Proportion of patients overall and by age meeting individual and collective criteria for frailty

Patients	n	Frail
Overall	2275	67.7
Age (yr)		
<40	306	44.4
40 to 50	352	61.1
50 to 60	440	66.4
60 to 70	570	74.2
70 to 80	475	78.1
>80	132	78.8

Table 3. Predictors of frailty[a]

Variable	OR	95% CI
Age	1.02	1.01 to 1.03
Female gender	1.55	1.27 to 1.88
Race		
white	1.0 (referent)	
black	0.90	0.72 to 1.13
Asian	0.56	0.30 to 1.05
other	1.01	0.26 to 3.92
BMI (kg/m^2)		
<19	1.41	0.93 to 2.13
19 to <25	1.0 (referent)	
25 to <30	0.98	0.78 to 1.22
≥30	1.00	0.77 to 1.30
Serum albumin concentration (g/dl)		
<3.2	1.89	1.43 to 2.49
3.2 to <3.5	1.32	1.00 to 1.76
3.5 to <3.9	1.06	0.84 to 1.35
≥3.9	1.0 (referent)	
Dialysis modality (PD)	0.80	0.65 to 0.97
Comorbidity		
diabetes	1.35	1.10 to 1.65
CAD	1.17	0.92 to 1.48
PAOD	1.19	0.88 to 1.60
CVA	1.55	1.05 to 2.29
cancer	1.39	0.95 to 2.04

[a]CVA, cerebrovascular accident; PAOD, peripheral arterial occlusive disease; PD, peritoneal dialysis.



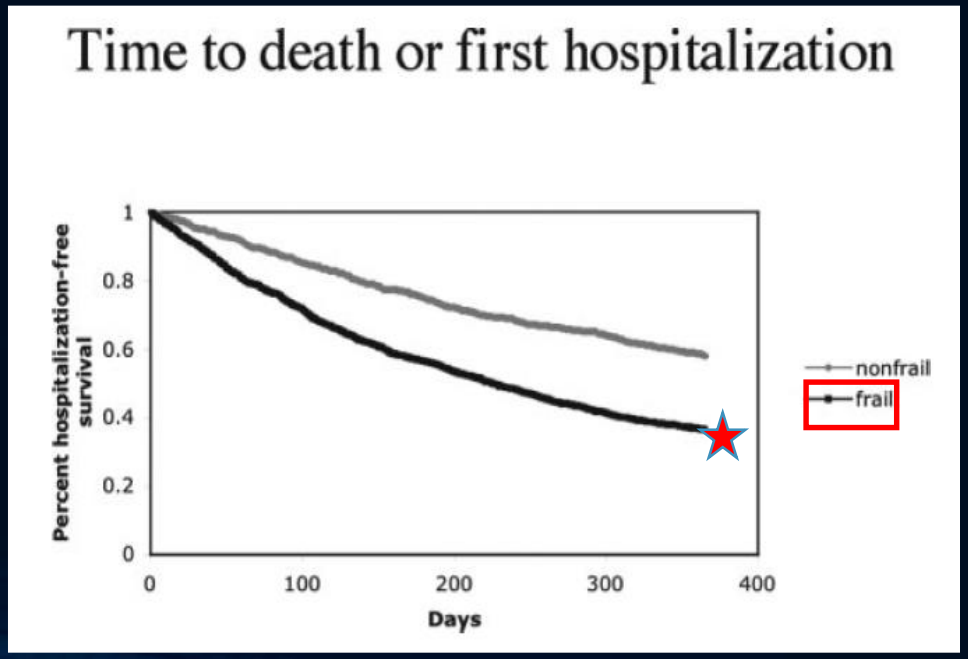


Table 4. Multivariable analysis of the association of frailty with 1-yr mortality

Variable	HR (95% CI)
Frailty	2.24 (1.60 to 3.15)
Age	1.03 (1.02 to 1.04)
Female gender	1.09 (0.86 to 1.38)
Race	
white	1.0 (referent)
black	1.01 (0.75 to 1.36)
Asian	0.91 (0.40 to 2.06)
other	0.84 (0.12 to 6.02)
Hispanic	1.20 (0.82 to 1.78)
BMI (kg/m^2)	
<19	1.11 (0.78 to 1.58)
19 to <25	1.0 (referent)
25 to <30	0.62 (0.46 to 0.82)
≥30	0.57 (0.40 to 0.81)
Serum albumin concentration (g/dl)[a]	
<3.2	1.83 (1.30 to 2.59)
3.2 to <3.5	1.09 (0.74 to 1.59)
3.5 to <3.9	1.04 (0.73 to 1.49)
≥	1.0 (referent)
Dialysis modality (PD)	1.03 (0.81 to 1. 31)
Comorbidity	
diabetes	1.10 (0.86 to 1.41)
CAD	1.36 (1.07 to 1.73)
peripheral vascular disease	1.55 (1.19 to 2.00)
CVA	1.13 (0.81 to 1.56)
cancer	1.26 (0.90 to 1.76)
Employment status	0.47 (0.25 to 0.87)
Marital status	0.86 (0.68 to 1.09)
Smoking	1.25 (0.88 to 1.77)

[a]To convert mg/dl to g/L, multiply by 10.

Components of Frailty	CHS	WHI	USRDS DMMS Wave 2
Slowness/ weakness	Slowness: Slowest quintile on a 15-ft walk test, stratified by gender and height Weakness: Weakest quintile in grip strength measured by handheld dynamometer, stratified by gender and BMI quartiles	Rand-36 PF <75. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf Lifting or carrying groceries Climbing several flights of stairs Climbing one flight of stairs Bending, kneeling, or stooping Walking more than a mile Walking several blocks Walking one block Bathing or dressing yourself	Rand-36 PF <75 =2points
Poor endurance/ exhaustion	Based on two questions from the CES-D Depression Scale: a. I felt that everything I did was an effort. b. I could not get going. How often in the last week did you feel this way? 0 = rarely or none of the time (<1 d) 1 = some or a little of the time (1 to 2 d) 2 = a moderate amount of the time (3 to 4 d) 3 = most of the time. Individuals answering 2 or 3 to either of these questions were categorized as meeting the exhaustion criterion.	Rand-36 Vitality <55 How much of the time during the last 30 d. . . Did you feel worn out? Did you feel tired? Did you have a lot of energy? Did you feel full of pep?	Rand-36 Vitality <55
Physical inactivity	Based on the short version of the Minnesota Leisure Time Activity questionnaire. The lowest quintile of activity stratified by gender was considered inactive.	Detailed physical activity questionnaire assessing frequency and duration of walking and mild, moderate, and strenuous activities. Kcal of weekly energy expenditure was calculated, and those in the lowest quartile were scored positive for inactivity.	How often do you *exercise* (do physical activity during your leisure time)? Daily or almost daily 4 to 5 times a week 2 to 3 times a week About once a week Less than once a week Almost never or never Individuals answering "almost never or never" were classified as inactive.
Unintentional weight loss	"In the last year, have you lost more than 10 pounds unintentionally (*i.e.*, not due to dieting or exercise)?" Individuals who responded "yes" met the weight loss criterion.	No measure was available at baseline. At follow-up, measured weight loss or subject-reported weight loss was used.	Undernourished or cachectic (malnourished), as assessed by data abstractor

