

## Review article

# Diet and physical activity interventions to improve cardiovascular disease risk factors in liver transplant recipients: Systematic review and meta-analysis

Lynsey N. Spillman<sup>a,b,\*</sup>, Emily Stowe<sup>c</sup>, Angela M. Madden<sup>d</sup>, Kirsten L. Rennie<sup>a</sup>, Linda M. Oude Griep<sup>a</sup>, Michael Allison<sup>b</sup>, Leia Kenney<sup>b</sup>, Ciara O'Connor<sup>b,1</sup>, Simon J. Griffin<sup>a,e</sup>

<sup>a</sup> MRC Epidemiology Unit, School of Clinical Medicine, University of Cambridge, Cambridge CB2 0QQ, UK

<sup>b</sup> Liver Transplant Unit, Cambridge NIHR Biomedical Research Centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge CB2 0QQ, UK

<sup>c</sup> Physiotherapy, Farleigh Hospice, Chelmsford CM1 7FH, UK

<sup>d</sup> School of Life and Medical Sciences, University of Hertfordshire, Hatfield AL10 9AB, UK

<sup>e</sup> Department of Public Health and Primary Care, Primary Care Unit, School of Clinical Medicine, University of Cambridge, Cambridge CB2 0SR, UK

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## ABSTRACT

**Background and aims:** Cardiovascular disease, associated risk factors and obesity are prevalent after liver transplant and modifiable through lifestyle changes. Understanding what lifestyle interventions and their respective components are effective is essential for translation to clinical practice. We aimed to investigate the effects of diet and physical activity interventions on weight, body mass index and other cardiovascular disease risk factors in liver transplant recipients, and systematically describe the interventions.

**Methods:** We systematically searched Embase, MEDLINE, Psycho Info, CINAHL, Cochrane central register of controlled trials, PeDro, AMED, BNI, Web of Science, OpenGrey, [ClinicalTrials.gov](http://ClinicalTrials.gov) and the international clinical trials registry from inception to 31 May 2023. Search results were screened by two independent reviewers: randomised control trials with interventions that targeted diet and physical activity behaviours in liver transplant recipients were considered eligible. Two independent reviewers extracted and synthesised data for study, participant and intervention details and results. We used the Revised Cochrane Risk of Bias Tool for Randomised Trials to assess risk of bias for outcomes and the GRADE approach to rate the quality of the body of evidence. When two or more studies reported findings for an outcome, we pooled data using random-effects meta-analysis.

**Results:** Six studies were included, reporting three physical activity and three combined diet and physical activity interventions. Participants were 2 months–4 years post-transplant. Interventions lasted 12 weeks–10 months and were delivered remotely and/or in-person, most commonly delivered to individual participants by health care or sports professionals. Five studies described individual tailoring, e.g. exercise intensity. Adherence to interventions ranged from 51% to 94%. No studies reported fidelity. Intervention components were not consistently reported. In meta-analysis, diet and physical activity interventions did not significantly reduce weight or body mass index compared to control groups, however no studies targeted participants with obesity. Diet and physical activity interventions reduced percentage body fat and triglycerides compared to control groups but did not reduce total cholesterol or increase activity. The GRADE quality of evidence was low or very low.

**Conclusion:** Diet and physical activity interventions reduced percentage body fat and triglycerides in liver transplant recipients. Further good quality research is needed to evaluate their effect on other cardiovascular disease risk factors, including weight and BMI. Interventions need to be better described and evaluated to improve evidence base and inform patient care.

**Abbreviations:** BCTs, Behaviour change techniques; BCTTv1, Behaviour Change Technique Taxonomy v1; BMI, Body mass index; BP, Blood pressure; CI, Confidence interval; CVD, Cardiovascular disease; HDL, High density lipoprotein; ITT, Intention-to-treat; LDL, Low density lipoprotein; LTRs, Liver transplant recipients; MD, Mean difference; PA, Physical Activity; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs, Randomised control trials; ROB, Risk of bias; TIDieR, Template for Intervention Description and Replication.

\* Corresponding author at: MRC Epidemiology Unit, School of Clinical Medicine, University of Cambridge, Cambridge CB2 0QQ, UK.

E-mail address: [lynsey.spillman@mrc-epid.cam.ac.uk](mailto:lynsey.spillman@mrc-epid.cam.ac.uk) (L.N. Spillman).

<sup>1</sup> Present address: Royal College of Surgeons Ireland, Beaumont Hospital, Dublin, D09 YD60, ROI.

