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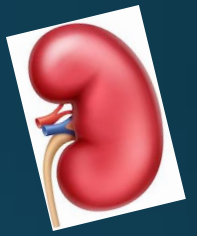
Ogden Surgical-Medical Society 2023

Lifestyle Modifications in Kidney Disease

Kidney



Patient

Disclosures

- I am not a dietician or exercise-sport scientist

- This presentation has no ineligible company content, promotes no ineligible company, and is not supported financially by any ineligible company. I receive no financial remuneration from any ineligible company related to this presentation.

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Objectives

- The learner will be able to describe appropriate dietary modifications for patients with CKD, dialysis and kidney transplants.
- The learner will discuss the benefits of exercise for patients with varying degrees of kidney disease.
- The learner will recognize barriers affecting the quality of life for patients with chronic kidney disease and renal replacement therapy.

Diet in CKD


KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation
eat right
Academy of Nutrition and Dietetics
KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE

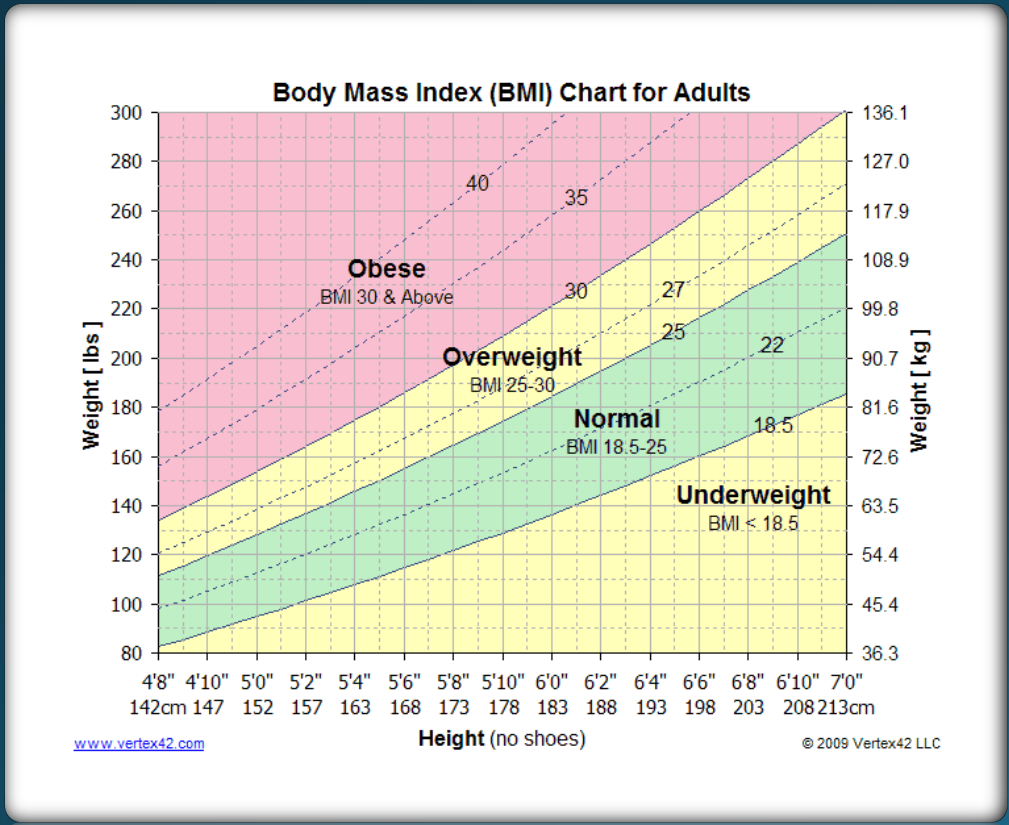
Nutrition Assessment

- In adults with CKD 3-5D or post-transplantation, it is reasonable that a registered dietitian nutritionist (RDN)… conduct a comprehensive nutrition assessment…at least within the first 90 days of starting dialysis, annually, or when indicated by nutrition screening or provider referral (OPINION).

Assessment of Nutrition

- Routine nutrition screening- Biannually to ID protein-energy wasting (OPINION)
  - Bioimpedance- preferably multi-frequency bioelectrical impedance(MF-BIA) for HD patients
  - Dual-Energy X-Ray Absorptiometry (DXA) for CKD and PD patients

Nutrition Assessment



- BMI
  - Underweight: predictor of higher mortality in PD patients
  - Overweight or obese: predicts lower mortality in PD
  - Underweight or morbid obesity: predicts higher mortality in HD patients
  - Underweight, overweight and obese: higher mortality prediction in post-transplant patients

Nutrition Labs

- Serum albumin
  - Low albumin levels = higher hospitalization & mortality in HD patients
- Serum pre-albumin
- Normalized protein catabolic rate (nPCR)
  - Used in HD patients

Complementary tools, not to be used in isolation

Composite Nutritional Indices

- 7-point Subjective Global Assessment (SGA)
  - Gold Standard
- Malnutrition Inflammation Score (MIS)

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Weight loss ____ kg in the past 6 months

Ratings	Weight loss
7	0%
6	<3%
5	3–<5%
4	5–<7%
3	7–<10%
2	10–<15%
1	≥15%

If ↑ weight trend, add 1 point, if ↓ weight trend within 1 month, minus 1 point

	RATINGS (circle one rating for each category)
	7 6 5 4 3 2 1
Dietary Intake (past 2 weeks) 7) Good (Full share of usual meal) 6) Good (> 3/4– < 1 share of usual meal) 5) Borderline (1/2–3/4 share of usual meal), but increasing 4) Borderline (1/2–3/4 share of usual meal), no change or decreasing 3) Poor (< 1/2 share of usual meal), but increasing 2) Poor (< 1/2 share of usual meal), no change or decreasing 1) Starvation (< 1/4 of usual meal)	7 6 5 4 3 2 1
Gastrointestinal symptoms (that persisted for > 2 weeks) Nausea: _____ Vomiting: _____ Diarrhea: _____ 7) No symptom 6) Very few intermittent symptoms (1x per day) 5) Some symptoms (2–3x per day)—improving 4) Some symptoms (2–3x per day)—no change 3) Some symptoms (2–3x per day)—getting worse 1–2) Some or all symptoms (> 3x per day)	7 6 5 4 3 2 1
Functional status (nutrition related) 6–7) Full functional capacity 3–5) Mild to moderate loss of stamina 1–2) Severe loss of functional ability (bedridden)	7 6 5 4 3 2 1
Disease state affecting nutritional requirements 6-7) No increase in metabolic demand (no or low stress) 3-5) Mild to moderate increase in metabolic demand (moderate stress) 1-2) Drastic increase in metabolic demand (high stress)	7 6 5 4 3 2 1
Muscle wastage: (at least 3 areas) 6–7) No depletion in all areas 3–5) Mild to moderate depletion 1–2) Severe depletion	7 6 5 4 3 2 1
Fat stores 6–7) No depletion in all areas 3–5) Mild to moderate depletion 1–2) Severe depletion	7 6 5 4 3 2 1
Edema: (nutrition related) 6–7) No edema 3–5) Mild to moderate edema 1–2) Severe edema	7 6 5 4 3 2 1

Nutritional Status: Well Nourished / Mildly to Moderately Malnourished / Severely Malnourished

Overall SGA Rating: 7 6 5 4 3 2 1 (circle one)

MIS

MIS Components	Score			
	0	1	2	3
(A) Medical history:				
1. Change in end dialysis dry weight (overall change in the past 3–6 months)	<0.5 Kg	0.5–1.0 Kg	≥1 Kg but <5%	≥ 5%
2. Dietary intake	Good appetite, no deterioration of dietary intake	Sub-optimal solid dietary intake	Moderate overall decrease to full liquid diet	Hypo-caloric liquid to starvation
3. Gastrointestinal symptoms	No symptoms with good appetite	Mild symptoms, poor appetite or nauseated occasionally	Occasional vomiting or moderate GI symptoms	Frequent diarrhea or vomiting or sever anorexia
4. Functional capacity (nutritionally related functional impairment)	Normal to improved functional capacity, feeling fine	Occasional difficulty with baseline ambulation, or feeling tired frequently	Difficulty with otherwise independent activities (e.g. going bathroom)	Bed/chair ridden, or little to no physical activity
5. Co-morbidity *	No comorbidity	Mild comorbidity (excluding MCC**)	Moderate comorbidity (including one MCC*)	Any sever multiple comorbidity (≥2 MCC*)
(B) Physical exam:				
6. Decreased fat stores or loss of subcutaneous fat (below eyes, triceps, biceps, chest)	No change	mild	moderate	sever
7. Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous)	No change	mild	moderate	sever
(C) Body size				
8. Body mass index (kg/m^2)	≥ 20	18–19.9	16–17.99	<16
(D) Laboratory parameters				
9. Serum albumin (g/L)	≥4	3.5–3.9	3.–3.4	<3.0
10. Serum total iron binding capacity (mg/dL)	≥ 250	200–249	150–199	<150
Total MIS = sum of the above 10 components, ranging from 0 (no malnutrition) to 30 (severely malnourished)				

*In the original MIS dialysis treatment age (vintage) contributes to the comorbid condition scoring: 0 if vintage <1 year, 1 if vintage 1 to 4 years, and at least 2 if vintage >4 years.

**Major co-morbid conditions (MCC) include CHF class III or IV, full blown AIDS, severe coronary artery disease, moderate to severe chronic obstructive pulmonary disease, major neurological sequelae, metastatic malignancy or recent chemotherapy

Nutrition Assessment

- In adults with CKD 3-5D or post-transplantation, it is reasonable that a registered dietitian nutritionist (RDN)… conduct a comprehensive nutrition assessment… at least within the first 90 days of starting dialysis, annually, or when indicated by nutrition screening or provider referral (OPINION).