Retrospective analysis
Cohort relatively young
Questionnaires (QoL, SF36)="self-reported" frailty

CLINICAL RESEARCH www.jasn.org J Am Soc Nephrol 25: 381–389, 2014

Association between Body Composition and Frailty among Prevalent Hemodialysis Patients: A US Renal Data System Special Study

Kirsten L. Johansen,*†‡ Lorien S. Dalrymple,§ Cynthia Delgado,*† George A. Kaysen,§ John Kornak,‡ Barbara Grimes,‡ and Glenn M. Chertow‖

*Department of Medicine, Division of Nephrology and ‡Department of Epidemiology and Biostatistics, University of California, San Francisco, California; †Nephrology Section, San Francisco Veterans Affairs Medical Center, San Francisco, California; §Division of Nephrology, University of California, Davis, California; and ‖Department of Medicine, Division of Nephrology, Stanford University School of Medicine, Stanford, California

Characteristic	Patients with Frailty and Body Composition Data[a] (*n*=638)
Age, yr	56.8 (14.5)
Women, %	42.0
Race, %	
White	24.6
Black	60.3
Other	15.0
BMI, kg/m^2	29.0 (7.1)
Serum albumin, g/dl	4.0 (0.4)
Serum creatinine, mg/dl	8.4 (2.7)
Dialysis vintage, yr	3.0 (0.1–30.1)
Comorbidity, %	
Diabetes	44.8
CHF	18.5
CAD	8.0
Hypertension	90.3
Frail, %	29.8

ACTIVE/ADIPOSE study
N=638 prevalent dialysis
Frailty measured: 30%
Frailty associated with age, diabetes, fat mass and intracellular water (=marker of muscle mass), but not BMI

Table 3. Multivariable correlates of frailty

Bioelectrical impedance spectroscopy

	Model 1 (No Body Composition) OR (95% CI)	Model 2 (BMI) OR (95% CI)	Model 3 (BIS) OR (95% CI)
Age, per 10 yr	1.31 (1.14 to 1.50)	1.32 (1.15 to 1.51)	1.16 (1.00 to 1.34)
Women	1.24 (0.86 to 1.78)	1.21 (0.84 to 1.74)	2.10 (1.25 to 3.70)
Race			
White	Reference	Reference	Reference
Black	0.98 (0.64 to 1.51)	0.95 (0.61 to 1.46)	0.86 (0.54 to 1.35)
Other	1.03 (0.59 to 1.81)	1.04 (0.59 to 1.83)	1.29 (0.72 to 2.30)
Diabetes	1.65 (1.13 to 2.40)	1.58 (1.08 to 2.30)	1.29 (0.87 to 1.91)
CHF	1.30 (0.83 to 2.00)	1.26 (0.80 to 1.98)	1.18 (0.74 to 1.89)
CAD	1.04 (0.55 to 1.97)	1.03 (0.54 to 1.95)	1.01 (0.52 to 1.93)
BMI, kg/m^2	—	1.02 (0.99 to 1.05)	—
Fat mass, per 10 kg	—	—	1.18 (1.02 to 1.37)
ICW, per kg	—	—	0.80 (0.73 to 0.87)
ECW, per kg	—	—	1.33 (1.20 to 1.47)
−2 Log likelihood	725.3	723.1	688.5

CHF, congestive heart failure; CAD, coronary artery disease.

« Self-reported » versus « measured » frailty

Hemodialysis International 2013; 17:41–49

A closer look at frailty in ESRD: Getting the measure right

Patricia PAINTER,[1] Michael KUSKOWSKI[2]

[1]*Department of Physical Therapy, University of Utah, Salt Lake City, Utah, USA;* [2] *Geriatric Research Education and Clinical Center (GRECC), Minneapolis VA Medical Center, Minneapolis, Minnesota, USA*

N=193 prevalent dialysis
Frailty measured: 33,7%
Frailty self-reported: 78,2%

AJKD

Am J Kidney Dis. 2014 Oct;64(4):600-7.

Original Investigation

Comparison of Self-report–Based and Physical Performance–Based Frailty Definitions Among Patients Receiving Maintenance Hemodialysis

Kirsten L. Johansen, MD,[1,2,3,4] Lorien S. Dalrymple, MD, MPH,[1,5] Cynthia Delgado, MD,[1,2,3] George A. Kaysen, MD, PhD,[1,5] John Kornak, PhD,[1,4] Barbara Grimes, PhD,[1,4] and Glenn M. Chertow, MD, MPH[1,6]

ACTIVE/ADIPOSE study
N=731 prevalent dialysis
Frailty measured: 29%
Frailty self-reported: 53%
Only 3% of frail when measured are not self-reported frail

Salter *et al. BMC Geriatrics* (2015) 15:52
DOI 10.1186/s12877-015-0051-y

BMC Geriatrics

RESEARCH ARTICLE Open Access

Perceived frailty and measured frailty among adults undergoing hemodialysis: a cross-sectional analysis

Megan L Salter[1,2,3*†], Natasha Gupta[3†], Allan B Massie[1,3], Mara A McAdams-DeMarco[1,3], Andrew H Law[1,3], Reside Lorie Jacob[5], Luis F Gimenez[6], Bernard G Jaar[1,4,6,7], Jeremy D Walston[2,8,9] and Dorry L Segev[1,3*]

N=146 prevalent dialysis
Very poor concordance between measured frailty, self-reported frailty and frailty estimated by nurses or nephrologists (especially in the elderly)

ORIGINAL RESEARCH

J Ren Nutr. 2013 Sep;23(5):356-62.

Association of Frailty With Body Composition Among Patients on Hemodialysis

Cynthia Delgado, MD, Julie W. Doyle, MS, and Kirsten L. Johansen, MD

N=80 prevalent dialysis
Frailty measured: 59%
Frailty self-reported: 63%
Frail by both: 55%

Kidney International (2016) **90,** 53–66;

www.kidney-international.org review

Screening for muscle wasting and dysfunction in patients with chronic kidney disease

Juan J. Carrero[1,2], Kirsten L. Johansen[3], Bengt Lindholm[1], Peter Stenvinkel[1], Lilian Cuppari[4] and Carla M. Avesani[5]

[1]Divisions of Renal Medicine and Baxter Novum, Karolinska Institutet, Stockholm, Sweden; [2]Center for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden; [3]Division of Nephrology, University of California, San Francisco, San Francisco, California, USA; [4]Division of Nephrology, Federal University of São Paulo, São Paulo, Brazil; and [5]Department of Applied Nutrition, Nutrition Institute, Rio de Janeiro State University, Rio de Janeiro, Brazil

Table 5| Studies on the prevalence of frailty among patients with CKD and ESRD, including definitions employed for its assessment