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## 1. Introduction

Cardiovascular disease (CVD) is a leading cause of death for liver transplant recipients (LTRs) and the presence of risk factors has a negative impact on health and quality of life [1,2]. CVD risk factors include obesity, hypertension, diabetes, and dyslipidaemia. Research undertaken in LTRs at least one-year post-transplant observed that 20–40% were obese, 50–80% had high blood pressure (BP), 20–50% had diabetes, and 40–60% had dyslipidaemia [3]. The incidence of obesity is high after liver transplant; studies report 15%–30% of patients with normal BMI become obese during the first year after liver transplant, increasing to over 40% at three years post-transplant [4–7]. In general populations, obesity increases the likelihood of developing other CVD risk factors, such as diabetes, hypertension and dyslipidaemia [8]. Obesity also increases the risk of CVD events and mortality independently of other CVD risk factors [8]. Obesity and other CVD risk factors are modifiable through diet and physical activity (PA) and therefore interventions that target these behaviours post-transplant may reduce CVD risk [9].

Interventions to change diet and PA behaviour are complex and usually involve multiple components that interact with each other. It is important to identify the detail of intervention content to establish which elements of the intervention were effective, understand the mechanism of behaviour change, build on research findings and replicate successful interventions.

We aimed to investigate the effects of diet and PA interventions with LTRs on:

- Primary outcomes: weight and body mass index (BMI).
- Secondary outcomes: total energy intake, diet quality score, PA in any format reported by studies (for example step count or MET-min/day), body fat, BP, blood glucose and blood lipids.

We also aimed to describe intervention characteristics, including behaviour change techniques used, and to investigate their effect on outcomes.

## 2. Materials and methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance to write this manuscript [10]. The protocol of this systematic review was registered in the international prospective register of systematic reviews (PROSPERO ID: CRD42022365619).

### 2.1. Inclusion criteria

We included randomised control trials (RCTs) with adult LTRs and diet and PA interventions. The control group could include usual care, no intervention or minimal intervention. Primary outcomes included weight and BMI. Secondary outcomes included total energy intake, diet quality score, PA in any format reported by studies (for example step count or MET-min/day), body fat, BP, blood glucose and blood lipids. We excluded studies reported as abstract only and studies not published in English.

### 2.2. Search strategy

The following databases were searched for literature published up to 31 May 2023: Embase, MEDLINE, Psycho Info, CINAHL, Cochrane central register of controlled trials, PeDro, AMED, BNI, Web of Science for published manuscripts; Web of Science and OpenGrey for grey literature (OpenGrey searched up to 1 December 2020); [ClinicalTrials.gov](#) and the international clinical trials registry platform for clinical trial protocols. The search strategy is presented in Table S1. The citation list of relevant review papers and included studies was searched to

identify any additional relevant studies.

### 2.3. Study selection

We collated results of the literature search in Endnote X8 (Clarivate, Philadelphia, United States). We exported deduplicated results to Rayyan for screening [11]. Two reviewers (LS and ES) independently screened titles, abstracts and full text articles. We resolved disagreements through discussion.

### 2.4. Data extraction

Two reviewers (LS and ES) independently extracted all data using piloted data extraction forms. We resolved disagreements through discussion. We extracted the following data: general details (author, year of publication, title, country, sample size, attrition rate, control group details, target population, target outcomes, dietary assessment method, PA assessment method, follow-up time); participants (mixed organ or liver-only transplant recipients, sex, age, time post-transplant, ethnicity, socioeconomic status, cause of liver disease, baseline weight and BMI); intervention (type (diet or PA), theoretical framework, delivery format, provider, location, duration, number of sessions, modifications, adherence, behaviour change techniques (BCTs)); and results (weight, BMI, total energy intake, total energy intake, diet quality score, PA in any format reported by studies (for example step count or MET-min/day), BP, glucose intolerance test, percent and kg body fat, blood levels of: fasting glucose, HbA1c, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides). We sought all results that were compatible with each outcome. We used the Template for Intervention Description and Replication (TIDieR) checklist to guide intervention characteristic data extraction [12]. We identified behaviour change techniques using the Behaviour Change Technique Taxonomy version 1 (BCTTv1) [13]. We contacted authors for missing data.

### 2.5. Risk of bias (quality) assessment

We used the Revised Cochrane Risk of Bias Tool for Randomised Trials (RoB 2.0) to assess risk of bias (ROB) for outcomes [14]. Two reviewers independently assessed ROB (LS and LK/CO). We resolved disagreements through discussion. We used the GRADE approach to rate the quality of the body of evidence for outcomes.