Protein Intake CKD

No Dialysis, no DM

- Protein <u>restriction</u> recommended
  - 0.55-0.60 g protein/kg of body weight/day OR
  - 0.28-0.43 g protein/kg body weight/day + keto acid/amino acid analogs for total of 0.55-0.60 g protein/kg of body weight/day
  - Reduces risk for progression to ESRD/death

No Dialysis, yes DM

- Protein <u>restriction</u> recommended
  - 0.6-0.80 g protein/kg of body weight/day

Protein Intake ESRD

HD and PD patients w/out DM	• **1.0-1.2 g/kg** of body weight per day
HD and PD patients with DM	• **1.0-1.2 g/kg** of body weight per day • May need adjustment to maintain glycemic control
No specific protein type (plant v animal) for nutrition, calcium or phosphorus levels	• Some suggest that plant proteins may have lower PO_4 levels

Nutritional Supplementation

- Trial of 3 months of oral nutritional supplements
- If oral trial fails:
  - Enteral tube feeding
  - TPN (CKD stage 1-5)
  - Intradialytic Parental Nutrition (IDPN)- CKD 5D on HD
  - Possible to add Amino Acid Dialysate for PD
    - Not recommended

Long Chain Omega-3 Polyunsaturated Fatty Acids

- Not recommended in ESRD or transplant patients for cardiovascular protection
- Reasonable to consider for CKD/ESRD/Transplant patients for improving lipid profile/TG
  - 2g/day for CKD 3-5 patients
  - 1.3-4 g/day in HD/PD patients
- No benefits in AVF/AVG patency
- No benefits to prevent transplant rejection

Vitamin Supplementation

- Diet first
- Multivitamin if necessary
  - Renal vitamin for dialysis patients
- Folate and B12
  - Only if deficient
- Vitamin C
  - If deficient:
    - 90 mg/day for males
    - 75 mg/day for females

Vitamin Supplementation

- Vitamin D
  - Only for deficiency
- Vitamin A and E
  - Not routine supplementation
  - Monitor for toxicity
- Trace Minerals
  - No routine selenium or zinc

Dietary Acid

- Chronic metabolic acidosis in CKD
  - Reduce acid intake
    - Increase fruit/vegetable intake
  - Increase alkali supplementation
    - Bicarbonate or citric acid/sodium citrate solution
      - Reduces rate of GFR decline
    - Maintain CO_2 levels 22-28 mmol/L

Calcium

- CKD 3-5
  - 800-1000 mg/day (dietary, supplements, binders)
- CKD 5D/ESRD
  - Adjust calcium intake to avoid hypercalcemia

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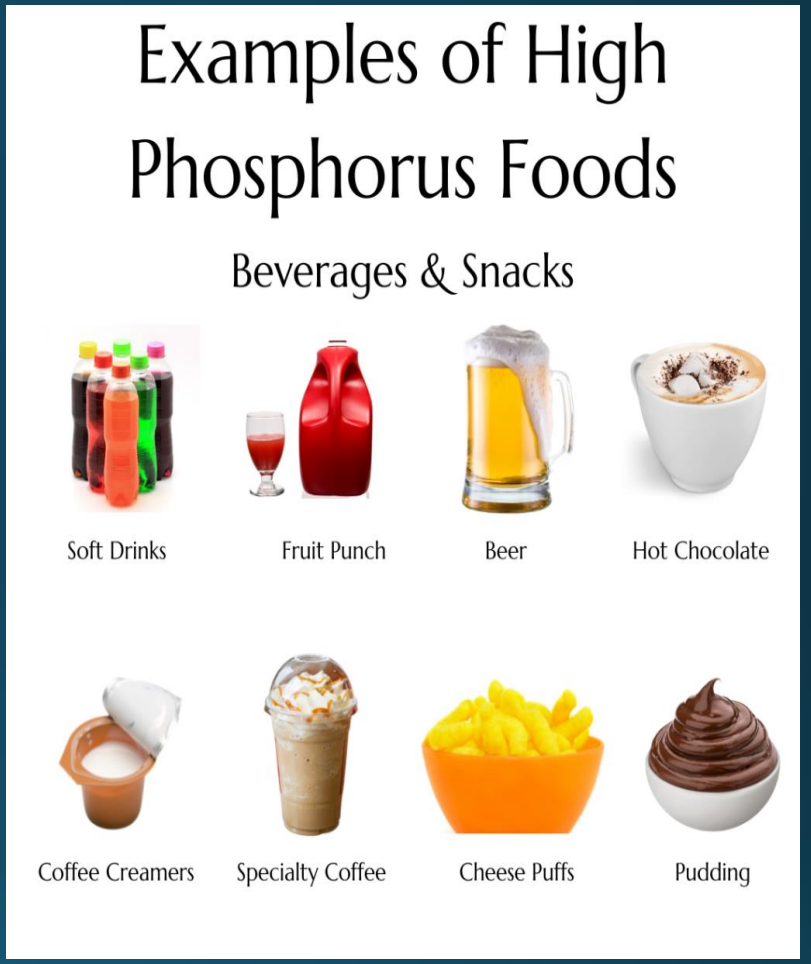
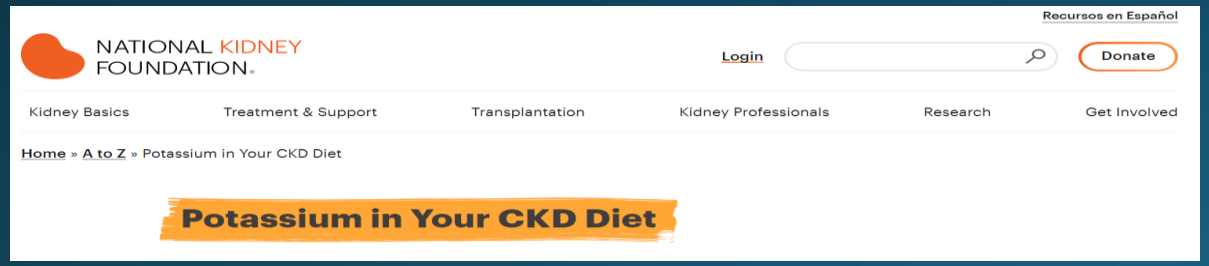
Phosphorus

- CKD 3-5D
  - Avoid high PO_4 foods
    - Processed food, packaged food, fast food, cola drinks
    - Binders when PO_4 is >4.5
      - Non-calcium binders > calcium based binders
    - Animal and additive PO_4 worse than plant based PO_4
- Post-transplant
  - Often with low PO_4
    - OK for high PO_4 intake or use of Neutra-Phos supplements



Potassium

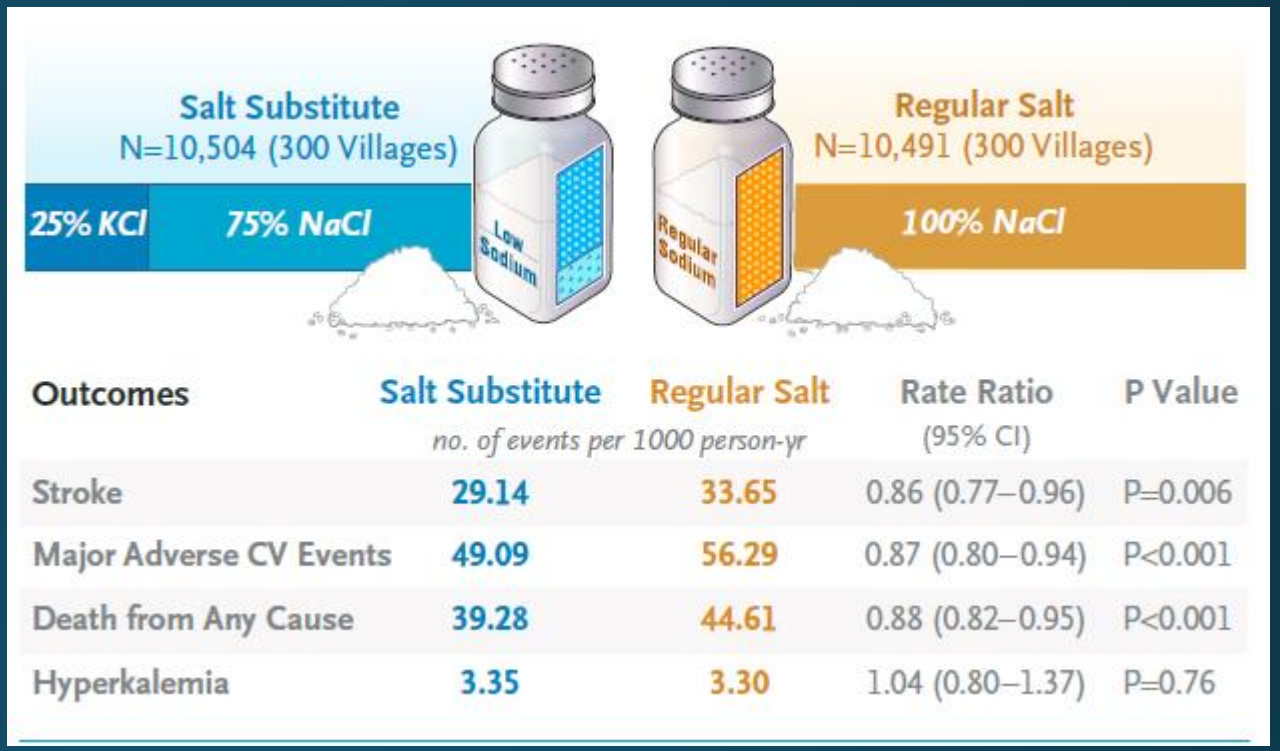
- Avoid when high K levels
- If diet doesn't reduce K, then use K binders
  - Veltassa
  - Lokelma
  - Kayexelate
  - Diuretics (Loop/Thiazides)



https://www.kidney.org/atoz/content/potassium-ckd-diet

Sodium

- <2300 mg daily
  - BP reduction
  - Proteinuria
  - Dry Body Weight



Outcomes	Salt Substitute	Regular Salt	Rate Ratio	P Value
	no. of events per 1000 person-yr		(95% CI)	
Stroke	29.14	33.65	0.86 (0.77–0.96)	P=0.006
Major Adverse CV Events	49.09	56.29	0.87 (0.80–0.94)	P<0.001
Death from Any Cause	39.28	44.61	0.88 (0.82–0.95)	P<0.001
Hyperkalemia	3.35	3.30	1.04 (0.80–1.37)	P=0.76

- If K levels will tolerate, recommend salt substitute
  - Salt Substitute and Stroke Study (SSaSS)- N Engl J Med 2021; 385:1067-1077
  - Meta-analysis- *Heart* 2022;108:1608-1615.

Exercise

- CKD patients:
  - Report 9 days of physical activity/month
- Dialysis patients
  - 43.9% report no exercise at all

Exercise

- Recommendation 2.2.1: We suggest that patients with high BP and CKD be advised to undertake moderate intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (2C).
  - "There may still be important health benefits even if physical activity falls below targets proposed for the general population."

