

December 5, 2025

ACPN x TSN 2025

Symposium: “Aging Gracefully, Is It Possible in Dialysis Patients?”

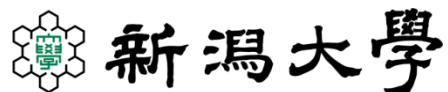
Prof. Philip Kam-Tao Li and Prof. Chia-Der Chao

Clinical assessment and practice gap of Frailty in dialysis patients

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APCN x TSN 2025 Disclosure

Suguru Yamamoto

Lecture Fees:

Ono Pharmaceutical Co., Ltd., Kaneka Corporation, Kissei Pharmaceutical Co., Ltd., Kyowa Kirin Co., Ltd., Ono Pharmaceutical Co., Ltd., Sanwa Kagaku Kenkyusho Co., Ltd., Fuso Pharmaceutical Industries, Ltd.

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Toagosei Co., Ltd., Kaneka Corporation, Kureha Corporation, Kyowa Kirin Co., Ltd., Toray Medical Co., Ltd.

CASE REPORT



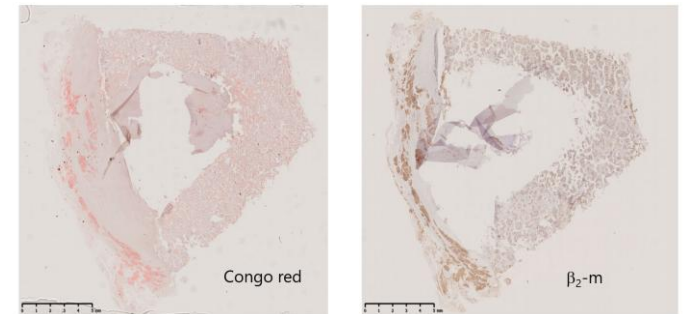
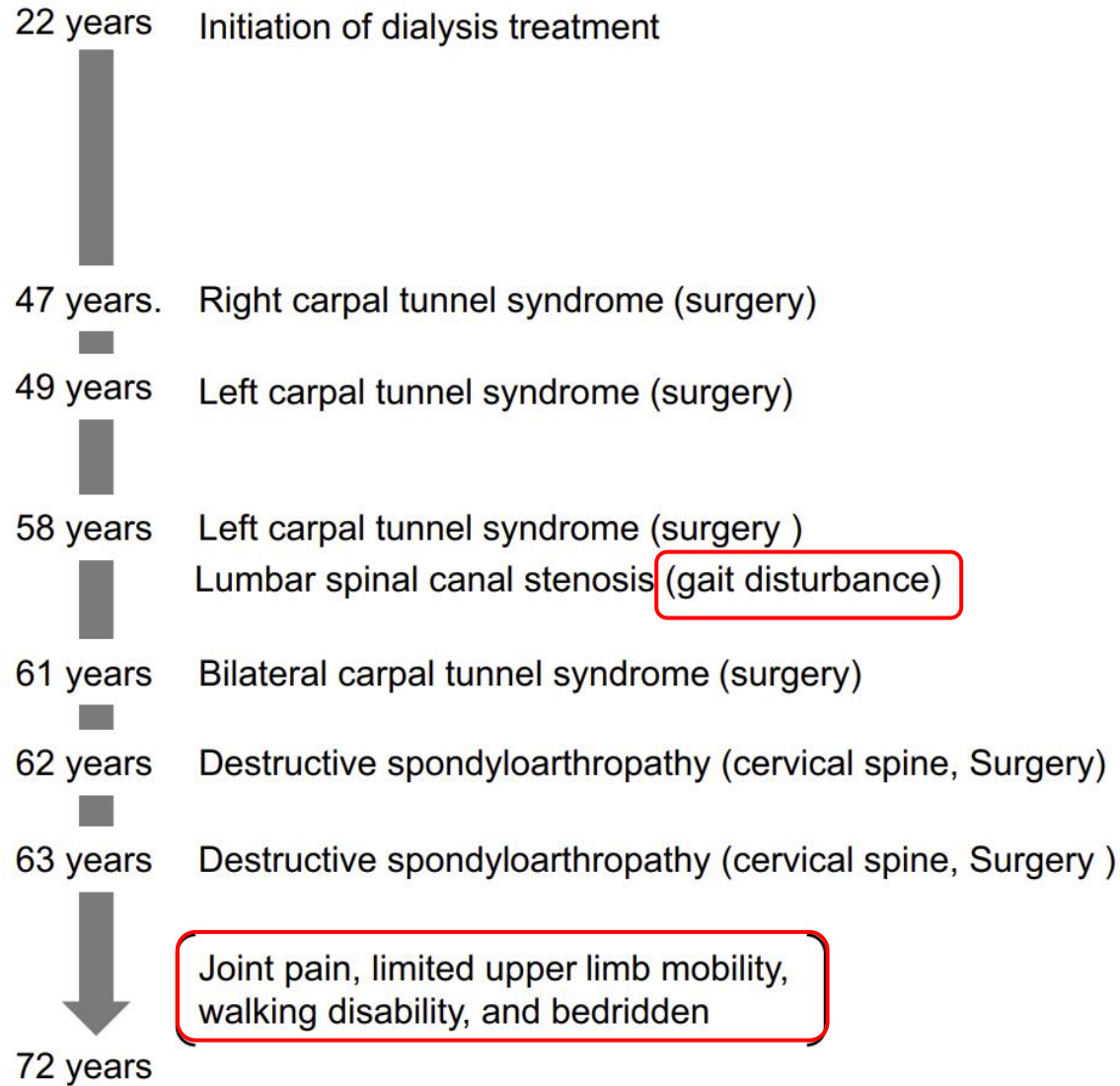
An end-stage kidney disease patient undergoing dialysis treatment for 50 years with dialysis-related amyloidosis in multiple organs

Toru Ito¹ · Takashi Kato² · Suguru Yamamoto¹ · Hisaki Shimada³ · Hideyuki Kabasawa⁴ · Shin Goto¹ · Riuko Ohashi² · Ichiei Narita¹

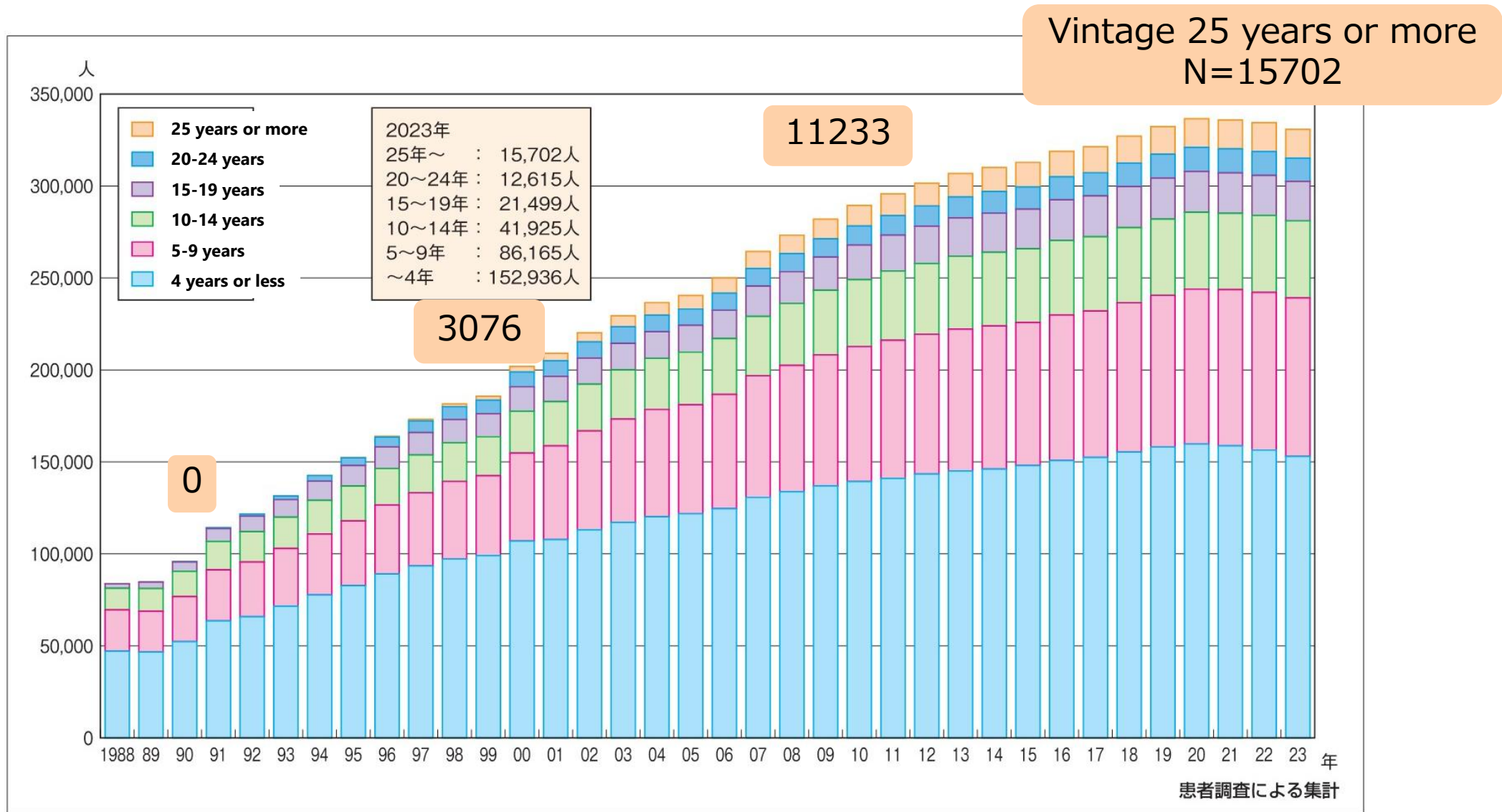
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Impaired ADL for 50 years dialysis treatment