### 2.6. Data synthesis and analysis

All eligible studies were included in the synthesis for the outcomes they reported with no restrictions. Extracted data for total cholesterol and triglycerides were converted from mg/dl to mmol/l for one study [15]. When two or more studies reported findings for an outcome we pooled data using random-effects meta-analysis to obtain mean differences (MD) with 95% confidence intervals (CI) using the Review Manager 5 software [16]. We calculated  $I^2$  statistic and  $P$  value, with  $P < 0.05$  indicative of substantial heterogeneity. We used funnel plots for outcomes included in meta-analysis to assess publication bias. For trials that were clinically heterogeneous or that included insufficient information for pooling we used narrative synthesis to present findings.

## 3. Results

### 3.1. Identification of studies

Our search identified 1488 unique publications, of which 21 were reviewed in full and 6 were included in the final review (see Fig. 1).

### 3.2. Study and intervention details

The characteristics of the six included studies are shown in Table 1.

Intervention characteristics according to the TIDieR framework are reported in Table S2.

The included studies were published between 2006 and 2022. Two of the studies included kidney transplant recipients as well as LTRs. A total of 497 participants were randomised, of which 72% were liver and 28% were kidney transplant recipients and 60% of participants were male. Sample size ranged from 30 to 151. The mean age of participants ranged from 35 to 56 years. Only two studies, both conducted in the USA ( $n = 246$ ), reported ethnicity; 63% of participants were white, 18% were African-American and 19% were Hispanic, Asian or other/unknown ethnicity [17,18]. One study ( $n = 151$ ) reported socio-economic status of participants and liver disease aetiology [17]. Mean BMI at baseline ranged from 24.5 to 33.9 kg/m<sup>2</sup>. Three PA-only interventions and three combined diet and PA interventions were included. Intervention duration ranged from 12 weeks to 10 months. One study enrolled LTRs with obesity and dyslipidaemia [15], and another only included LTRs aged 18–45 years [19].

### 3.3. Risk of bias

The ROB results for primary and secondary outcomes are in Fig. 2 and Table S3, respectively. Overall, no outcomes were at low ROB.

#### 3.3.1. Publication bias

Funnel pots for primary and secondary outcomes are shown in Fig. S1.

### 3.4. Meta-analysis of the effect of diet and physical activity interventions on CVD risk factors

#### 3.4.1. Primary outcomes

Diet and PA interventions did not significantly reduce body weight (MD -0.21 kg, 95% CI -4.71 to 4.3 kg,  $I^2 = 0\%$ ) or BMI (MD -0.11 kg/m<sup>2</sup>, 95% CI -1.64 to 1.43 kg/m<sup>2</sup>,  $I^2 = 22\%$ ) compared with the control group

(Figs. 3 and 4), with GRADE very low-quality evidence (Table 2).

#### 3.4.2. Secondary outcomes

Diet and PA interventions significantly decreased percentage body fat (MD -3.93%, 95% CI -5.72 to -2.14%,  $I^2 = 32\%$ , GRADE low-quality) and triglycerides (MD -0.34 mmol/L, 95% CI -0.45 mmol/L to -0.23 mmol/L,  $I^2 = 0\%$ , GRADE low-quality). The interventions however did not increase PA from baseline when measured using a pedometer (MD 445 steps per day, 95% CI -780 to 1670,  $I^2 = 28\%$ , GRADE very low-quality). Interventions did not significantly reduce total cholesterol (MD -0.09 mmol/L, 95% CI -1.39, 1.20,  $I^2 = 92\%$ , GRADE very low-quality). Other secondary outcomes were either reported by one study or were not reported therefore meta-analysis was not possible. Table S4 presents a summary of findings for secondary outcomes including the certainty of the evidence. Meta-analyses are shown in Figs. S2–S5.

#### 3.4.3. Sensitivity and meta-regression analysis

There were no studies assessed as low ROB for the primary outcomes weight and BMI therefore it was not possible to run sensitivity analysis for studies with low ROB. There were <10 studies included in the review therefore we were unable to complete meta-regression analysis to explore sources of heterogeneity, including type and number of BCTs used, time post-transplant, and type of organ transplant recipient.