KDIGO 2021

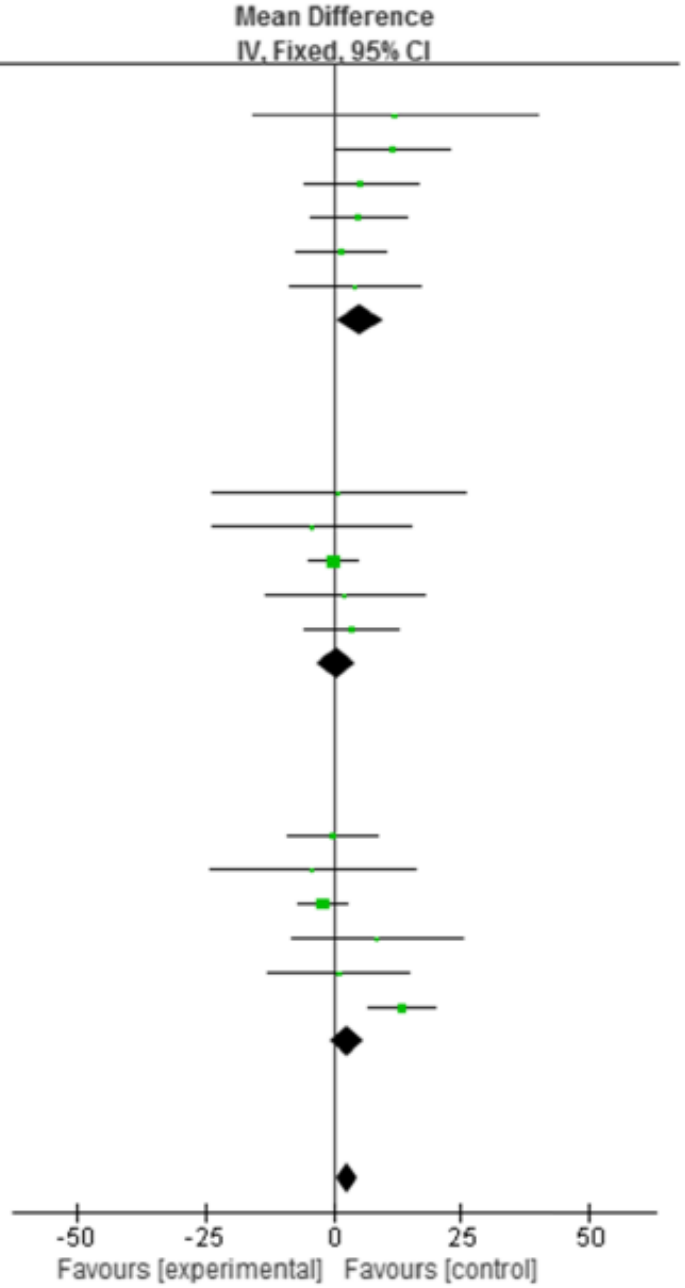
Exercise CKD

- Meta-analysis- Zhang et al. BMC Nephrology (2019) 20:398
  - 13 RCTs, representing 421 patients with non-dialysis CKD
    - >18 y.o., CKD 2-5 not on dialysis
    - Aerobic or resistance exercise
    - 1x/week for >1 month

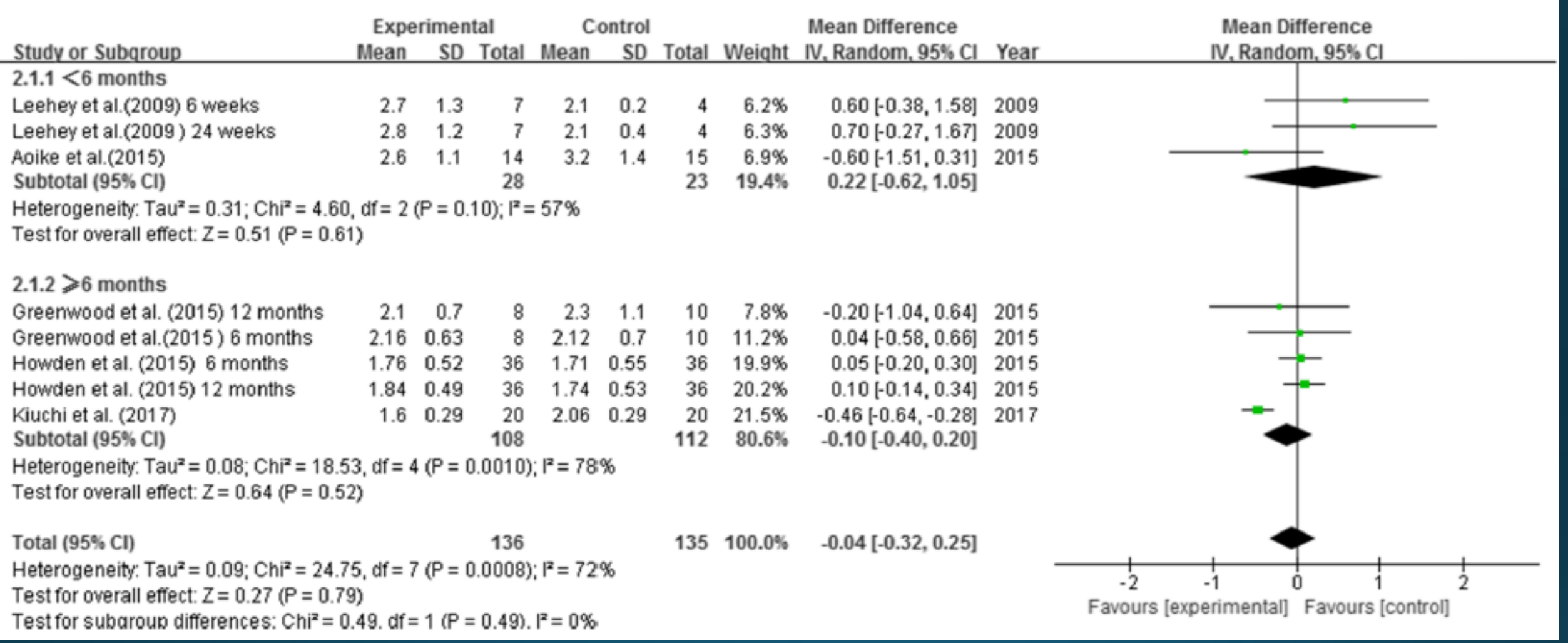
	Median (CI)	P-value
eGFR (mL/min)	2.62 (0.42-4.82)	0.02
SBP (Δ mmHg)	-5.61 (-8.99 to -2.33)	0.001
DBP (Δ mmHg)	-2.87 (-3.65 to -2.08)	<0.00001
BMI	-1.32 (-2.39 to -0.25)	0.02

eGFR

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
1.1.1 exercise duration≤3months									
Leehey et al.(2009) 6 weeks	1	33.78	7	-11	12.38	4	0.6%	12.00 [-15.81, 39.81]	2009
Toyama et al. (2010)	8.2	15.55	10	-3.3	8.98	9	3.8%	11.50 [0.22, 22.78]	2010
Baria et al.(2014)	3.6	8.75	10	-1.8	14.53	9	4.0%	5.40 [-5.53, 16.33]	2014
Aoike et al.(2015)	3.5	12.78	14	-1.4	12.84	15	5.5%	4.90 [-4.43, 14.23]	2015
Van Craenenbroeck et al. (2015)	1.1	13.74	19	-0.4	14.19	21	6.4%	1.50 [-7.16, 10.16]	2015
Leehey et al. (2016) 12 weeks	0.9	17.76	14	-3.3	19.17	18	2.9%	4.20 [-8.64, 17.04]	2016
Subtotal (95% CI)			74			76	23.4%	5.22 [0.68, 9.77]	
Heterogeneity: Chi² = 2.16, df = 5 (P = 0.83); I² = 0%									
Test for overall effect: Z = 2.25 (P = 0.02)									
1.1.2 3<exercise duration≤6months									
Leehey et al.(2009) 24 weeks	-5	31.43	7	-6	8.25	4	0.8%	1.00 [-23.65, 25.65]	2009
Headley et al.(2012) 24 weeks	1	19.57	10	5.1	25.64	11	1.3%	-4.10 [-23.51, 15.31]	2012
Howden et al. (2015) 6 months	0.5	9.17	36	0.5	10.79	36	22.6%	0.00 [-4.63, 4.63]	2015
Greenwood et al.(2015) 6 months	0.3	12.37	8	-2	20.75	10	2.0%	2.30 [-13.16, 17.76]	2015
Miele et al. (2017)	5.4	16.72	25	1.8	14.76	21	5.8%	3.60 [-5.50, 12.70]	2017
Subtotal (95% CI)			86			82	32.5%	0.65 [-3.20, 4.51]	
Heterogeneity: Chi² = 0.75, df = 4 (P = 0.94); I² = 0%									
Test for overall effect: Z = 0.33 (P = 0.74)									
1.1.3 6<exercise duration≤12months									
Hiraki et al. (2017)	-1.9	11.16	14	-1.6	12.56	14	6.2%	-0.30 [-9.10, 8.50]	2007
Headley et al.(2012) 48 weeks	1	19.14	10	5	27.24	11	1.2%	-4.00 [-24.00, 16.00]	2012
Howden et al. (2015) 12 months	-1.8	9.76	36	0.2	10.86	36	21.2%	-2.00 [-6.77, 2.77]	2015
Greenwood et al. (2015) 12 months	3.7	16.21	8	-4.8	19.51	10	1.8%	8.50 [-8.00, 25.00]	2015
Leehey et al.(2016) 52 weeks	-1.9	19.37	14	-3.1	20.25	18	2.5%	1.20 [-12.60, 15.00]	2016
Kiuchi et al. (2017)	8.9	11.94	20	-4.5	9.07	20	11.2%	13.40 [6.83, 19.97]	2017
Subtotal (95% CI)			102			109	44.1%	2.69 [-0.62, 6.00]	
Heterogeneity: Chi² = 15.31, df = 5 (P = 0.009); I² = 67%									
Test for overall effect: Z = 1.59 (P = 0.11)									
Total (95% CI)			262			267	100.0%	2.62 [0.42, 4.82]	
Heterogeneity: Chi² = 20.49, df = 16 (P = 0.20); I² = 22%									
Test for overall effect: Z = 2.34 (P = 0.02)									
Test for subgroup differences: Chi² = 2.26, df = 2 (P = 0.32), I² = 11.6%									