Reference	Population	Weight loss	Exhaustion	Physical activity	Gait speed	Grip strength	Prevalence
Studies in the ESRD population							
Johansen *et al.*, 2007[115]	Incident dialysis	Malnourished according to provider assessment	SF-36 Vitality	Inactive (single question about frequency of activity)	SF-36 PF scale	SF-36 PF scale	67.7%
Bao *et al.*, 2012[116]	Incident HD	No	SF-12 Vitality	Human Activity Profile	SF-12 PF	SF-12 PF	73%
McAdams-Demarco *et al.*, 2013[117]	Prevalent HD	Yes	CES-D	MMLTA	Over 15 ft	Yes	41.8%
Johansen *et al.*, 2014[97]	Prevalent HD	Yes	CES-D	MMLTA	Over 15 ft	Yes	30%
Johansen *et al.*, 2014[118]	Prevalent HD	Yes	SF-36 Vitality	MMLTA	SF-36 PF	SF-36 PF	53%
Painter and Kuskowski, 2013[119]	Prevalent HD	BMI ≤18.5 kg/m^2	SF-36 Vitality	Detailed self-report of no activity beyond self-care	SF-36 PF >6 m	SF-36 PF Chair stand test (5 repetitions)	78% 24%

Standardization

- In the definition (FRIED)
- We think that physiological measurements (strict adherence to FRIED criteria) are better than self-reported for standardization
- Standardization of the measurement

Frailty as a predictor is confirmed

Frailty, Dialysis Initiation, and Mortality in End-Stage Renal Disease

Yeran Bao, MD; Lorien Dalrymple, MD, MPH; Glenn M. Chertow, MD, MPH; George A. Kaysen, MD, PhD; Kirsten L. Johansen, MD

Arch Intern Med. 2012;172(14):1071-1077.

N = 1576, 73% frail (63%if <40y)
Comprehensive Dialysis Study
Median follow-up 2.9 years
Score on questionnaires…#

Frailty as a Novel Predictor of Mortality and Hospitalization in Individuals of All Ages Undergoing Hemodialysis

Mara A. McAdams-DeMarco, PhD,*† Andrew Law, ScM,*† Megan L. Salter, PhD,*† Brian Boyarsky, BA,* Luis Gimenez, MD,‡§¶ Bernard G. Jaar, MD, MPH,†‡§¶ Jeremy D. Walston, MD,** and Dorry L. Segev, PhD, MD*†

J Am Geriatr Soc 61:896–901, 2013.

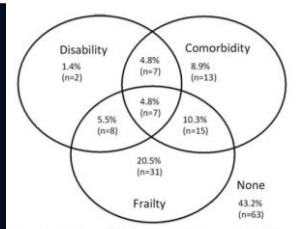


Figure 2. Overlap of frailty, comorbidity, and disability. Frailty is defined as three or more components as defined by Fried. Disability is defined as the need for assistance in two or more activities of daily living categories. Comorbidity is defined as four or more conditions as specified in Methods. The total represents 164 study participants undergoing hemodialysis.

Prevalent, prospective design
N = 146, 41,8% frail (35,4%if <65y)
Median follow-up 3,0 years
« True score »

Frailty and Cognitive Function in Incident Hemodialysis Patients

Mara A. McAdams-DeMarco,*† Jingwen Tan,* Megan L. Salter,*† Alden Gross,* Lucy A. Meoni,‡§ Bernard G. Jaar,*§‖ Wen-Hong Linda Kao,*a Rulan S. Parekh,§¶** Dorry L. Segev,*† and Stephen M. Sozio§

Clin J Am Soc Nephrol 10: 2181–2189, 2015.

Incident, prospective design
N = 323, 34% frail
Mortality at one-year: NS
« True score », 50% lost of follow-up

ORIGINAL RESEARCH

The Prevalence, Association, and Clinical Outcomes of Frailty in Maintenance Dialysis Patients

So-Young Lee, MD, PhD,* Dong Ho Yang, MD, PhD,* Eunah Hwang, MD, PhD,† Seock Hui Kang, MD, PhD,‡ Sun-Hee Park, MD, PhD,§ Tae Woo Kim, MD, PhD,¶ Duk Hyun Lee, MD, PhD,** Kisoo Park, MD, PhD,†† and Jun Chul Kim, MD, PhD‡‡

Journal of Renal Nutrition, Vol 27, No 2 (March), 2017: pp 106-112

Prevalent, prospective design
N = 1658 (n=403 PD), 34,8% frail
Median follow-up 17,1 months
Score on questionnaires…

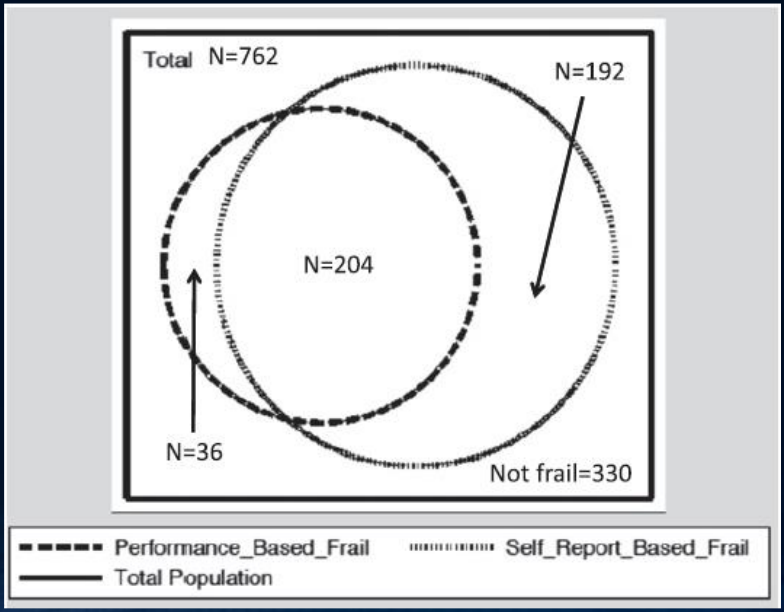
« Self-reported » versus « measured » frailty

Association of Performance-Based and Self–Reported Function–Based Definitions of Frailty with Mortality among Patients Receiving Hemodialysis

Kirsten L. Johansen,†‡ Lorien S. Dalrymple,§ David Glidden,‡ Cynthia Delgado,*† George A. Kaysen,§ Barbara Grimes,‡ and Glenn M. Chertow‖*

Clin J Am Soc Nephrol 11: 626–632, 2016.

ACTIVE/ADIPOSE study
N=762 prevalent dialysis
Frailty measured: 31%
Frailty self-reported: 52%
Median follow-up: 1,7 y



HR for mortality (n=106)(adjusted)
Measured: 2,16 [95% CI: 1,41 to 3,29]
Self-reported: 1,93 [95% CI: 1,24 to 3,00]

Self-reported frail but not measured: NS
Both self-reported and measured: 2,46 [95% CI: 1,51 to 4,01]

Longitudinal data

Factors Associated with Frailty and Its Trajectory among Patients on Hemodialysis

Kirsten L. Johansen,†‡ Lorien S. Dalrymple,§ Cynthia Delgado,*† Glenn M. Chertow,‖ Mark R. Segal,‡ Janet Chiang,†¶ Barbara Grimes,‡ and George A. Kaysen**††*

Clin J Am Soc Nephrol 12: 1100–1108, 2017.