### 3.5. Narrative synthesis of secondary outcomes

Studies reported no significant differences between intervention versus control group for any of the following outcomes: fat mass ( $25.4 \pm 11.6$  kg vs.  $26.04 \pm 10.1$  kg,  $p > 0.05$ ) [12]; total energy intake ( $1909.6 \pm 750.3$  kcal/day vs.  $1923.8 \pm 897.6$  kcal/day,  $p > 0.05$ ) [17]; Mediterranean diet score ( $7.7 \pm 2.5$  vs.  $5.9 \pm 3.2$ ,  $p > 0.05$ ) [20]; systolic BP ( $128 \pm 16$  vs.  $131 \pm 12$ ,  $p > 0.05$ ) [20]; diastolic BP ( $81 \pm 11$  vs.  $83 \pm 9$ ,  $p > 0.05$ ) [20]; fasting blood glucose ( $5.4 \pm 0.7$  vs.  $5.5 \pm 1.0$ ,  $p > 0.05$ ) [20]; LDL cholesterol ( $2.8 \pm 0.6$  vs.  $2.1 \pm 0.8$ ,  $p > 0.05$ ) [20]; HDL

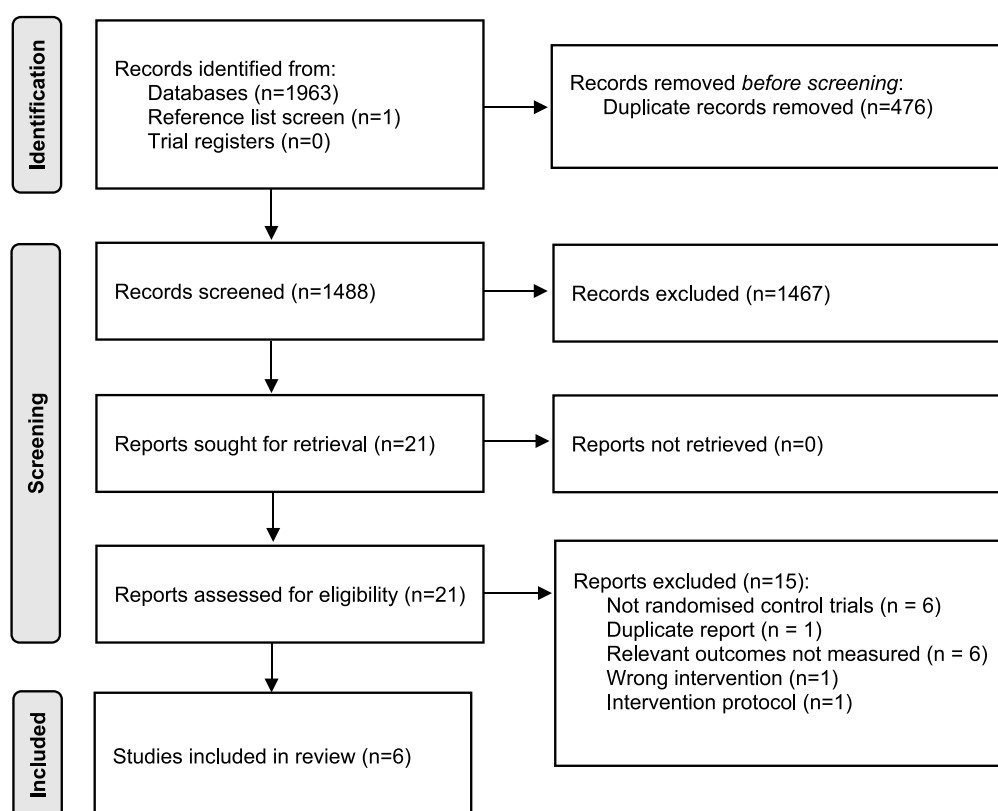


Fig. 1. PRISMA (2020) flow diagram of studies identified, screened, excluded and included in the review.

