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Effectiveness of the perioperative encounter in promoting regular exercise and physical activity: a systematic review and meta-analysis

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Summary

Background Low levels of physical activity (PA) are associated with poorer health outcomes. The perioperative encounter (extending from initial contact in primary care to beyond discharge from hospital) is potentially a good time to intervene, but data regarding the effectiveness of interventions are scarce. To address this, we systematically reviewed existing literature to evaluate the effectiveness of interventions applied perioperatively to facilitate PA in the medium to long-term (at least six months after the intervention).

Methods In this systematic review and meta-analysis, we searched Central Register of Controlled Trials (CENTRAL, Cochrane Library), MEDLINE, CINAHL, Embase, PsycInfo, and SPORTDiscus from database inception to October 22nd 2020, with an updated search done on August 4th 2022. We searched clinical trials registers, and conducted forward- and backward-citation searches. We included randomised controlled trials and quasi-randomised trials comparing PA interventions with usual care, or another PA intervention, in adults who were scheduled for, or had recently undergone, surgery. We included trials which reported our primary outcomes: amount of PA or whether participants were engaged in PA at least six months after the intervention. A random effects meta-analysis was used to pool data across studies as risk ratios (RR), or standardised mean differences (SMDs), which we interpreted using Cohen. We used the Cochrane risk of bias tool and used GRADE to assess the certainty of the evidence. This study is registered with PROSPERO, CRD42019139008.

Findings We found 57 trials including 8548 adults and compared 71 interventions facilitating PA. Most interventions were started postoperatively and included multiple components. Compared with usual care, interventions may slightly increase the number of minutes of PA per day or week (SMD 0.17, 95% CI 0.09–0.26; 14 studies, 2172 participants; I^2 = 0%), and people's engagement in PA at the study's end (RR 1.19, 95% CI 0.96–1.47; 9 studies, 882 participants; I^2 = 25%); this was moderate-certainty evidence. Some studies compared two different types of interventions but it was often not feasible to combine data in analysis. The effect estimates generally indicated little difference between intervention designs and we judged all the evidence for these comparisons to be very low certainty. Thirty-six studies (63%) had low risk of selection bias for sequence generation, 27 studies (47%) had low risk of bias for allocation concealment, and 56 studies (98%) had a high risk of performance bias. For detection bias for PA outcomes, we judged 30 studies (53%) that used subjective measurement tools to have a high risk of detection bias.

Interpretation Interventions delivered in the perioperative setting, aimed at enhancing PA in the medium to long-term, may have overall benefit. However, because of imprecision in some of the findings, we could not rule out the possibility of no change in PA.

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Research in context

Evidence before this study

We searched the Cochrane Library, MEDLINE, CINAHL, Embase, PsycINFO and SPORTDiscus from inception until October 22 2020 for terms related to "physical activity" or "exercise" and the "perioperative period". We found no published meta-analyses evaluating the effectiveness of physical activity interventions, applied during the perioperative period across a broad spectrum of surgeries, to facilitate physical activity in the medium to long-term.

Added value of this study

This systematic review and meta-analysis of 55 randomised controlled trials and two quasi-randomised trials, including 8548 participants, is the first to synthesise empirical data for physical activity interventions given during the perioperative period before or after such a range of surgical types. Results from pooled analyses indicate that interventions may slightly increase the amount of physical activity, engagement in physical activity, and improve health-related quality of life beyond surgery. These interventions probably increase the amount of physical activity for up to 12 months after surgery. Interventions may also improve fitness and pain outcomes. Few studies reported adherence and adverse events, and certainty of these findings was very low. Although infrequently reported, participants generally provided positive feedback about the interventions. We could not determine if differences between study designs, patient characteristics and the various and differing components of intervention types led to heterogeneity within some of the data.

Implications of all the available evidence

In general, the findings for all outcomes showed a trend in favour of physical activity interventions. These data might be used to inform decision making by primary and secondary care coordinators within the perioperative pathway, augmenting provision to safely facilitate a more active lifestyle beyond surgery. The heterogeneity between studies calls for greater methodological cohesion in this field; the development of a core outcome set and more distinguishable interventions is needed to improve future quantitative analysis.

Introduction

More than half of UK adults do not achieve the recommended amount of physical activity (PA).[1,2] Inactivity costs UK healthcare as much as £1.2 billion per year, with a wider impact on the UK economy of up to £1.5 billion.[1] Low levels of PA are associated with poorer physical and mental health, with inactivity directly contributing to one in every six deaths in the UK.[3] Small increases in PA in adults can benefit health, lowering all-cause mortality[4]; increased PA can reduce the risk of developing heart and circulatory diseases by as much as 35%.[5] For older adults, increases in PA can protect against falls and frailty, with communal activities reducing social isolation.[4] Furthermore, active travel reduces congestion and air pollution.[2] PA has been labelled as a 'miracle cure' for health promotion.[2]