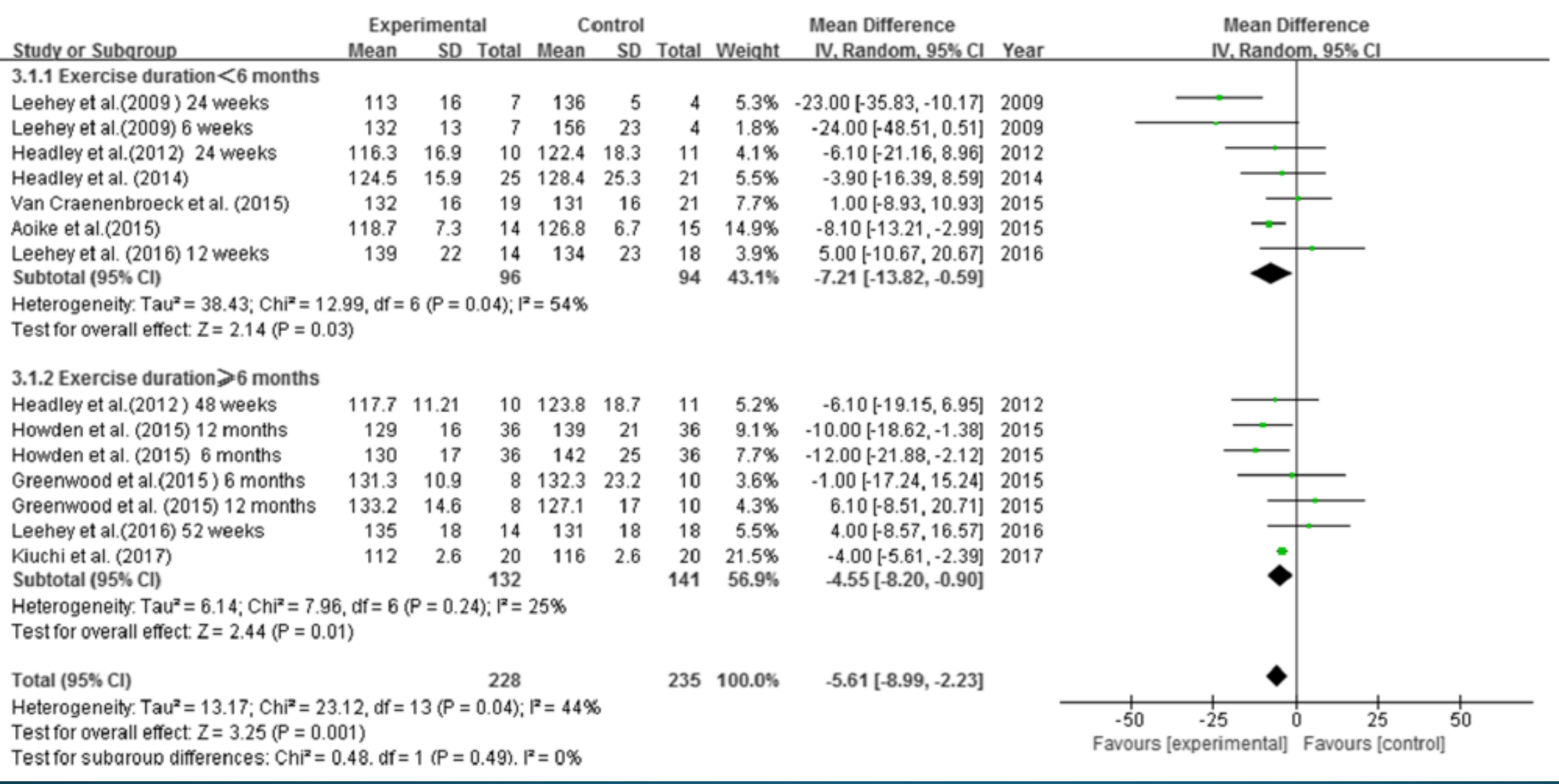


Nakamura, K. et al, Sci Rep (2020)10, 18195.



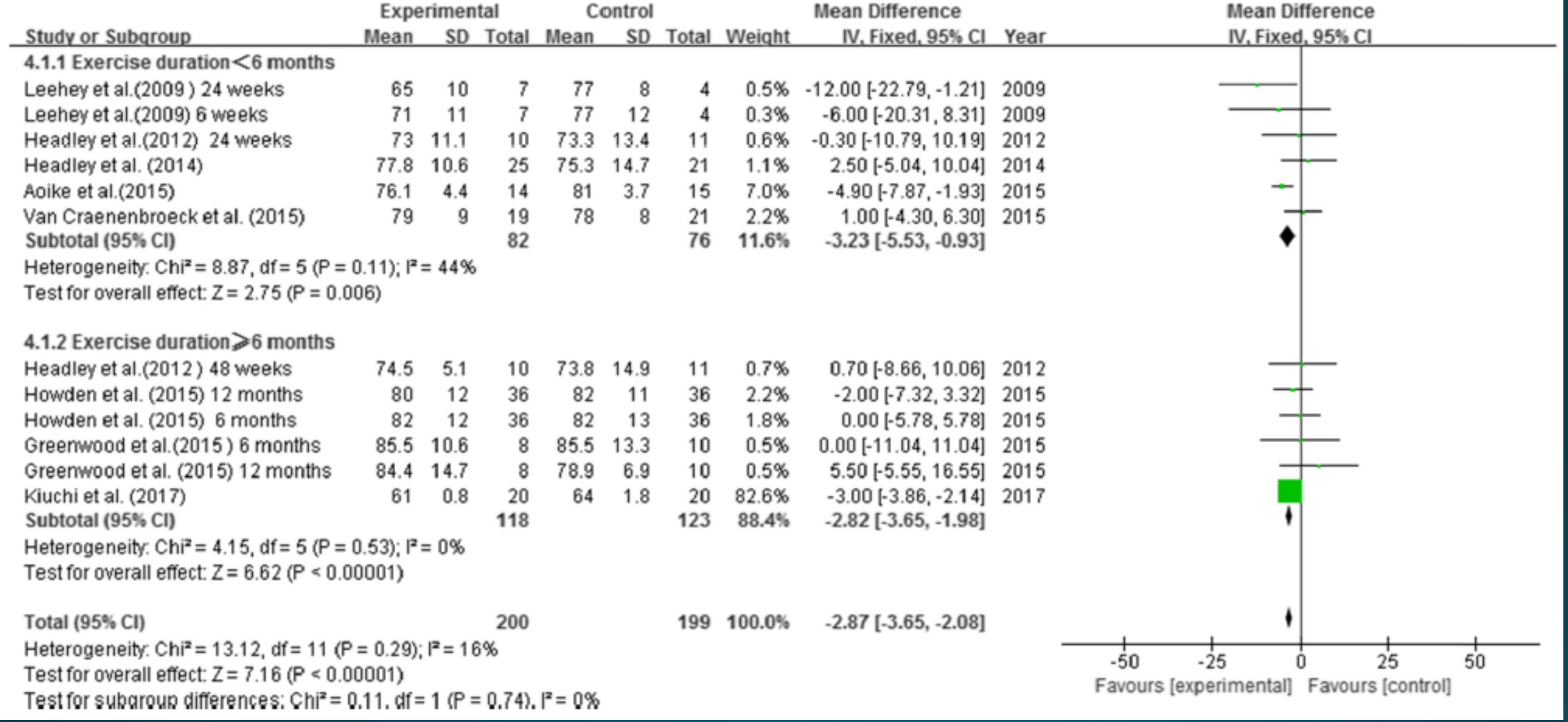
Serum Creatinine

Nakamura, K. et al, Sci Rep (2020)10, 18195.



SBP

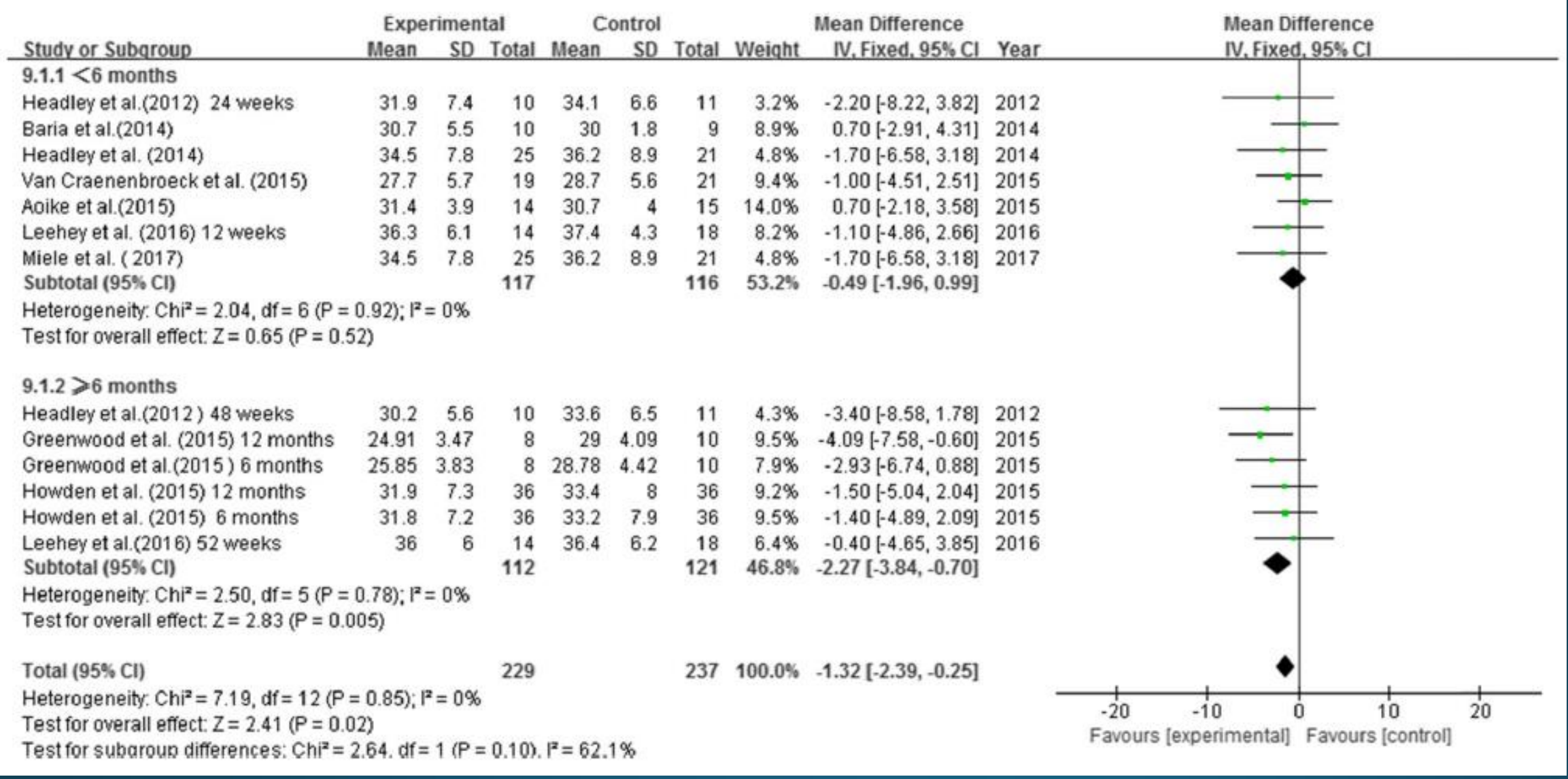
Nakamura, K. et al, Sci Rep (2020)10, 18195.