**Table 1**  
Characteristics of included studies.

| Study                         | Country   | Sample size | Organ transplanted                         | Start of intervention post-transplant | Intervention | Intervention duration | BCT used according to BCTTv1: number and description                                                                                                                                                                                                                                                                                                                                                                                                       | Outcomes of interest                                                                                |
|-------------------------------|-----------|-------------|--------------------------------------------|---------------------------------------|--------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| Krasnoff, 2006 [16]           | USA       | 151         | Liver                                      | 2 months                              | Diet and PA  | 10 months             | 1.1 Goal setting, 1.2 Problem solving, 1.5 Review of behavioural goals, 2.3 Self-monitoring of behaviour, 3.1 Social support (unspecified), 8.7 Graded tasks, 9.1 Credible source                                                                                                                                                                                                                                                                          | Weight, BMI, percent body fat, fat mass, total energy intake                                        |
| Basha, 2015 [14]              | Egypt     | 30          | Liver                                      | 6 months                              | PA           | 12 weeks              | 2.3 Self-monitoring of behaviour, 4.1 Instructions on how to perform behaviour, 6.1 Demonstration of behaviour, 8.7 Graded tasks, 9.1 Credible source                                                                                                                                                                                                                                                                                                      | Percent body fat, total cholesterol, triglycerides                                                  |
| Moya-Najera, 2017 [20]        | Spain     | 54          | Liver                                      | 6 months                              | PA           | 24 weeks              | 4.1 Instructions on how to perform behaviour, 6.1 Demonstration of behaviour, 8.1 Behavioural practice and rehearsal, 8.7 Graded tasks, 9.1 Credible source                                                                                                                                                                                                                                                                                                | Weight, BMI, percent body fat                                                                       |
| Serper, 2020 [17]             | USA       | 127         | Liver ( $n = 62$ ) and kidney ( $n = 65$ ) | 9.5 months                            | Diet and PA  | 12 weeks              | 1.1 Goal setting, 10.11 Future punishment, 14.3 Remove reward                                                                                                                                                                                                                                                                                                                                                                                              | Weight, PA                                                                                          |
| Hickman, 2021 [19]            | Australia | 35          | Liver                                      | 4 years                               | Diet and PA  | 12 weeks              | 1.1 Goal setting, 1.4 Action planning, 1.5 Review of behavioural goal(s), 1.6 Discrepancy between current behaviour and goal, 2.3 Self-monitoring of behaviour, 3.1 Social support (unspecified), 3.2 Social support (practical), 4.1 Instruction on how to perform behaviour, 6.1 Demonstration of the behaviour, 7.1 Prompts and cues, 8.1 Behavioural practice/rehearsal, 8.7 Graded tasks, 9.1 Credible source, 12.5 Adding objects to the environment | Weight, BMI, diet quality, BP, fasting blood glucose, total, LDL and HDL cholesterol, triglycerides |
| Wesołowska-Górniak, 2022 [18] | Poland    | 100         | Liver ( $n = 28$ ) and kidney ( $n = 72$ ) | 1–5 years                             | PA           | 3 months              | 2.3 Self-monitoring of behaviour                                                                                                                                                                                                                                                                                                                                                                                                                           | BMI, percent body fat, PA                                                                           |

BCT: Behaviour change technique; BCTTv1: Behaviour Change Technique Taxonomy Version 1; BMI: body mass index; BP: Blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PA: physical activity. BCT number and description taken from Michie et al. [11].

cholesterol ( $1.3 \pm 0.4$  vs.  $1.2 \pm 0.3$ ,  $p > 0.05$ ) [20]. There was no significant mean change in total PA from baseline to follow-up between intervention and control group ( $-78.5 \pm 556.5$  MET-min/day vs.  $396.7 \pm 796.9$ ,  $p > 0.05$ ) [19].

#### 4. Discussion

This systematic review and meta-analysis reports the effect of diet and PA interventions for LTRs on CVD risk factors. Of the six studies included, meta-analysis of five RCTs showed no reduction in body weight or BMI compared to the control group. In meta-analysis of secondary outcomes, diet and PA interventions showed improvements in body fat percentage and serum triglycerides but not in daily steps or total serum cholesterol, compared with the control group. Descriptive analysis found no significant improvements in any other CVD risk factors for intervention compared with control groups.

No studies included in the meta-analyses for weight or BMI targeted LTRs with obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) and the average BMI of participants was categorised as normal ( $\text{BMI} 18.5 - < 25 \text{ kg/m}^2$ ) [19] or overweight ( $\text{BMI} 25 - < 30 \text{ kg/m}^2$ ) [17,18,20,21]. Research has found a high prevalence (up to 40%) and incidence (up to 40%) of obesity after liver transplant [3–7]. If studies that aim to achieve weight loss target LTRs living with obesity the intervention is likely to be more effective than targeting LTRs with a normal or overweight BMI [22].

BMI is commonly used to identify obesity. However, BMI does not distinguish between lean and fat mass and has low sensitivity to identify body fat (~50%) [23]. Research has found that the combination of

normal BMI and high body fat is associated with CVD risk [24]. We found diet and PA interventions significantly improved percent body fat, with a mean difference of  $-3.93\%$  in meta-analysis. Only one study ( $n = 30$ ) targeted LTRs with obesity. These findings suggest that beneficial body composition changes are experienced with diet and PA interventions despite no significant improvements observed in weight or BMI. This underpins that body fat is an important outcome for evaluation of future lifestyle interventions for LTRs.