ACTIVE/ADIPOSE study
N=762 prevalent dialysis
Mean age: 57±14y
40,7% women
61,5% of African-Americans
53,4% of diabetes

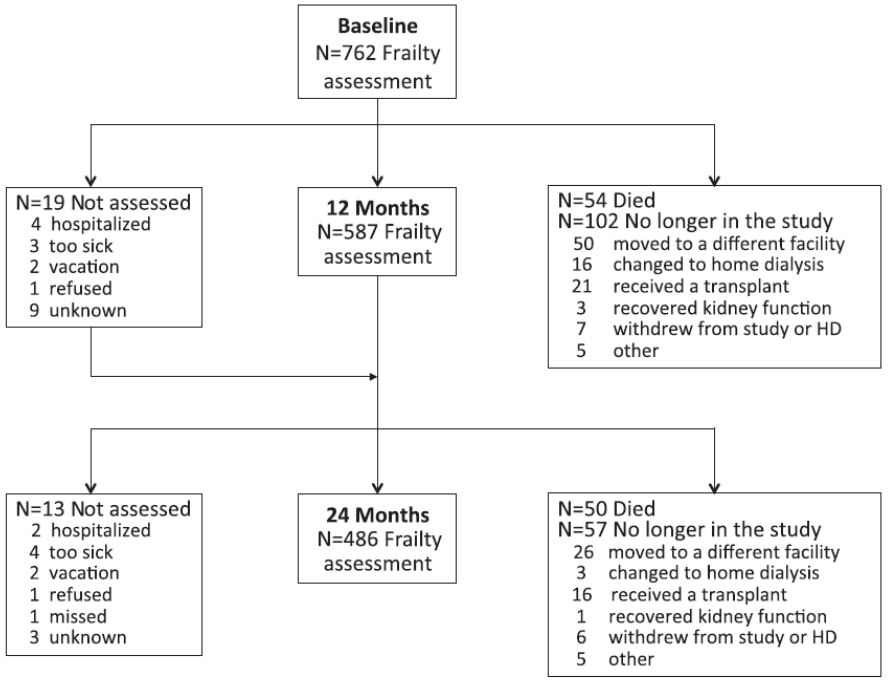
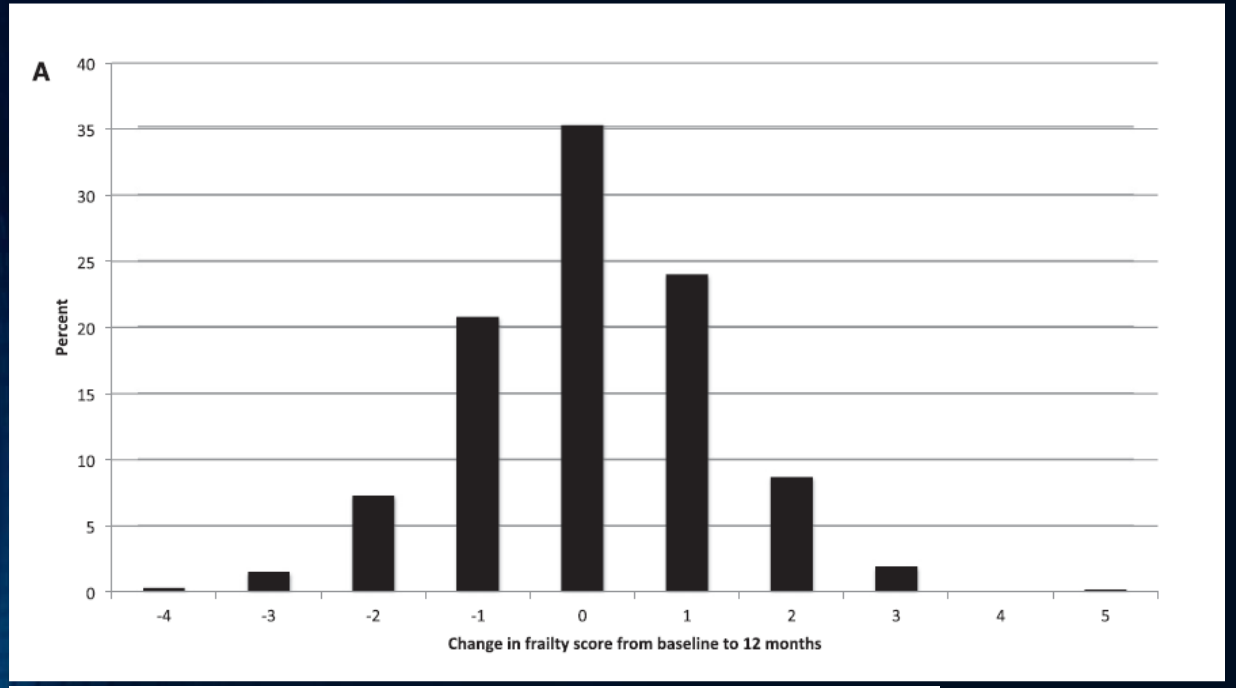
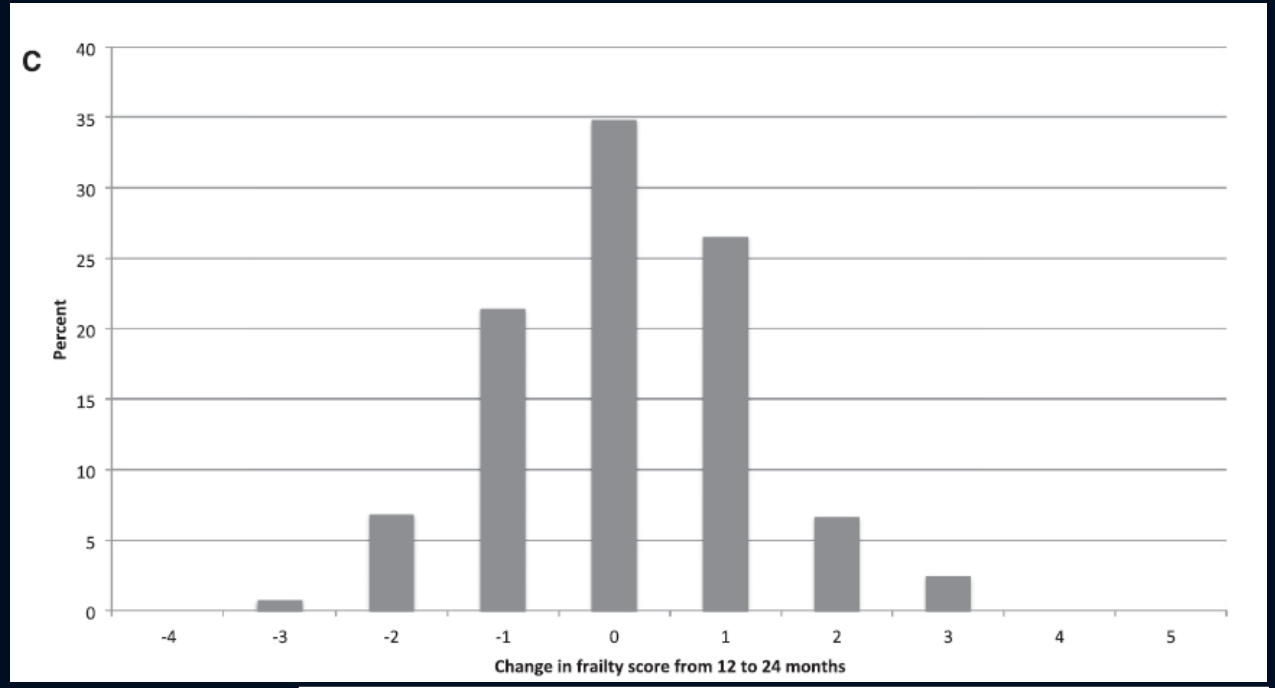
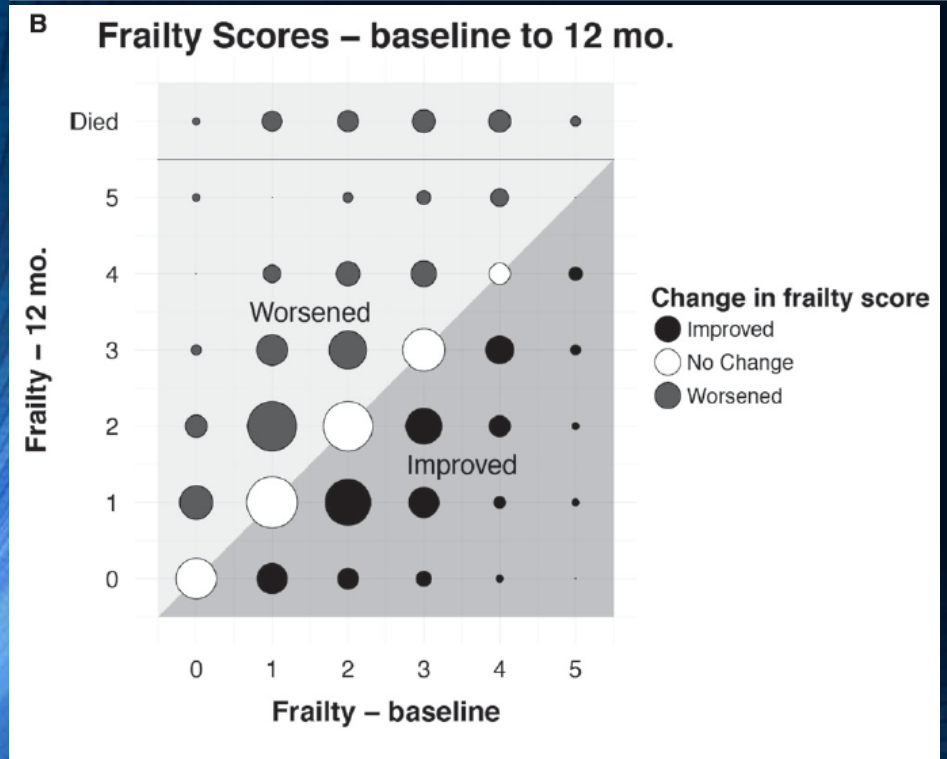