Despite PA being central to the UK's health promotion strategy,[2,6] around 60 percent of adults are unaware of the Government's PA guidelines,[1] and the UK compares poorly to other nations.[7] The benefits of exploiting every healthcare encounter are well stated,[8] and the Chief Medical Officer's 'Moving Medicine' initiative participates in this strategy.[9] The NICE PA promotion guidance asks: 'What infrastructures and systems help increase the number of assessments of PA undertaken and the delivery of brief advice?'.[10] Furthermore, the National Institute for Health Research (NIHR), prioritises questions such as: "How can pre-operative exercise of fitness training, including physiotherapy, improve outcomes after surgery?".[11]

With over four million hospital admissions leading to surgery each year in England alone,[12] the perioperative encounter (extending from the initial contact in primary care and continuing beyond discharge from hospital) has potential to address this. Work exists on primary-secondary care co-ordination in general,[13] and on primary care interventions to improve postoperative outcomes,[14] but the potential for collaborative working to improve health in the longer term has not been studied in this perioperative context. Understanding is required around how to integrate models of care which optimise not only surgical outcomes, but also the longer-term health benefits of increased PA, into a perioperative pathway. We systematically reviewed evidence from randomised controlled trials to determine the potential for promoting PA and exercise in the medium to long-term (at least six months after the intervention) in people undergoing elective surgery.

Methods

Search strategy and selection criteria

We performed a systematic review and meta-analysis of randomised controlled trials (RCTs) and quasi-RCTs examining the medium to long-term effects of PA and exercise promotion on adults during the perioperative period. The findings are reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[15] The protocol was registered on PROSPERO (international prospective register of systematic reviews) and is available online (www.crd.york.ac.uk/prospero, CRD42019139008).[16] This review formed part of a wider evidence synthesis including observational research.[17]

We searched Cochrane Central Register of Controlled Trials (CENTRAL, Cochrane Library), MEDLINE (Ovid SP), CINAHL (EBSCOhost), Embase (Ovid SP), PsycInfo (EBSCOhost), and SPORTDiscus (EBSCOhost) from database inception until 22 October 2020, applying no restrictions on language or publication status. We also searched ClinicalTrials.gov[18] on 7 January 2020 and World Health Organization International Clinical Trials Registry Platform[19] on 24 January 2020. We also conducted forward citation searches of included studies and backward citation searching of key articles and reviews using Web of Science citation index, as well as grey literature searching[20] using 'opengrey'.[21] See supplementary file 1 for search strategies. We conducted an additional top-up search of databases on 4 August 2022, re-assessed studies previously identified as ongoing or awaiting classification, and included the results in this report.

We included RCTs and quasi-RCTs in adults who were scheduled for surgery or had recently undergone surgery. Interventions encouraged participants to engage in PA or exercise which we defined as a planned, structured activity which takes place regularly with the purpose of improving physical fitness.[22] We compared any PA intervention with either another PA intervention, usual care, or both. In order to ensure our review objectives were addressed, we only included studies that reported our primary outcomes (amount of PA and PA engagement), with available data at least six months after surgery (when the intervention was started post-surgery), or six months after the beginning of the intervention (when the intervention was started pre-surgery). We included studies of mixed surgical and non-surgical populations if at least 60% were in a surgical pathway (see supplementary file 2).

Data analysis and quality assessment

We used Covidence 2018[23] software to assess study eligibility, extract data, and assess risk of bias according to the Cochrane 'Risk of bias' tool.[24] We assessed the risk of publication bias by visual inspection of funnel plots. We used the GRADE[25] approach to assess the certainty of the evidence at the end of follow-up for: amount of PA completed; number of people engaged in PA; level of physical fitness; health-related quality of life; pain; adverse events; and overall adherence to the intervention. We did not report data for a planned outcome (cancellation of surgery) which was not reported in any of our included studies.

One author extracted study characteristics and outcome data which were checked by a second author for accuracy. All other review stages were conducted independently by two authors and consensus reached through discussion.

We conducted meta-analyses using the Mantel-Haenszel random-effects model[26] in Review Manager 5.4[27] when comparable effect measures were available from more than one study. We did not pool studies with high levels of methodological or clinical heterogeneity, or statistical heterogeneity ($I^2 \geq 75\%$) (judged using the Chi^2 test and I^2 statistics[28]). We reported dichotomous data using risk ratios (RRs) and continuous data using mean differences (MDs). In order to account for different surgical populations, random effects meta-analysis was used to pool data across studies. The standardised mean difference (SMD) was used when measurement tools differed, which we interpreted using Cohen.[29] We reported 95% confidence intervals (CI) alongside point estimates and used a P value of 0.05 or less to judge whether a result was statistically significant. Data for participant experiences were described narratively.

Interventions were compared according to the types of control group interventions. Thus, we included two comparison groups in the review and analysed data separately for these groups: intervention versus usual care; intervention versus intervention.

For studies with multiple intervention arms within the same comparison, we selected one intervention arm (the most enhanced) to use in the meta-analysis. We used the latest time point reported in the studies because our intention was to establish the long-term effect of interventions. If study authors used more than one tool to measure an outcome, we selected the tool that provided the most objective assessment, or which was the most commonly used tool in the analysis. We used sensitivity analysis to explore the effect of these decisions. We also explored whether the time point of data collection affected outcomes (if measured immediately after the end of the intervention, or when there is a delay between the end of the formal intervention period and data collection), and the impact of risk of bias assessments (by excluding studies at high risk of attrition bias, and studies at high or unclear risk of selection bias).