For the two studies reporting PA as an outcome, the intervention failed to influence PA levels; there was no difference in steps per day measured using an objective method [18,19] or total PA measured using a subjective validated questionnaire [19]. This can be explained by the intervention limitations. In the study by Serper et al, the step goal was capped at 7000 steps per day with some participants already achieving this at baseline [18]. Furthermore, the authors report the control group tracked steps which was outside of the control group protocol and a component of the intervention. Wesołowska-Górniak et al. used a single behaviour change technique, self-monitoring, which on its own has not been found to be effective for increasing daily steps [25]. Furthermore, this study recruited LTRs who were young and had a high mean daily step count at baseline [19].

Hickman et al. reported a greater improvement in mean Mediterranean diet score for the intervention group compared to the control group [20]. Krasnoff et al. found no differences in nutrient intakes between groups at 12-month follow-up after individualised counselling to achieve an ideal body weight and low fat, high fibre dietary intake; only 51% of participants adhered to the recommended total energy intake

| Weight and BMI           | D1 | D2 | D3 | D4 | D5 | Overall |
|--------------------------|----|----|----|----|----|---------|
| Krasnoff, 2006           | SC | SC | HR | LR | SC | HR      |
| Moya-Najera, 2017        | SC | SC | LR | LR | SC | SC      |
| Serper, 2020             | SC | HR | HR | LR | C  | HR      |
| Hickman, 2021            | LR | SC | HR | LR | SC | HR      |
| Wesołowska-Górniak, 2022 | SC | SC | LR | LR | SC | SC      |

Fig. 2. Risk of bias for weight and BMI.

HR: High risk; LR: Low risk; SC: Some concerns.

Domain 1 (D1) Randomisation process. Some concerns: studies reported participants randomised but no information about the randomisation process/allocation concealment.

Domain 2 (D2) Deviations from the intended interventions. For all studies participants and intervention providers aware of assigned intervention. Some concerns: no information about deviation from intended intervention. High risk Serper 2020: deviation from intended intervention; control group tracked steps outside of the study protocol.

Domain 3 (D3) Missing outcome data. High risk: missing outcome data and no analysis/information reporting if results biased by missing data. Krasnoff 2006: loss to follow-up related to participants' health state; Hickman 2021: More participants in the intervention group had missing data; 7 were lost to follow-up compared to 1 in the control group.

Domain 4 (D4) Measurement of the outcome.

Domain 5 (D5) Selection of the reported result. Some concerns: no prespecified analysis plan available.

and energy from saturated and total fat [17]. Frequency of support and differences in intervention design could have influenced dietary adherence; Hickman et al. uniquely provided a starter pack of key Mediterranean diet ingredients and dietitian support was more frequent than in the Krasnoff et al. study (fortnightly vs. every other month). Additionally, dietary adherence may have been influenced by differences in study duration, Hickman et al. report a 12-week study and Krasnoff report a 10-month study; short-term dietary changes are often not maintained long-term [26]. Interventions are unlikely to improve outcomes if the intervention is not measurably effective at improving the target behaviours. Future dietary interventions should include methods to achieve higher levels of long-term dietary adherence.

In our narrative analysis we found no effect of a combined PA and diet intervention on BP, fasting blood glucose, LDL or HDL, however results were from one small pilot study ( $n = 23$ ), not powered to detect

differences in these outcomes [20]. A body of evidence from systematic review studies has consistently demonstrated the benefits of diet and PA on CVD risk for general populations and adults at high risk of CVD [9,27–32]. Meta-analyses have shown that different dietary interventions modify different CVD risk factors; reduction in saturated fat intake reduced serum LDL cholesterol and cardiovascular events [30]; Low-carbohydrate diets improved weight, HDL and triglycerides compared to low-fat diets, but low-fat diets were more effective at reducing LDL and total cholesterol [31]; and a Mediterranean diet compared to no diet intervention reduced total cholesterol and BP but had no effect on LDL, HDL or triglycerides [32]. These studies suggest that well designed and adequately powered studies are required in LTR populations, with appropriate dietary interventions for the outcome. For example, if reducing LDL is the target outcome then the intervention should include replacing saturated fat with polyunsaturated fat [30].

