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Systematic Review

Do Exercise, Physical Activity, Dietetic, or Combined Interventions Improve Body Weight in New Kidney Transplant Recipients? A Narrative Systematic Review and Meta-Analysis

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Abstract: Weight gain within the first year of kidney transplantation is associated with adverse outcomes. This narrative systematic review and meta-analysis examines the effect of exercise, physical activity, dietary, and/or combined interventions on body weight and body mass index (BMI) within the first year of kidney transplantation. Seven databases were searched from January 1985 to April 2021 (Prospero ID: CRD42019140865), using a 'Population, Intervention, Controls, Outcome' (PICO) framework. The risk-of-bias was assessed by two reviewers. A random-effects meta-analysis was conducted on randomized controlled trials (RCTs) that included post-intervention body weight or BMI values. Of the 1197 articles screened, sixteen met the search criteria. Ten were RCTs, and six were quasi-experimental studies, including a total of 1821 new kidney transplant recipients. The sample sizes ranged from 8 to 452. Interventions (duration and type) were variable. Random-effects meta-analysis revealed no significant difference in post-intervention body weight (−2.5 kg, 95% CI −5.22 to 0.22) or BMI (−0.4 kg/m^2, 95% CI −1.33 to 0.54). Despite methodological variance, statistical heterogeneity was not significant. Sensitivity analysis suggests combined interventions warrant further investigation. Five RCTs were classified as 'high-risk', one as 'some-concerns', and four as 'low-risk' for bias. We did not find evidence that dietary, exercise, or combined interventions led to significant changes in body weight or BMI post kidney transplantation. The number and quality of intervention studies are low. Higher quality RCTs are needed to evaluate the immediate and longer-term effects of combined interventions on body weight in new kidney transplant recipients.

Keywords: kidney transplant; weight gain; body weight; systematic review; physical activity; meta-analysis

1. Introduction

Weight gain within the first year of solid organ (kidney, liver, heart, and lung) transplantation has been associated with adverse clinical events and poor transplant outcomes [1,2]. Whilst weight gain presents as a clinical issue for all solid organ transplant (SOT) recipients, the experiences of weight gain vary across the SOT groups. Liver transplant recipients tend to have a reduction in body weight in the first six months associated with the removal of ascites, followed by a period of weight gain [3]. In contrast, kidney,

heart, and lung transplant recipients demonstrate rapid weight gain in the acute-post operative period [3].

Increased body weight and body mass index (BMI) is associated with poor transplant outcomes. A retrospective analysis of 25,539 adult kidney transplant recipients (KTRs) in the United Kingdom (UK) reported a BMI of greater than 25 kg/m^2 was an independent risk factor for both delayed graft function and primary graft non-function [4]. In addition, underweight and obese KTRs were reported to have poorer graft survival [4].

Weight gain within the first year of receiving a kidney is a critical health issue [5]. KTRs who gain more than 15% of their body weight within the first year of transplant surgery are at an increased risk of death with a functioning kidney [6]. The factors underlying post kidney transplant weight gain include reduced physical function [7] and physical activity (PA) [8], increased appetite [9], steroid medication use [10], and the lifting of dietary restrictions [11].

Results from a recent UK survey of all transplant centres revealed clinicians believed that kidney transplant outcomes were adversely affected by obesity. [4] Despite this recognised clinical need, dedicated pathways to address weight management for KTRs were sparse with variable access [4].

Previous literature reviews [12,13], systematic reviews [14,15], and meta-analyses [16,17] that examine the effects of exercise [12,15–17] or PA interventions [13,14] for KTRs have shown a favourable effect on cardiorespiratory fitness and exercise tolerance [13,15–17], muscle strength and function [16,17], health-related quality of life [13,15,16], maximum heart rate [15], and arterial stiffness [17]. Exercise studies have failed to show significant effects on body weight or composition [15]. However, combined interventions that included any combination of either exercise, physical activity, and/or dietary interventions were excluded in these reviews.

A Cochrane review of dietary interventions for adults with end-stage kidney disease (including KTRs), concluded clinical dietary care recommendations could not be made for KTRs due to insufficient evidence [18]. This Cochrane review excluded dietary interventions that incorporated strategies to implement lifestyle behaviour-change.

Currently, there are no systematic reviews and meta-analyses that consider the impact of either exercise, physical activity, dietary, or combined interventions on body weight and BMI in KTRs within the first year of receiving a kidney transplant. The research question for this systematic review was 'do exercise, physical activity, dietetic, or combined interventions improve body weight in new kidney transplant recipients?' The aim of this narrative systematic review and meta-analysis was to provide a synthesis and pooled effect of post-transplant interventions on body weight and BMI within the first year of kidney transplantation and suggest recommendations for future research.

2. Materials and Methods

2.1. Search Protocol and Registration

A pre-specified protocol was published on the 9th September 2019 (www.crd.york.ac.uk/PROSPERO, accessed on 9 September 2019, id: CRD42019140865). This narrative systematic review and meta-analysis was undertaken as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance [19], (Supplementary Material, Table S1). Eligibility criteria were based on the 'Population, Intervention, Controls, Outcome' (PICO) framework [20,21], and are summarised in Table 1. The population of interest was new KTRs within the first year of kidney transplantation. Post-transplant interventions consisted of either exercise, physical activity, dietary interventions, or a combination thereof. PA was defined as any habitual or planned activity of the body such as occupational, transportation, domestic, and social [22]. In contrast, exercise interventions were defined as any planned, structured, prescriptive activity designed to improve a specific aspect of physical fitness [22,23]. Dietary interventions included dietary modifications, advice, nutritional counselling, and education regarding food-based interventions [18]. Combined interventions refer to any combination of exercise, PA, and/or dietary interven-

tions. They may also include behaviour change techniques (BCTs) designed to address PA and/or healthy eating behaviour(s) [24].

Table 1. Eligibility criteria based on the PICO framework.

PICO(s)	Inclusion	Exclusion	Reasons for Exclusion
Population	KTRs within the first 12 months of transplantation	>12 months post-transplant <18 years of age Mixed samples (e.g., dialysis and transplant patients)	WG occurs within first year Different populations (adults vs. paediatric) Difficult to isolate effects to just KTR in mixed sample unless information provided by authors
Intervention	Complex interventions involving either exercise, activity, nutrition, diet, behaviour-change, or combined interventions designed to prevent WG occurring	Treatments including pharmacological intervention	Difficult to isolate effects of the other components of the treatment
Comparator	Usual care or standard care or no intervention	No comparator available	Difficult to determine the treatment effect(s)
Outcomes-Primary outcome	WG from baseline to short term (3 months) baseline to long term (6–12 months)	No reported BW or BMI at baseline or follow-up (3–12 months)	Unable to determine change in BW or BMI
Study Types	RCTs, non-RCTs (quasi-experimental)	Exclude literature reviews Exclude trials with no control group	Outside scope of this review
Language	English		Limited resources for this project
Year	Published after 1985		Changes to standards of care

Note. KTR indicates kidney transplant recipient, BW = body weight, WG = weight gain, CKD = chronic kidney disease, RCTs = randomised controlled trials, Non-RCTs = nonrandomised controlled trials.

