A Systematic Review of Scope and Consistency of Outcome Measures for Physical Fitness in Chronic Kidney Disease Trials

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Introduction: Impaired physical fitness is prevalent in people with chronic kidney disease (CKD), associating with an increased risk of mortality, falls, and hospitalization. A plethora of physical fitness outcomes have been reported in randomized trials. This study aimed to assess the scope and consistency of physical fitness outcomes and outcome measures reported in trials in CKD.

Methods: A systematic review of randomized trials reporting physical fitness outcomes in adults with CKD (not requiring kidney replacement therapy) receiving hemodialysis (HD) or peritoneal dialysis and kidney transplant recipients was conducted. Studies were identified from MEDLINE, Embase, and the Cochrane Library from 2000 to 2019. The scope, frequency, and characteristics of outcome measures were categorized and analyzed.

Results: From 111 trials, 87 tests/measurements were used to evaluate 30 outcomes measures that reported on 23 outcomes, categorized into five domains of physical fitness: neuromuscular fitness (reported in 76% of trials), exercise capacity (64%), physiological-metabolic (49%), body composition (36%), and cardiorespiratory fitness (30%). Neuromuscular fitness was examined by 37 tests/measurements including the physical function component of questionnaires (27%), one-repetition maximum (9%), and hand-grip strength (9%). Outcome measures were assessed by lab-based (58% of all trials), field-based (31%), and patient-reported measures (11%), and commonly evaluated at 12 (30%), 26 (23%) and 52 weeks (10%), respectively.

Conclusion: There is large heterogeneity in the reporting of physical fitness outcomes, with inconsistencies particularly in the definitions of outcome measures. Standardization in the assessment of physical fitness will likely improve the comparability of trial outcomes and enhance clinical recommendations.

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Impaired physical fitness is prevalent in patients with CKD and is associated with an increased risk of mortality, progression of kidney disease requiring kidney replacement therapy, falls, and hospitalization.[1–11] Patients with kidney disease experience greater rates of functional decline and accelerated ageing compared to the general population.[12–18] The reasons are multifactorial including uremic muscle dysfunction, shared cardio-metabolic risk factors, and complications of the disease process itself.[16,18]

Physical fitness broadly implies that an individual has acquired the attributes needed to perform a given physical task, at an acceptable level, within a certain physical, social, and psychological environment.[19] The reporting of physical fitness in the nephrology literature has lacked clarity due to the lack of standard definitions, the absence of an agreed classification system of the subcomponents of physical fitness, and

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poor identification of the appropriate tools to measure outcomes. For example, there appears to be haphazard use of terms such as functional capacity, aerobic capacity, and exercise performance, and it is important to determine what aspect of fitness (e.g., cardiorespiratory fitness or exercise capacity) is being reported. Outcomes relating to physical fitness, such as mobility, were identified as important by patients, caregivers, and health professionals through the Standardized Outcomes in Nephrology initiative.[20–22] How to best assess such metrics in a standardized way is as yet unclear and critical to allow reporting of patient important outcomes.

Although interventions to improve physical fitness have been assessed in randomized controlled trials (RCTs),[23–27] outcomes must be consistent, standardized, and patient-important to allow meaningful comparisons across studies and to inform clinical decision-making. The aim of this study is to assess the scope and consistency of outcomes and outcome measures used to assess physical fitness in RCTs in patients with CKD.

METHODS

Selection Criteria

An electronic search using MEDLINE, Embase, and the Cochrane Library databases without language restriction was conducted using search strategies provided in the Supplemental Material. Randomized trials (including *post hoc* analyses of RCTs) that reported at least one physical fitness outcome in adult patients aged 18 years or older at any stage of kidney disease (CKD not requiring kidney replacement therapy, HD, peritoneal dialysis, kidney transplantation) published from March 2000 to March 2019 were eligible. This time frame was chosen to capture the outcome measures used in contemporary trials as they were more likely to reflect current clinical practice. Relevant systematic reviews were screened to identify additional RCTs published within the specified time frame. Review articles, observational studies, conference abstracts, study protocols, and non–English language publications were excluded. The full list of articles is provided in Supplementary Table S1.