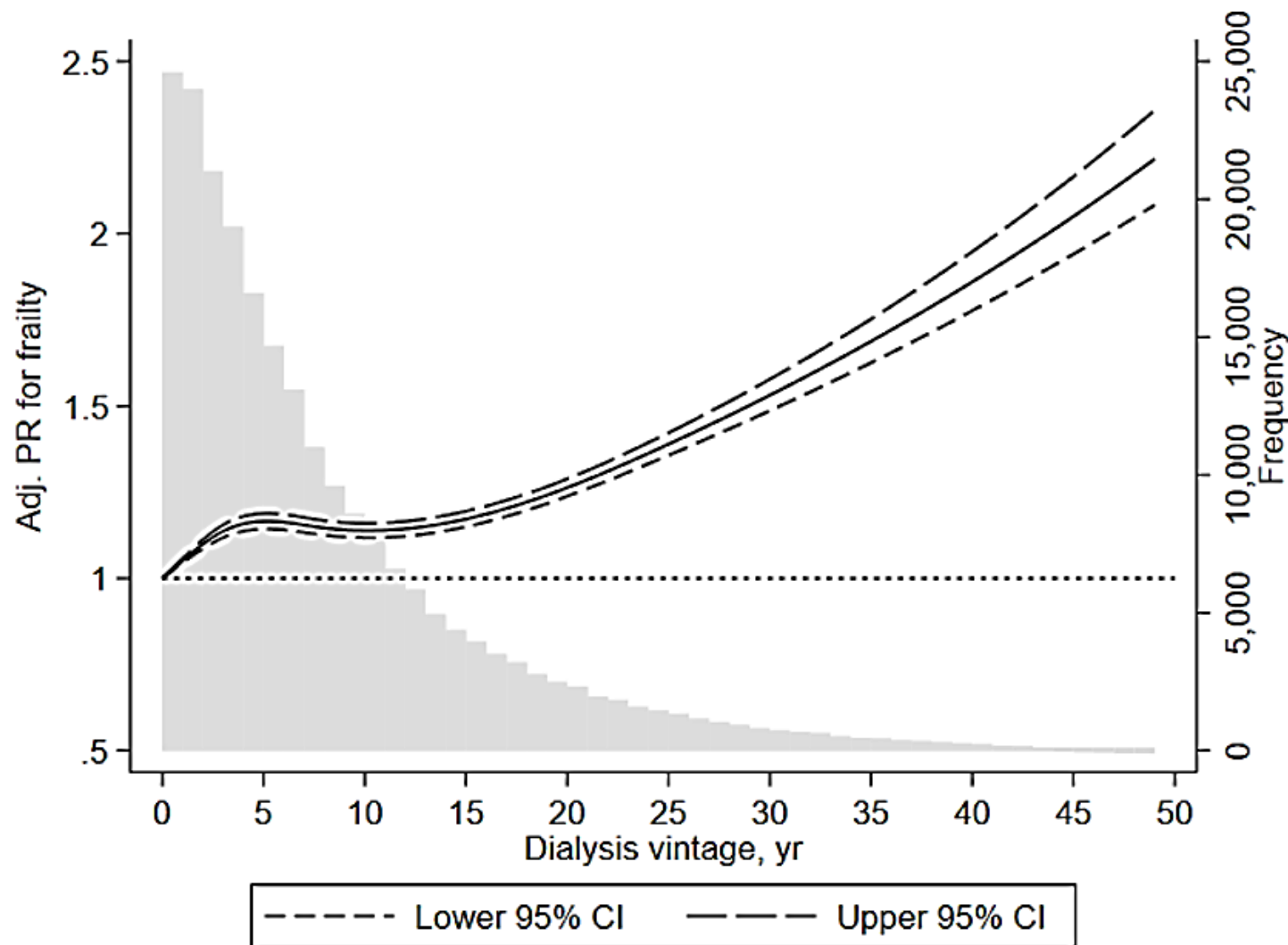


Increasing patients with long-term dialysis



一般社団法人日本透析医学会「わが国の慢性透析療法の現況（2023年12月31日現在）」

Frailty and dialysis treatment



Adjusted for age, sex, corrected calcium, phosphorus, parathyroid hormone, β 2MG, creatinine index, albumin, diabetes, dementia, ischemic heart disease, cerebral hemorrhage, cerebral infarction, limb amputation, carpal tunnel syndrome, hip fracture, and vascular access type.

ECOG PS

0	Normal activity	
1	Symptomatic and ambulatory; cares for self	
2	Ambulatory >50% of time; occasional assistance	
3	Ambulatory ≤50% of time; nursing care needed	
4	Bedridden	

Frailty

West H, JAMA Oncol, 2015

Yamamoto S, Am J Kidney Dis, 2024

Frailty-related clinical factors in dialysis patients

	PR	95% CI	
Dialysis vintage			
<5 years	Ref.		
5- <10 years	1.06	1.05-	1.08
10- <20 years	1.10	1.08-	1.11
20- <30 years	1.14	1.10-	1.17
≥30 years	1.67	1.60-	1.73
Demographics			
Age (year)	1.02	1.02-	1.02
Male sex	1.20	1.19-	1.22
Biomarkers			
Albumin (per mg/L)	0.72	0.71-	0.73
Cr index (per mg/kg/day)	0.85	0.85-	0.85

	PR	95% CI	
Comorbidities			
Diabetes	1.23	1.21-	1.24
Dementia	1.62	1.60-	1.64
Ischemic heart disease	1.03	1.02-	1.05
Cerebral hemorrhage	1.40	1.37-	1.42
Cerebral infarction	1.34	1.32-	1.35
Limb amputation	1.55	1.51-	1.59
Hip fracture	1.21	1.19-	1.23
Carpal tunnel syndrome	1.06	1.02-	1.10

Yamamoto S, Am J Kidney Dis, 2024

Contributions to frailty in patients on dialysis

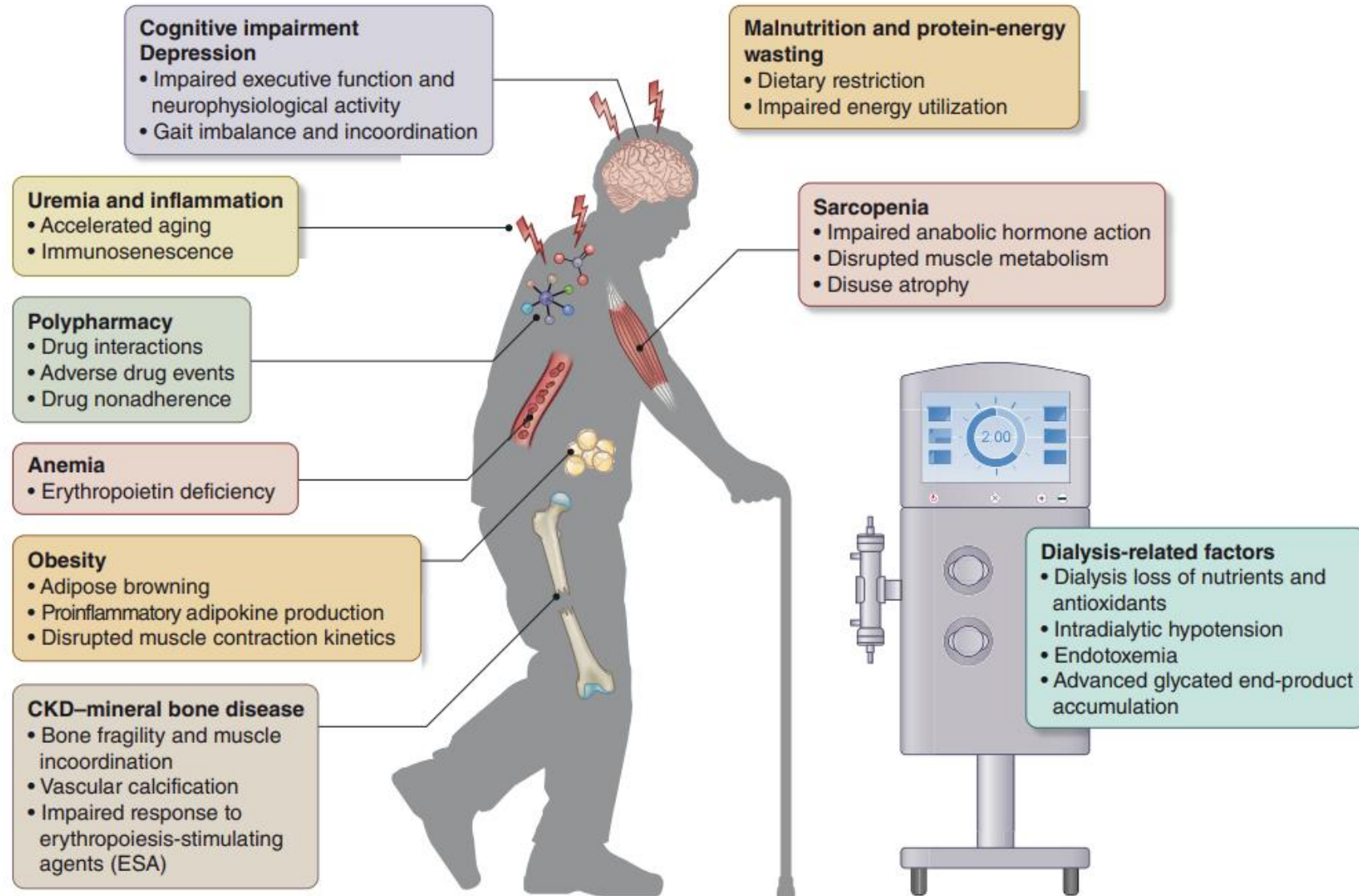


Figure 2 | Contributors to frailty in patients on dialysis. CKD, chronic kidney disease.