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
4.1.1 Exercise duration<6 months									
Leehey et al.(2009) 24 weeks	65	10	7	77	8	4	0.5%	-12.00 [-22.79, -1.21]	2009
Leehey et al.(2009) 6 weeks	71	11	7	77	12	4	0.3%	-6.00 [-20.31, 8.31]	2009
Headley et al.(2012) 24 weeks	73	11.1	10	73.3	13.4	11	0.6%	-0.30 [-10.79, 10.19]	2012
Headley et al. (2014)	77.8	10.6	25	75.3	14.7	21	1.1%	2.50 [-5.04, 10.04]	2014
Aoike et al.(2015)	76.1	4.4	14	81	3.7	15	7.0%	-4.90 [-7.87, -1.93]	2015
Van Craenenbroeck et al. (2015)	79	9	19	78	8	21	2.2%	1.00 [-4.30, 6.30]	2015
Subtotal (95% CI)			82			76	**11.6%**	-3.23 [-5.53, -0.93]	
Heterogeneity: Chi² = 8.87, df = 5 (P = 0.11); I² = 44%									
Test for overall effect: Z = 2.75 (P = 0.006)									
4.1.2 Exercise duration≥6 months									
Headley et al.(2012) 48 weeks	74.5	5.1	10	73.8	14.9	11	0.7%	0.70 [-8.66, 10.06]	2012
Howden et al. (2015) 12 months	80	12	36	82	11	36	2.2%	-2.00 [-7.32, 3.32]	2015
Howden et al. (2015) 6 months	82	12	36	82	13	36	1.8%	0.00 [-5.78, 5.78]	2015
Greenwood et al.(2015) 6 months	85.5	10.6	8	85.5	13.3	10	0.5%	0.00 [-11.04, 11.04]	2015
Greenwood et al. (2015) 12 months	84.4	14.7	8	78.9	6.9	10	0.5%	5.50 [-5.55, 16.55]	2015
Kiuchi et al. (2017)	61	0.8	20	64	1.8	20	82.6%	-3.00 [-3.86, -2.14]	2017
Subtotal (95% CI)			118			123	**88.4%**	-2.82 [-3.65, -1.98]	
Heterogeneity: Chi² = 4.15, df = 5 (P = 0.53); I² = 0%									
Test for overall effect: Z = 6.62 (P < 0.00001)									
Total (95% CI)			200			199	**100.0%**	-2.87 [-3.65, -2.08]	
Heterogeneity: Chi² = 13.12, df = 11 (P = 0.29); I² = 16%									
Test for overall effect: Z = 7.16 (P < 0.00001)									
Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.74), I² = 0%									

DBP

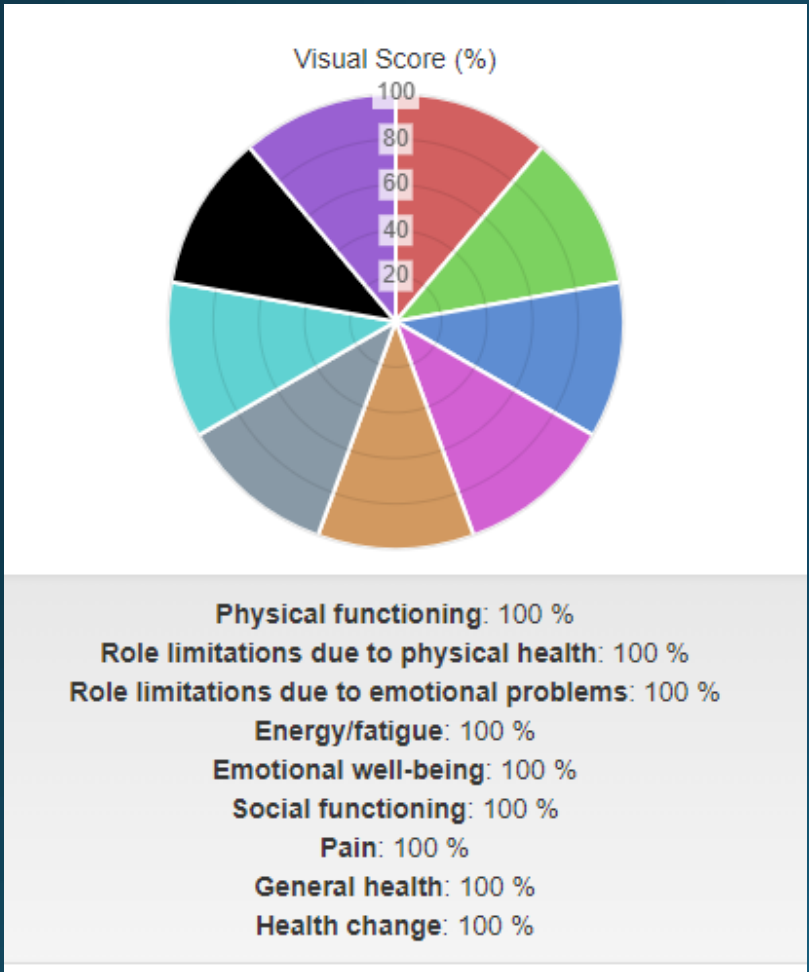
Nakamura, K. et al, Sci Rep (2020)10, 18195.



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
9.1.1 <6 months									
Headley et al.(2012) 24 weeks	31.9	7.4	10	34.1	6.6	11	3.2%	-2.20 [-8.22, 3.82]	2012
Baria et al.(2014)	30.7	5.5	10	30	1.8	9	8.9%	0.70 [-2.91, 4.31]	2014
Headley et al. (2014)	34.5	7.8	25	36.2	8.9	21	4.8%	-1.70 [-6.58, 3.18]	2014
Van Craenenbroeck et al. (2015)	27.7	5.7	19	28.7	5.6	21	9.4%	-1.00 [-4.51, 2.51]	2015
Aoike et al.(2015)	31.4	3.9	14	30.7	4	15	14.0%	0.70 [-2.18, 3.58]	2015
Leehey et al. (2016) 12 weeks	36.3	6.1	14	37.4	4.3	18	8.2%	-1.10 [-4.86, 2.66]	2016
Miele et al. (2017)	34.5	7.8	25	36.2	8.9	21	4.8%	-1.70 [-6.58, 3.18]	2017
Subtotal (95% CI)			**117**			**116**	**53.2%**	**-0.49 [-1.96, 0.99]**	
Heterogeneity: Chi² = 2.04, df = 6 (P = 0.92); I² = 0%									
Test for overall effect: Z = 0.65 (P = 0.52)									
9.1.2 ≥6 months									
Headley et al.(2012) 48 weeks	30.2	5.6	10	33.6	6.5	11	4.3%	-3.40 [-8.58, 1.78]	2012
Greenwood et al. (2015) 12 months	24.91	3.47	8	29	4.09	10	9.5%	-4.09 [-7.58, -0.60]	2015
Greenwood et al.(2015) 6 months	25.85	3.83	8	28.78	4.42	10	7.9%	-2.93 [-6.74, 0.88]	2015
Howden et al. (2015) 12 months	31.9	7.3	36	33.4	8	36	9.2%	-1.50 [-5.04, 2.04]	2015
Howden et al. (2015) 6 months	31.8	7.2	36	33.2	7.9	36	9.5%	-1.40 [-4.89, 2.09]	2015
Leehey et al.(2016) 52 weeks	36	6	14	36.4	6.2	18	6.4%	-0.40 [-4.65, 3.85]	2016
Subtotal (95% CI)			**112**			**121**	**46.8%**	**-2.27 [-3.84, -0.70]**	
Heterogeneity: Chi² = 2.50, df = 5 (P = 0.78); I² = 0%									
Test for overall effect: Z = 2.83 (P = 0.005)									
Total (95% CI)			**229**			**237**	**100.0%**	**-1.32 [-2.39, -0.25]**	
Heterogeneity: Chi² = 7.19, df = 12 (P = 0.85); I² = 0%									
Test for overall effect: Z = 2.41 (P = 0.02)									
Test for subgroup differences: Chi² = 2.64, df = 1 (P = 0.10), I² = 62.1%									

BMI

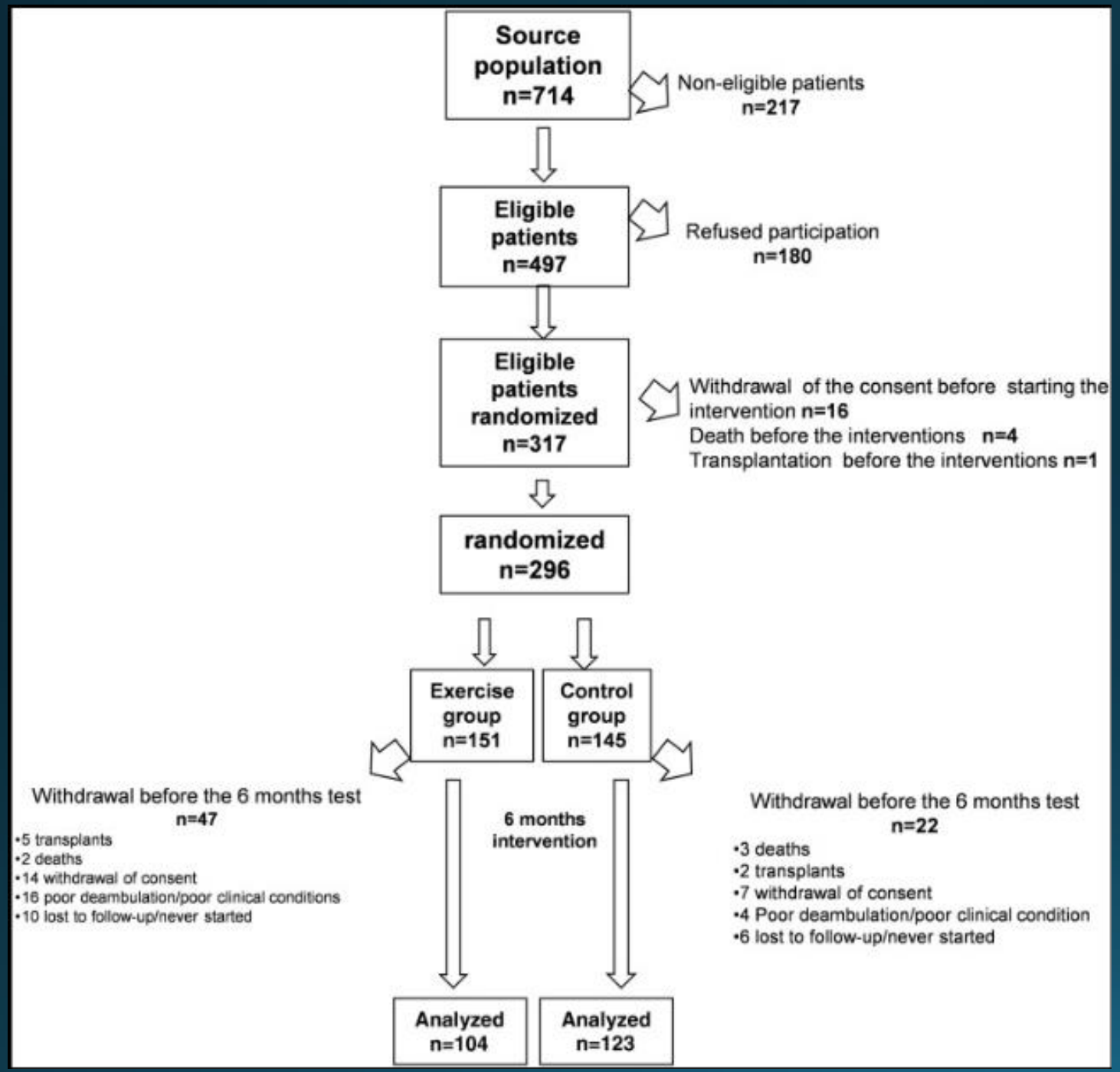
Nakamura, K. et al, Sci Rep (2020)10, 18195.



Exercise on Quality of Life

- KDQOL-36 survey:
  - Standardized Mean Difference (SMD) 3.56 (P = 0.02) on Effects of Kidney Disease
- SF-36 survey:
  - SMD 6.66 (P = 0.02) on Physical Functioning

Nefrología, 2020, 40 (3), 237-252.



Exercise for Dialysis

JASN 2017, 28(4):1259-1268.