Data Extraction

Trial characteristics were extracted by two reviewers (DKJ and RM), including first author, year of publication, participating countries, sample size, stage of kidney disease, baseline fitness levels, study duration, type of intervention, timing of intervention (intradialytic vs. nondialytic for HD trials), and all outcomes. Each physical fitness outcome measure had accompanying data extracted including assessment type (e.g., field test, lab-based test, or patient-reported measure), specific measure (e.g., distance walked in meters), method of aggregation (e.g., mean or median), and time point of measurement.

Classification of Outcome Measures and Tests

Individual outcomes assessing similar aspects of physical fitness were grouped together by one reviewer (DKJ). The grouping was reviewed by three reviewers (DKJ, RM, and JSC), and discrepancies were discussed to reach agreement. Outcome measures were identified and categorized into five domains according to the framework for health-related physical fitness endorsed by Exercise & Sports Science Australia: cardiorespiratory fitness (e.g., objectively measured or estimated peak oxygen uptake, anaerobic threshold), exercise capacity (e.g., peak power output, time on test, distance travelled, and number of steps), neuromuscular fitness (e.g., strength, power, strength endurance, balance, and submaximal speed), body composition (e.g., fat mass, lean muscle mass, and bone mineral density), and physiological-metabolic (e.g., glycemic parameters, lipid metabolism, and cardiovascular and respiratory function) domains.[28] Outcome measures that were defined by terms such as physical functioning, functional capacity, physical performance, physical capacity, physical fitness, exercise tolerance, and work performance were confusing to interpret. To minimize overlaps and to further categorize these terms, outcome measures were reclassified according to the tests/measurements they were assessed by and their relevant physical fitness domains as outlined in Table 1. The list of outcomes was reviewed and agreed upon by five additional reviewers (RK, AT, AV, DWJ, and NI). Categories and classifications were finally agreed on by all reviewers. Tests/measurements were classified into field tests, lab-based tests, and patient-reported outcome measures by reviewers DKJ and JSC. Tests that required specialized equipment such as a dynamometer (e.g., hand grip strength [HGS]) or weights were also classified as lab-based tests.

RESULTS

Trial Characteristics

We included 111 relevant RCTs involving 6049 participants (1644 CKD; 3716 HD; 121 peritoneal dialysis; and 568 kidney transplantations) (Figure 1). Trial characteristics are provided in Table 2. Trials were conducted in 25 countries, including Brazil (23 [21%] trials), United States (22 [20%]), Greece (10 [9%]), United Kingdom (8 [7%]), and Canada (8 [7%]). The median duration of trials was 4 (interquartile range: 3–6) months, and the median sample size was 39 (interquartile range: 26–60) patients. Studies included interventions that mostly involved aerobic training

Table 1. Tests/Measurements Used Across the Trials, Reclassified Into Physical Fitness Domains and Subdomains (%)

Neuromuscular Fitness				**Physiological-Metabolic**		**Exercise Capacity**		**Cardiorespiratory Fitness**	
Strength		Power		Vascular structure/function		Submaximal exercise capacity		Aerobic power	
Maximal torque		TUG	8	Pulse wave velocity	18	Distance travelled		VO_2 max/peak	
Quad strength	12	Power rig	<1	Arterial stiffness index	3	6MWT	57	Maximal or submaximal test	76
HGS	10								
Maximal weight lifted		Balance		Arterial FMD	3	NSRI walk	4	Exercise threshold	
1-RM	5	Tinetti balance instrument	1	Baroreflex sensitivity	3	Number of steps		Anaerobic, ventilatory or lactate threshold	
Repetition maximum		1-leg balance test	1	Artery/vein diameter	3	Stair climbing test	4	Maximal or submaximal test	17
5-RM	1	Berg balance scale	1	Toe-brachial index	3	2-minute step test	4	HR response	
Squat test <1		Four square step test	<1	CIMT	1	2-minute stair climb	1	HR max	
Submaximal speed		Balance confidence scale	<1	Doppler flow	1	4-minute step test	1	Maximal exercise test	7
Gait speed	3	Mini-BEST	<1	Vein distensibility	1	Incremental step test	1	Body composition	
Function		Static GSI	<1	Respiratory parameters		Time		Fat	
Physical function component of [a]	27	Dynamic GSI	<1	Maximal inspiratory and expiratory pressure	11	Normal walking test	1	BMI	26
Barthel ADL index	<1	Strength endurance		Spirometry	10	Fast walking test	1	DEXA	15
FIM	<1	30-s STS	8	Lipid metabolism		Maximal exercise capacity		BIA	5
Flexibility		60-s STS	4	Serum lipids	7	Time on test		Waist to hip ratio	5
Sit and reach test	3	10 times STS	5	Glycemic parameters		Graded exercise treadmill or ergometer	11	Air displacement plethysmography	3
Shoulder flexibility	<1	5 times STS	4	Fasting glucose	10	ISWT	7	Skinfold thickness	3
Hamstring flexibility	<1	Arm curl test	2	HbA1c	4	METs		CT abdomen	1
		Heel rises	1	OGTT	3	Peak METs	6	Muscle	
		Chair stands	1	Fasting insulin	3	Maximal speed		DEXA	16
		Toe lifts	<1	Muscle characteristics		Graded exercise test	1	CSA/volume — US, CT or MRI	14
		Forearm endurance	<1	Histology	7			BIA	6
		Leg extensor endurance	<1	Resting muscle VO_2	1			Muscle circumference	5
				Cardiac function				Bone density	
				TTE	4			BMD	1
				HR variability	4				