Table 2 | Commonly used diagnostic tools for frailty: physical performance-based

Assessment tool	Description	Advantages	Disadvantages
Fried phenotype ³⁰	Criteria • Unintentional weight loss >10 lbs per year • Exhaustion • Physical inactivity with reduced energy expenditure • Prolonged walking time • Weakness (reduced grip strength) Interpretation: • Fulfilling 2 criteria: pre-frail • Fulfilling ≥3 criteria: frail	• Objective • Non-operator dependent • Widely used • Often regarded as the gold standard of diagnosis	• Severity cannot be graded • Labor-intensive • Requires dedicated tool, such as dynamometer • Time-consuming • Requires direct patient contact • Psychosocial aspect is not captured
Short Physical Performance Battery test ³¹	Criteria • Balance test ■ Side-by-side stand ■ Semi-tandem stand ■ Heel-to-toe stand • Gait-speed test • Chair stand test	• Objective • Non-operator dependent • Easy to use	• Not designed to screen frailty • Focus is on functional aspect only • Requires dedicated tool • Upper-limb function is not evaluated • Ceiling and floor effects • Time-consuming • Requires direct patient contact • Mental aspect is not captured • Cutoff requires validation

Fried phenotype : 5 criteria

Short physical performance battery : 3 criteria

Table 3 | Commonly used diagnostic tools for frailty: cumulative deficits-based model

Assessment tool	Description	Advantages	Disadvantages
Clinical Frailty Scale (CFS) ³²	9-point scale from 1 (very fit) to 9 (terminally ill) Interpretation: • Grade 1: mild fit • Grade 6: moderately frail • Grade 7-9: severely frail	• Easy to use • More-comprehensive evaluation • Does not require dedicated tools • Can be performed by any healthcare professional • Grades frailty severity • Easy to deliver • Comprehensive evaluation of different domains • Does not require direct patient contact	• Subjective assessment (assessor-dependent) • Diagnosed perceived frailty but not measured frailty • Requires direct patient contact
Groningen Frailty Indicator (GFI) ³³	15 dichotomous items Assess different domains, such as mobility, vision, hearing, nutrition, comorbidity, cognition, psychosocial, and physical fitness Total score from 0 (no frailty) to 15 (completely disabled) Interpretation: Frail: total score ≥ 4	• Simple and easy • Quick to deliver • Assessor training not required • Does not require face-to-face contact	• Does not stage severity • Subjective, potential bias by subject's affective functioning
FRAIL Scale ³⁴	Contains 5 domains: • Fatigue • Resistance • Ambulation • Illness • Loss of weight Interpretation: • 1-2 points: prefrail • ≥ 3 points: frail	• Simple and easy • Quick to deliver • Assessor training not required • Does not require face-to-face contact	• Subjective • Weighing of each component depends on center and/or population studied • Disregard social aspects • Does not grade severity
Edmonton Frail Scale (EFS) ³⁵	Contains 9 domains with 11 items: • Cognition • General health status • Functional independence • Polypharmacy • Nutrition • Mood • Continence • Functional performance Interpretation: • 6-7 points: vulnerable • 8-9 points: mildly frail • 10-11 points: moderately frail • 12-17 points: severely frail	• Combination of subjective and objective assessment • Captures different domains, such as cognition and medication use • Captures social aspect • Grades severity	• Assessor training required • Requires direct contact
Frailty Score ³⁶	30 dichotomous items that cover various aspects of physical functioning and self-care capability Interpretation: • 6-8 points: mildly frail • 9-11 points: moderately frail • 12 points: severely frail	• Multidimensional • Easy to administer • Can be delivered by remote contact	• Disregards objective functional part • Validation for specific population required