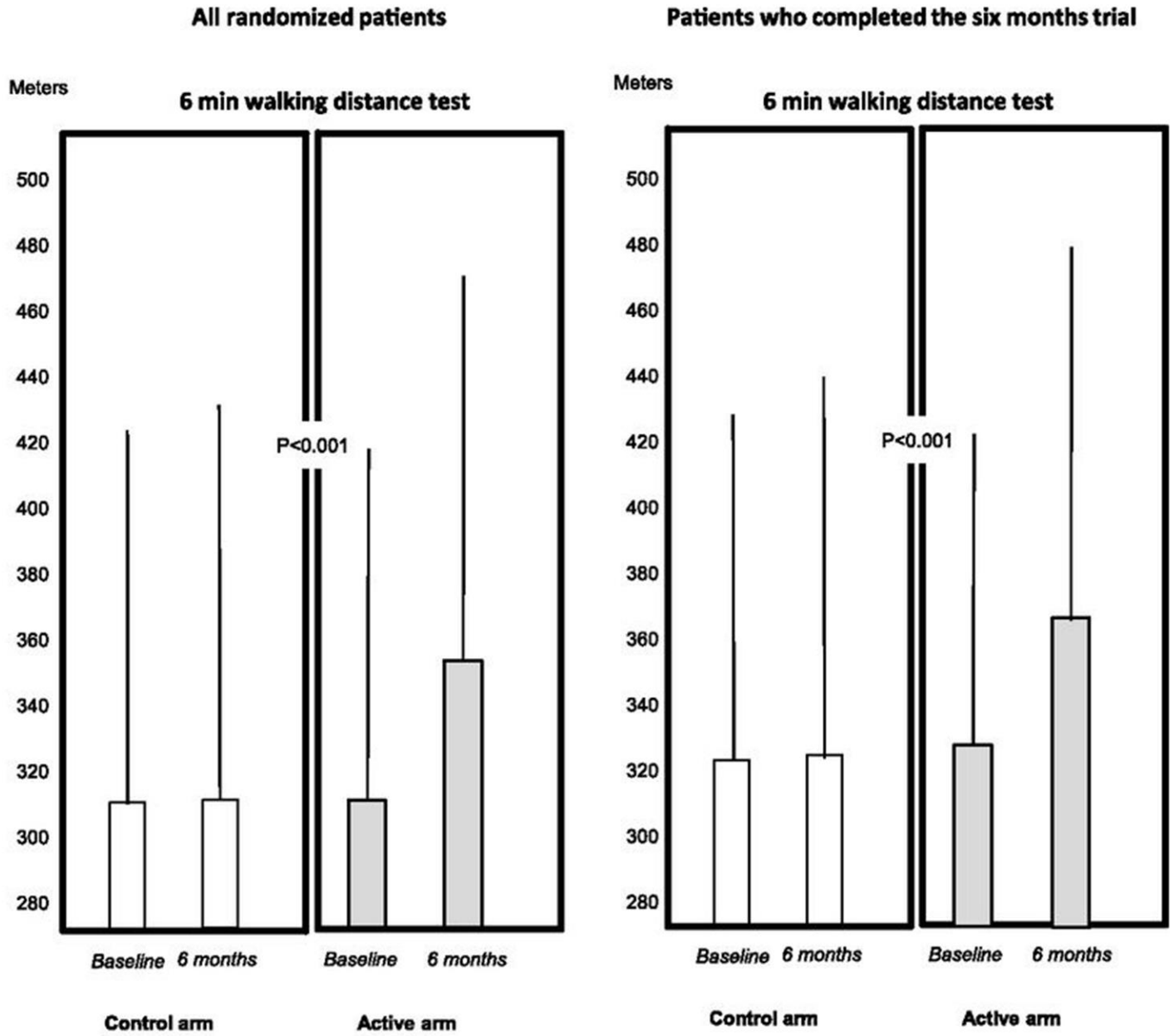
- 296 patients to normal physical activity (control; n=145) or walking exercise (n=151);
- 227 patients- 77% (exercise n=104; control n=123) repeated the 6-month evaluations

EXCITE

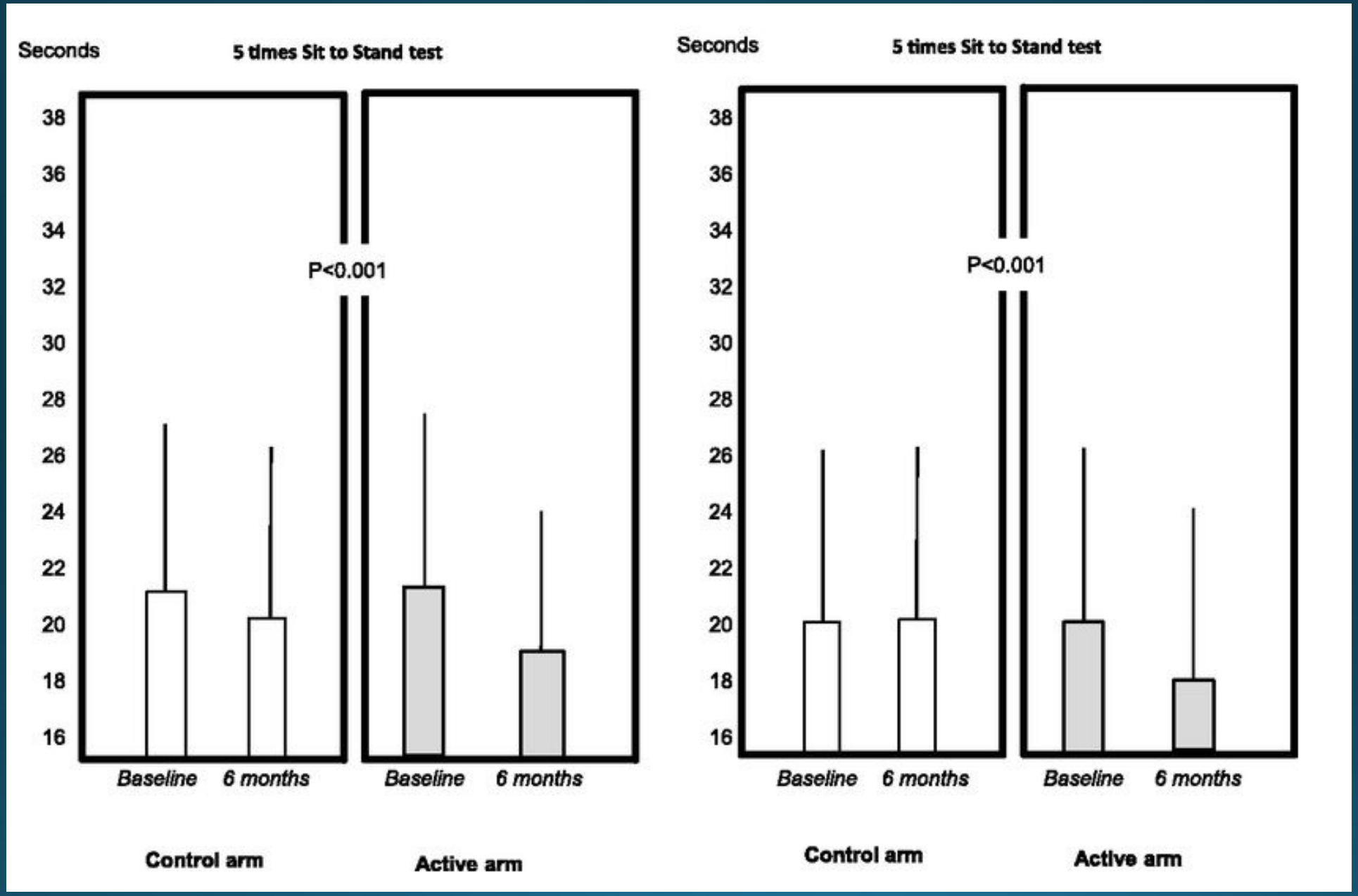
Table 4. Stepping up of the exercise program

Functioning Capacity Level	Normal	Moderate	Low	Very Low
6 min distance walked at baseline, m	>300 to ≤550	<300 to >200	<200	<200 +severe symptoms
Number of training sessions per d (always on nondialysis days)	2	2	2	2
Duration of training sessions, min	10	10	10	10
Frequency, times per wk	3	3	3	3
Training speed				
Baseline, km/h	2.8	2.0	1.4	1.4
Miles per h	1.7	1.2	0.9	0.9
wk 1–14, steps/min	72–120	66–100	56–80	56–80
wk 15–24, steps/min	90–120	80–100	60–80	60–80
wk 1–14				
Work/rest time, min	5:1	5:1	5:1	2:1
No. of repetitions	2	2	2	5
wk 15–24				
Work/rest time, min	10:0	10:0	10:0	5:1
No. of repetitions	1	1	1	2

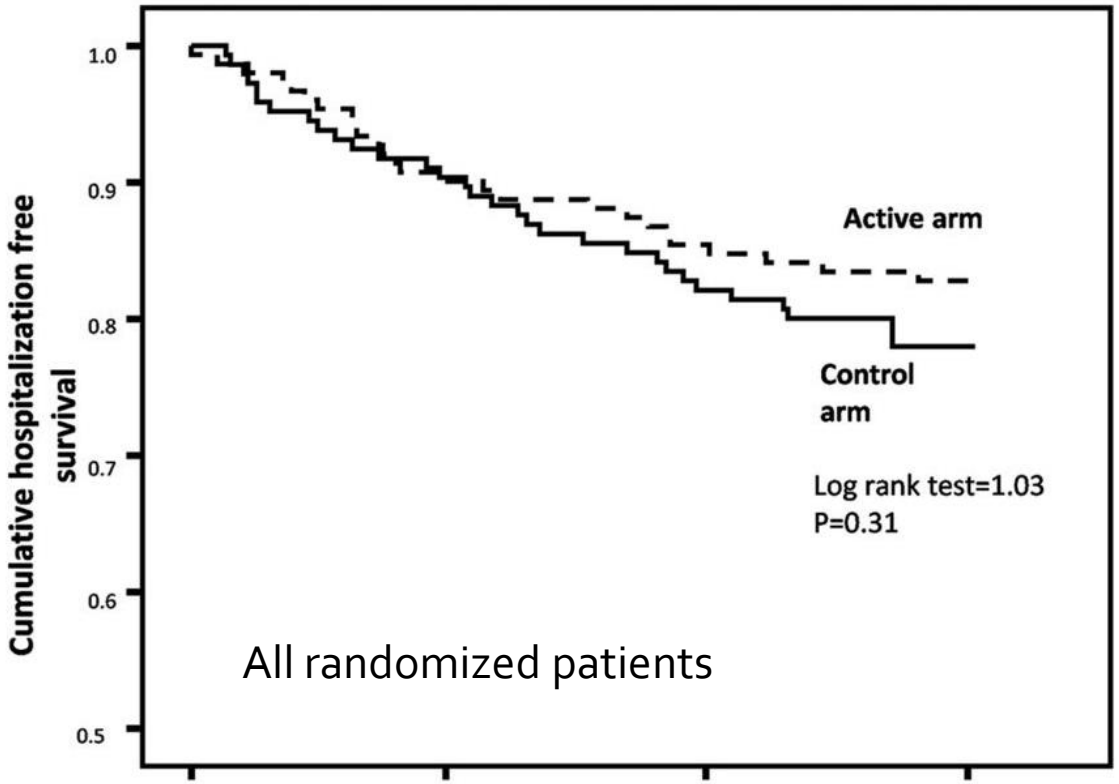
JASN 2017, 28(4):1259-1268.