6MWT, 6-minute walk test; ADL, activities of daily living; BEST, balance evaluation systems test; BIA, bio-electrical impedance analysis; BMD, bone mineral density; BMI, body mass index; CIMT, carotid intima-media thickness; CSA, cross-sectional area; CT, computed tomography; DEXA, dual-energy x-ray absorptiometry; FIM, functional independence measure; FMD, flow-mediated dilation; GSI, global stability index; HbA1c, glycosylated hemoglobin; HGS, hand grip strength; HR, heart rate; ISWT, ; MET, metabolic equivalent; MRI, magnetic resonance imaging; NSRI, North Staffordshire Royal Infirmary; OGTT, oral glucose tolerance test; RM, repetition maximum; STS, sit to stand; TUG, timed up and go; TTE, transthoracic echocardiography; US, ultrasound; VO_2, peak oxygen uptake;

[a]Kidney disease quality of life, short form 36, short-form 8, Spitzer index, sickness impact profile.

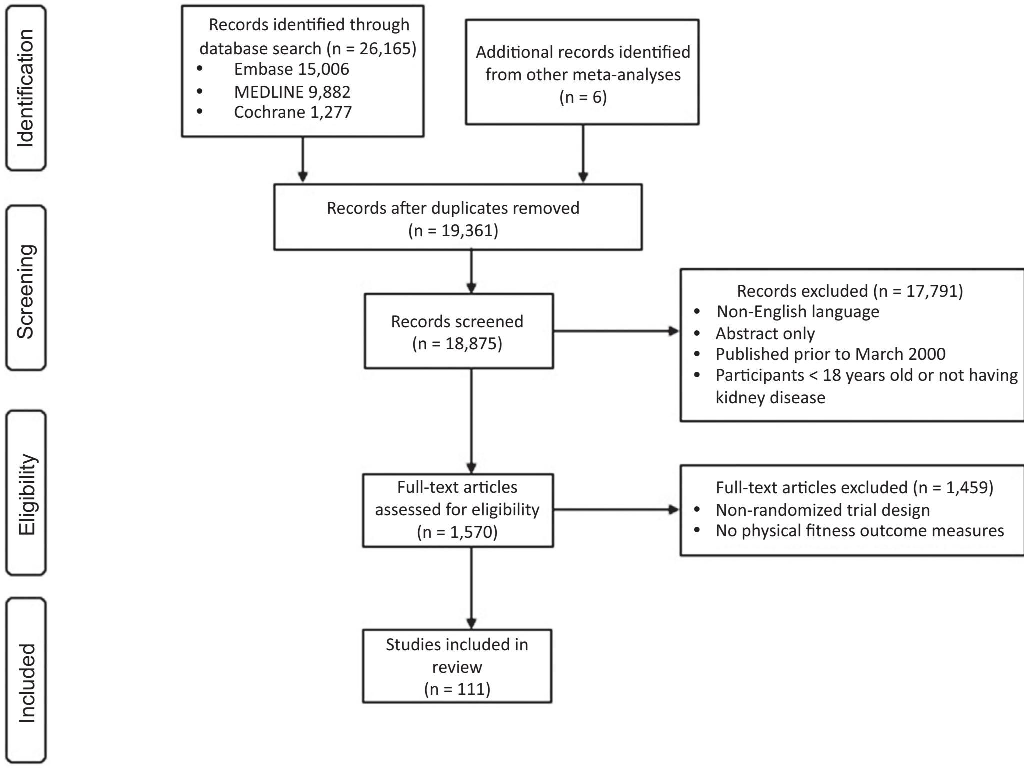

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the systematic review.