As weight gain is of clinical concern, particularly within the first year of receiving a kidney transplant, interventions were included if they were offered within the first year of receiving the kidney transplant. Table S2 demonstrates the search strategy. Randomised Controlled Trials (RCTs) and quasi-experimental studies (non-RCTs) with a comparator group were included. The primary outcome of interest was post-intervention measures of body weight or BMI. Long-term follow-up of body weight and BMI were included if available. Secondary outcomes included body composition, physical function, PA levels, self-efficacy toward PA, and mood. This systematic review will focus on body weight and BMI from the RCTs. Secondary outcomes and non-RCTs will be presented briefly.

2.2. Study Identification

MEDLINE, Embase, Psychinfo, CINAHL, SCOPUS, The Cochrane Library, and Web of Science were searched from the 1st January 1985 to the 6th April 2021. Grey literature was searched using OpenGrey. A combination of free text searching, subject headings, and Boolean operators were used. This search strategy was piloted and refined by authors and subject matter experts, with assistance from librarians. Search terms were adapted to each database. The final search was conducted by two authors (E.M.C. and J.G.). Conference abstracts were searched for full text publications, and reference lists were hand-searched.

2.3. Study Selection, Data Extraction, and Risk-of-Bias

All stages of the review were recorded on an Excel spreadsheet and Endnote software. Duplicate citations were removed. The remaining citations were assessed against the pre-defined eligibility criteria. Title and abstracts that did not meet the search criteria were excluded. The remaining full text articles were assessed for eligibility (E.M.C. and J.G.). Table S3 depicts the screening form.

Data were extracted from the full text publications and tabulated, based on the 'characteristics included in studies table' in the Cochrane Handbook for Systematic Reviews of Interventions [25]. In addition, ten percent of titles and abstracts, and ten percent of the full

text citations were selected using a random number generator and assessed for eligibility by two subject matter experts (J.C. and S.G.). When missing data were encountered, the corresponding author was contacted via email. If no response was received, this was repeated with secondary and senior manuscript authors.

Two reviewers (E.M.C. and E.Mc.) independently assessed the final full text publications using version two of the Cochrane risk-of-bias tool for randomized studies [26] and the risk-of-bias in non-randomized studies of interventions tool [27]. If disagreements occurred, both reviewers would discuss until consensus was achieved. Where consensus could not be achieved, a third reviewer (S.G.) would resolve disagreements.

2.4. Statistical Analysis

The Cochrane handbook [28] was utilised to calculate standard deviations (SD) based on the available data reported. RCTs that reported post-intervention body weight (n = 8) and post-intervention BMI (n = 8) for an intervention group (either diet, PA, exercise, or combined interventions) and a comparator group (usual care or no intervention) were included in the meta-analysis. This allowed for calculation of an estimate of pooled effect of the interventions on body weight and BMI, with associated confidence intervals to demonstrate precision. Meta-analysis was not completed for secondary outcomes in this systematic review due to the variation in measurement scales.

Post-intervention values (body weight and BMI) were used rather than change scores for the meta-analysis. There was inadequate data from the studies to calculate confidence intervals for change-scores in body weight and BMI values in all RCTs. Secondly, meta-analyses with post-intervention values have been shown to have more a conservative estimate of effect than change scores [29]. For the studies with more than one treatment arm, guidance was used to combine means and SDs to form an intervention group mean with SD [30,31].

Meta-analyses were conducted using RevMan software [32]. The inverse model for continuous data and the Der Simonian and Laird [33] random-effects model were used to produce a pooled estimate of effect. A random-effects model was selected due to the anticipated heterogeneity caused by clinical and methodological differences between the RCTs [34].

Forrest plots, with chi squared and I^2 statistics were used to assess heterogeneity before proceeding with the meta-analysis as per the Cochrane handbook [35]. Due to the small number of RCTs included in each meta-analysis, and the methodological variation in trial designs, sub-group analysis was not completed. Heterogeneity and publication bias were explored using funnel plots [34]. A post hoc exploratory sensitivity analysis was performed to examine the potential influence of different intervention types on body weight and BMI values.

3. Results

3.1. Search Results and Study Characteristics

After the removal of duplicates, 1198 citations were reviewed for eligibility. This systematic review revealed eighteen publications, from sixteen studies that met the search inclusion criteria. Four publications [36–39] were from two studies. O'Connor et al. [39] reported a long-term follow-up of the same participants of the original study by Greenwood et al. [38]. Therefore, these two studies [38,39] were considered as one intervention for the purpose of this systematic review and meta-analysis. Painter et al. [36,37] were publications from the same trial, and were also considered as one intervention. Figure 1 summarises the study selection process utilising a PRISMA diagram [40].

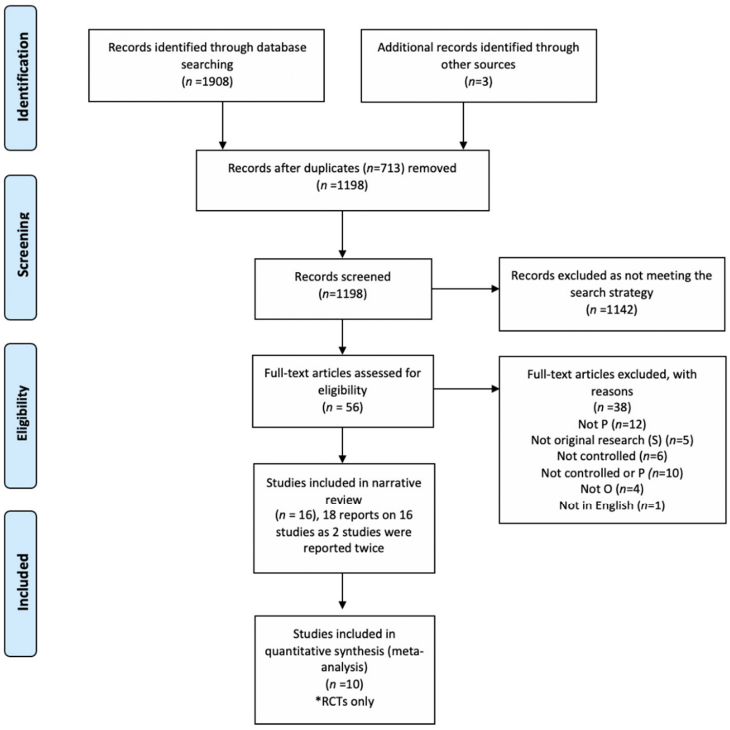


Figure 1. Flow chart of study selection process with reasons for exclusion. Where *n* = number of studies, P = population of interest, S = study design, O = outcome of interest, Randomised Controlled trials (RCTs) only included in this analysis. Figure adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffman TC, Mulrow CD, et al. The PRIMSA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71, doi:10.1136/bmj.n71. For more information visit http://www.prisma-statement.org/.