JASN 2017, 28(4):1259-1268.

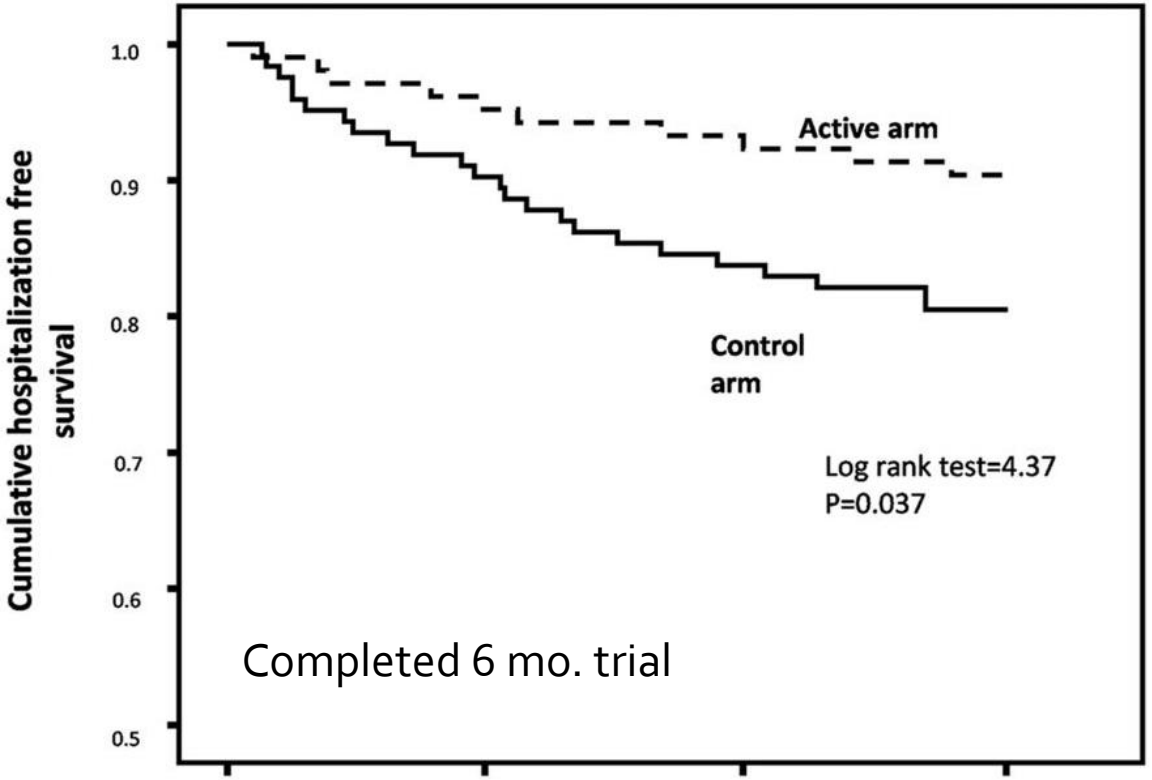


JASN 2017, 28(4):1259-1268.



Number of patients at risk

Active arm	151	136	128	125
Control arm	145	131	119	113



Number of patients at risk

Active arm	104	99	96	94
Control arm	123	111	103	99

Kaplan–Meier survival curves of hospitalizations in the active and control arms of the trial. The left panel shows analysis of all randomized patients. The right panel shows analysis of patients who completed the 6-month trial.

JASN 2017, 28(4):1259-1268.

Resistance Training Dialysis

- Nandrolone and Exercise Trial (NEXT)- 2006
  - 12-week intervention, 79 patients @ UCSF (~20/group)
  - 2x2 design- anabolic steroid, exercise, steroid + exercise, placebo
    - Steroid and/or Exercise increased Quadricep cross-section
    - Exercise DID NOT improve: gait speed, stair climbing, or ability to rise from a chair

JASN 2006 Aug;17(8):2307-14.

Resistance Training Dialysis

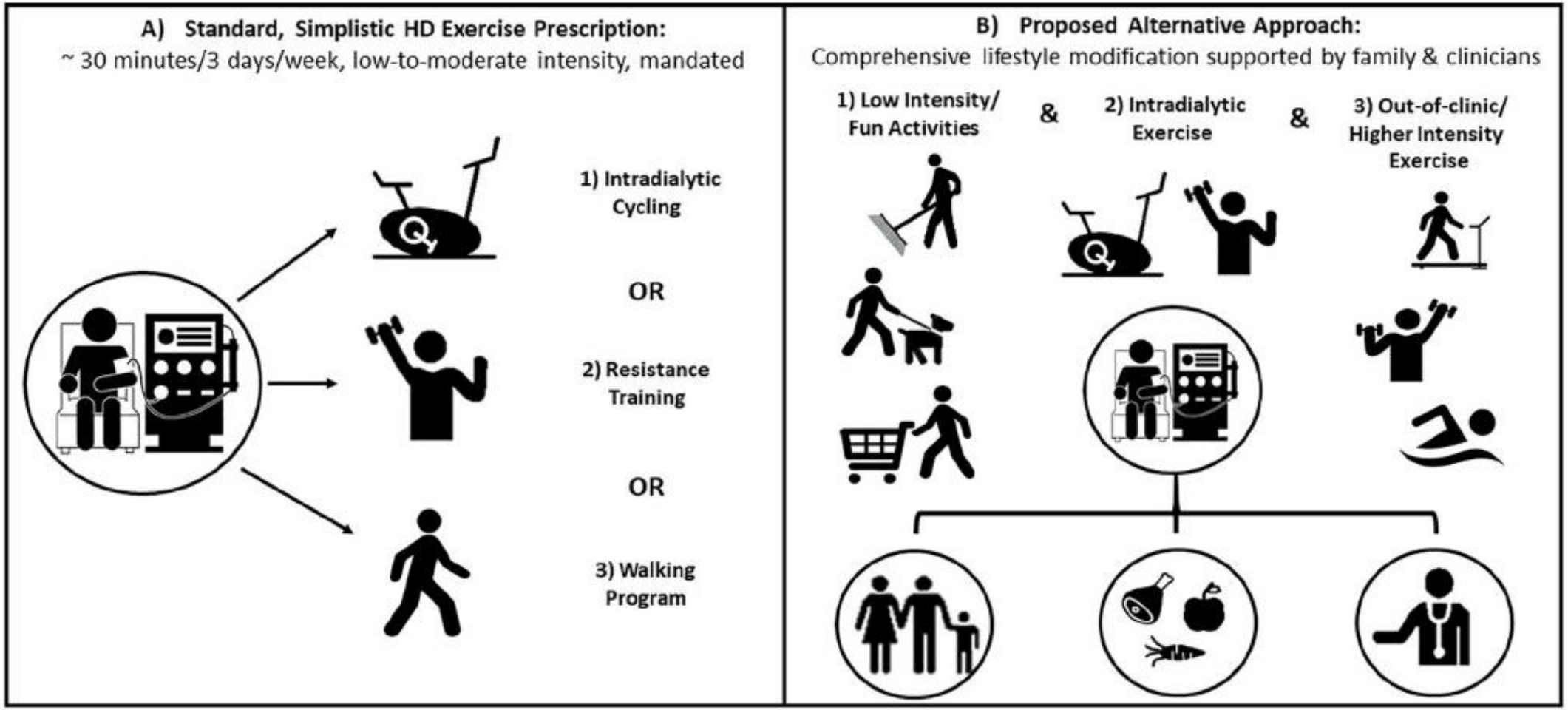
- Progressive exercise for anabolism in kidney disease (PEAK)
  - 12-week intervention- JASN 2007
    - 49 patients, 24- exercise, 25- usual care
      - No improvement in muscle cross sectional area
      - Improvement in muscle "quality"- lower muscle lipid infiltration. Leg muscle strength was also improved.
      - No improvement in 6-minute walk test
  - 24-week intervention- AJKD 2007
    - No significantly improved muscle cross-sectional area or intramuscular lipid content

JASN 2007 May;18(5):1594-601.
AJKD 2007 Oct;50(4):574-84.

Exercise Takeaways

- Probably a good idea
  - Supervised exercise with PT ideal
  - Something >nothing
- Suggestion of improved:
  - Decreased CKD progression
  - BP control
  - BMI
  - Improved QoL parameters
- Endurance exercise > Resistance Training (?)
- "Starting an exercise program when a patient reaches the need for dialysis might be too late … it is reasonable to assume that bigger gains could be made by focusing exercise interventions in the non-dialysis CKD patients."

Exerc Sport Sci Rev. 2020 Jan; 48(1): 28–39.



Exerc Sport Sci Rev. 2020 Jan; 48(1): 28–39.

Symptoms v Scores

- What to target?
  - Providers: Kt/V, PTH, PO_4, Hgb (CMS reportable parameters)
  - Patients: bothersome symptoms

Standardized Outcomes in Nephrology (SONG)

- Fatigue
- Depression
- Pain
- Anxiety
- Cramps
- Itching
- Nausea
- Anemia
- Sexual function
- Lack of food enjoyment
- Mobility
- Restless legs syndrome
- Dialysis-free time
- Ability to work or travel
- Sleep disturbance
- Reduced cognitive function
- Impact on family/friends
- Hospitalization
- Feeling “washed out”

Fatigue

Clin Kidney J, Volume 16, Issue 1, January 2023, 30–40.