(39%), and were supervised (78%) and delivered during HD sessions (90% of trials that included patients receiving HD; 58% of all trials). Of the 73 trials that studied exercise in people receiving HD, 77% had outcomes measured on dialysis days (91% intradialytic), 16% on nondialysis days, and 7% on either day or not specified.

Outcomes, Measures, Tests, and Domains

Nonspecific outcome measures were frequently reported, including functional capacity (17 trials), physical function (reported in 15 trials), physical performance (12 trials), physical capacity (seven trials), physical fitness (three trials), exercise tolerance (three trials), and work performance (one trial). Heterogeneity in outcome measure assessment was also noted. The 6-minute walk test (6MWT), as a measure of distance walked, was reported to be an assessment of functional capacity (24% of trials), walking capacity (16%), exercise capacity/tolerance (16%), physical functioning (14%), physical performance (10%), physical capacity (8%), aerobic capacity (6%), exercise performance (2%), function (2%), and muscular endurance (2%). Similarly, HGS was reported as an assessment of muscular strength (63%), physical functioning (21%), physical performance (5%), exercise capacity/tolerance (5%), and physical fitness (5%) (Supplemental Table S1).

After reclassification, we identified that 87 different tests/measurements were used to evaluate 30 outcome measures that reported on 23 physical fitness outcomes over 17 separate time points across the trials. The breakdown of outcomes, tests/measurements, assessment types, and time points within each physical fitness domain are summarized in Figures 2 and 3, respectively. Lab-based tests were the most common assessment type (58% of all trials), followed by field tests (31%), and patient-reported outcome measures (11%). Outcome measures were most frequently assessed at 12 weeks (30%), 26 weeks (23%), and 52 weeks (10%). Tests/measurements that were used to assess the different fitness domains (neuromuscular fitness, exercise capacity, cardiorespiratory fitness, body composition, and physiological-metabolic) and their respective subdomains are presented in Table 2.

Neuromuscular Fitness

Neuromuscular fitness was reported as nine different outcome measures and at 14 separate time points. The examined subdomains were strength (28%, reported as maximal torque [22%], maximum weight lifted [5%], and repetition maximum [1%]), function (28%), strength endurance (25%), power (9%), balance (5%),

Table 2. Characteristics of Included Trials

Trial Characteristic	n (%)
Year of Publication	
2000–2004[a]	14 (13)
2005–2009	9 (8)
2010–2014	31 (28)
2015–2019[a]	57 (51)
Country	
Brazil	23 (21)
United States	22 (20)
Greece	10 (9)
United Kingdom	8 (7)
Canada	8 (7)
Australia	7 (6)
Other[b]	33 (30)
Kidney disease cohort	
HD	69 (62)
CKD	27 (24)
KT	9 (8)
HD and PD	3 (3)
PD	1 (1)
CKD and HD	1 (1)
CKD and KT	1 (1)
Sample size	
1–50	76 (68)
51–100	21 (20)
101–150	7 (6)
≥151	7 (6)
Study duration, months	
≤1	6 (5)
>1 to ≤3	38 (35)
>3 to ≤6	44 (39)
>6 to <12	7 (6)
≥12	16 (14)
Intervention type[c]	
Exercise	
Aerobic	44 (39)
Resistance	34 (30)
Combined	30 (27)
Other[d]	40 (36)
Number of outcome measures reported in each trial	
1–3	58 (53)
4–6	37 (33)
7–11	16 (14)