Using information collected during data extraction, we attempted to explore differences between study population (oncological surgery versus other types of surgery; BMI below or above 30 kg/m^2; less than or over 60 years of age) and intervention characteristics (interventions initiated before or after surgery; or interventions lasting less or at least six months). In order

to draw meaningful results from tests for subgroup interactions, we only conducted subgroup analysis when we had more than 10 studies.[30]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MP, SL and AR had access to the dataset. All study authors had final responsibility for the decision to submit for publication.

Results

Study selection and characteristics

After removal of duplicates from the search results, we screened 22,186 titles and abstracts which included forward and backward citation searches and searches of clinical trials registers. We reviewed the full text of 389 records and selected 57 studies (with 117 records), for inclusion, based on review criteria.[31–146] We identified 35 ongoing studies (see supplementary file 3), found 24 studies for which we were not able to effectively assess eligibility (see supplementary file 4), and excluded 211 records (see Fig. 1; supplementary file 5).

The 57 eligible studies included 8548 participants. The most common operations were for cancer (12 studies; 21%), cardiac (12 studies; 21%), bariatric (10 studies; 17%), and hip and knee replacement (13 studies; 23%). In more than two-thirds of studies, PA interventions were started postoperatively; few studies had preoperative initiation of the intervention (4 studies; 7%), or a mixture of pre- and postoperative initiation (10 studies; 18%). The interventions more often involved multiple components or modes of delivery (32 studies; 56%). We grouped these components into three main categories: education and advice (45 studies; 79%), which included written or verbal information, PA recommendations, or a formal exercise prescription; behavioural mechanisms (35 studies; 61%), which focused on behaviour change theories, usually through therapeutic approaches including counselling or motivational interviewing; or direct PA instruction (26 studies; 46%) with group or one-to-one classes.

Fifty (88%) studies compared one or more interventions with usual care (Table 1), and seven (12%) compared an intervention with another intervention (Table 2).

We judged 36 studies (63%) to have low risk of selection bias for sequence generation, and 27 studies (47%) to have low risk of bias for allocation concealment. Because it was generally not feasible to blind participants and personnel to the intervention, we judged 56 studies (98%) to be at a high risk of performance bias. For detection bias for PA outcomes, we judged 30 studies (53%) that used subjective measurement tools to have a high risk of detection bias. We report the risk of bias assessment for individual trials in supplementary file 6. Fig. 2 shows a summary of risk of bias assessment.

Intervention vs usual care

Forty-one studies (5543 participants) reported amount of PA at the end of study follow-up, using a range of measurement values (e.g., minutes per day/week; steps per day; responses to questionnaires) which we pooled in separate analyses. We found moderate-certainty evidence, with a consistent finding across all measures, that PA interventions may increase the likelihood of people doing more PA at six to 24 months after surgery (Table 3). Most evidence was reported as minutes/day or week at six to 12 months after surgery, with a small increase in PA when participants received the intervention (SMD 0.17, 95% CI 0.09–0.26; 14 studies, 2172 participants; I^2 = 0%; see Fig. 3). In subgroup analysis, we found no evidence of a difference according to whether these interventions were given for at least six months or for less time, whether initiated pre- or post-surgery, according to the indication for surgery, or the age of the participants (younger than 60 years or at least 60 years) (Table 4).

We also found moderate-certainty evidence that interventions probably slightly increase people's engagement in PA compared with usual care (RR 1.19, 95% CI 0.96–1.47; 9 studies, 882 participants; I^2 = 25%; see supplementary file 7). Thus, 60 more participants per 1000 would still be engaging in PA six to 24 months later. However, the wide CI in this effect estimate indicates that some people who received the intervention did less PA.

Again, for the secondary outcome of physical fitness, various measures were used which prohibited complete pooling of data; the variety of outcome measures may reflect the age of participants in different studies, the indications for surgery, or both. In general, we noted a similar trend that suggested interventions may lead to an improvement in fitness (e.g., when measured in two studies using an exercise tolerance test, SMD was 0.82 (95% CI 0.23–1.40); see supplementary file 8). The low-certainty evidence for physical fitness included the possibility that interventions may or may not improve physical fitness at six to 12 months after surgery.