From the sixteen final studies, ten were RCTs, and six were non-RCTs (quasi-experimental studies) with a total of 1821 KTR participants within the first year of kidney transplantation. The individual study sample sizes ranged from eight [41] to 452 participants [42]. Two of the four studies include other transplant populations [43,44]; however, one author was able to provide data for the KTR sub-group on request [43].

There was variation across the sample characteristics that could limit the generalisability (see Tables 2 and 3). Some trials excluded KTRs with diagnosed diabetes [45–48], another study included hyperlipidaemic KTRs [45], and two studies included only overweight or obese KTRs [42,49]. See Table S4 for detailed study sample characteristics.

Six studies reported body weight only [39,41,44,47,48,50], four reported BMI [43,45,49,51], and six reported both body weight and BMI [36,42,43,46,52,53] post-intervention. Seven out of the sixteen studies recorded body weight or BMI at an interim time point of three to six months, and at a one-year follow-up [36,39,45,49,50,52,54]. Only three trials [39,50,52] included a long-term follow-up of body weight or BMI after the intervention cessation, making it difficult to determine longer-term intervention effects. Table 2 summarizes the study characteristics of the included RCT studies (*n* = 10).Table S5 (Supplementary Material) summarizes the non-RCTs (*n* = 6).

Table 2. Summary of characteristics of included RCTs (n = 10).

First Author, Year (Country of Origin)	Study Duration (Months)	Sample	Groups	Outcomes (Primary and Secondary)	Results (for Primary and Secondary Outcomes)	Comments
Lawrence et al. [45] (UK)	12	n = 38, KTRs with hyperlipidaemia	IG: Dietitian only for 12 months CG: Usual care, no dietary intervention	Primary: Dietary intake (24-h recall assessed for total energy intake, fibre intake, protein, carbohydrate, fat and distribution of fat intake) and fasting lipids Secondary: BW, BMI, medications, Renal function	Primary: No significant difference between groups in total cholesterol, HDL cholesterol, or plasma triglyceride levels LDL cholesterol was significantly lower in the IG at 1 month after Tx Significant improvement in polyunsaturated-to-unsaturated fat ratio in the IG Change in dietary intake not associated with changes in serum lipid levels Fibre intake significantly higher at 3 months in the IG Secondary: No difference in BMI, medication, or kidney function between groups at any time Both groups reduced average consumption of cigarettes and alcohol	AEs not reported Limited reporting of blinding, allocation, analysis plan, treatment, protocol deviations, and statistical plan
Painter et al. [36] (USA)	12	n = 167	IG: 12-months ET, home based AT CG: no ET	Primary: Not stated Secondary: VO_2 peak, Muscle strength, BC (DEXA), QoL (SF-36), PA reporting (active or inactive)	Primary/Secondary: No difference in BW, BMI, or BC, all participants increased BW, BMI, FM, LTM, % FM IG had greater gains in VO_2 peak and muscle strength IG had higher % classified as active at follow-up No difference in QoL	AEs not reported High dropout rate 42% did not complete assessment at all three timepoints Painter 2003 duplicate paper from this study
Tzvetanov et al. [49] (USA)	12	n = 17, Obese KTRs	IG: 12-month combined Rx (lifestyle, exercise, behaviour, and nutrition guidance) CG: Nutritional guidance only	Primary: Not stated? feasibility Secondary: Physical (weightlifting capacity) and vascular function (PWV and CiMT), BC, QoL (SF-36), kidney function, blood lipid markers, and adherence	Primary/Secondary: No significant difference in BMI at 12 months Greater adherence to follow-up in IG (100%) vs. CG (25%) Improved weightlifting and PWV (IG only) significant difference in CiMT (IG only) Improvement in QoL (p = 0.008) and employment rate (p = 0.02) in IG vs. CG No significant differences between groups in kidney function or lipids	AEs not reported Small sample t-tests used, not ITT High dropouts in CG vs. IG Missing data (BC, PWV, CiMT) in CG
Karelis et al. [46] (Canada)	≈4	n = 24, non-diabetic KTRs, excluded smoking history	IG: Exercise only for 16 weeks (RT)CG: Instructed not to perform any structured exercise	Primary: Feasibility outcomes (adherence, injuries, drop-outs) Secondary: BC (DEXA), OGTT, Lipid profile, BP, QoL, Anthropometrics, Muscle strength (leg press), VO_2 peak	Primary: 47% consent rate 80% compliance IG 17% dropout IG Secondary: No difference in BW or BMI, BC, VO_2 peak, lipids, OGTT or QoL Both groups increased FM (BC) IG associated with increase in muscle strength (p = 0.003)	No AEs or injuries reported Short study duration (16 weeks) Small sample size
O'Connor et al. [39] (UK)	12	n = 47 of the original 60 ExeRT cohort [38]	IG1: Supervised AT for 12 weeks IG2:Supervised RT for 12 weeks CG: No ET for 12 weeks	Primary: PWV and VO_2 peak Secondary: Anthropometrics, BP	Primary: Significant difference in PWV in IG2 (RT) vs. CG (p = 0.03) Favourable difference in VO_2 peak IG1 (AT) vs. CG (p = 0.02) Secondary: No difference between-groups in BW or BP BMI not reported No difference in BMI reported in original study manuscript [38]	No AEs Long-term follow-up data from the ExeRT cohort [38] Dropouts ANCOVA used