HD, hemodialysis; PD, peritoneal dialysis; KT, kidney transplantation; CKD, chronic kidney disease.
[a]March 2000 to March 2019.
[b]Other countries included Italy (4 trials), Japan (4), Tunisia (3), Taiwan (2), Iran (2), China (2), Spain (2), France (2), Denmark (2), Mexico (2), Turkey (1), Belgium (1), Czech Republic (1), Hong Kong (1), Netherlands (1), South Korea (1), Sweden (1), Switzerland (1), and Thailand (1).
[c]Sum is greater than 100% as some trials compared different interventions (e.g., aerobic versus resistance training was regarded as two separate interventions).
[d]Other interventions included electromyostimulation (5 trials), supplements (5), flexibility (4), respiratory muscle training (4), balance training (3), lifestyle counseling (3), stretching (2), whole body vibration (1), antidepressant (1), steroid withdrawal (1), L-carnitine infusion (1), blood flow restriction (1), Quran recitation (1), dopamine agonist (1), and progressive muscle relaxation (1).

flexibility (3%), and submaximal speed (2%). Neuromuscular fitness was assessed using 37 different tests/measurements including the physical function component of patient questionnaires (27%), quadriceps strength (12%), HGS (10%), and timed up-and-go tests (8%).

Exercise Capacity

Exercise capacity was reported as six different outcome measures and at 13 separate time points. Distance travelled was the most common outcome measure (60%), followed by time on test (19%), number of steps (11%), metabolic equivalents from time on test or peak power (6%), walking time (2%), and speed (1%). Exercise capacity was assessed using 13 different tests/measurements including 6MWT (57%), graded exercise treadmill or ergometer (19%), and incremental shuttle walk test (7%).

Cardiorespiratory Fitness

Cardiorespiratory fitness was reported as three different outcome measures, peak oxygen uptake (VO_2 max/peak, [76%]), anaerobic/ventilatory/lactate threshold (17%), and heart rate maximum (7%). These outcomes were measured at nine separate time points and were all assessed through maximal or submaximal exercise tests.

Body Composition

Body composition was reported as five different outcome measures and at six separate time points. Muscle mass (measured in millimeters or percent of body weight) was the most commonly reported outcome measure (41%), followed by fat mass (26%, measured in millimeters or percent of body weight), weight for height (26%), waist-to-hip ratio (5%), and bone mineral density (1%). The most frequently reported tests/measurements were dual-energy x-ray absorptiometry (DEXA) (33%), body mass index (26%), and muscle cross-sectional area (14%, measured by ultrasound, computed tomography, or magnetic resonance imaging).

Physiological-Metabolic

Components of the physiological-metabolic domain were reported as seven different outcome measures and at 11 separate time points. These included vascular structure/function (36%), glycemic parameters (19%), respiratory muscle strength (11%), and respiratory function (10%). The most commonly used tests/measurements were pulse wave velocity (18%), spirometry (11%), and respiratory manometry (11%).

Patient-Reported Outcomes

Patient-reported outcomes were evaluated by 11% of all tests/measurements and reported exclusively in trials that assessed neuromuscular fitness. The physical function component of the kidney disease quality of life, short-form 36 (SF-36), short-form 8 (SF-8), Spitzer index, and the sickness impact profile accounted for 96% of patient-reported outcomes, with one trial using "Barthel activities of daily living" and another trial reporting on the "functional independence measure."