We found moderate-certainty evidence that PA interventions probably slightly increase health-related quality of life (SMD 0.11, 95% CI –0.03 to 0.24; 18 studies, 2638 participants; I^2 = 58%; see supplementary file 9). In formal tests for subgroup interactions for this outcome, we found no evidence of a difference between subgroups (Table 5). Again, the findings for pain tended to favour the intervention (SMD 0.20, 95% CI –0.07 to 0.47; 8 studies, 765 participants; I^2 = 73%; see supplementary file 10). However, the estimates were all imprecise and included possible benefits as well as harms; the certainty of this evidence was low. Fifteen studies (796 participants) reported adherence to the

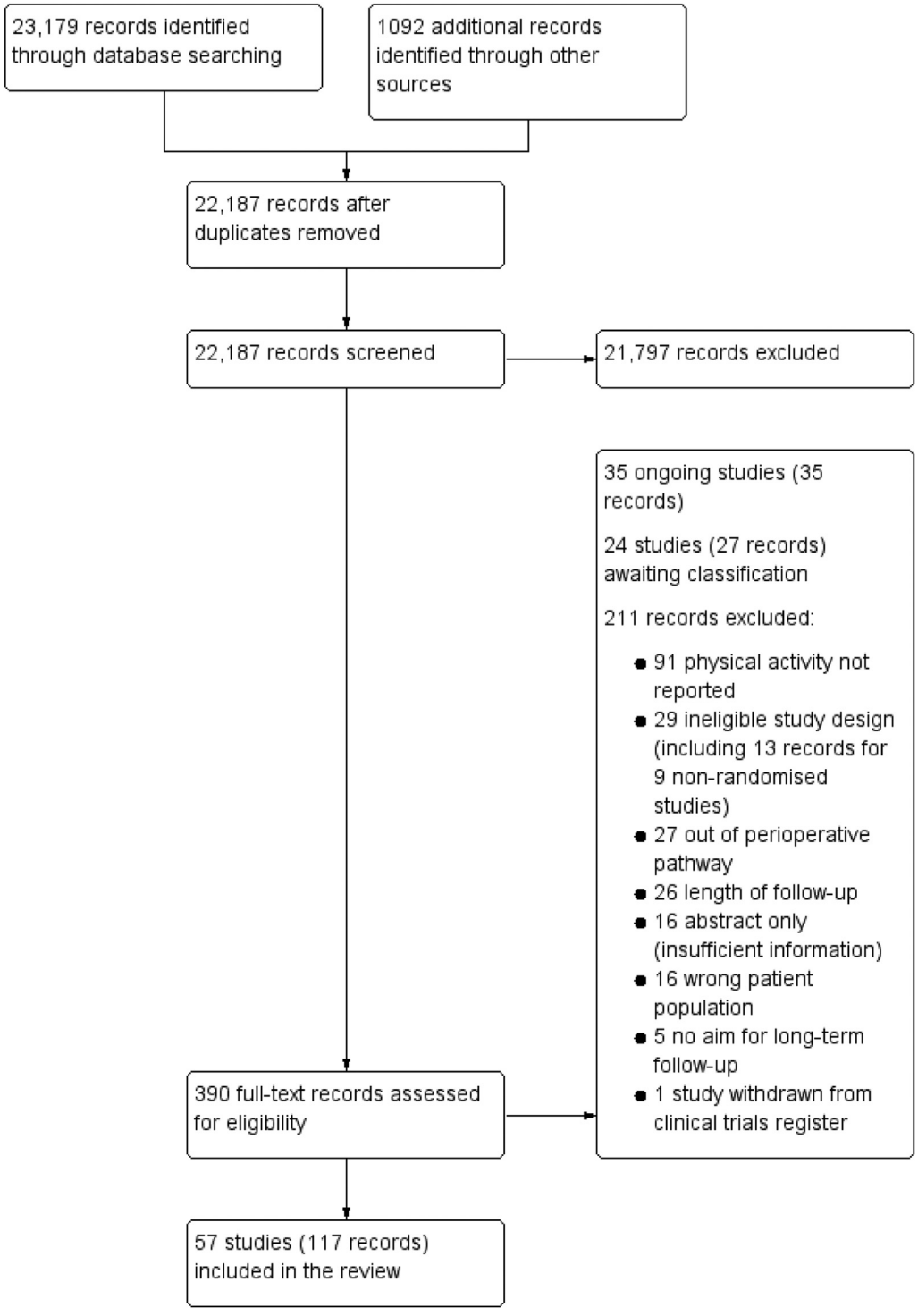

Fig. 1: Selection of studies for inclusion in review.

intervention which ranged from 47% to 93% (see supplementary file 11). It was not reasonable to draw confident conclusions about adherence because of differences in definitions for this outcome and the variation in intervention designs, and we judged the certainty of this evidence to be very low. Most adverse events, reported in 11 studies (1634 participants) with very low-certainty evidence, were described as not