Symptom	Treatment	Efficacy/safety	Approval/off-label for treatment of symptom?
Fatigue	Non-pharmacologic interventions: sleep hygiene, energy conservation, acupressure	Limited evidence of efficacy in small-scale studies [54]	NA
	Pharmacologic interventions: hematopoietics, antidepressants, anxiolytics, levocarnitine, human growth hormone, more frequent dialysis	Hematopoietics and antidepressants show some efficacy in patients with underlying anemia or depression	Treatments approved for underlying conditions such as anemia and depression [54]
		Levocarnitine and human growth hormone have limited evidence of efficacy in small-scale studies	
		Increased dialysis frequency has demonstrated efficacy but also increases overall time on dialysis [54]	

Restless Legs

Restless legs syndrome	Non-pharmacologic: exercise, near-infrared light, vibration and massage	Limited evidence of efficacy in small-scale studies [62]	NA
	Pharmacologic: dopamine agonists, levodopa and iron supplements	Limited evidence of efficacy in small-scale studies [62]	Off-label treatment
	Parathyroidectomy	Limited evidence of efficacy in small-scale studies [62]	NA

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Nausea and Sleep

Nausea	Ondansetron, metoclopramide and haloperidol	Evidence of efficacy for uremia-associated nausea [63]	Approved in general population
Sleep disturbance	Non-pharmacologic: exercise and sleep hygiene	Evidence of efficacy in the general population, limited evidence in dialysis populations [64]	NA
	Pharmacologic: treatment of underlying disorders, e.g. restless legs syndrome, pruritus or use of hypnotics	Evidence of efficacy in the general population, limited evidence in dialysis populations [64]	Several medications approved for insomnia in the general population—only eszopiclone is approved for longer-term use [64]

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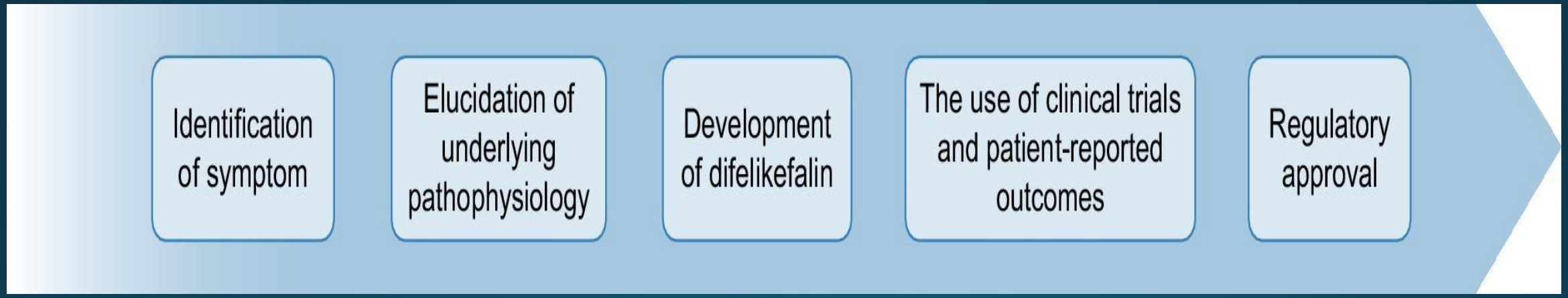
Pruritis

Pruritus	Difelikefalin	Robust clinical efficacy and safety data from large well-designed Phase 3 RCTs [13, 46, 48]	Only treatment that is FDA-approved by regulatory authorities for treatment of CKD-aP
	Gabapentinoids (pregabalin and gabapentin)	Effective for reduction of itch intensity	Not approved for CKD-aP, off-label treatment
		Risk of potentially serious adverse effects, particularly at higher doses, including altered mental status, falls and fractures [57]	

Figure 1: Outline of the difelikefalin pathway, from symptom identification to regulatory approval.



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https://doi.org/10.1093/ckj/sfac187

Figure 2: Pathophysiology of the itch mechanism through activation of kappa-opioid receptors in response to inflammation in CKD-aP.

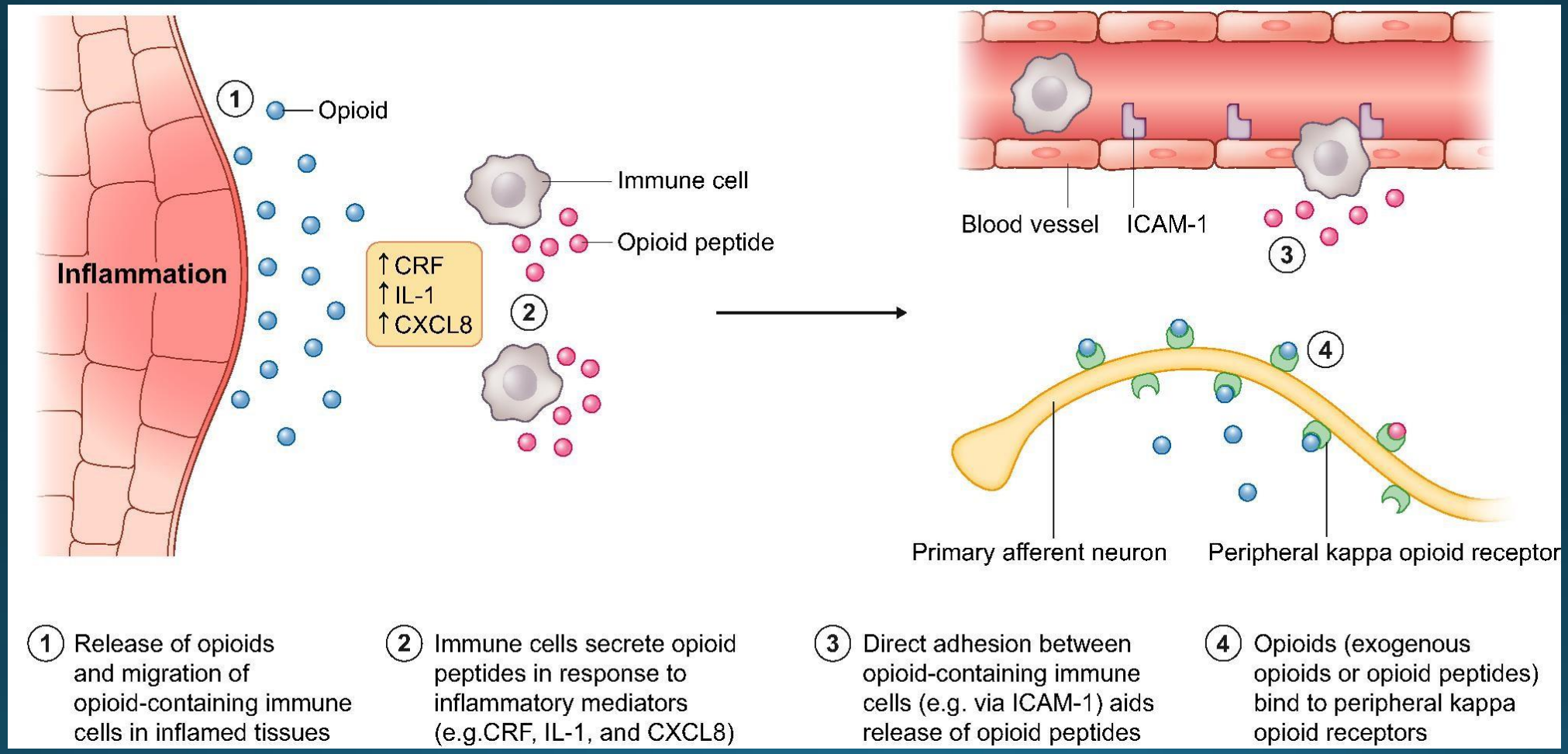

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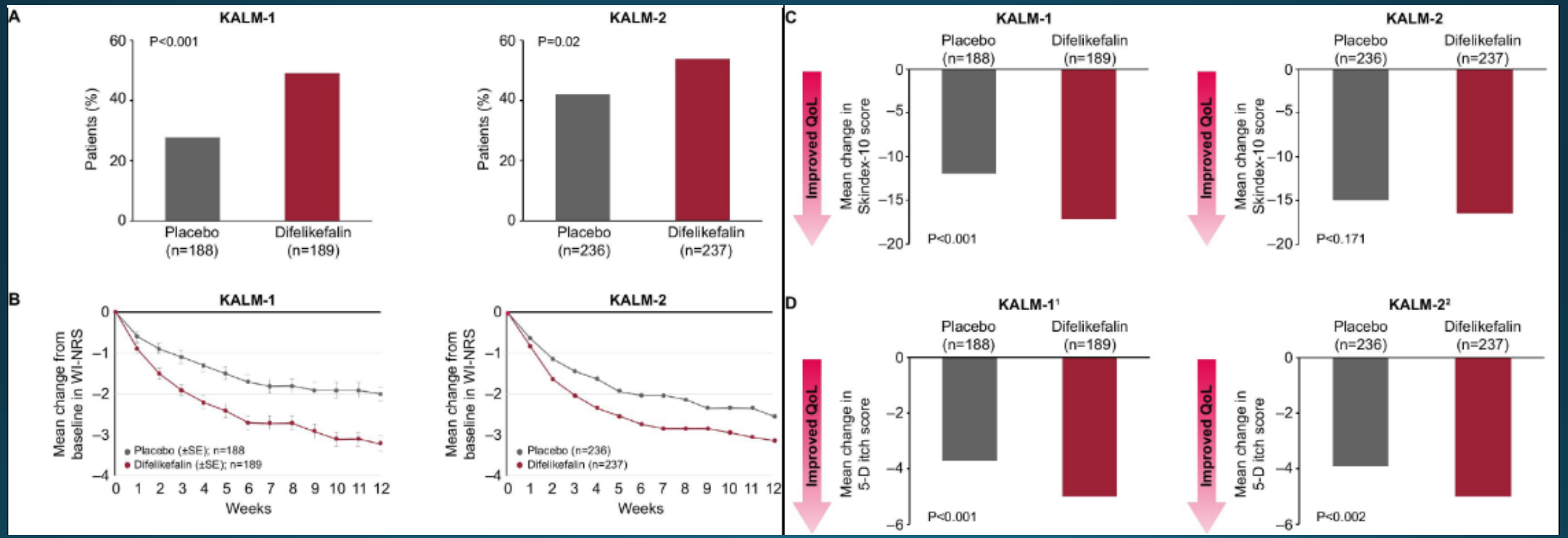
Figure 4: Improvement in itch severity and itch-related QoL with difelikefalin versus placebo



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Summary

- Dietary guidelines for CKD 3-5D
  - Protein, Phosphorus, Potassium, Pharmaceuticals
  - Involve a Renal Dietician
- Exercise in CKD/Dialysis
  - Start now, before it's too late
- Symptom approach to CKD care
  - Not just a numbers game
  - Difelikefalin- proof of concept


Questions?

Depression

Depression	Psychotherapy	Some evidence of efficacy, although quality of evidence is low [55]	NA
	SSRIs	Limited evidence of efficacy in the dialysis population [55]	Approved in general population

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Pain

Pain	Conservative management, e.g. exercise, massage, heat/cold therapy, cognitive behavioral therapy	Some evidence of efficacy, although quality of evidence is low [56]	NA
	Analgesics: opioid analgesics are indicated if pain control is not optimal with other methods	Evidence of efficacy in the general population, limited evidence in dialysis populations [56]	Approved in general population
	Gabapentin/pregabalin	Demonstrated efficacy in several small, short-term randomized trials conducted in patients on HD [57]	Recommended for the treatment of neuropathic pain in patients with kidney failure [58]
		Associated with increased risk of mental state changes and falls [57]	

Anxiety

Anxiety	Psychotherapy	Some evidence of efficacy [59]	NA
	Pharmacologic agents, including SSRIs and benzodiazepines	Evidence of efficacy in the general population, limited evidence in dialysis populations	Approved in general population
		Treatment with benzodiazepines is not suitable for long-term treatment [59]	

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Cramping

Cramps	Hypertonic solutions	Evidence of efficacy in patients on HD	NA
		Mild post-dialysis hyperglycemia and hypernatremia have been reported [60]	
	Pharmacologic agents	Limited evidence of efficacy of quinine, vitamin E supplementation and L-carnitine [60, 61]	Off-label treatment

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