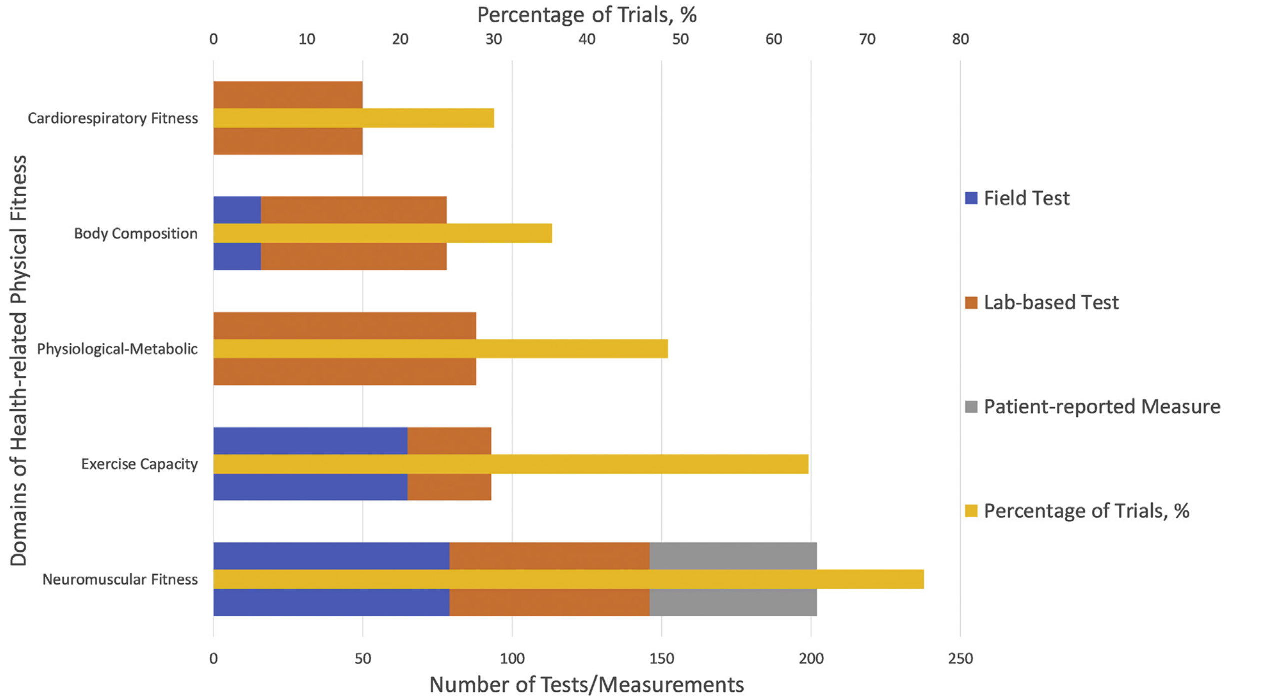

Figure 2. The reported frequency of each domain (as percentage of all trials) and the number of tests/measurements reported within each domain (categorized according to assessment type — field test, lab-based test, or patient-reported measure).

Tests/Measurements Across Stages of Kidney Disease

The frequency and distribution of tests/measurement were similar between the stages of kidney disease (Supplementary Table S2): HD/ peritoneal dialysis (6MWT [11%], SF-36 [10%], VO_2 peak/max [6%], quadriceps strength [5%], HGS [5%], and DEXA [5%]); CKD (VO_2 peak/max [13%], 6MWT [9%], body mass index [7%], SF-36 [5%], and DEXA [5%]); kidney transplantation (VO_2 peak/max [14%], body mass