Clinical frailty scale : 1 scale, but subjective

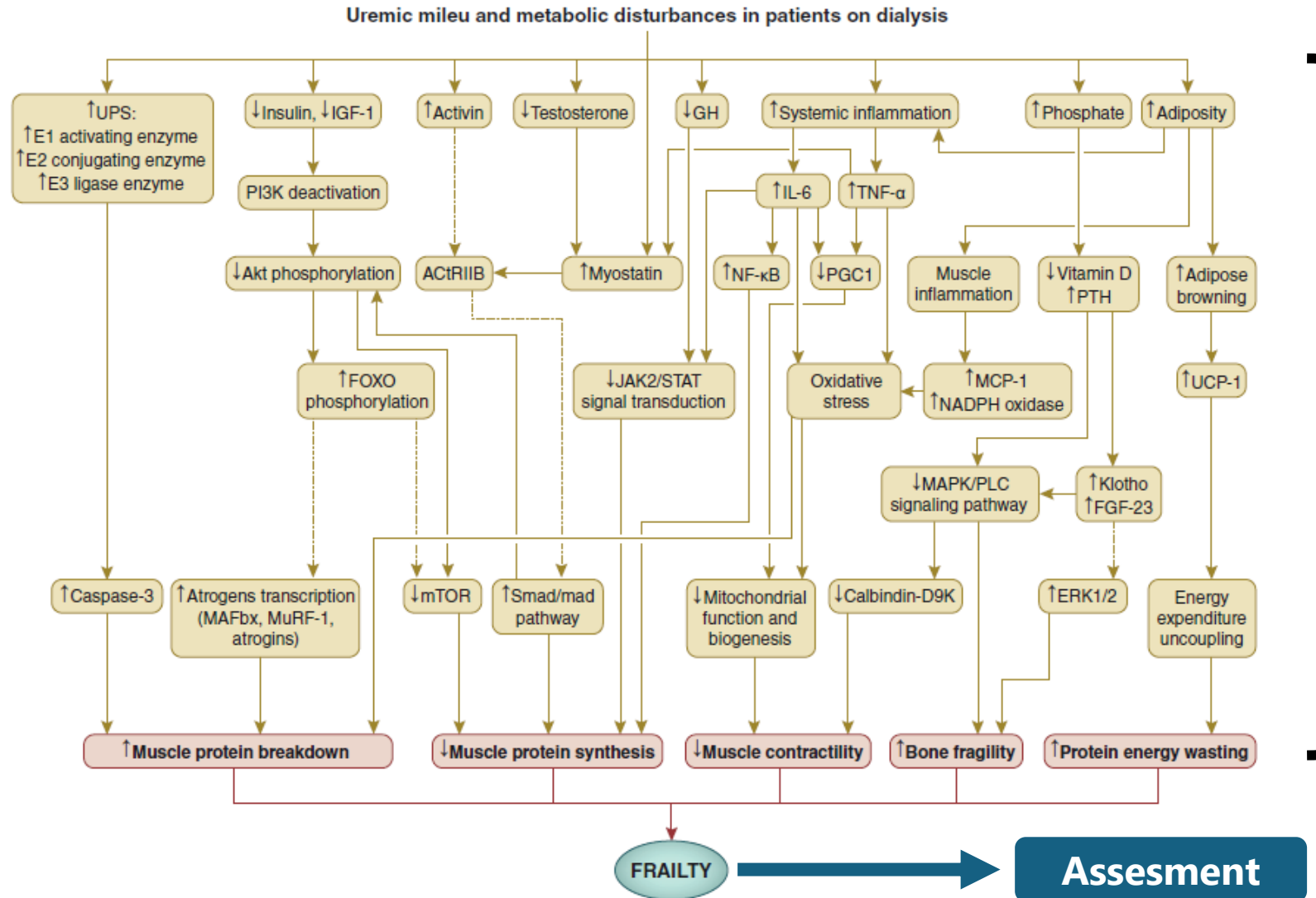
Groningen frailty indicator : 15 items

FRAIL scale : 5 domains

Edmonton frail scale : 9 domains with 11 items

Frail score : 30 items

Pathophysiology of frailty in patients on dialysis

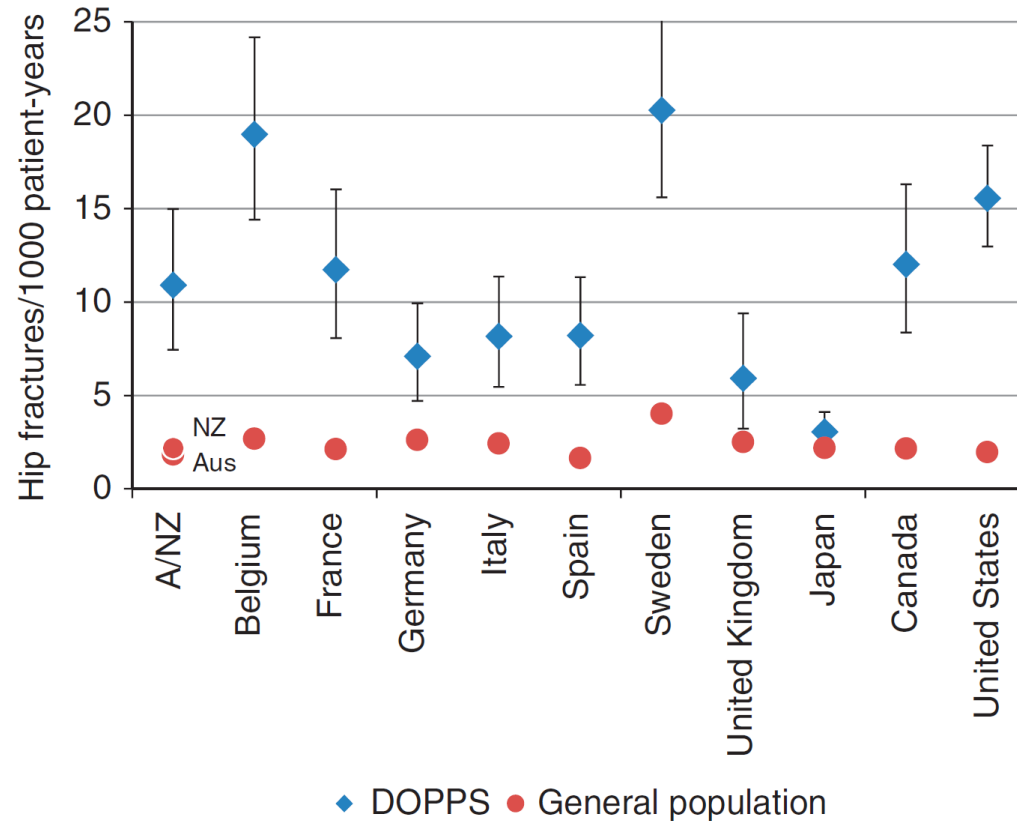


CKD-related systemic disorders are often under-recognized and undertreatment

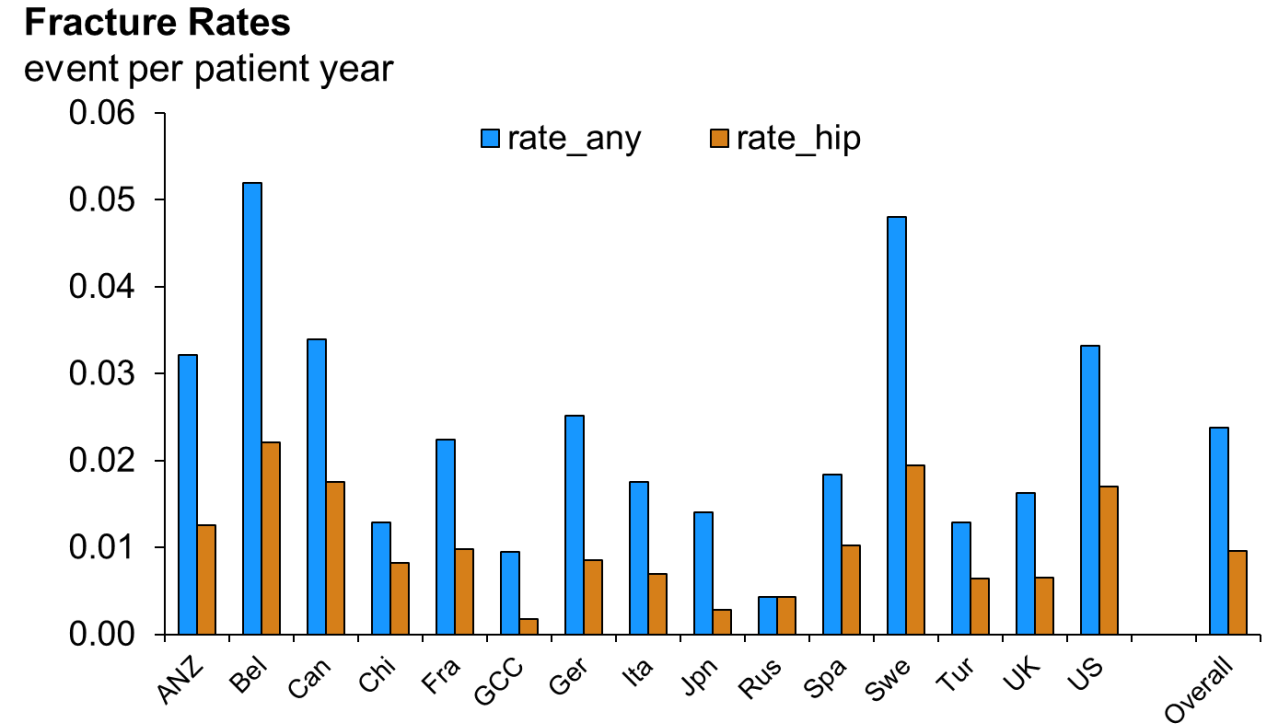
PTH and fracture

β2-m and amyloidosis

Fractures in patients with dialysis

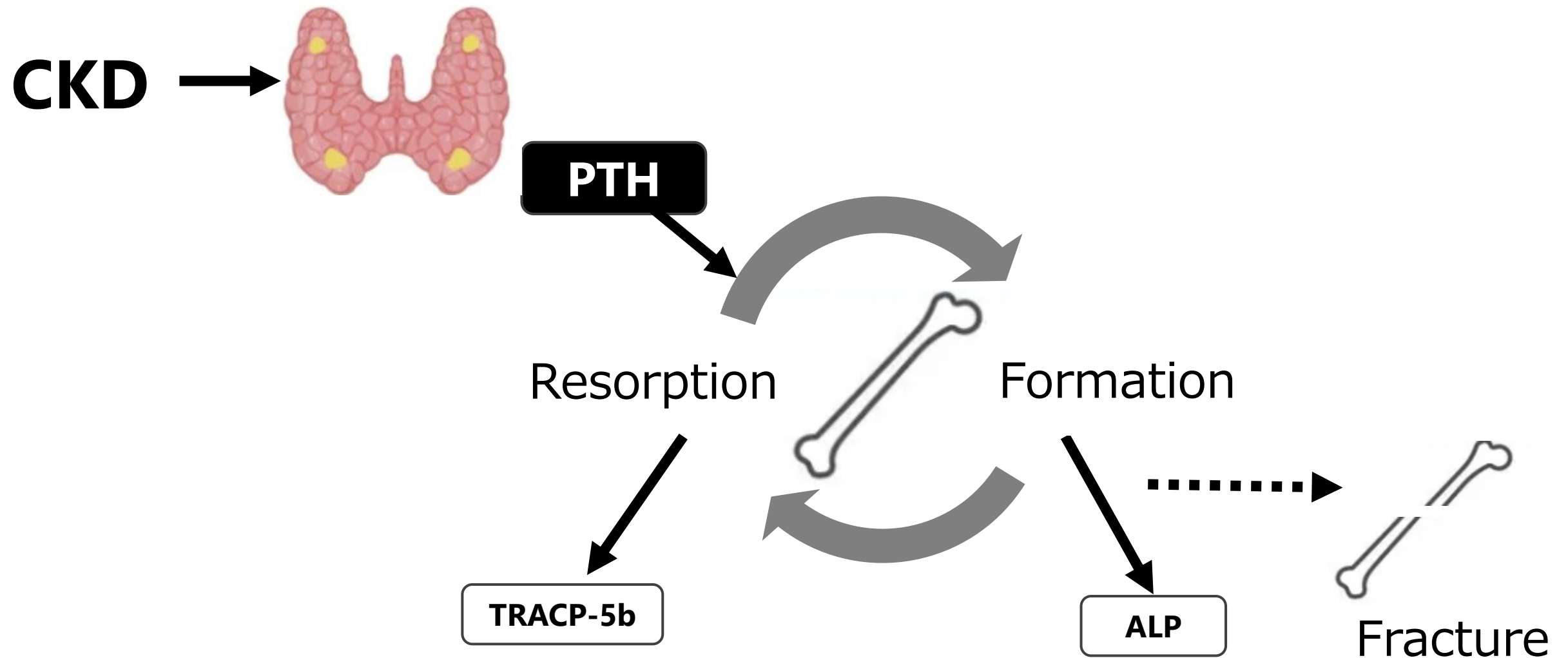


Tentori F, Kidney Int 2013



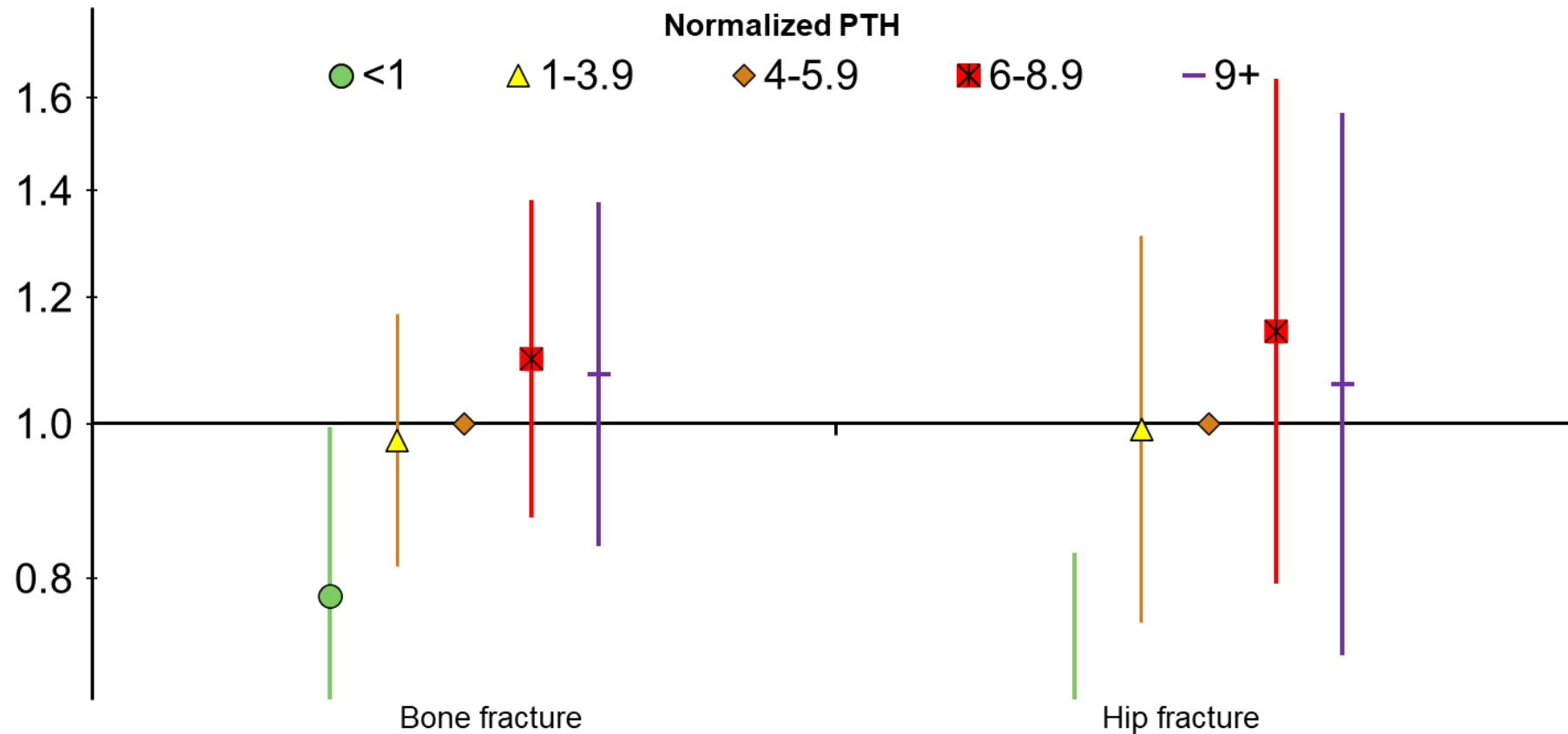
Komaba H, J Bone Miner Res, 2023

Secondary hyperparathyroidism

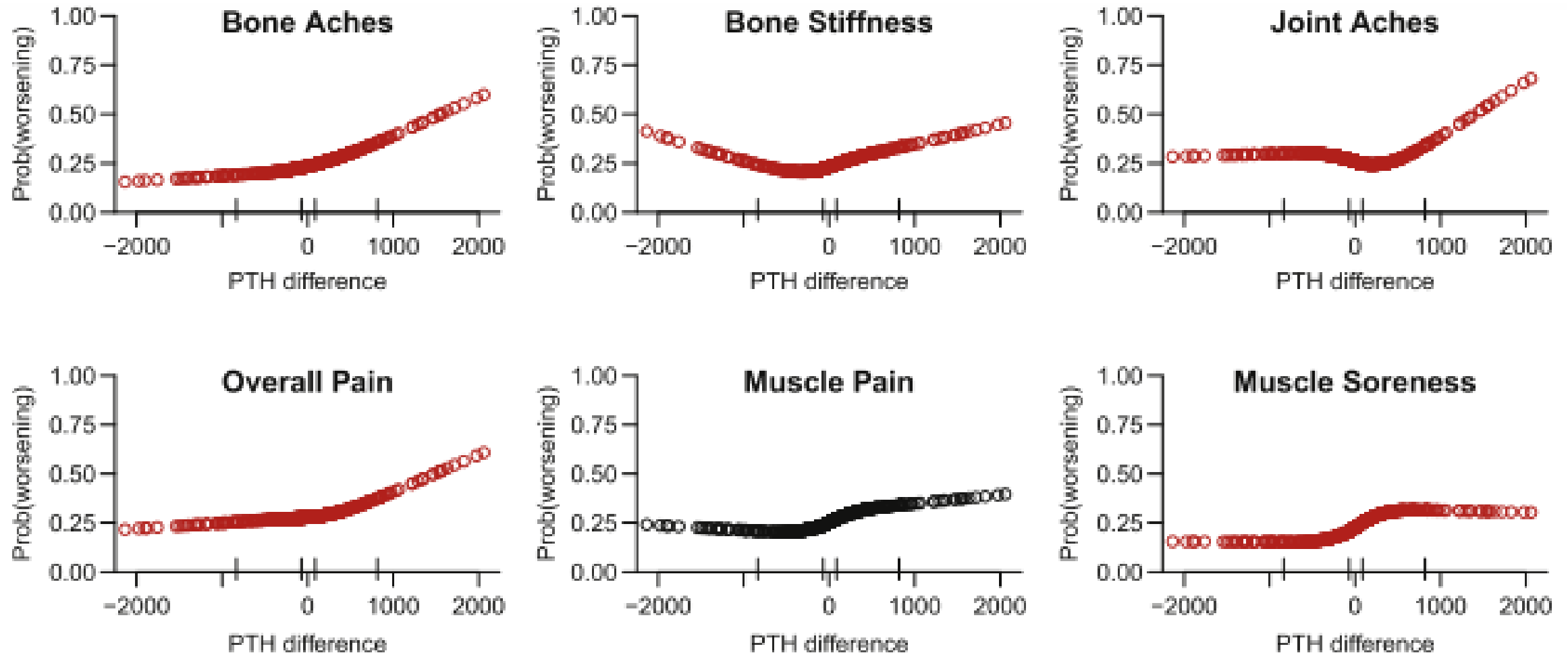


PTH and fractures in patients with dialysis

Hazard Ratio (95% CI)



PTH and osteoarticular symptoms



PTH and weight loss, association with frailty?

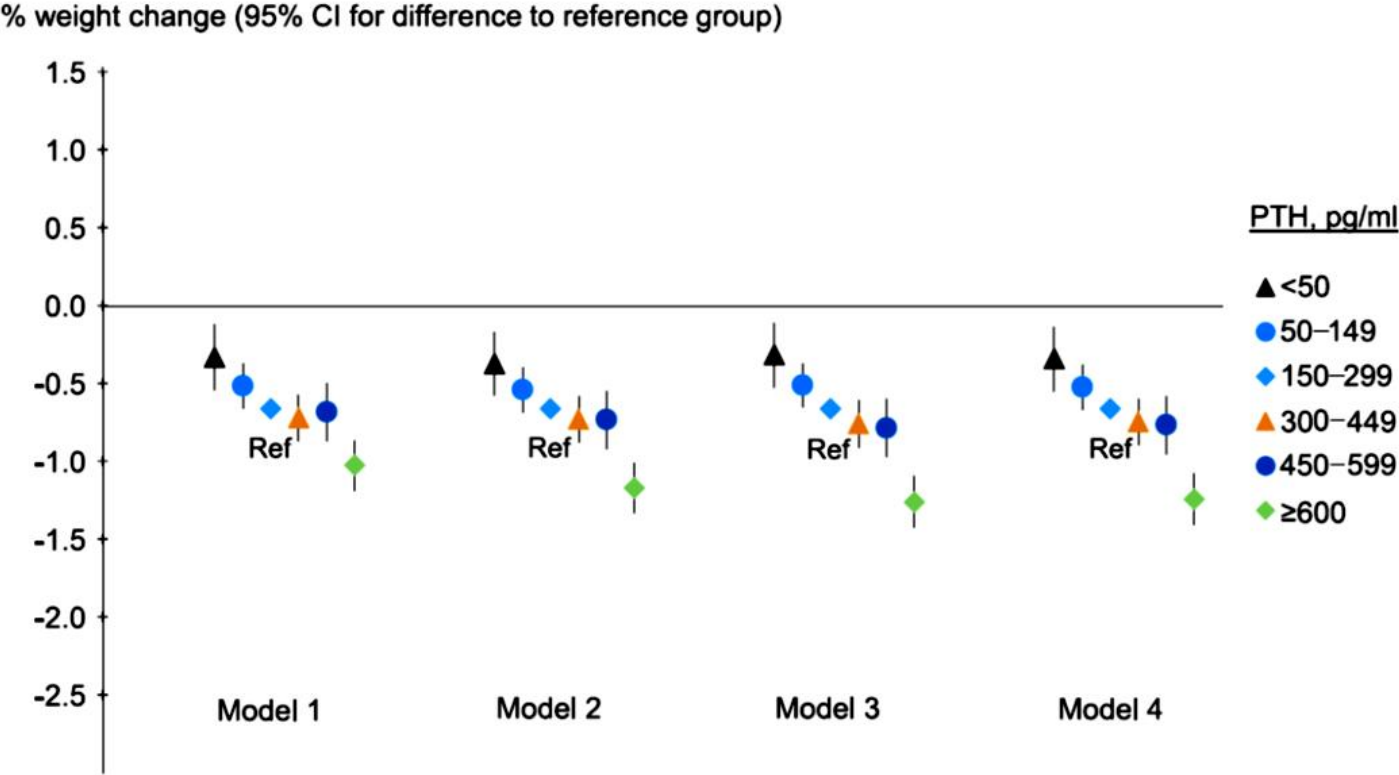