Study ID	Population Characteristics	Total sample	Follow-up (months)	Age (years)[a]: intervention; control	Intervention (educational, behavioural, instruction); duration		Comparator
Artz et al.[32]	TKA	46	6	70.0 (57–81); 67.2 (51–82)[b]	Edu, instr; 6 weeks		Usual care
Baillot et al.[33]	Bariatric	30	12	44.5 (±8.8); 41.1 (±10.3)	Edu, behav and instr; 18 months		Usual care
Barberan-Garcia et al.[34]	Major intestinal surgery	144	6	71 (±11); 71 (±10)	Edu, behav and instr; 4–6 weeks		Usual care
Barnason et al.[35]	CABG	280	6	71.21 (±4.91)[c]	Edu, behav; 6 weeks		Usual care
Bellicha et al.[36]	Bariatric	76	60	NR	Instr; 18 weeks		Usual care
Bond et al.[38]	Bariatric	80	6	44.2 (±9.2); 48.1 (±8.1)	Edu, behav; 6 weeks		Usual care
Brandes et al. Q-RCT[39]	THA & TKA	65	6	70.7 (68.0–73.5); 69.9 (67.3–72.5)[d]	Edu, behav; mean (SD): 19.4 (±1.4) days		Usual care
Cadmus et al.[40]	Breast cancer	50	6	54.5 (±8.2); 54.0 (±10.9)	Edu, behav; 6 months		Usual care
Carnero et al.[41]	RYGB	128	6	39.4 (±9.7); 41.7 (±9.8)	Edu, instr; 6 months		Education sessions
Christiansen et al.a[43]	TKA	43	6	67 (±7); 67 (±7)	Edu, behav; 7–8 months		Usual care
Christiansen et al.b[42]	Dysvascular TTA	38	6	62 (59–65); 65 (60–71)[d]	Edu, behav; 12 weeks		Telephone session with physical therapist
Courneya et al.[44]	Breast cancer	242	6	49 (30–75)[b] 49.5 (25–76)[b] 49 (26–78)[b]	Aerobic instr; 1 month	Resistance instr	Usual care
Creel et al.[45]	Bariatric	150	6 1/2	43.6 (±11.9) 41.8 (±10.8) 44.2 (±11.0)	Edu, behav; 26 weeks	Edu	Usual care
Demark-Wahnefried et al.[46]	Breast and prostate cancer	543	12	57 (±10.4); 56.9 (±11.2)	Edu; 10 months		Non-tailored materials
Duculan et al.[47]	Complex lumbar surgery	230	12	64 (NR); 63 (NR)	Edu, behav; 12 months		Information
Eakin et al.[48]	Lumpectomy and mastectomy	143	12	51.7 (±9.0); 54.1 (±8.7)	Edu, behav; 8 months		Usual care
Engblom et al.[49]	CABG	201	12	54 (±6); 54 (±6)	Edu, behav, instr; 9 months		Usual care
Foster et al.[50]	Myocardial revascularization	40	12	56.0 (±8.6); 58.2 (±10.4)	Edu, instr; 6 months		Supervised training
Goedendorp et al.[51]	Various cancers	240	6	57.1 (±10.0) 55.6 (±11.3) 57.3 (±11.1)	Edu; 3 months	Edu, behav; 6 months	Usual care
Golsteijn et al.[52]	Colorectal and prostate cancer	478	6	66.55 (±7.07); 66.38 (±8.21)	Behav; 3 months		Usual care
Hackshaw-McGeagh et al.[53]	Prostatectomy	81	6	65.5 (±5.5); 62.5 (±6.9)	Edu, behav; 6 months		Usual care
Hauer et al.[54]	Hip fracture or elective THA	28	6	81.7 (±7.6); 80.8 (±7.0)	Instr; 12 weeks		Placebo activities
Hawkes et al.[55]	Colorectal cancer	410	12	64.9 (±10.8); 67.8 (±9.2)	Edu, behav; 6 months		Usual care
Heiberg et al.[56]	THA	68	60	65 (63–68); 66 (63–69)[d]	Instr; 6 weeks		Usual care
Hoorntje et al.[57]	UKA & TKA	120	6	58.6 (±5.0); 58.2 (±4.6)	Behav; 3–12 months		Usual care
Hubbard et al.[58]	Colorectal cancer	41	6	67.9 (±11.49); 64.2 (±11.10)	Edu, behav, instr; 6–12 weeks		Usual care
Husebo et al.[59]	Mastectomy or lumpectomy	67	6	50.8 (±9.7); 53.6 (±8.8)	Edu, behav; 16.7 (±7.6) weeks		Usual care
Ilves et al.[60]	Lumbar spine fusion	104	12	59 (±12); 58 (±12)	Edu, behav, instr; 3 months		Usual care
Jiménez-Loaisa et al. Q-RCT[61]	Bariatric	40	13	47.5 (±8.8); 42.6 (±10.9)	Edu, behav, instr; 6 months		Usual care
Kong et al.[65]	Breast cancer	152	6	47.3 (±8.5);46.8 (±7.6)	Edu, behav; 5 weeks		Usual care
Kummel et al.[67]	CABG	173	12	Male: 70.2 (±3.9), female: 70.3 (±3.9); male: 70.2 (±4.0), female: 71.5 (±4.1)	Edu, behav; 12-months		Usual care
Lear et al.[68]	CABG	302	12	64.8 (±8.8); 63.4 (±10.2)	Edu, behav, instr; 12 months		Usual care
Li et al.[69]	TKA	50	6	NR	Edu; NS		Usual care
Lier et al.[70]	Bariatric	99	12	43.5 (±11.1); 42.4 (±9.1)	Edu, behav; 25 months		Usual care
Lindback et al.[71]	Degenerative lumbar spine disorder	197	12	58 (±13.3); 61 (±11.5)	Behav, instr; 9 weeks		Usual care

(Table 1 continues on next page)