Table 2. *Cont.*

First Author, Year (Country of Origin)	Study Duration (Months)	Sample	Groups	Outcomes (Primary and Secondary)	Results (for Primary and Secondary Outcomes)	Comments
Henggeler et al. [54] (NZ)	12	n = 37 KTRs with a BMI of > 18.5 and <40 kg/m^2	IG: 12-month combined Rx including standard care + dietitian appointments (12 sessions in total) and exercise sessions CG: Standard care (4 sessions in 12 months) with renal dietitian	Primary: BW at 6 months adjusted for baseline weight, obesity, and gender Secondary: Change in Anthropometrics and BC (DEXA), resting energy expenditure, physical function (grip, 25-feet gait speed, STS), PA (NZ PA questionnaire), serum biochem, QoL (SF-36)	Primary: No significant difference in BW or BC between groups at 6 months Secondary: No between-group difference in BC or energy expenditure Both groups increased total body fat and % body fat No significant difference in biochemistry Whole sample HbA1c and fasting glucose increased, cholesterol decreased Whole sample improved physical function, body protein, and QoL	No AEs CG greater than clinical practice in the UK May require formal ET/PA to elicit training response ANCOVA used
Kuningas et al. 2019 [48] (UK)	6	n = 130 nondiabetic KTRs	IG: 6-month exercise and nutrition education +BCTs CG: Passive education (booklet) on healthy eating, exercise, and risks of PTDM	Primary: 6-month change in insulin sensitivity, secretion, and disposition index (OGTT) Secondary: PA (GPPAQ), Physical function (DASI), QoL (EQ-5D), Beck depression inventory, situational motivational score, safety issues, BW, BC (skinfolds and bioimpedance)	Primary: No between-group difference in 6-month glucose metabolism Secondary: Significant between-group difference in BW favouring IG vs. UC (p = 0.02) Significant between-group difference in FM IG vs. CG (p = 0.03) Clinically significant reduction in PTDM, halved in IG vs. CG No between-group difference in any questionnaires	No safety concerns Dropout out rate 20.8% Pre–post study design with no long-term follow up Excluded non-diabetic KTRs Single centre study No reporting of BMI at 6 months
Schmid-Mohler et al. [43] (Switzerland)	12	n = 123 KTR and Kidney-pancreas Tx (120 KTR)	IG: Control + 8-month nurse-led intervention including dietary and PA counselling with motivational interviewing and action planning CG: A single nurse-led education session with booklet	Primary: Difference in BMI (baseline to 8 months) in patients with a BMI of ≥18.5 kg/m^2 Secondary: change in BMI baseline to 12 months, Rx adherence, satisfaction with counselling, BC (bioimpedance), PA (IPAQ), patient assessment of chronic illness care PACIC)	Primary: No significant between-group difference in change in BMI or BC from baseline to 8 months, or Baseline to 12 months Secondary: No significant differences between-group in BC, steps or IPAQ IG more chronic care related activities (PACIC) High acceptability IG 88.5% IG received ≥7 sessions Significant difference in PACIC in all but one score IG vs. CG No difference between groups in satisfaction with counselling	AEs not reported Sample includes kidney-pancreas Tx Means and SD for KTR (n = 120) provided on request. There was no significant between-group in BW or BMI at any timepoint in KTRs
Serper et al. [44] (USA)	4	n = 127 KTR and Liver Transplants (65 KTR). Participants needed to own a smartphone compatible with wearable accelerometer	IG1: Device only group, access to online portal with education materials and questions + control education IG2: Control education + Intervention 1 + 2 plus bi-weekly texts, step goals and financial incentives CG: standard education on healthy diet, food hygiene and PA	Primary: Change in BW from baseline to 4 months Secondary: Daily steps—proportion of patients achieving > 7000 steps/day, and continuous daily step data	Primary: No significant difference in weight gain between all three groups (IG1, IG2 and CG) Secondary: Significantly higher step count reported in IG2 vs. IG1 (p < 0.001) Retention rate 92.1% Adherence final study weight assessment 88% 74% IG2 adhered to their step targets Study increased motivation to monitor weight and increase PA Some participants disappointed with randomisation Some IG patients requested ability to track different activities, and have non-step related goals	No AEs associated with study Combined sample (KTR and Liver Transplant) Unique approach with financial incentives Diet education not designed for weight management No longer-term follow-up BMI not reported

Table 2. *Cont.*

First Author, Year (Country of Origin)	Study Duration (Months)	Sample	Groups	Outcomes (Primary and Secondary)	Results (for Primary and Secondary Outcomes)	Comments
Gibson et al. [53] (USA)	6	n = 10 KTR, 6–12 months post-transplant, Mean age 44 years, BMI >22 kg/m^2,	IG: 6-month combined Rx via telehealth (dietitian-led, 12 weeks of one-hour weekly calls and PA classes). Followed by 12 weeks of maintenance. Provided with tablet to track food and veg intake, whole grains intake, water intake, steps, and PA weekly CG: Standardised education to follow healthy eating and PA. Provided with tablet and tracking (as above). Did not receive weekly video calls or PA classes	Primary: Primary outcomes relate to feasibility (recruitment, adherence, attendance) Secondary: Provide estimates of Rx effectiveness including changes to PA, food intake (fruit, veg, whole-grain, and water). Secondary outcomes included weight gain (baseline to six months), BW, BMI, BP, PA (accelerometer), QoL, Dietary intake (3-day food diary), qualitative interviews for strengths and weakness of intervention	Primary: 78% attendance telehealth sessions (IG) 86% adherence to weekly behaviour tracking via tablet All patients attended week 12 study assessments Tracking increased awareness but some had problems All would recommend trial to others Tailored education and the ability to complete Rx at home was valued Secondary: Weight gain and BMI greater in IG versus CHG QoL improvements greater in CG versus IG No difference in BP and PA between groups Improved diet quality in both groups	Specific recruitment criteria included the ability to take part in six-month trial, ability to report data weekly (by phone, fax, email), access to the internet, English speaking, willingness to be randomised One participant withdrew due to time commitments

Note. KTRs = kidney transplant recipient, IG = intervention Group, CG = control group, BW = body weight (kg), BMI = body mass index (kg/m^2), HDL = high-density lipoprotein, LDL = low-density lipoprotein, Tx = transplant, AE = adverse event, AT = aerobic exercise training, Vo2 peak = peak oxygen update, FM = fat mass, LTM = lean tissue mass, BC = body composition, DEXA = dual-energy X-ray absorptiometry, QoL = quality of life, SF-36 = short form 36, PA = physical activity, PWV = pulse wave velocity, CiMT = carotid intima-media thickness via ultrasound, ITT = intention to treat analysis, KTx = kidney transplant, RT = resistance training, OGTT = oral glucose tolerance test, BP = blood pressure, ET = exercise training, ANCOVA = analysis of covariance analysis, STS = sit to stand test, NZPA = New Zealand physical activity questionnaire, HbA1c = haemoglobin A1c, PTDM = post-transplant diabetes mellitus, GPPAQ = General Practice Physical Activity Questionnaire, DASI = Dukes Activity Status Index, EQ-5D = EuroQoL five dimension scale, BAME = black, Asian and minority ethnicity, IPAQ = international physical activity questionnaire, PACIC = patient assessment of chronic illness care questionnaire, SD = standard deviation, Rx = Intervention.

3.2. Characteristics of Interventions

Methodological variation was evident across the ten RCTs included in this systematic review and meta-analysis. One study included a 12-month diet only intervention [45], three studies [36,39,46] included exercise only interventions ranging from three to twelve months, and six RCTs included combined interventions [43,44,48,49,53,54]. The RCTs with combined interventions varied significantly in duration between fourteen weeks [44], six months [48,53], eight months [43], and one year [49,54]. Two studies [48,54] did not report the specifics of the PA component of the combined intervention.

Two RCTs [39,44] included three treatment arms. O'Connor et al. [39] compared three months of either aerobic training or resistance training to usual care. Serper et al. [44] randomised kidney and liver transplant recipients into the following three groups: (1) education, (2) access to an online platform and a step tracking device, and (3) access to the online platform and step tracking device, plus text message support, automated step goals, and financial incentives [44]. However, limited information was provided on the education content within the treatment website.

The healthcare professionals providing interventions was variable. Some were dietitian-led face-to-face visits or telephone calls [45,48,54], one was provided by a physiotherapist [39], two were provided by exercise professionals [46,49], and one RCT did not specify the intervention provider [36]. Two recent RCTs [43,53] included combined interventions with a digital delivery component. Serper et al. [44], provided both the two intervention groups with access to a combined online platform. Gibson et al. [53] provided both groups with a tablet to track healthy behaviours weekly. The intervention group were provided with dietary and PA interventions delivered by video teleconference calls [53].