Figure 1. | Study flow diagram. Patients with a frailty score or death at 12 or 24 months contributed outcome information during follow-up. HD, hemodialysis.


A
Percent
Change in frailty score from baseline to 12 months


C
Percent
Change in frailty score from 12 to 24 months


B
Frailty Scores – baseline to 12 mo.
Died
Worsened
Improved
Frailty – 12 mo.
Frailty – baseline
Change in frailty score
Improved
No Change
Worsened

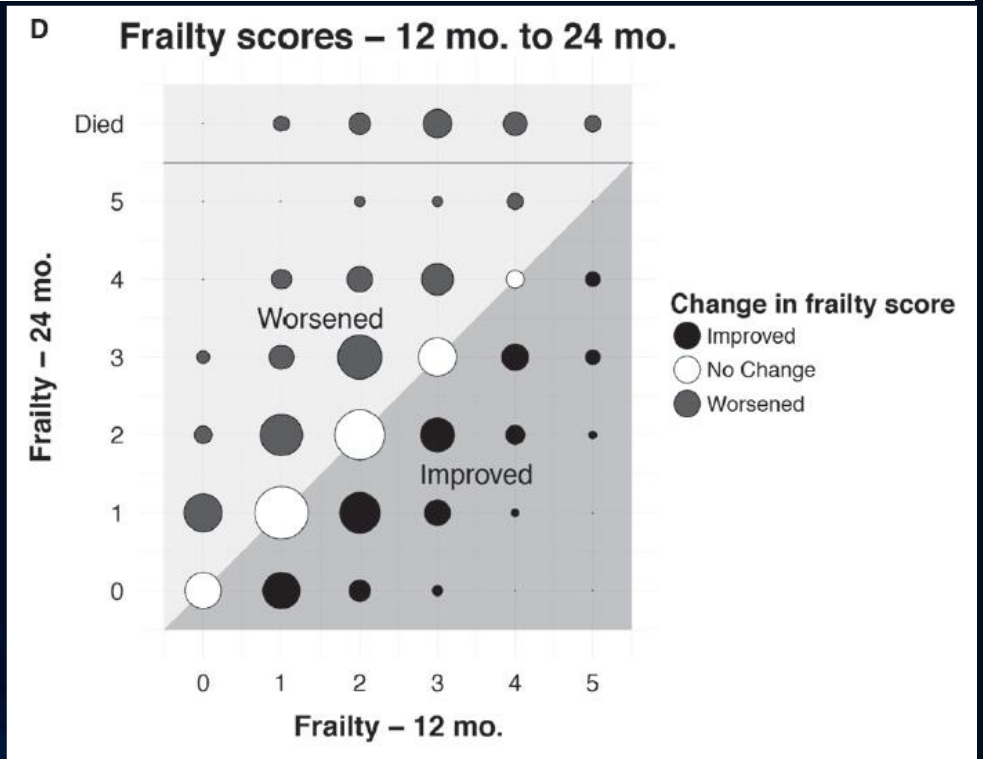

D
Frailty scores – 12 mo. to 24 mo.
Died
Worsened
Improved
Frailty – 24 mo.
Frailty – 12 mo.
Change in frailty score
Improved
No Change
Worsened