Study ID	Population Characteristics	Total sample	Follow-up (months)	Age (years)[a]: intervention; control	Intervention (educational, behavioural, instruction); duration			Comparator
(Continued from previous page)								
Losina et al.[72]	TKA	202	6	65.0 (±6.9); 65.0 (±8.3); 65.7 (±8.1); 65.8 (±6.9)	Behav; 6 months	edu	Edu, behav	Attention control
Lotzke et al.[73]	Lumbar fusion	118	6	44.8 (±8.2); 46.7 (±8.5)	Edu, behav; 14 weeks			Usual care
Mundle et al.[74]	Cardiac	50	6	NR	Edu; 30 days			Usual care
Olsen et al.[75]	RYGB	122	12	39.7 (±11.3); 40.2 (±10.8)	Edu, behav; 12 months			Usual care
Painter et al.[76]	Renal transplantation	167	12	39.7 (±12.6); 43.7 (±10.7)	Edu; 12 months			Usual care
Piva et al.[77]	TKA	240	6	69 (±6); 70 (±7); 70 (±7)	Edu, instr; 12 weeks	Instr		Usual care
Possmark et al.[78]	RYGB	259	24	43.6 (±10.7); 45.1 (±10.1)	Behav; 4 weeks			Usual care
Santa Mina et al.[79]	Prostatectomy	86	6	61.2 (±8.0); 62.2 (±6.9)	Edu; 4–8 weeks			Usual care
Smith et al.[81]	THA & TKA	224	12	63.3 (±8.6); 68.5 (±8.8)	Behav, instru; 6 weeks			Usual care
Stolberg et al.[82]	RYGB	60	24	42.4 (±9.0); 42.3 (±9.4)	Instr; 26 weeks			Usual care
Taraldsen et al.[83]	Hip fracture	143	6	84.0 (±6.6); 82.7 (±5.7)	Edu, instr; 10 weeks			Usual care
Turunen et al.[84]	Hip fracture	81	24	80.9 (±7.7); 79.1 (±6.4)	Edu, behav; 12 months			Usual care
Turunen et al.[85]	Joint replacement and back surgery	117	12	79.9 (±8.4); 79.7 (±8.1)	Edu, behav, instr; 6 months			Usual care
Van der Walt et al.[86]	THA & TKA	202	6	67 (±9); 66 (±9)	Edu; 6–8 weeks			Usual care
Yates et al.[87]	CABG	35	6	64 (33–77); 66 (40–77)[b]	Behav, instr; 3 weeks			Usual care

SD = standard deviation; NR = not reported; TKA = total knee arthroplasty; CABG = coronary artery bypass graft; RYGB = Roux-en-Y gastric bypass; TTA = transtibial amputation; AAA = abdominal aortic aneurysm; UKA = unicompartmental knee arthroplasty; CAD = coronary artery disease; THA = total hip arthroplasty; CI = confidence interval[a]Mean (SD), unless otherwise noted. [b]Median (range). [c]Baseline characteristics of overall analysed study participants. [d]Mean (95% CI).

Table 1: **Summary of included randomised controlled trials (intervention vs control).**

serious and unrelated to the intervention. The few events described as possibly related to the intervention (e.g., muscle soreness and musculoskeletal injury) were reported for only 30 participants (see supplementary file 12). Very few studies reported details of participants' experiences (4 studies, 159 participants). Feedback was generally positive, and participants were satisfied and/or felt that they had benefited from being able to engage with the intervention. We did not downgrade the certainty of this narrative evidence (see supplementary file 13).

Intervention vs intervention

Only seven studies compared one PA intervention with another type of PA intervention, and the differences in these interventions meant that it was often not feasible

Study ID	Population Characteristics	Total sample	Follow-up (months)	Mean (SD) age (years): intervention; control	Intervention (educational, behavioural, instruction); duration		Comparator
Archer et al.[31]	Laminectomy	248	12	62.94 (±11.50); 61.44 (±12.22)	Behav; 6 weeks		Edu
Boesch et al.[37]	CABG	51	24	55.4 (±9) 60.9 (±10) 54.3 (±12)	Objective/subjective; 1 month	Self-regulated	Heart-rate reserve
Johansson et al.[62]	Standard lumbar discectomy	59	12	43 (35–47); 38 (31–43)[a]	Edu, instr; 8-weeks		Edu
Jolly et al.[63]	PTCA/CABG	525	24	60.3 (±10.5); 61.8 (±11.0)	Edu, behav, instr; 8–12 weeks		Edu
Kinsey et al.[64]	CABG	48	48	56.2 (NR); 53.8 (NR)	Walking programme; 12 weeks		Cycling programme
Kraal et al.[66]	CABG	90	12	57.7 (±8.7); 60.5 (±8.8)	Centre-based training; 12 weeks		Home-based training
Smith et al.[80]	CABG	242	72	63.4 (±8.8); 65.1 (±9.0)	Centre-based training; 6 months		Home-based training

NR = not reported; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty. [a]Median (range).