Whilst some interventions describe common strategies to promote behaviour-change such as goal setting [43,48,53,54] and motivational interviewing techniques [43,54], only three trials [43,48,54] explicitly described BCTs in reference to the BCT taxonomy [55]. Self-monitoring, 'SMART goals' [56], action planning, social support, and revision of goals were the most common BCTs. Table 3 summarises the interventions of the RCTs. See Table S6 for tabulated descriptions of the interventions for the non-RCTs.

Table 3. Detailed description of interventions RCTs (n = 10).

Study	Rx type	Rx Description	Rx Behaviour Components	Provider	Duration (Months)	Frequency	Intensity	Type of ET	Time (Minutes)
Lawrence et al. [45]	Diet	Written and verbal edu to reduce hyperlipidaemia Diet: 30% total energy from fat and 50% from carbohydrates Mode: NI, assume F2F	NI	RD	12 s	NI	NA	NA	NA
Painter et al. [36]	Exercise	Home ET (independent) Fortnightly phone calls Mode: Telephone	Self-monitoring behaviour (diaries) Phone calls for encouragement	NI	12	4x week	60–65% HRM, ↑ 75–80% HRM	AT	≥30
Tzvetanov et al. [49]	Combined	Combination of 1:1 ET + CBT + nutrition Topics include reduce sodium, emotional eating, increase protein, reduce cholesterol, and balanced meals Aims of Rx; build muscle tissue, change thoughts, and empowerment Mode: F2F	CBT details not provided	P.Tr	12	ET 2x week	Not specified	RT	60
Karelis et al. [46]	Exercise	ET programme of 7 exercises Upper and lower limb RT Mode: F2F supervised	NI	Kinesiology student	16 weeks (≈3.68 months)	3x week (1x week supervised)	80% 1RM	RT	45–60
O'Connor et al. [39]	Exercise	2 intervention groups; AT and RT compared with UC Mode: F2F	Motivational interviewing	PT	3	3x week (2x supervised group, 1x not supervised)	AT: 80% HRR RT: 80% 1RM 1–2 sets 10 reps, ↑ to 3 sets	AT or RT vs. UC	60 AT or RT 30 min/week edu (AT and RT)
Henggeler et al. [54]	Combined	Multi-professional and components 12 sessions (4x UC sessions, plus 8 additional nutrition sessions) with RD Exercise and PA component Mode: NI, assume F2F	SMART goal setting and revision of goals Motivational interviewing Action planning Self-monitoring	RD Ex.Phys: ET and PA	12	12x RD follow-ups 3x ET with Ex.Phys	'Tailored PA advice', No further detail	NI	NI PA

Table 3. *Cont.*

Study	Rx type	Rx Description	Rx Behaviour Components	Provider	Duration (Months)	Frequency	Intensity	Type of ET	Time (Minutes)
Kuningas et al. [48]	Combined	Combined lifestyle Rx to prevent PTDM, Dietary habits, Personalised healthy eating, edu based on Diabetes UK and Public Health England, Graded ET, Exercise diary, Mode: F2F and phone follow-up	BCTs used: Information on consequences, feedback on personal information prompting intention formation, SMART goals, graded tasks, self-monitoring, revision of goals, social support	RD	6	4x F2F 1:1 with RD RD phone consultant between each F2F session	Specifics not Reported	AT	NI
Schmid-Mohler et al. [43]	Combined	Developed brochure edu food types and hygiene, and encouraging PA Initial 1:1 edu session with brochure as per UC group +8 APN-led sessions Mode: F2F or phone	BCTs used: goal setting, problem solving, action planning, review behaviour and outcome goals, feedback on behaviour, self-monitoring of behaviour, instruction on how to perform behaviour, information about health consequences, prompts/cues, habit formation and reversal, focus on past success, self-monitoring of behaviour social support	APN (trained in motiva-tional interview-ing)	8	Combination of F2F and phone follow-up 9 sessions in total.	Specifics PA not reported	NI	35
Serper et al. [44]	Combined + online	IG1: Device only: Step-counting device, Website with resources on healthy eating and PA, Health knowledge questionnaires Mode: online IG2. Device and Rx: As above + Financial incentives, + Automated step goals, + Bi-weekly text messages, for health questionnaire Mode: online and text	prompts/cues (text), financial incentives (rewards)	1. Website 2. website and text messages (auto-mated) by research team	14 weeks (≈3.22 months)	1. Online website, step-recording device 2. online website, step-recording device and text support	1. Device only—no prescription 2. Device and Rx: baseline steps increased 15% every 2 weeks until reached 7000 steps/day	AT- steps	NI

Table 3. *Cont.*

Study	Rx type	Rx Description	Rx Behaviour Components	Provider	Duration (Months)	Frequency	Intensity	Type of ET	Time (Minutes)
Gibson et al. [53]	Combined +tracking +video calls	both groups given tablets for weekly tracking (fruit/veg, wholegrains, water, steps, and PA) IG: 6-months video calls: Tracking, 12 weeks of diet Edu (DASH diet), 12 weeks group PA, 12 weeks maintenance using tracking only Mode: video calls	Rx informed by the Social Cognitive Theory [57] and self-efficacy [58] Self-monitoring Goal setting	Tracking (not supervised) on tablet Diet Edu (RD), group PA (exercise professional)	6	Weekly	Moderate intensity (3–6 metabolic equivalent of task)	NI	Diet 1:1 and group PA 30 min/week (total 60 min/week) Encouraged to do 10–15 min PA/day

Note. Rx indicates treatment, ET = exercise training, Edu = education, F2F = face-to-face, NI = no information, RD = renal dietitian, NA = not applicable, KTx = Kidney transplant, PT = Physiotherapist, Ax = assessment, AT = aerobic training, HR = hear rate, RT = resistance training, BCTs = behaviour change techniques, HRM = heart rate max, Phys. = Physician, 1:1 = one on one (individual treatment), CBT = cognitive behavioural therapy, P.Tr = Personal trainer, PA = physical activity, 1RM = one repetition maximum, UC = usual care, HRR= heart rate reserve, reps = repetitions, SMART goals = specific measurable achievable realistic and timed goals, Ex. Phys = Exercise Physiologist, PTDM = post-transplant diabetes mellitus, APN = advanced practice nurse, IG = intervention group, DASH = dietary approaches to stop hypertension diet.

4. Risk-of-Bias

Minor disagreements between the two reviewers (E.M.C. and E.Mc.) on quality assessments were resolved through discussion, with no need to involve a third reviewer. Four RCTs were classified as 'low-risk' [43,48,53,54], one was classified as 'some concerns' [44] for risk of bias, and five were classified as 'high-risk' overall [36,39,45,46,49]. The 'High-risk' assessment was predominantly due to inadequate reporting on deviation from protocol and missing data. There was a wide variation in the risk-of-bias for the non-RCTs (Supplementary Material, Figure S1). Figure 2 demonstrates the risk-of-bias plots created using the risk-of-bias visualisation tool [59].