Table 2. Predictors of frailty and change in frailty score over time

Variable	Model 1[a]		Model 2	
	Difference in Frailty Score, Points	Change in Frailty, Points per Year[b]	Difference in Frailty Score, Points	Change in Frailty, Points per Year[b]
Age, per 10 yr	0.2 (−0.1 to 0.5)	0.0 (−0.1 to 0.1)	0.2 (0.1 to 0.3)	0.0 (−0.1 to 0.1)
Women	0.3 (−0.0 to 0.6)	0.1 (−0.1 to 0.3)	0.4 (0.0 to 0.7)	0.1 (−0.1 to 0.2)
Race, nonwhite	0.1 (−0.3 to 0.6)	−0.0 (−0.3 to 0.3)	0.0 (−0.4 to 0.5)	0.0 (−0.2 to 0.3)
Ethnicity, Hispanic	0.6 (0.0 to 1.1)	−0.1 (−0.5 to 0.2)	0.6 (0.1 to 1.2)	−0.1 (−0.4 to 0.2)
BMI, kg/m^2				
<20	−0.1 (−0.3 to 0.5)	0.3 (−0.2 to 0.6)	0.0 (−0.7 to 0.6)	0.3 (−0.2 to 0.7)
20 to <25	Reference	Reference	Reference	Reference
25 to <30	0.0 (−0.4 to 0.4)	0.2 (0.0 to 0.4)	0.0 (−0.4 to 0.4)	0.2 (0.0 to 0.5)
≥30	0.1 (−0.3 to 0.5)	0.2 (−0.1 to 0.4)	0.1 (−0.3 to 0.4)	0.1 (−0.1 to 0.4)
Diabetes	0.7 (0.3 to 1.0)	−0.1 (−0.3 to 0.1)	0.6 (0.3 to 0.9)	−0.1 (−0.3 to 0.1)
ASHD	0.2 (−0.2 to 0.5)	0.1 (−0.2 to 0.2)	0.0 (−0.2 to 0.2)	0.0 (−0.2 to 0.2)
Heart failure	0.3 (0.0 to 0.6)	0.0 (−0.2 to 0.2)	0.3 (−0.1 to 0.6)	0.0 (−0.2 to 0.2)
Dialysis *via* catheter	0.3 (−0.1 to 0.7)	0.3 (−0.2 to 0.7)	0.1 (−0.3 to 0.5)	0.1 (−0.3 to 0.5)
Serum albumin, g/dl	−1.1 (−1.5 to −0.7)	−0.4 (−0.8 to −0.1)	−0.6 (−1.1 to −0.2)	−0.1 (−0.5 to 0.3)
Hospitalization in last year	—	—	0.6 (0.3 to 1.0)	0.6 (0.3 to 0.8)
IL-6, pg/ml	—	—	0.3 (0.2 to 0.5)	0.3 (0.1 to 0.4)
nPCR, g/kg	—	—	−0.4 (−0.9 to 0.1)	−0.4 (−0.9 to 0.1)

There were n=732 patients with complete data for all covariates. BMI, body mass index; ASHD, atherosclerotic heart disease; nPCR, normalized protein catabolic rate.

[a]-, these variables were not included in model 1.

[b]For nonvarying predictors, change in frailty represents the interaction term between time and each variable. For time-updated variables, this column shows the association with the change in that variable over time.

POTENTIAL LIMITATIONS

- Better than age?
- Better than comorbidities/Charlson score?
- Better than each criteria alone?
- Adding value compared to sarcopenia, malnutrition, protein-energy wasting syndrome?
- Better than the doctor's feeling?
- Are norms strictly applicable to dialysis patients?
- Isolation, cognitive impairment and depression
- Few longitudinal data
- Few data available in Europe

Prevalence of frailty in CHU Liège n = 108

56%

n =108	Hommes : n=71	Femmes : n=37
% de Fragiles	38/71 (53%)	23/37 (62%)
Fragiles à 3 critères / 5	20%	16%
Fragiles à 4 critères / 5	23%	35%
Fragiles à 5 critères / 5	11%	11%
Fragiles de moins de 50 ans	5/31 (16%)	
Fragiles de plus de 50 ans	58/77 (75%)	
Fragiles de plus de 60 ans	51/64 (80%)	
Fragiles de plus de 70 ans	29/34 (84%)	

56%

Tableau 3 : Prévalence de patients fragiles, ventilation sur la base du genre, de l'âge et du score obtenu selon les critères de Fried.

66% of men
Age: 64 [28] y
BMI: 24 [7] kg/m²

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Perspectives

- Identification of patient at risk for (diverse) adverse outcomes
- Role in the decision to start or not dialysis? to be grafted or not?
- To be interventional

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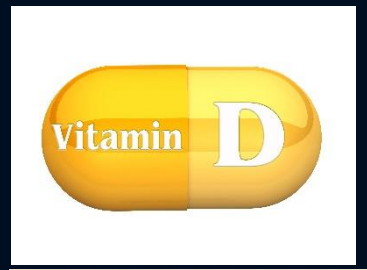
Special Article

Frailty Consensus: A Call to Action

John E. Morley MB, BCh [a,*], Bruno Vellas MD [b,c], G. Abellan van Kan MD [b,c], Stefan D. Anker MD, PhD [d,e], Juergen M. Bauer MD, PhD [f], Roberto Bernabei MD [g], Matteo Cesari MD, PhD [b,c], W.C. Chumlea PhD [h], Wolfram Doehner MD, PhD [d,i], Jonathan Evans MD [j], Linda P. Fried MD, MPH [k], Jack M. Guralnik MD, PhD [l], Paul R. Katz MD, CMD [m], Theodore K. Malmstrom PhD [a,n], Roger J. McCarter PhD [o], Luis M. Gutierrez Robledo MD, PhD [p], Ken Rockwood MD [q], Stephan von Haehling MD, PhD [r], Maurits F. Vandewoude MD, PhD [s], Jeremy Walston MD [t]

- Exercise (resistance and aerobic)
- Caloric and protein support
- Vitamin D
- Reduction of polypharmacy



Perspectives: to be interventional !

AJKD
In Practice

Exercise and CKD: Skeletal Muscle Dysfunction and Practical Application of Exercise to Prevent and Treat Physical Impairments in CKD

Baback Roshanravan, MD, MS, MSPH,[1] Jorge Gamboa, MD, PhD,[2] and Kenneth Wilund, PhD[3]

Patients with chronic kidney disease experience substantial loss of muscle mass, weakness, and poor physical performance. As kidney disease progresses, skeletal muscle dysfunction forms a common pathway for mobility limitation, loss of functional independence, and vulnerability to disease complications. Screening for those at high risk for mobility disability by self-reported and objective measures of function is an essential first step in developing an interdisciplinary approach to treatment that includes rehabilitative therapies and counseling on physical activity. Exercise has beneficial effects on systemic inflammation, muscle, and physical performance in chronic kidney disease. Kidney health providers need to identify patient and care delivery barriers to exercise in order to effectively counsel patients on physical activity. A thorough medical evaluation and assessment of baseline function using self-reported and objective function assessment is essential to guide an effective individualized exercise prescription to prevent function decline in persons with kidney disease. This review focuses on the impact of kidney disease on skeletal muscle dysfunction in the context of the disablement process and reviews screening and treatment strategies that kidney health professionals can use in clinical practice to prevent functional decline and disability.

Am J Kidney Dis. 69(6):837-852.

INDEX WORDS: Kidney disease; physical function; muscle; exercise; prevention; frailty; CKD; ESRD; older adults; muscle dysfunction; recommendations.

Perspectives: to be interventional !

- Exercise (resistance and aerobic)
- Caloric and protein support
- Vitamin D
- Reduction of polypharmacy

- Correction of acidosis?
- Testosterone or other androgenic compounds? GH? Carnitine?
- Future anabolic therapy?
- Place for biomarkers?