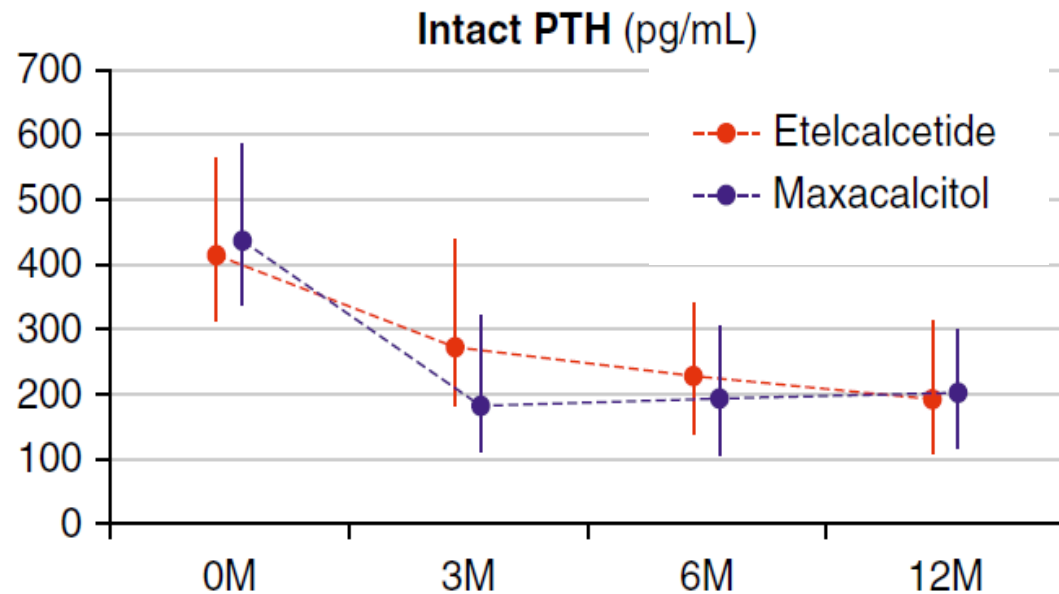
Figure 3 Association of baseline PTH with 12-month percent weight change. PTH, parathyroid hormone; Ref, reference. Model 1 adjusted for country, study phase, and electronic health record data source (US Phases 4–6 only), accounting for facility clustering. Model 2 adjusted for covariates in Model 1 plus age, sex, time on dialysis, 13 comorbid conditions, single-pool *Kt/V*, and dry weight. Model 3 adjusted for covariates in Model 2 plus albumin, haemoglobin, creatinine, calcium, and phosphorus. Model 4 adjusted for covariates in Model 3 plus calcium-based binder, sevelamer, lanthanum, other phosphate binders, active vitamin D derivatives, and calcimimetics. The *P* value for trend was <0.001 for each model. The mean actual weight change was shown for the reference group, and other groups were plotted relative to the reference group based on adjusted model results.