Five of the included studies describe tailoring the intervention, for example, tailoring PA intensity, providing individualised dietary advice, and altering goals based on the individual's behaviour. Liver transplant is medically and surgically complex and individual patients have differing needs; nutritional status, frailty, complications and recovery vary between individuals and therefore tailoring diet and PA support is likely to be important. Qualitative research with LTRs suggests tailoring is an important aspect of a behavioural intervention for this population as tailored advice is a facilitator of behaviour change and similarly, advice and support that is not personalised is a barrier [33,34]. Further research investigating factors influencing LTRs diet and PA behaviours, including qualitative research, would help to identify how to best tailor interventions. For example, research to investigate whether the return of health and appetite, the lifting of dietary restrictions for liver disease or anti-rejection medications influence dietary intake.

Diet and PA interventions are complex and require careful development; the Medical Research Council recommends good theoretical underpinning, intervention piloting with feasibility assessment and intervention evaluation [35]. One study included in our review, a pilot RCT, has evidence of this strategy with previous feasibility work [36] and a qualitative evaluation of the intervention [37]. We recommend that future lifestyle interventions for LTRs follow these development guidelines for improved effectiveness.

We have identified three other systematic reviews investigating the impact of PA interventions on outcomes for LTRs, but no reviews studied the effectiveness of diet interventions [38–40]. Our review has the most recent literature search and is the most comprehensive, including more recent studies and diet as well as PA interventions.

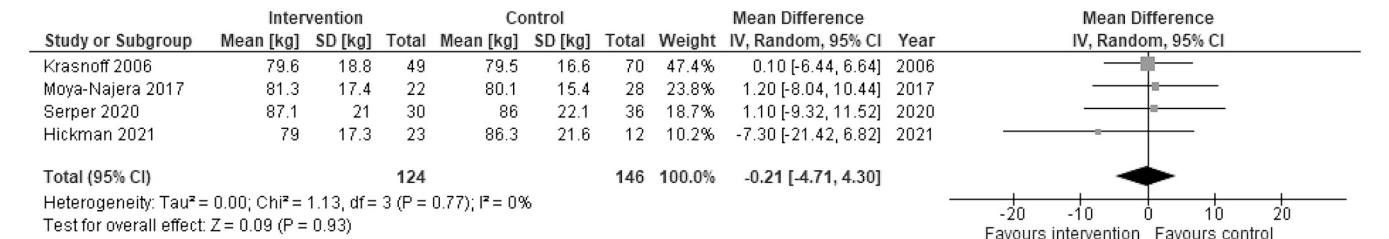


Fig. 3. Forest plot for weight (kg).

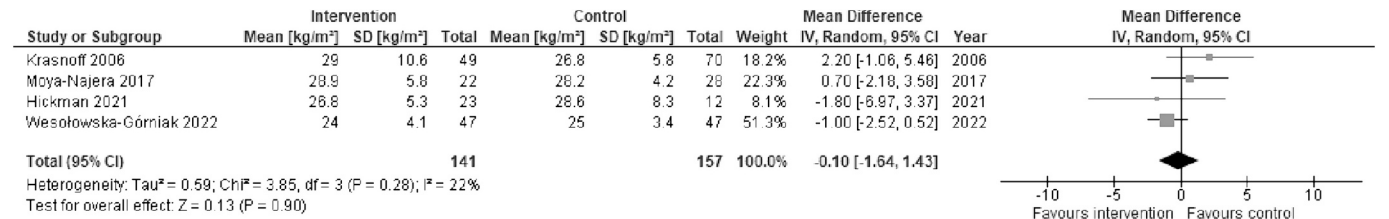


Fig. 4. Forest plot for BMI (kg/m²).

**Table 2**  
Summary of findings for primary outcomes.

| Diet and physical activity interventions compared to usual care or minimal intervention for liver transplant recipients |                                                             |                                                                   |                               |                                   |
|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------|-----------------------------------|
| <b>Patient or population:</b> LTRs                                                                                      |                                                             |                                                                   |                               |                                   |
| <b>Setting:</b> all settings, including in hospital and at home                                                         |                                                             |                                                                   |                               |                                   |
| <b>Intervention:</b> diet and PA interventions                                                                          |                                                             |                                                                   |                               |                                   |
| <b>Comparison:</b> usual care or minimal intervention                                                                   |                                                             |                                                                   |                               |                                   |
| <b>Anticipated absolute effects*</b><br>(95% CI)                                                                        |                                                             |                                                                   |                               |                                   |
| Outcomes                                                                                                                | Risk with usual care or minimal intervention                | Risk with diet and PA interventions                               | No. of participants (studies) | Certainty of the evidence (GRADE) |
| Weight follow-up: range 12 weeks to 10 months                                                                           | The mean weight ranged from <b>79.5 to 86.3 kg</b>          | MD <b>0.21 kg lower</b> (4.71 lower to 4.3 higher)                | 270 (4 RCTs)                  | ⊕⊕⊕⊕<br>Very low <sup>a,b</sup>   |
| BMI follow-up: range 12 weeks to 10 months                                                                              | The mean BMI ranged from <b>25 to 28.6 kg/m<sup>2</sup></b> | MD <b>0.11 kg/m<sup>2</sup> lower</b> (1.64 lower to 1.43 higher) | 304 (4 RCTs)                  | ⊕⊕⊕⊕<br>Very low <sup>b,c</sup>   |