Conclusions

- Frailty according FRIED criteria: relatively simple tool (subjective/objective)
- Frailty is (very) frequent in dialysis patients (even in young patients)
- Seems predictive of adverse events also in dialysis patients (even in young patients)
- We are at the beginning of the story…
- The ultimate goal is to have (try, test) interventions (probably multiple) to improve frailty status (and maybe mortality)

Jupiler

Questions?
Interest to collaborate?
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Version courte du Minnesota

Type d'activité	**Durée totale cumulée sur les 2 dernières semaines (min)**
Marche pour faire les courses ou pour le plaisir	
Prendre les escaliers (montée)	
Randonnée à pied	
Tâches ménagères énergiques	
Danse	
Gymnastique à domicile	
Gymnastique dans un club de gym	
Jogging	
Ski	
Jardinage	
Entretien du jardin, creuser, pelleter	
Ratisser les feuilles	
Tondre la pelouse (tondeuse non à moteur)	
Pelleter la neige	
Chasse	
Pêche	
Vélo	
Autre :	

Low physical activity determination Kilocalorie per week (kcal/week) expenditures were calculated for each activity using its metabolic equivalent (MET) score (a measure of exercise intensity) (15,16):

$$\begin{aligned} &\text{activity} - \text{specific MET (kcal / (kg} \times \text{hour))} \\ &\times \text{body weight (kg)} \\ &\times \text{activity duration (minutes) / 60} \\ &\times \text{number of sessions in past two we} \\ &\times \text{number of months per year / 12.} \end{aligned}$$

performed during a typical day. The limitations of each

Label	SF-36 QUESTIONS
GH1	**1.** In general, would you say your health is:
HT	**2.** Compared to one year ago, how would you rate your health in general now?
	3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? Is so, how much?
PF01	**a.** Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports
PF02	**b.** Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
PF03	**c.** Lifting or carrying groceries
PF04	**d.** Climbing several flights of stairs
PF05	**e.** Climbing one flight of stairs
PF06	**f.** Bending, kneeling, or stooping
PF07	**g.** Walking more than a mile
PF08	**h.** Walking several blocks
PF09	**i.** Walking one block
PF10	**j.** Bathing or dressing yourself
	4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?
RP1	**a.** Cut down on the amount of time you spent on work or other activities
RP2	**b.** Accomplished less than you would like
RP3	**c.** Were limited in the kind of work or other activities.
RP4	**d.** Had difficulty performing the work or other activities (for example, it took extra effort)
	5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)
RE1	**a.** Cut down on the amount of time you spent on work or other activities
RE2	**b.** Accomplished less than you would like
RE3	**c.** Didn't do work or other activities as carefully as usual
SF1	
	6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered

performed during a typical day. The limitations of each physical activity were classified into 3 categories: "limited a lot," "limited a little," and "not limited at all," and each response yielded a score of 0, 50 or 100, respectively. The final score was determined by summing the scores for the 10 physical activity items and dividing the total by 10. A score lower than 75 on the PF scale of the SF 36 was considered to indicate slowness and weakness, thus counting for 2 points. Exhaustion was measured with vitality scale, consisting of four questions about how the respondent feels and how things have been during the previous 4 weeks as follows: "Did you feel full of pep?", "Did you have a lot of energy?", "Did you feel worn out?", and "Did you feel tired?" The average score for these 4 questions was calculated; exhaustion was indicated if the score was lower than 55, and the patient then received 1 point.

	with your normal social activities with family, frends, neighbors, or groups?
BP1	**7.** How much bodily pain have you had during the past 4 weeks?
BP2	
	8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
	9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks—
VT1	**a.** Did you feel full of pep?
MH1	**b.** Have you been a very nervous person?
MH2	**c.** Have you felt so down in the dumps that nothing could cheer you up?
MH3	**d.** Have you felt calm and peaceful?
VT2	**e.** Did you have a lot of energy?
MH4	**f.** Have you felt downhearted and blue?
VT3	**g.** Did you feel worn out?
MH5	**h.** Have you been a happy person?
VT4	**i.** Did you feel tired?
SF2	
	10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
	11. How TRUE or FALSE is each of the following statements for you?
GH2	**a.** I seem to get sick a little easier than other people
GH3	**b.** I am as healthy as anybody I know
GH4	**c.** I expect my health to get worse
GH5	**d.** My health is excellent

SF-36 RESPONSE CHOICES

1.	Excellent, Very good, Good, Fair, Poor
2.	Much better now than one year ago, Somehwat better now than one year ago, About the same as one year ago, Somewhat worse now than one year ago, Much worse now than one year ago
3.	Yes, limited a lot; Yes, limited a little; No, not limited at all
4. & 5.	Yes, No
6.	Not at all, Slightly, Moderately, Quite a bit, Extremely
7.	None, Very mild, Mild, Moderate, Severe, Very severe
8.	Not at all, A little bit, Moderately, Quite a bit, Extremely
9.	All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the item
10.	All of the time, Most of the time, Some of the time, A little of the time, None of the time
11.	Definitely true, Mostly true, Don't know, Mostly false, Definitely false

SF-36 Scales	Abbreviation	Number of items in scale	Maximum number of items imputed
Physical Health			
Physical Functioning	PF	10	5
Role Physical	RP	4	2
Bodily Pain	BP	2	1
General Health	GH	5	2
Mental Health			
Vitality	VT	4	2
Social Functioning	SF	2	1
Role Emotional	RE	3	1
Mental Health	MH	5	2

Raw scores are calculated as the sum of (re-coded) scale items and transformed to a 0 to 100 scale according to the formula:

$$\text{Transformed score} = \frac{\text{Raw score} - \text{Minimum possible raw score}}{\text{Possible raw score range}} * 100$$

Table 3. Sarcopenia, cachexia, protein-energy wasting and frailty

	Dynapenia	Sarcopenia	Protein-energy wasting	Frailty	Cachexia
Low fat-free mass					X
Fatigue/exhaustion				X	X
Decreased muscle strength	X	X		X	X
Malnutrition			X		X
Abnormal biochemistry			X		X
Low BMI/weight loss			X	X	X
Decreased gait speed	X	X		X	
Decreased muscle mass		X	X		
Decreased physical activity				X	

Table 1. Operational definitions of sarcopenia

Author	Appendicular lean mass	Gait	Physical performance
Baumgartner *et al.* [9]	Appendicular skeletal muscle mass/height^2 >2 SD average of a young reference population is sarcopenic threshold		
Newman *et al.* [10]	A measure of relative LM (LM, kg) was derived by adjusting for fat mass (FM, kg) in addition to height (m)		
Delmonico *et al.* [11]	Appendicular skeletal muscle mass/height^2 categorized by sex-specific lowest 20% of the health aging and body composition study		
European Working Group on Sarcopenia in Older People [5]	Low appendicular skeletal muscle mass using the Baumgartner's criteria (ASM/height^2 ≤5.45 kg/m^2)	Gait speed ≤0.8 m/s	Grip strength cutoff of 20 kg (via dynamometer)
European Society for Clinical Nutrition and Metabolism Special Interest Group [12]	>2 SD average of a young reference population for appendicular skeletal muscle mass/height^2	Gait speed ≤0.8 m/s	
International Working Group on Sarcopenia [13]	Appendicular skeletal muscle mass/height^2 categorized by sex-specific lowest 20% of the health aging and body composition study	Gait speed ≤1 m/s	
Foundation of NIH Sarcopenia Project [6]	Appendicular lean mass Men: <0.789 Women: <0.512	Gait speed ≤0.8 m/s	Grip strength Men: <26 kg Women: <16 kg