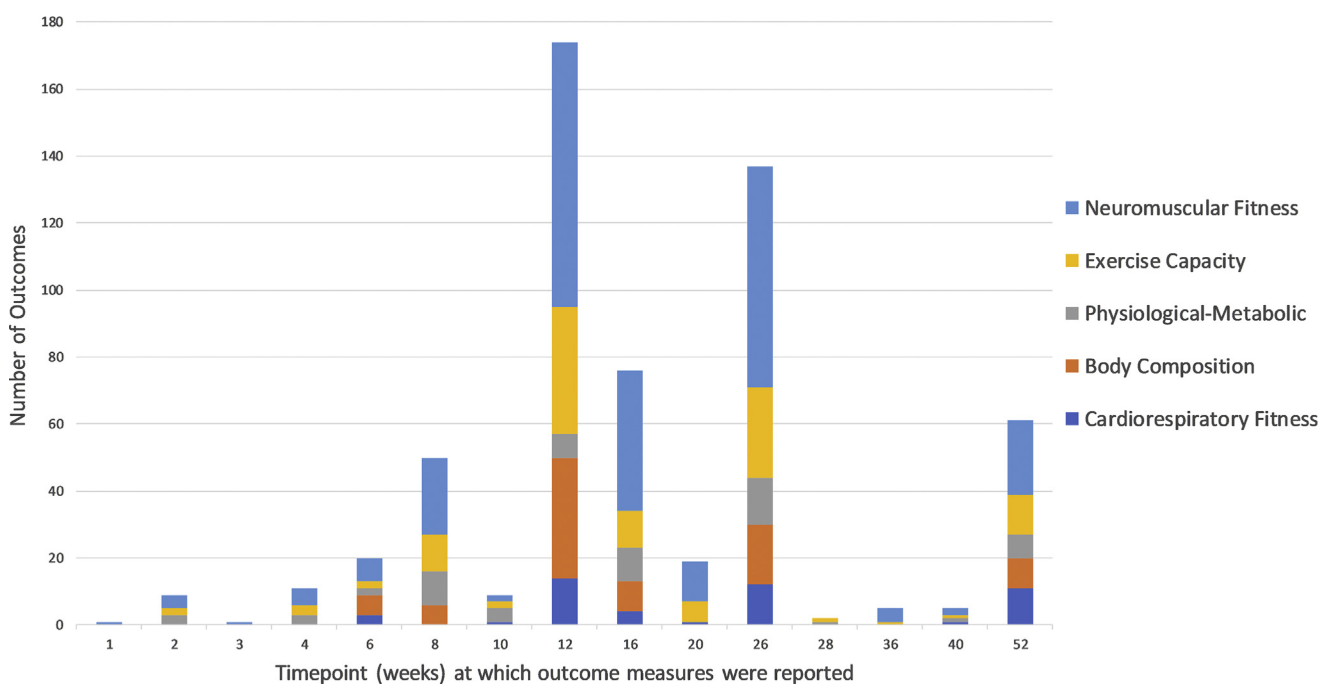

Figure 3. The number of outcomes measured at different time points, after baseline testing, separated by physical fitness domain. Additionally, three outcome measures were recorded at 208 weeks (not shown).

index [9%], DEXA [9%], SF-36 [7%], pulse wave velocity [7%],dual and quadriceps strength [7%]).

DISCUSSION

This review highlights the prevalent use of non-standardized terms to define physical fitness outcome measures in RCTs of adult patients across the spectrum of kidney disease. Overall, 87 tests/measurements were used to assess 30 different outcome measures across 112 RCTs. Physical fitness outcome measures have primarily assessed the domains of neuromuscular fitness, followed by exercise capacity, physiological-metabolic, body composition, and cardiorespiratory fitness. These outcomes have generally been assessed using lab-based and field tests, with few patient-reported outcome measures included. The findings of this systematic review emphasize the inconsistency and diversity in the measurement and reporting of outcome measures in trials of physical fitness interventions in people with kidney disease. Furthermore, the metric, method of aggregation, and time point of when outcomes were measured varied considerably. Finally, the trials were small (87% had 100 or fewer participants) and short (79% running for 6 months or less). Overall, these inconsistencies and limitations restrict the ability to accurately assess the efficacy of an intervention and compare different interventions, ultimately impairing the quality of clinical recommendations.

Categorization of outcome measures and tests/measurements within fitness domains was a critical first step to analyzing the data in this review. Cardiorespiratory fitness is a very specific component of physical fitness, defined as the integrated ability to transport oxygen from the atmosphere to the mitochondria to perform physical work.[29] It is either measured directly with a gas analyzer or estimated from the heart rate response of a submaximal test. Exercise capacity is another component of physical fitness that refers to the ability to complete a physical task (e.g., peak work rate achieved on a graded cycle ergometer test, "time on test" during a standard incremental treadmill protocol, or from a field test such as the 6MWT). Although tests of exercise capacity can be used to estimate VO_2 max/peak using formulae, they were often inappropriately reported as measures of cardiorespiratory fitness. For classifying tests into neuromuscular fitness subdomains, consideration was given to the contribution of the different energy systems based on the usual time taken to complete the test. For example, the five times sit to stand test would take approximately 10 to 15 seconds in older individuals; therefore, it relies more on the anaerobic glycolysis system leading to its classification as strength endurance, whereas the time up-and-go test is classified as a measure of power as it would usually be completed in less than 10 seconds.

In addition, outcome measures that were defined by terms such as physical functioning, functional capacity, physical performance, physical capacity, physical fitness, exercise tolerance, and work performance were frequently reported but did not reflect a standardized outcome measure or domain of physical fitness. For example, the term "physical functioning" was used to report outcome measures of (i) neuromuscular fitness; (ii) composite of neuromuscular fitness and exercise capacity; and (iii) composite of neuromuscular fitness, exercise capacity, and cardiorespiratory fitness. Similarly, "functional capacity" was reported as an outcome measure of (i) exercise capacity; (ii) composite of exercise capacity and neuromuscular fitness; and (iii) neuromuscular fitness. Furthermore, the tests/measurements used to assess these outcome measures were also heterogenous. To rationalize these inconsistencies, we propose that physical fitness outcome measures should be defined by what the test or measurement was designed to measure, and not the other way around (e.g., the 6MWT to be reported as a measure of "distance travelled" or "submaximal exercise capacity" [Table 1], rather than "physical performance" or "exercise performance"). Categorization into physical fitness domains provides further granularity to the outcome measures. The use of nonspecific outcomes such as physical performance, physical capacity, or exercise performance must be more clearly defined and ideally avoided. The proposed model of using tests/measurements and domains to classify outcome measures offers a structured and comprehensive approach for future physical fitness research (Table 1).