Table 2: **Characteristics of included randomised controlled trials (intervention vs intervention).**

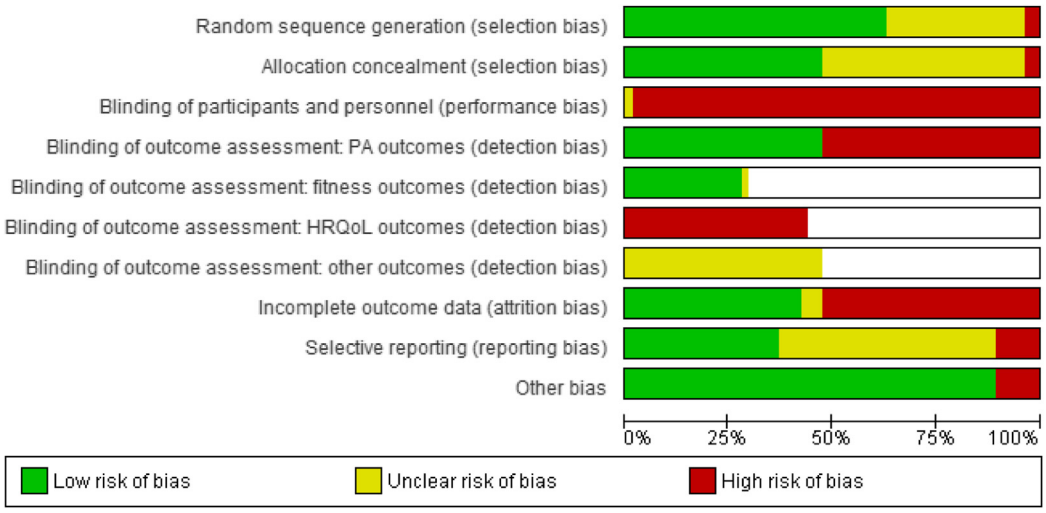

Fig. 2: Summary of risk of bias assessment across all included trials. Detection bias was judged at the outcome level and was not reported in all studies; therefore, percentages for these domains are not complete.

to combine data in analysis. The effects from most studies generally indicated little difference between intervention designs. One study[62] found improved engagement with PA after using a clinic-based intervention compared to a home-based intervention (RR 1.25, 95% CI 1.03–1.52; 57 participants; see supplementary file 14). For secondary outcomes, one study[66] found a small improvement in health-related quality of life with a home-based intervention compared to a clinic-based intervention (MD 0.32, 95% CI 0.27–0.37; 78 participants; see supplementary file 15), and another study[62] found improvement in pain with a home-based compared to a centre-based intervention (P value = 0.04; 57 participants; see supplementary file 16). But these findings were not comparable to other studies (Table 6), and we judged all the evidence, which was sparse and generally inconclusive, to be very low certainty.

Sensitivity analysis

Sensitivity analysis showed differences in some effects when comparing a PA intervention with usual care. For the amount of PA, measured as a change from baseline in minutes of PA per day or week, we found that effect estimates more clearly favoured the intervention when we excluded a study at high risk of attrition bias (MD 6.04, 95% CI 0.19–11.88; 2 studies, 150 participants; I^2 = 0%); this study was also the only study in which the outcome was measured immediately after the end of the intervention period (see supplementary file 17). When measured as steps per day, we found that the effect estimate was less precise when we included only studies with a period of delay after the formal completion of the intervention period (MD 553.35, 95% CI –18.82 to 1125.51; 3 studies, 232 participants; I^2 = 0%. See supplementary file 18). We also found a less precise effect estimate when studies with high or unclear risk of selection bias were excluded from the primary analysis of PA (measured as steps per day). In addition, we noted that when using data from alternative intervention groups in one study,[72] there was also less evidence of a difference between groups (see supplementary file 18). When PA was measured using questionnaires, we found a less precise result when we excluded studies with an unclear risk of selection bias (SMD 0.23, 95% CI –0.04 to 0.51; 4 studies, 401 participants; I^2 = 40%. See supplementary file 19).

In sensitivity analysis for HRQoL, we noted that the effect estimates more clearly favoured the intervention group when we excluded studies that were at high or unclear risk of selection bias for random sequence generation (SMD 0.25, 95% CI 0.00–0.29; 13 studies, 2350 participants; I^2 = 60%), or we excluded studies at high risk of attrition bias (SMD 0.27, 95% CI 0.00–0.54; 7 studies, 1096 participants; I^2 = 73%) (See supplementary file 20.)

If we used more consistent time points across studies, rather than using data at the end of study follow-up, we noted an improvement in physical fitness when measured using walking tests (SMD 0.99, 95% CI 0.47–1.51; 4 studies, 215 participants; I^2 = 69%; see supplementary file 21).