Table 5. Examples of recent exercise studies performed with those who have chronic kidney disease

Reference		Days/ weeks	Duration/ day	Duration/ total (week)	Intensity	Outcome
Van Craenenbroeck *et al.* [43]	Aerobic	Daily	4, 10-min bouts	12	90% heart rate at anaerobic threshold	↑ VO2peak ↑ QOL ↔ Vascular function
Gregory *et al.* [44]	Aerobic	3×	Up to 55 min	48	50–60% VO2peak	↔ IGF ↔ Kidney function ↔ VO2peak ↔ BMI ↑ VO2peak
Headley *et al.* [45]	Aerobic	3×	Up to 55 min	16	50–60% VO2peak	↑ VO2peak ↔ Vascular function
Watson *et al.* [46]	Resistance	3×	3 sets of 10 reps	8	70% predicted max	↑ Muscle volume ↑ Vcross-sectional area (8%) ↑ Strength
Balakrishnan *et al.* [47]	Resistance	3×	3 sets of 8 reps		80% 1 rep max	↑ mtDNA copy number

QOL, Quality of Life; IGF, Insulin-like growth factor.

Table 3. Exercise Recommendations for CKD and ESRD Patients

Type	Frequency	Intensity	Time
Aerobic (cycling, walking, swimming)	wk 1-2: 2×/wk wk 3-5: 3×/wk	wk 1-2: moderate (RPE 11-13 on scale of 6-20), 55%-70% max HR wk 3-5: moderate (RPE 11-16), 55%-90% of max HR	20 min/d (or bouts of 3-5 min of intermittent exercise)
Resistance (multijoint exercises affecting >1 muscle group and targeting agonist and antagonist muscles)	2×/wk	60%-70% of 1-RM or 5RM	Minimum of 1 set of 10-15 repetitions; gradually increase to 2-4 sets choose 8-10 different exercises to work major muscle groups; rest 2-3 min between sets; rest ≥ 48 h between sessions
Flexibility (combine with aerobic and resistance when possible)	5×/wk		10 min/d

Note: Special considerations: for patients using β-blockers, use RPE instead of HR. Patients using vasodilators (eg, α-blockers or calcium channel blockers) would require an extended cool-down period after exercise. Arms with active dialysis access can be exercised during nondialysis times. Peritoneal dialysis patients may have more effective exercise with smaller dwell volumes, although fluid in the abdomen is not a contraindication to exercise. Exercise recommendations based on Smart et al,[96] Koufaki et al,[97] and Thompson et al.[101]

Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease; HR, heart rate; max, maximum; RPE, relative perceived exertion; RM, repetition maximum.

Study	Population	Intervention/Control	Results	Monitoring	Adherence/Adverse Events
		Control: usual care			
Kouidi et al[125] (2009)	ESRD on dialysis (n = 63); excluded DM	Intervention: 10 mo supervised in-center aerobic and resistance exercise; aerobic in-center cycling during dialysis 3×/wk 90 min/session during first 2 h of HD; target RPE of 13 of 20 on Borg scale; heart rate on exercise 60%-70% of maximum; isometric & isotonic resistance exercise of abdomen and lower limbs 30 min while in seated position gradual increase to 3 sets of 15 repetitions per exercise with goal RPE of 13 Control: not specified	Exercise time; Vo_{2peak}; left ventricular ejection fraction; improved heart rate variability	2 exercise trainers specialized in physical rehabilitation supervised training sessions; continuous heart rate monitoring telemetrically during exercise	88.3% adherence; 59 completed study (2 discontinued in training and 2 lost to follow-up in control); no complications
Ouzouni et al[126] (2009)	ESRD on dialysis (n = 35); excluded DM	Intervention: 10 mo supervised aerobic and resistance training during first 2 h of dialysis; aerobic cycling exercise for 30 min targeting RPE of 13-14 on Borg scale; resistance exercise for abdominal and lower-limb muscles; Control: not specified	Exercise time; Vo_{2peak}; physical component score of SF-36; QoL index and life satisfaction index; decreased self-reported depression (Beck Depression Inventory)	Supervised exercise sessions by 2 exercise physiologists	2 participants dropped out (reason not given) and unclear which group; no adverse events
Matsumoto et al[127] (2007)	ESRD on HD (n = 55, 22 training, 33 control)	Intevention:12 mo supervised in-center cycling performed predialysis; started at 2-5 min/session until 20 min of continuous cycling/session; increased intensity based on RPE with heart rate check targeting 60%-70% peak heart rate Control: usual care (none)	QoL: Physical Functioning, Role-Physical, Vitality, Mental Health of SF-36; muscle mass (creatinine generation rate); greater serum albumin	Not indicated	Adherence not recorded; 6 patients dropped out (5 in training and 1 in control); no adverse events

Abbreviations: ACSM, American College of Sports Medicine; BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; METS; metabolic equivalents; PD, peritoneal dialysis; QoL, quality of life; RPE, relative perceived exertion; SF-36, 36-Item Short Form Health Survey; VO_{2peak}, peak oxygen consumption.

Table 1. The Canadian Society of Health and Aging CFS

CFS Score	Interpretation
1	Very fit: robust, active, energetic, well motivated, and fit; fittest in their age group
2	Well: without active disease but not as fit as those in category 1
3	Well: with treated comorbid disease
4	Apparently vulnerable: not dependent but has symptoms from comorbid disease (such as being slowed up)
5	Mildly frail: limited dependence on others for instrumental activities of daily living
6	Moderately frail: help is needed for instrumental activities of daily living and activities of daily living
7	Severely frail: completely dependent on others for instrumental activities of daily living and activities of daily living or terminally ill

CFS, Clinical Frailty Scale.

5. Frailty and the kidney transplant recipient

Three studies have investigated frailty in kidney transplant recipients. McAdams De-Marco et al. (McAdams-DeMarco, Law, & Salter, 2013b) demonstrated that incident frailty increased the risk of hospital readmission amongst kidney transplant recipients (Relative Risk = 1.61, 95% CI 1.18–2.19). This risk persisted after adjustment for age, gender, co-morbidity, time spent on dialysis and donor factors. Another study by Garonzik-Wang et al. (Garonzik-Wang, Govindan, & Grinnan, 2012) showed that frailty was an independent risk factor for delayed graft function (RR = 1.94, 95% CI 1.13–3.36). A second study by McAdams De-Marco et al. (McAdams-DeMarco, Isaacs, & Darko, 2015) investigated the change in frailty status after kidney transplantation. It found that the prevalence of frailty in the cohort decreased at 3 months of follow up and that patients who were frail before transplantation were twice as likely to have improvement in frailty score after transplantation (HR: 2.55 [95% CI: 1.71–3.82]) (McAdams-DeMarco, Isaacs et al., 2015).