PTH-lowering treatment

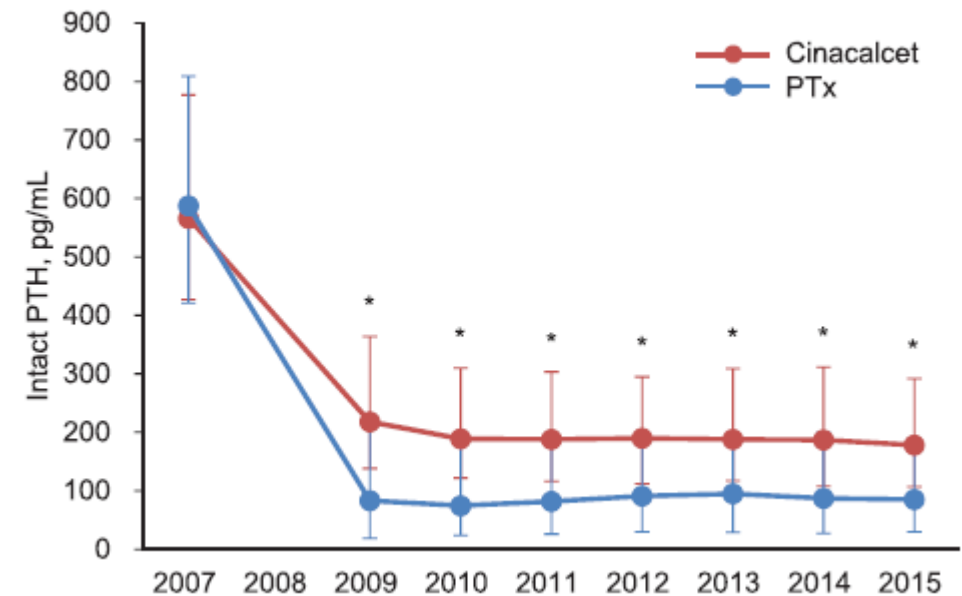
Calcimimetics

Vitamin D

Parathyroidectomy

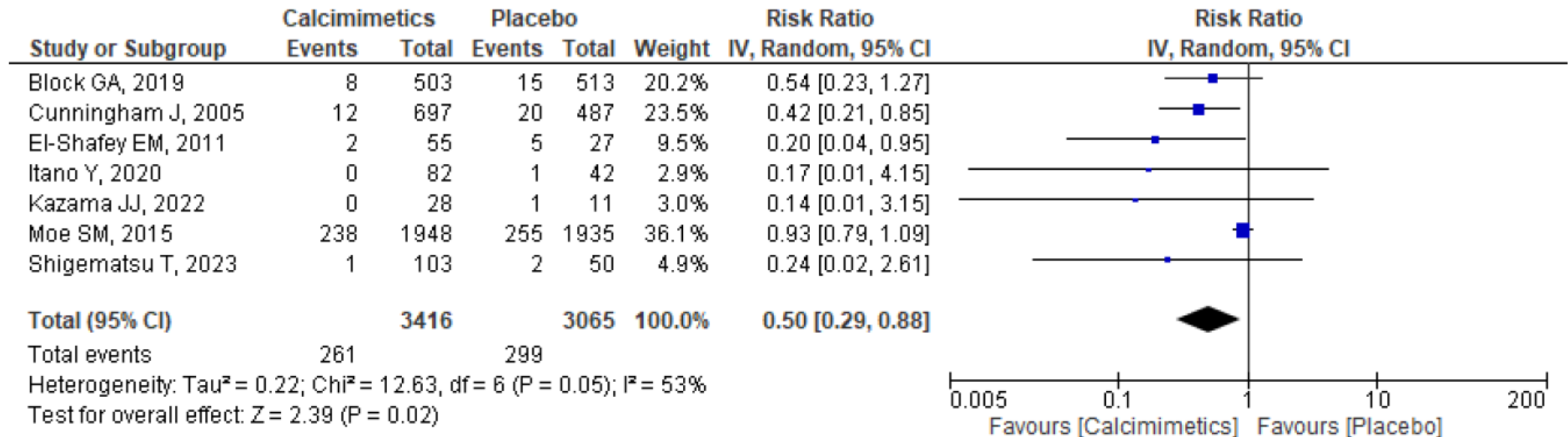


Shoji T, Clin J Am Soc Nephrol, 2021



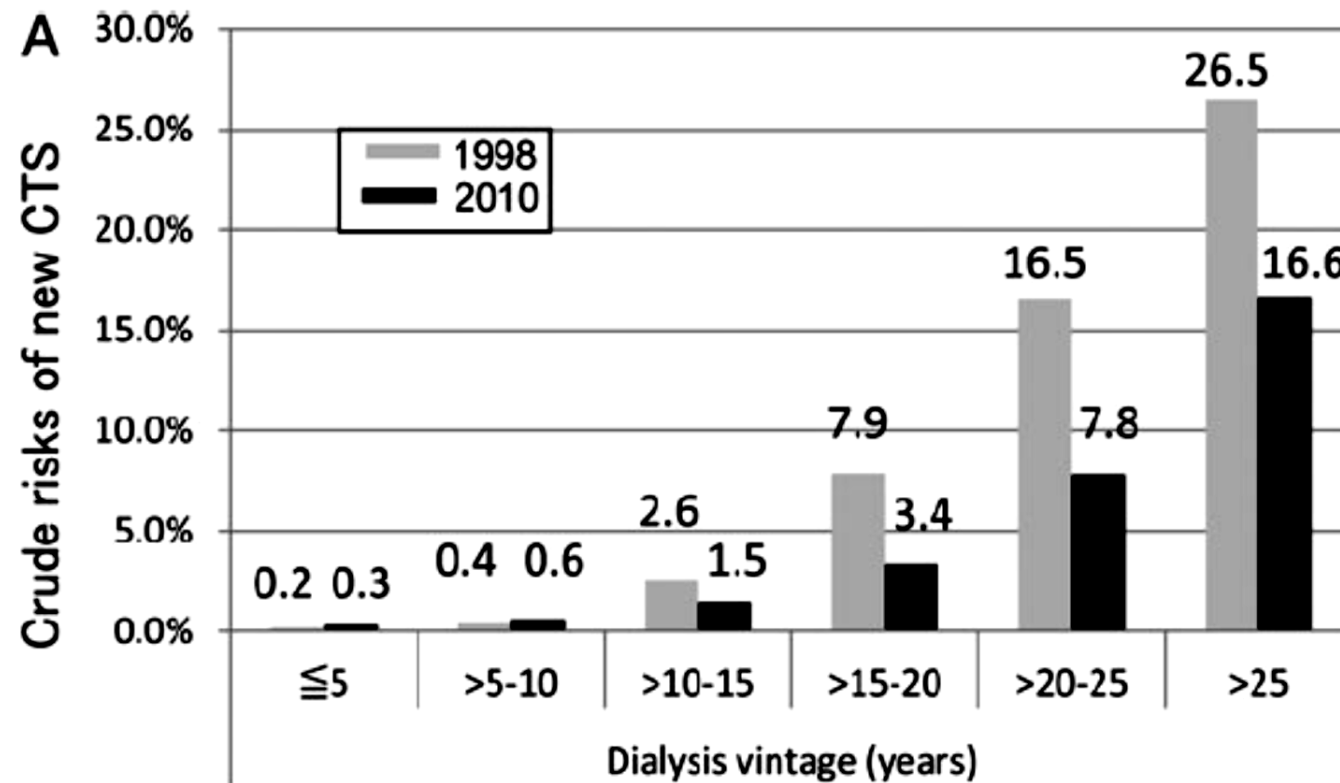
Komaba H, J Clin Endocrinol Metab, 2022

Effect of calcimimetics on fracture prevention

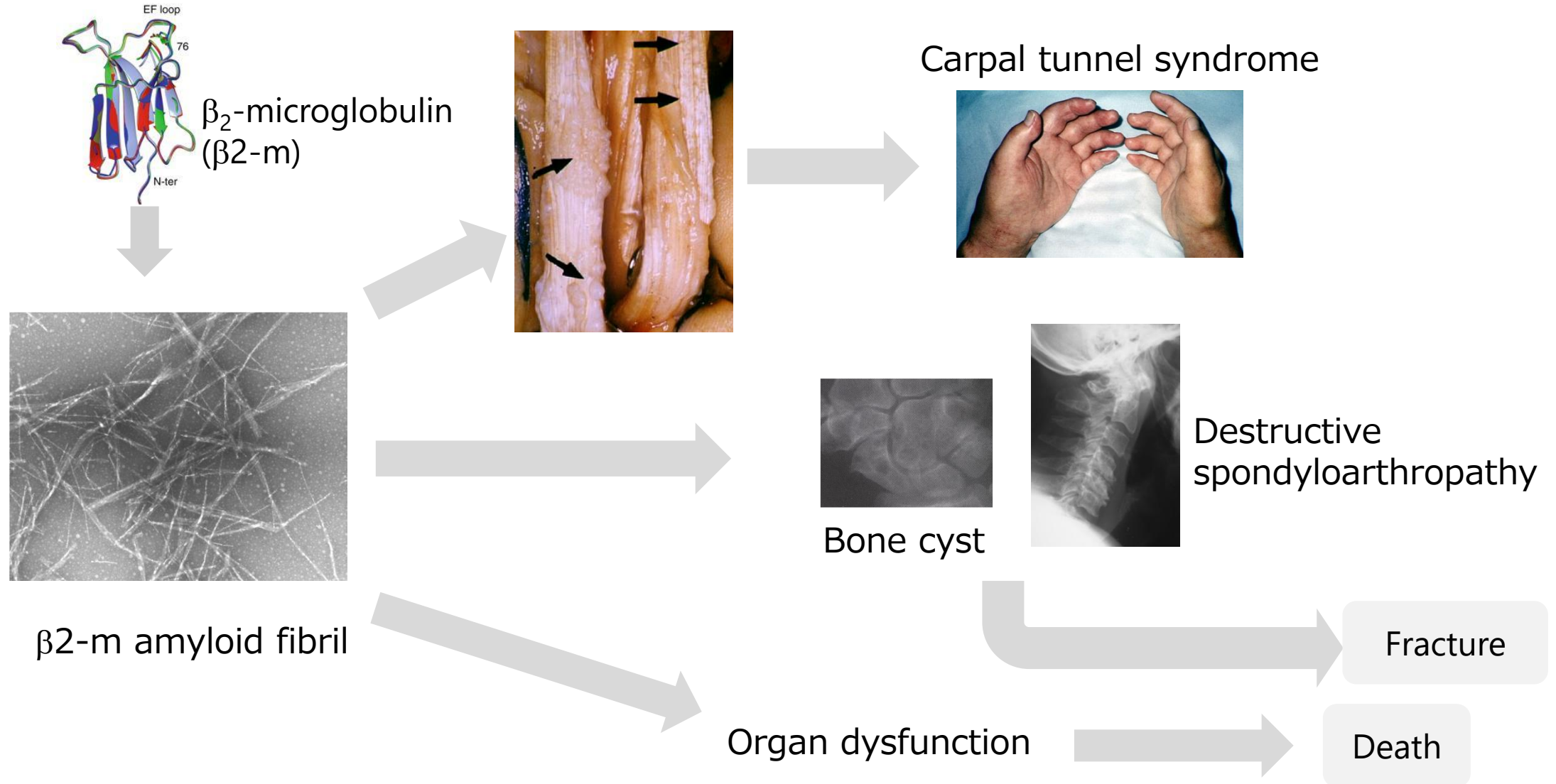


Wakamatsu T, Yamamoto S, *J Bone Mine Metab*, 2024

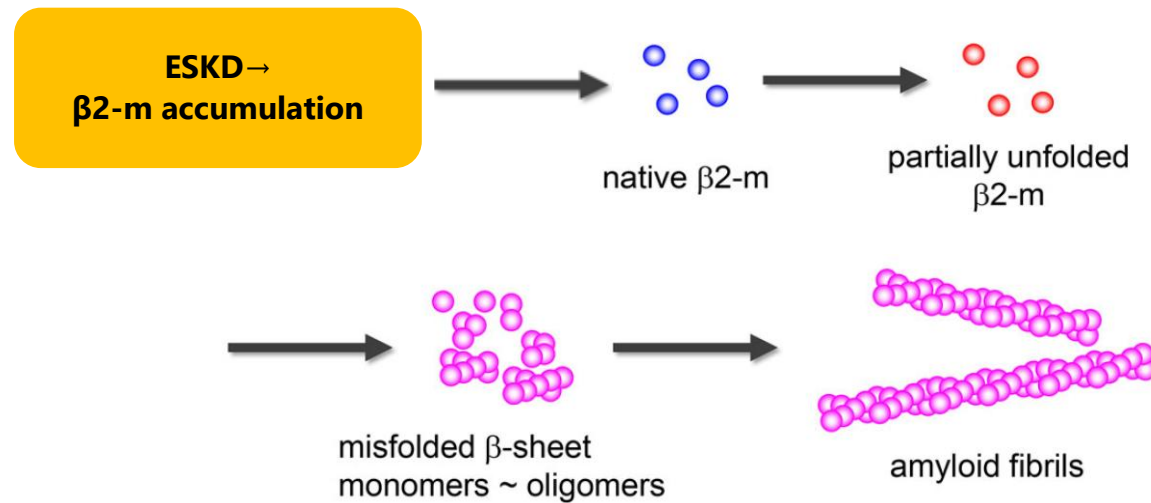
Carpal tunnel syndrome in patients with dialysis treatment in Japan