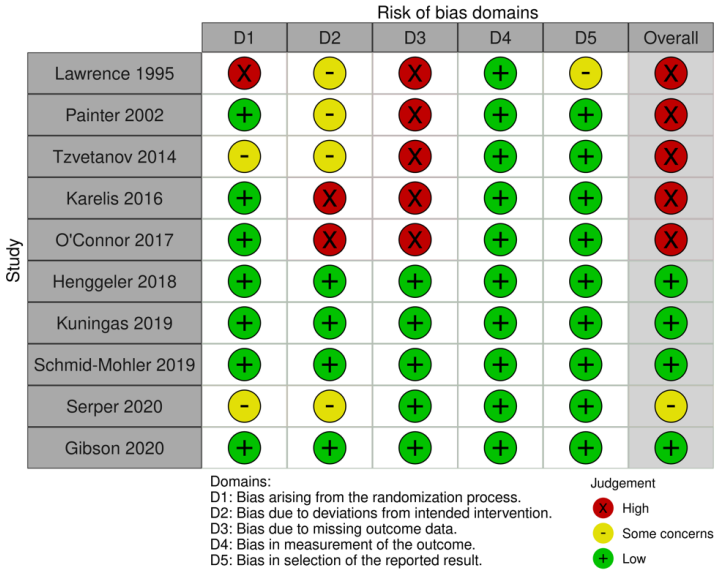


Figure 2. Risk−of−bias plot for RCTs (n = 10).

5. Body Weight and BMI

Nine [36,39,43–46,49,53,54] of the ten RCTs reported no effect of interventions on body weight or BMI values. However, Kuningas et al. [48] reported a change to these measures

as a secondary outcome. A total of 130 non-diabetic KTRs were randomised to either a passive education booklet or a dietitian-led six-month intervention involving dietary education, PA plans, and BCTs [48] (Figure 3). Whilst the study revealed no significant difference in its primary outcome of glucose metabolism, the authors report a significant difference in the change in body weight over the 6-month study of −2.47 kg (95% CI 0.401 to −0.92, $p = 0.002$) [48]. BMI post-intervention values were not presented by the authors. However, there was a significant mean difference in fat mass favouring the intervention group participants [48]. The risk-of-bias was categorised as 'low'.

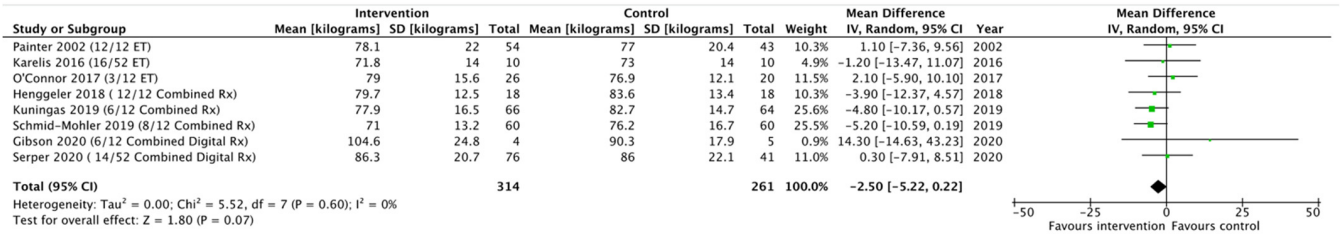


Figure 3. Meta-analysis body weight (post-intervention values). Note. Post-intervention values used for meta-analysis. Scheme 45. and Henggeler et al. [54]. Schmid-Mohler et al. [43] provided BW and BMI data for KTR alone ($n = 120$) on request. Studies with multiple intervention arms [39,44] were combined. Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx = intervention.

6. Meta-Analyses Body Weight and BMI

Eight out of the ten final RCTs [36,39,43,44,46,48,53,54] reported post-intervention body weight values. Eight reported post-intervention BMI values [36,38,43,45,46,49,53,54] and were included in the meta-analysis. Despite variation in the methods and participant characteristics between the included RCTs, the measures of statistical heterogeneity were not significant for BW (Chi2 7, $n = 575$, $p = 0.6$, $I^2 = 0\%$) or BMI (Chi2 7, $n = 383$, $p = 0.43$, $I^2 = 0\%$). The pooled data from 575 KTRs (Figure 3) revealed a non-significant mean difference in body weight (effect size, −2.50 kg, 95% confidence interval (95% CI) −5.22 to 0.22). The pooled data from 383 KTRs revealed a non-significant mean difference in BMI (−0.4 kg/m^2, 95% CI –1.33 to 0.53). See Figure 4.

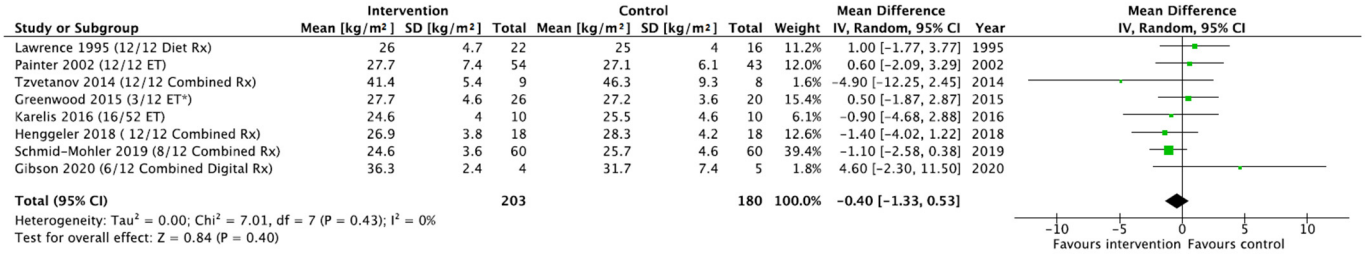
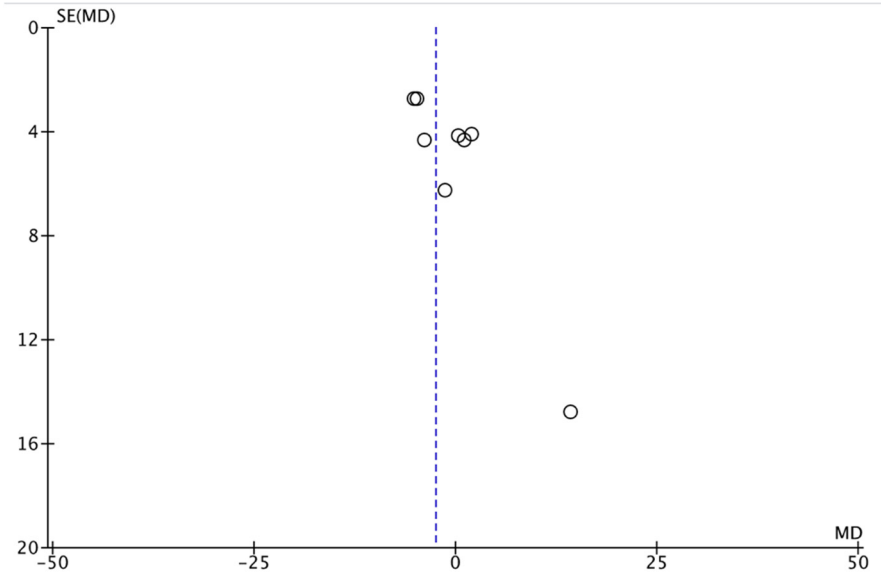


Figure 4. Meta-analysis BMI (post-intervention values). Note. Post-intervention values used for meta-analysis. BMI was not reported in O'Connor et al. [39]. Therefore, * indicates BMI from primary study manuscript [38]. BMI values from Tzvetanov et al. [49] were calculated from mean change and baseline values. Standard deviations were calculated from SEM in Henggeler et al. [54]. Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx = intervention.