The timing of outcome measurement was also inconsistent across trials, particularly relevant in people receiving HD. The cardiovascular physiology of an individual treated with HD varies considerably, depending on the time of day (especially if pre-, intra- or immediately post-HD) and day of the week (particularly in relation to when they last dialyzed).[30] For instance, in a cross-sectional study of 156 people receiving HD, there was a significant reduction in HGS over the duration of a single HD session.[31] The timing of outcome measurement, regardless of physical fitness domain, is thus likely to influence the interpretation of results. This is therefore an important consideration when comparing study outcomes, particularly in trials involving participants treated with HD.

This review also highlights the apparent disconnect between trial design and patient preferences. For instance, a survey of 423 dialysis patients in Canada found that 70% of HD patients preferred to exercise at home.[32] In contrast, fewer than 10% of HD trials in this review evaluated home-based interventions. Similarly, although combined aerobic and resistance training was the most preferred type of exercise (selected by 40% of surveyed HD patients), this was the least trialled intervention (28%) across all the included studies.[32] Overall, it remains unclear the extent to which patients were involved in the selection of outcomes in these trials. It is plausible that increased consumer engagement at the trial design stage may improve the relevance of the research, its external validity, and dissemination of findings as well as the uptake of effective interventions.[33] Critically important outcomes identified from the Standardized Outcomes in Nephrology initiative such as mortality, fatigue, hospitalization, life participation, ability to work, sleep quality, and ability to travel were mostly not reported in any of the trials, and how to best incorporate these patient important outcomes warrants further study.[20–22] It would be pertinent to evaluate these outcomes in conjunction with physical fitness outcomes in future trials.

Study Limitations

There are some potential limitations. We limited the search to trials published with a 20-year time frame from March 2000 because we focused on contemporary trials. However, the inclusion of nonrandomized and older trials would likely further increase heterogeneity and inconsistency, and thus be unlikely to change the conclusion of this study.

CONCLUSION

Compromised physical fitness in patients with CKD needs ongoing high-quality research to ensure that effective interventions and improved patient outcomes can be translated to routine clinical practice. It is apparent that there is considerable heterogeneity in the outcome measures used to report on physical fitness in kidney disease trials. A multitude of outcome measures have been presented, often to assess different outcomes, with disparity in how these measures report on the key domains of physical fitness. Given the multidimensional nature of physical fitness, a cumulative measure that combines a battery of tests, covering a variety of domains, is most likely required. Furthermore, there are limited patient-reported outcome measures for assessing physical fitness, and it is not clear if these are directly measuring factors that are important to patients.

Future research should firstly aim to identify the physical fitness outcome measures that are valid, reliable, and patient-important. Classifying outcomes within an accepted framework for physical fitness offers the first step to better defining and informing the selection of outcome measures in this process. Further investigation into the validity, reliability, and practicality of outcome measures is necessary. Defining consistent, relevant, and patient-important outcome measures will potentially allow for more meaningful comparisons across studies to inform clinical decisions. These advances will lay the foundation for more effective clinical trials, ultimately aspiring towards improving the physical fitness of people with kidney disease.

DISCLOSURES

DKJ has received travel sponsorship from Roche. DWJ has received consultancy fees, research grants, speaker's honoraria and travel sponsorships from Baxter Healthcare and Fresenius Medical Care, consultancy fees from Astra Zeneca and AWAK, speaker's honoraria and travel sponsorships from ONO, and travel sponsorships from Amgen. He is a current recipient of an Australian National Health and Medical Research Council (NHMRC) Practitioner Fellowship. NI has received consultancy fees, speaker's honoraria and travel sponsorship from Alexion Pharmaceuticals. RK has received consultancy fees, speaker's honoraria and travel sponsorship from Baxter Healthcare and travel sponsorship from Amgen. The remaining authors declare that they have no relevant financial interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Summary of intervention type, fitness outcome and assessment method across the studies.

Table S2. Distribution of tests/measurements across the stages of kidney disease.

PRISMA Checklist

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