BMI: Body mass index; CI: confidence interval; LTRs: liver transplant recipients; MD: mean difference; RCTs: randomised control trials.  
GRADE Working Group grades of evidence.  
**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.  
**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.  
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.  
**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.  
<sup>a</sup> **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).  
<sup>a</sup> Risk of Bias: Three trials at high risk, and one trial with some concerns, (downgraded two levels due to methodological limitations).  
<sup>b</sup> Large confidence intervals.  
<sup>c</sup> Risk of Bias: Two trials at high risk and two trials with some concerns, (downgraded two levels due to methodological limitations).

4.1. Strengths and limitations

Due to the systematic search that was conducted and inclusion of only RCTs, this paper provides a comprehensive overview of the research investigating the effect of diet and PA interventions on CVD risk factors in LTRs, highlighting the strengths and limitations of research in this area and the need for future research.

It is important to interpret the findings of our review within the context of the limitations. All study outcomes were considered at high or some concerns of ROB and the certainty of evidence according to GRADE was low or very low. There were only six published studies that contributed to the body of the evidence. Due to the limited number of published eligible studies we were unable to explore sources of heterogeneity, for example the influence of BCTs or TiDieR components on intervention effect. However, the use of BCTTv1 and TiDieR frameworks in this review provides detailed intervention information to inform future interventions and progress this area of study. In studies involving other adult populations, the most effective BCTs vary across populations and may be different for initial behaviour change compared to behaviour change maintenance [41–43]. It is therefore important to identify the most effective BCTs to support LTRs with healthy lifestyles in future research.

PA interventions included aerobic exercise (*n* = 2) or combined

aerobic and strength exercise (*n* = 4). Adherence to PA interventions ranges from 52% to 94% and adherence to diet interventions ranged from 57% to 71%. Low adherence is likely to limit the intervention effect. No studies reported the fidelity of intervention content; it is not possible to know if the intervention is ineffective without implementation reporting. Process evaluation of interventions is recommended, including fidelity to the intervention, to understand what works, in what context, through what mechanism, and why an intervention may not be effective [44]. For combined diet and PA interventions, intervention evaluation would help to identify whether diet, PA or the combination of these behaviours is important for this patient population.

There was variation in the average time of recruitment post-transplant (two months–four years) and this is likely to be a relevant source of heterogeneity which we were unable to explore using meta regression due to the limited number of eligible studies. At two months post-transplant LTRs are still malnourished, frail and recovering from the transplant operation and therefore have different diet and PA needs compared to four years post-transplant when most LTRs have recovered. Furthermore, immunosuppressive therapy, diet and PA behaviours are likely to be different early compared to longer-term post-transplant. Based on exclusion criteria, studies likely recruited more LTRs with better health compared to the health of the overall LTR population. Two studies included kidney as well as liver transplant recipients and it was not possible to extract findings for LTRs only for these studies. One eligible study was excluded as it was published as an abstract with no further information available from the authors [45]. It was not possible to assess publication bias due to four or fewer studies included in meta-analyses.

5. Conclusions

Further good quality research is needed to evaluate the effect of diet and PA interventions on CVD risk factors in LTRs, including weight and BMI. However, results from this systematic review suggest interventions reduced percentage body fat and serum triglycerides in LTRs. Interventions need to be better described and tools such as the BCTTv1 and TiDieR should be used to facilitate consistent reporting. Careful consideration is needed when selecting participants and designing an intervention so that it is likely to modify the target behaviour and in turn the chosen outcome. To improve the likelihood of effectiveness, interventions should be developed and evaluated using evidence-based guidelines for complex intervention development and evaluation.

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Declaration of competing interest

The authors have no conflicts of interest relevant to this article to disclose.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.trre.2024.100852>.

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