Exploratory post hoc sensitivity analysis was performed on pooling the effects of the combined interventions and the single modality interventions (exercise or diet alone) to further explore the body weight and BMI values. Sensitivity analysis (Supplementary Material, Table S7) revealed that combined interventions [43,44,48,53,54] could have the potential to influence post-intervention body weight values. These findings were not echoed in the sensitivity analysis for the post-intervention BMI values. Funnel plots were completed to assess publication bias (Figure 5A,B). These demonstrated the potential for publication bias.

(**A**)



(**B**)

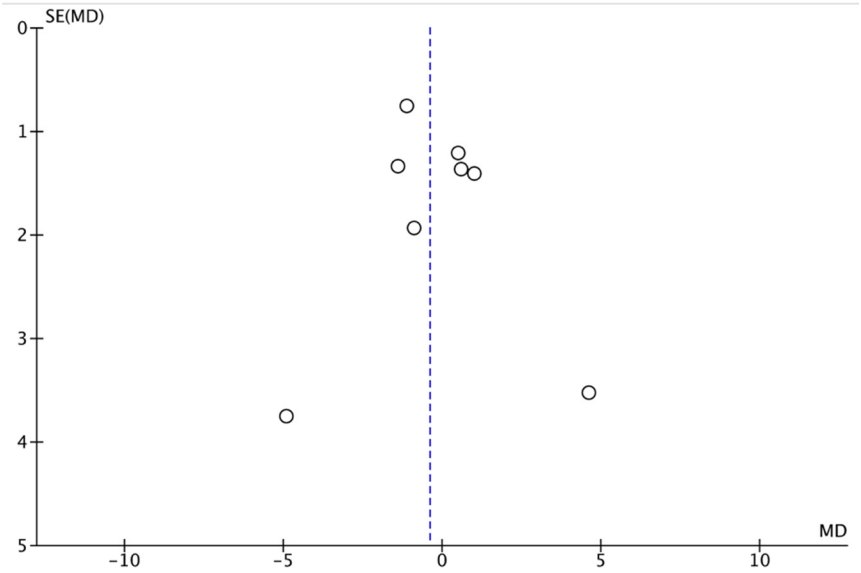


Figure 5. Funnel plots to assess publication bias. (**A**). Funnel plot for post−intervention body weight (kg). (**B**). Funnel plot for post−intervention BMI(kg/m^2). Note. Where SE = standard error, MD = mean difference.

7. Secondary Outcomes

Meta-analyses were not performed on secondary outcomes due to the large variation of measurement tools utilised (refer to Tables 2 and 3), and the limited number of RCTs. Five RCTs assessed body composition [36,43,46,48,54]. No studies reported a significant difference in lean tissue mass. Kuningas et al. [48] reported a significant mean difference in fat mass favouring the treatment group in their dietitian-led combined intervention (mean difference −1.54 kg (−2.95 to −0.13), $p = 0.033$). Another study [49] reported a marginal decrease in the percentage fat mass; however, this outcome was only captured in the treatment group due to significant loss to follow-up. Four studies reported an increase in fat mass in all the participants [36,41,46,54].

Four studies measured physical function [48,49,51,54] using different measures. One study reported a significant difference in physical function; however, data were only available for the intervention group [49].

Three studies used different questionnaires to measure PA [43,48,54]. One study [52] reported an increase in the PA of the treatment group but provided no further information. Another study [47] reported a significant increase in the percentage of participants achieving two hours or more of PA per-week (28% vs. 71%, $p < 0.001$); however the data are not presented for the comparator group. One study [36] reported a higher proportion of self-reported PA levels at twelve months in the treatment group versus the usual care group (67% vs. 36%, $p = 0.02$). Three studies reported no significant between-group difference in PA [43,48,53]. One RCT demonstrated a high step count of over ten thousand steps-per-day in both groups [43]. Serper et al. [44] reported the group receiving the step tracker, website, and online-intervention had a higher step count than the group receiving the device alone ($p < 0.001$).

No studies assessed self-efficacy. One study [48] reported no between-group difference in the questionnaires assessing situational motivation scores and depression symptoms. Another study [49] reported motivation via the index of personality styles questionnaire in the intervention group only.

8. Discussion

8.1. Summary of Main Findings

The current evidence evaluating interventions to address post-transplant weight gain are limited, with only ten RCTs. These studies had mainly small samples, limited power, a lack of long-term follow-up, variable sample characteristics, and variable intervention types and duration. This limits the ability to perform pooled estimates. The meta-analyses of post-intervention body weight and BMI values revealed no significant effect on body weight or BMI. Whilst the meta-analysis revealed no significant statistical heterogeneity, there was methodological heterogeneity across the included RCTs. When performing exploratory post hoc sensitivity analysis, the combined interventions revealed the potential to influence body weight, but not BMI in new KTRs.

A study by Kuningas et al. [48] was the only RCT to show a significant difference in body weight following a six-month complex intervention involving dietetic education, physical activity plans, and BCTs. The authors reported a significant mean difference in change in weight of −2.47 kg at six months, and a significant mean difference in fat mass favouring the treatment group. Whilst this study was powered for insulin sensitivity, the relatively large sample of 130 participants and it's 'low risk' of bias provides some confidence in its findings. Whilst the study excluded diabetic KTRs and did not include a long-term follow-up, it provides a promising basis of intervention design for future research in this field.

The study design could have impacted the ability for RCTs using combined interventions [43,44,49,53,54] to effect post-intervention body weight and BMI values. The lack of between-group treatment effect in Henggeler et al. [54] could have been influenced by the higher standard of usual care, and the exercise component may not have been of a sufficient dose to elicit change. Schmid-Mohler et al. [43] acknowledged that irrespective

of the treatment groups, both groups had high levels of PA, which could have influenced their results.

Tzvetanov et al. [49] reported no significant between-group difference in BMI between the 12-month combined intervention group and the control group. Change in body weight was not reported. This study was assessed to have 'high-risk' with the risk of bias due to its small sample size (n = 12) and large number of dropouts, particularly in the control group, impacting data collection on important outcomes such as body composition.