Dialysis-related amyloidosis



β 2-m amyloid fibril formation and molecular interaction



Naiki H, *Pathol Int*, 2020

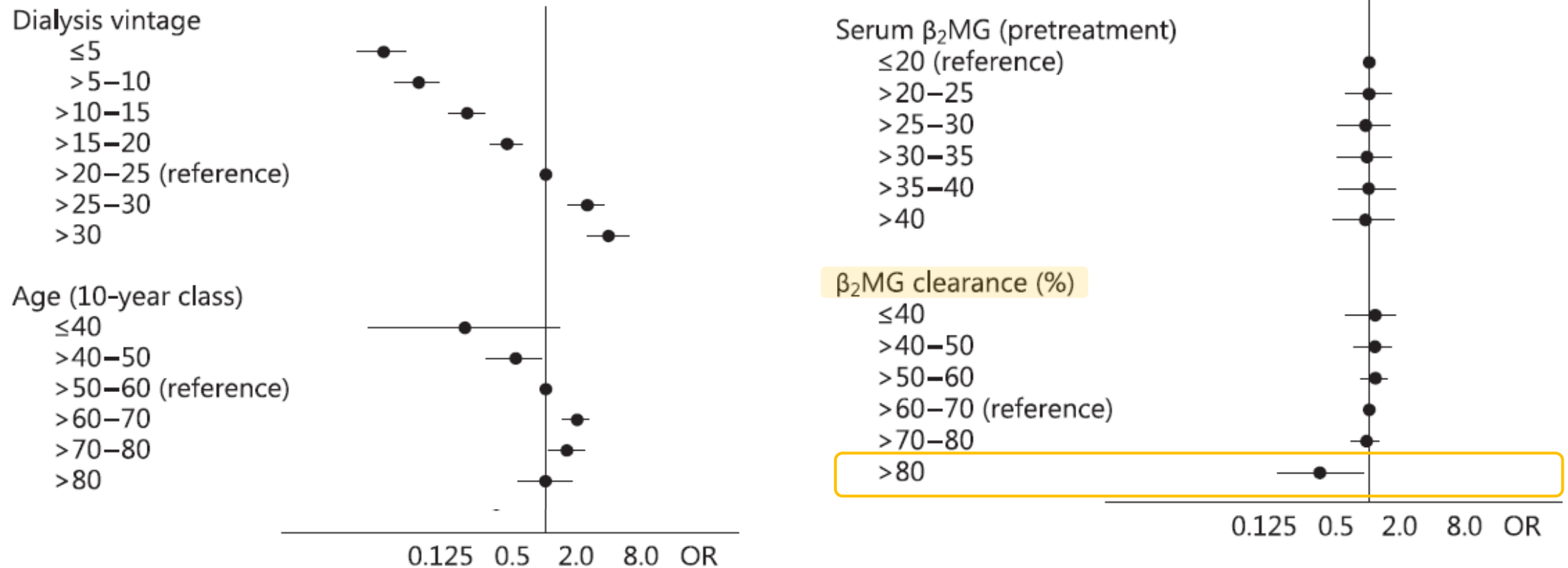
Accelerate

Proteoglycan	<i>Kidney Int</i> (2003)
Glycosaminoglycan	<i>J Am Soc Nephrol</i> (2004)
Sodium dodecyl sulfate	<i>Biochemistry</i> (2004)
Lysophosphatidic acid	<i>Nephrol Dial Transplant</i> (2008)
Non esterified fatty acid	<i>Biochem J</i> (2008)
Type 1 collagen	<i>J Biol Chem</i> (2008)
Polyphosphate	<i>PNAS</i> (2019)
Uremic serum	<i>Nat Commun</i> (2022)

Inhibition

AGE	<i>Amyloid</i> (1999)
α_2 -macroglobulin	<i>J Biol Chem</i> (2011)
Albumin	<i>Nat Commun</i> (2022)

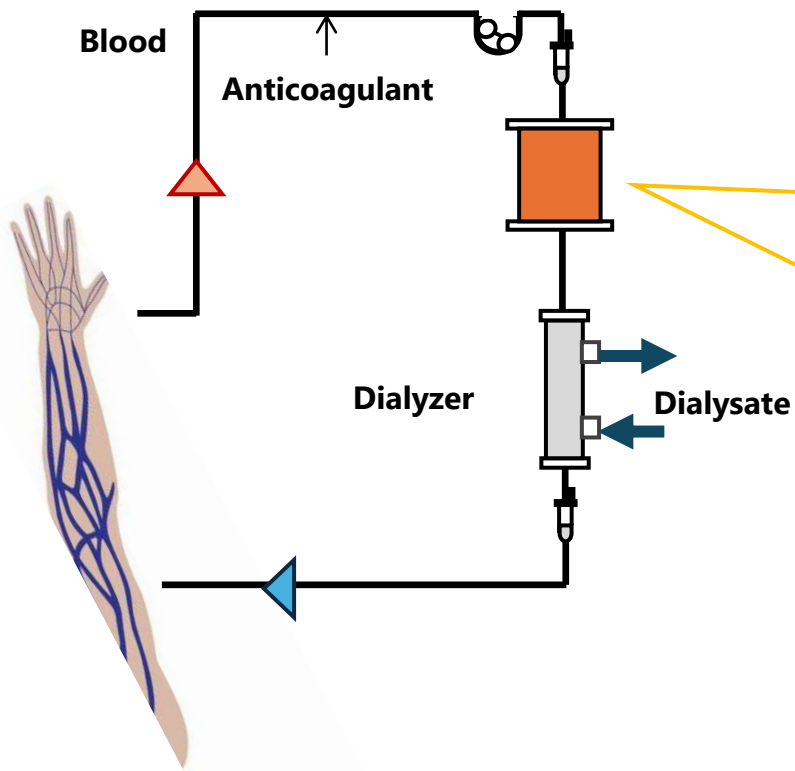
Clinical factors associated with carpal tunnel syndrome



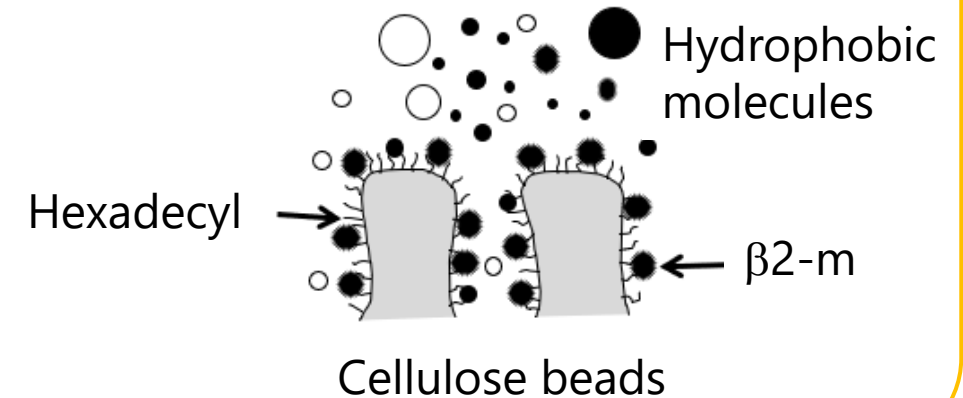
Hoshino J, Am J Nephrol, 2014

➔ Increase of β 2-m removal may be a therapeutic strategy for dialysis-related amyloidosis

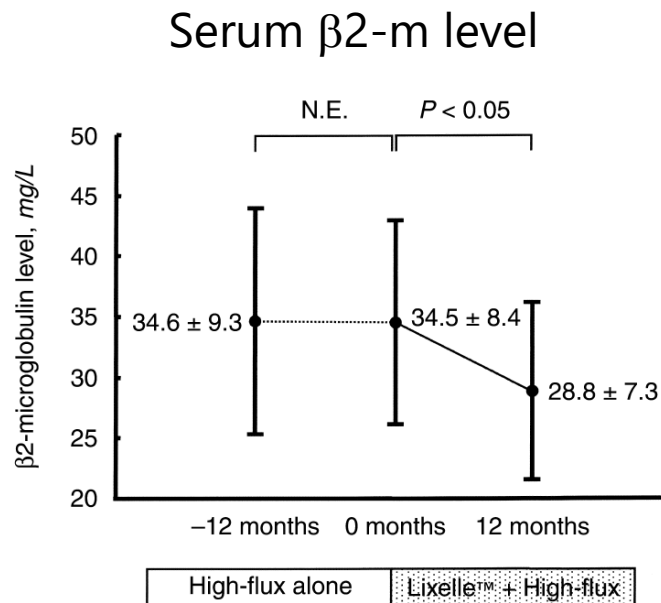
β 2-m adsorption column for dialysis-related amyloidosis