Serper et al. [44] reported no significant between-group difference in the change in body weight from baseline to four months. The authors acknowledged that the dietary component of the online intervention was not designed for weight management, the intervention was relatively short in duration (14 weeks), and there was no long-term follow-up [44]. In addition, there was the potential of contamination bias, with some of the control group participants purchasing wearable step trackers or using smart phone applications in response to randomisation [44]. The participants randomised into the step tracker device with the text message and financial incentives displayed a greater number of steps than those in the step tracking device group, suggesting a potential benefit of the text reminders and financial incentives on PA behaviour. This study was assessed as 'some-concerns' for risk of bias. However, KTR data are not presented in isolation of the combined transplant sample, making it difficult to determine the effects of the intervention on KTRs alone.

Gibson et al. [53] reported that the intervention group, who received six months of combined intervention with video teleconference calls, increased their body weight and BMI in comparison to the usual care group. Measures of body composition were not included in this trial. This feasibility RCT had a small sample (n = 10). It does, however, provide evidence of strong adherence rates in the intervention group and qualitative findings to support further investigation into online interventions to support new KTRs.

Previous systematic reviews of exercise interventions in KTRs have shown favourable effects on exercise clinical outcomes but no consistent change in body weight [15,17]. Therefore, it is unsurprising that our systematic review confirmed that exercise or PA interventions alone [36,39,46] did not show favourable effects on body weight or BMI. This is likely due to the trial and intervention design, with exercise specific outcomes being selected to align with exercise intervention targets [60], rather than targeting behaviour change. It is also unsurprising that the one RCT [45] included in this systematic review that compared 12 months of dietary intervention with usual care did not show a significant impact in BMI [45]. Combined interventions are likely to be needed to address the complex clinical problem of acute post-transplant weight gain.

A recent Cochrane review by Conley et al. [61] reviewed interventions for weight loss in obese and overweight participants living with chronic kidney disease (including KTRs). The authors [61] reported no difference in total weight loss when comparing weight loss interventions (dietary, physical activity, behavioural, or combined) to usual care in KTRs. However, this systematic review focused on people who were already classified as overweight and obese, investigated weight loss rather than weight gain prevention, and included participants with older transplants, making it difficult to infer the effects on weight gain in the acute post-transplant period.

8.2. Implications for Clinical Practice

Fear of harming the new kidney transplant has been reported by KTRs [11,62,63]. KTRs have reported receiving limited education from clinicians regarding the type and dose of recommended exercise after kidney transplant [62]. KTRs have expressed the need for early interventions that support PA behaviour-change [14] and a healthy lifestyle post-transplantation [11]. Routine access to both physiotherapists and dietitians is not available for KTRs in the UK. A recent survey of the UK transplant units conducted by Kostakis et al. [4] revealed that despite clinicians agreeing that obesity and a high BMI negatively affects transplant outcomes, there was limited clinical support for weight control

for new KTRs. Thus, data regarding the effect of interventions to prevent weight gain in new KTRs are limited and are urgently needed to inform clinical practice.

8.3. Implications for Future Research

This systematic review and meta-analysis suggest that there is insufficient evidence to advise clinical practice in this field, and that more research is warranted. Sufficiently powered RCTs, with clear reporting of complex multi-component interventions using recognised checklists such as the CReDECI criteria [64], the TiDieR checklist [65], and reference to the BCT taxonomies [55] are required. It would be of particular interest for future studies to include combined interventions, with recognised BCTs, similar to those displayed in Kuningas et al. [48], to address both physical activity and healthy eating behaviours. In addition, only one RCT in this review [39] reported a twelve-month follow-up after a period of intervention cessation. There is, therefore, a need for RCTs to investigate longer-term outcomes.

There was significant variation in the methods utilised to assess body composition, physical function, and physical activity in new KTRs, precluding the ability to perform a meta-analysis for these secondary outcomes. Whilst weight gain is a clinically important issue for new KTRs, future studies would benefit from including the patient-centred outcomes, such as 'life participation', that have been listed as a core outcome measure by a group of international KTRs and healthcare professionals from the Standardized Outcomes in Nephrology (SONG) Transplantation group [66].

Given there is no recognised intervention to prevent weight gain in new KTRs, an exploration of other modes of delivery, such as online interventions, would benefit from further research. Only two studies [44,53] identified in this systematic review included an element of digital delivery to the intervention group. Despite both RCTs not revealing significant differences in body weight or BMI, they did demonstrate improved PA levels [44], acceptability, and good adherence rates to the online interventions [44,53].

A recent Cochrane systematic review [67] evaluated the risks and benefits of online e-health interventions for people living with kidney disease (including KTRs). The review [67] concluded that there is low quality evidence for e-health interventions, and further research with interventions that utilise theoretical frameworks, self-monitoring and personalised education are warranted. Given the recent need for virtual clinics to support transplant patients during the COVID-19 pandemic [68], research exploring the use of online delivery of interventions to support KTRs requires further investigation.

8.4. Strengths and Limitations

To our knowledge, this is the first systematic review and meta-analysis that included exercise, PA, dietary, or combined interventions and their effect on body weight in new KTRs. Previous reviews have focused on either exercise or PA alone, [15–17] or excluded combined interventions [18]. There is a need for further research on dietary management for KTRs [18,69,70]. This systematic review focused on body weight and BMI as primary outcomes. Therefore, it is possible that further studies reporting secondary outcomes, but not body weight or BMI, were excluded in this search.

This systematic review focused on KTRs rather than all SOTs. However, KTRs have requested specific education and support [11,71], experience a unique fear avoidance pattern associated with PA [63], and experience rapid weight gain in the acute post-operative period [3]. Furthermore, this review focused on KTRs within the first year of transplant surgery. Studies that include participants with an older transplant vintage were excluded, which may have precluded additional insight into this research area. However, as weight gain within the first year is associated with adverse clinical outcomes [6,72], the authors felt it was important to investigate the first year post kidney transplantation.

The authors acknowledge the impact that the methodological variation between the final RCTs (sample characteristics, intervention type, dose, and duration) may have had on the validity of the pooled effects of interventions on body weight or BMI. Statistical

heterogeneity was not significant. By performing the meta-analyses on body weight and BMI, and exploring this with sensitivity analysis, this systematic review provides novel implications for future research studies in this field.

9. Conclusions

This is the first systematic review and meta-analysis to examine the evidence on either dietetic, exercise, or combined interventions on body weight and BMI within the first year of receiving a kidney transplant. There is limited evidence in the field, and we encourage further adequately powered theoretically informed RCTs, with pragmatic inclusion criteria, clear reporting of intervention components, and long-term follow-up, to further answer this important clinical question of acute weight gain post kidney transplantation.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/kidneydial1020014/s1, Figure S1: Risk-of-bias plots for Non-RCTs (n = 6), Table S1: PRISMA checklist, Table S2: Search strategy, Table S3: Screening form, Table S4: Detailed sample characteristics, Table S5: Study characteristics of non-RCTs, Table S6: Details of intervention non-RCTs (n = 6), Table S7: Sensitivity analysis.

Author Contributions: The search was conducted by E.M.C. and J.G. who collected the data. Quality assessments were independently conducted by E.M.C. and E.M. on individual papers. All authors (E.M.C., E.M., J.G., K.B., J.C. and S.A.G.) contributed to the writing of the manuscript and the search protocol. All authors have read and agreed to the published version of the manuscript.

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