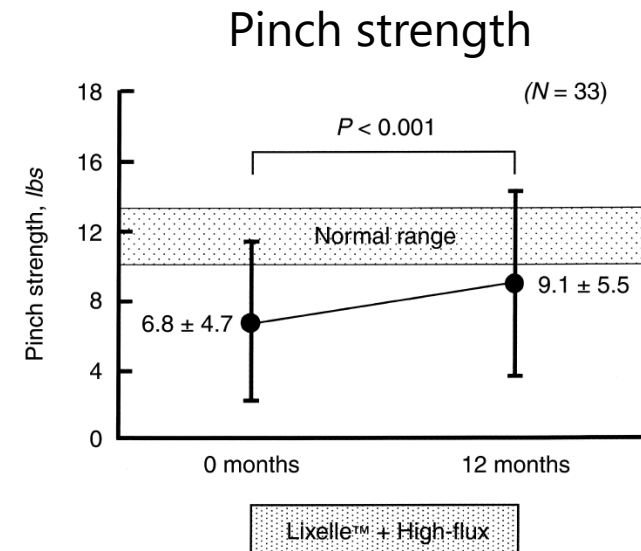
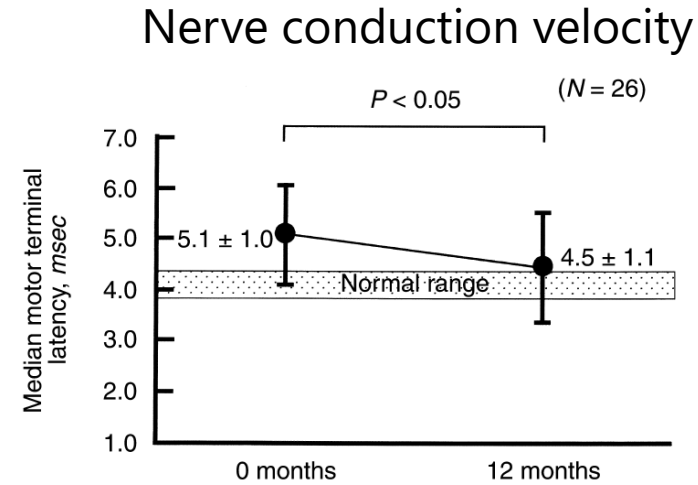
**Hexadecyl-immobilized
cellulose beads (HICB)**



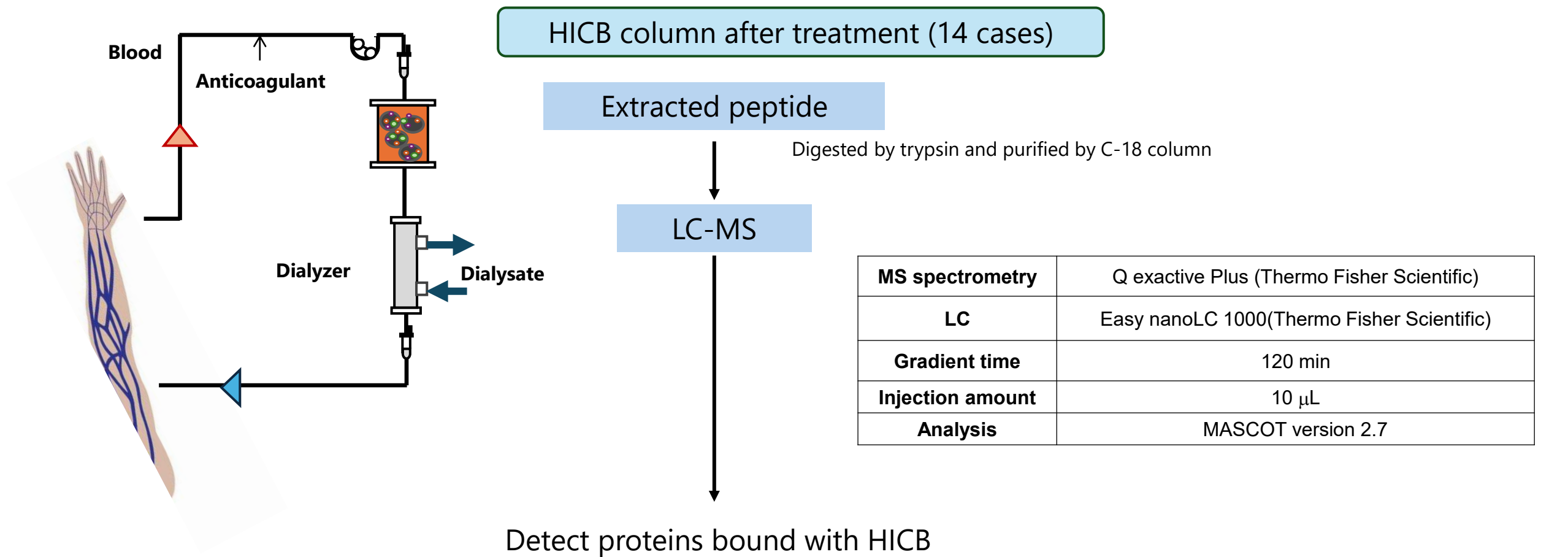
β 2-m adsorption column and clinical symptoms



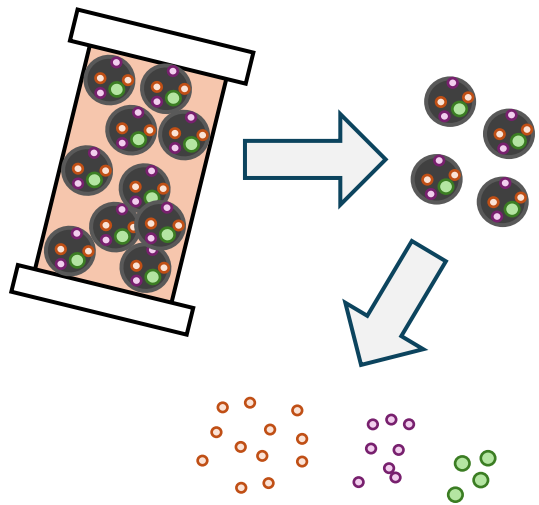
Abe T, Kidney Int, 2003



Proteomic analysis for the proteins bound with HICB column



HICB column after treatment, 14 cases



Detected at least in one case

661



Common in 9 and more of 14 cases

352

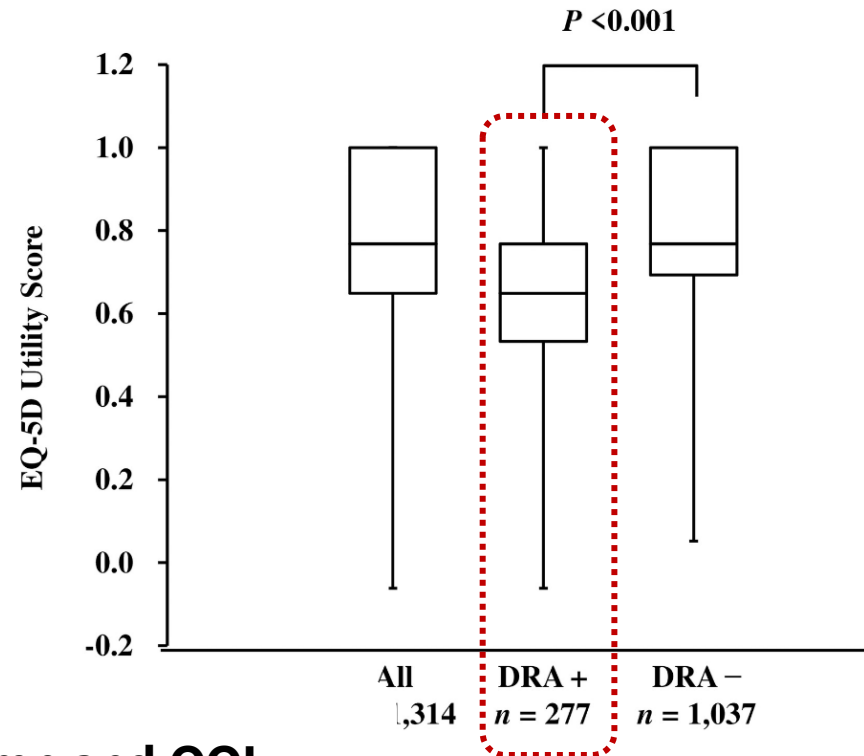


Selected SIN>1

200 proteins

Official gene symbol	Gene name	SIN
ALB	Albumin	296.6 ± 61.5
APOA4	apolipoprotein A4	204.4 ± 46.7
B2M	beta-2-macroglobulin	193.9 ± 143.4
RBP4	retinol binding protein 4	172.9 ± 55.4
LYZ	Lysozyme	156.5 ± 47.8
CFD	complement factor D	109.4 ± 41.9
APOC3	apolipoprotein C3	106.2 ± 58.9
IGLC2	immunoglobulin lambda constant 2	89.9 ± 66.0
CST3	cystatin C	88.8 ± 32.2
APOA1	apolipoprotein A1	82.3 ± 26.9
TMSB4X	thymosin beta 4, X-linked	75.5 ± 51.3
ANG	Angiogenin	70.2 ± 27.0
IGKC	immunoglobulin kappa constant	66.3 ± 32.9
AMBP	alpha-1-microglobulin/bikunin precursor	59.6 ± 20.4
RNASE1	ribonuclease A family member 1, pancreatic	52.7 ± 31.0
TF	Transferrin	50.6 ± 16.7
APOA2	apolipoprotein A2	48.6 ± 30.2
DEFA1	defensin alpha 1	47.0 ± 27.7
IGFBP4	insulin like growth factor binding protein 4	43.1 ± 14.3
APOH	apolipoprotein H	38.9 ± 11.0
SERPINA1	serpin family A member 1	34.2 ± 10.8
ORM1	orosomucoid 1	33.9 ± 23.5
MGP	matrix Gla protein	32.3 ± 25.9
TTR	Transthyretin	32.1 ± 17.5
RNASE4	ribonuclease A family member 4	31.7 ± 10.9
FGA	fibrinogen alpha chain	31.1 ± 9.7
REG1A	regenerating family member 1 alpha	30.8 ± 18.5
RARRES2	retinoic acid receptor responder 2	30.0 ± 11.9
GC	GC, vitamin D binding protein	27.9 ± 7.8
IGFBP2	insulin like growth factor binding protein 2	27.1 ± 8.0

Use of β 2-m adsorption column inhibits impairment of QOL



β 2-m adsorption column and QOL

β 2-m adsorption column	Mean change (95% CI)	Difference (95% CI)	P value
Use	-0.05 (-0.19 to 0.08)	0.08 (0.01 to 0.15)	0.017
No use	-0.14 (-0.26 to -0.01)	Reference	

For Aging Gracefully in Dialysis Patients

Clinical assessment and practice gap of **Frailty** in dialysis patients

Frailty is not routinely assessed or diagnosed

A simpler and more sustainable diagnostic tool is needed

Effect of exercise and nutritional interventions are often limited

→ Insufficient understanding and treatment of CKD-related pathologies.

PTH and fracture

β 2-m and amyloidosis

A comprehensive approach is required, including

- targeted management of diverse CKD-related conditions
- appropriate assessment
- integrated exercise and nutritional interventions