Certainty of the evidence

Using GRADE, we downgraded the certainty of the evidence owing to the unavoidable high risk of performance and detection bias. The sensitivity analyses on other risk of bias assessments did not impact most results such that our interpretation was altered. However, for HRQoL, this sensitivity analysis made us more

Outcome[a]	No. of studies	Sample size		Effect size (95% CI)
		Intervention group	Control group	
Amount of PA (minutes per day or week)[40,46,51,52,55,58,61,65,67,70,72,75,78,85]	14	1103	1069	SMD: 0.17 (0.09–0.26); I^2 = 0%; P < 0.0001
Amount of PA (minutes per day or week; based on change-from-baseline)[36,41,73]	3	120	126	MD: 2.42 (–3.87 to 13.20); I^2 = 67%; P = 0.66
Amount of PA (steps per day)[33,39,42,69,72,78]	6	206	178	MD: 909.58 (305.82–1513.35); I^2 = 41%; P = 0.003
Amount of PA (steps per day; based on change-from-baseline)[41,73]	2	105	109	MD: 187.48 (–410.09 to 785.06); I^2 = 0%; P = 0.54
Amount of PA using energy expenditure measures[35,53,68,77,79]	5	372	323	SMD: 0.17 (–0.16 to 0.50); I^2 = 76%; P = 0.32
Amount of PA using energy expenditure measures (based on change-from-baseline)[41]	1	46	50	MD: –84.00 (–192.79 to 24.79)
Amount of PA using various questionnaires[32,34,51,54,56,81]	6	264	221	SMD: 0.34 (0.08–0.60); I^2 = 43%; P = 0.010
Amount of PA using IPAQ-SF (METS/mins/week)[33,59,75]	3	72	73	MD: 276.21 (–614.32 to 1166.74); I^2 = 0%; P = 0.54
Amount of PA using a daily activity score[51]	1	30	25	MD: 2.50 (–10.17 to 15.17)
Engagement in PA[44,48–50,67,70,76,84,85]	9	460	422	RR: 1.19 (0.96–1.47); I^2 = 25%; P = 0.11
Physical fitness using 6 MWT (based on change-from-baseline)[33]	1	13	12	MD: 50.90 (0.55–101.25)
Physical fitness using 5 MWT (based on change-from-baseline)[73]	1	59	59	MD: 0.50 (–65.62 to 66.62)
Physical fitness using TUG test (seconds)[42,54,73]	3	88	87	MD: –0.09 (–0.98 to 0.80); I^2 = 0%; P = 0.84
Physical fitness using an exercise tolerance test[33,50]	2	32	21	SMD: 0.82 (0.23–1.40); I^2 = 0%; P = 0.006
Physical fitness using performance-based tests[77,85]	2	142	98	SMD: 0.19 (–0.08 to 0.45); I^2 = 0%; P = 0.16
Physical fitness using sit-to-stand test[33]	1	13	12	MD: 2.50 (–1.30 to 6.30)
Physical fitness using arm curl test[33]	1	13	12	MD: 0.50 (–3.86 to 4.86)
Physical fitness using leg press[54]	1	12	12	MD: 42.00 (–1.61 to 85.61)
Physical fitness using VO_2 peak[76]	1	52	43	MD: 3.60 (–0.22 to 7.42)
Physical fitness using VO_2 peak (based on change-from-baseline)[41]	1	46	50	MD: 188.00 (55.57–320.43)
HRQoL using various measurement tools[32–34,39,40,44,46,52,55,56,58,61,76–79,81,86]	17	1277	1178	SMD: 0.12 (–0.03 to 0.24); I^2 = 58%; P = 0.12
HRQoL using various measurement tools (based on change-from-baseline)[36,71,73]	3	181	179	SMD: –0.14 (–0.35 to 0.07); I^2 = 0%; P = 0.19
HRQoL using FACT-B+4 (based on change-from-baseline)[48]	1	66	60	MD: 3.70 (–1.48 to 8.88)
Pain using various measurement tools[32,39,40,56,79,81,86]	8	426	339	SMD 0.20 (–0.07 to 0.47); I^2 = 67%; P = 0.15
Pain using VAS (based on change-from-baseline)[71,73]	2	158	157	Back pain (MD): 5.45 (–1.03 to 11.92); I^2 = 0%; P = 0.10 Leg pain (MD): 2.00 (–6.19 to 10.18); I^2 = 0%; P = 0.63

CI = confidence interval; SMD = standardised mean difference; MD = mean difference; IPAQ-SF=International Activity Questionnaire – short form; RR = relative risk; METS = metabolic equivalent tasks; 6 MWT = 6-min walk test; 5 MWT = 5-min walk test; TUG = Timed up-and-go; VO2 peak = peak oxygen uptake; HRQoL = health-related quality of life; EQ-5D = five-dimensional EuroQol questionnaire; FACT-B4=Functional Assessment of Cancer Therapy-Breast Cancer; VAS = visual analogue score. [a]Data reported as a set of post-intervention value scores unless otherwise stated.

Table 3: **| Intervention vs control.**

confident that PA may slightly improve quality of life. We were not surprised by the high levels of statistical heterogeneity in some of the effect estimates; this was likely caused by our decision to pool studies with different surgical populations as well as different intervention components. Subgroup analyses were inconclusive, although we noted in one analysis for 'amount of PA' that this inconsistency may have been caused by studies at high risk of bias. Imprecision was evident in some findings, with the effect estimates including the possibility of harms as well as benefits, and we downgraded the certainty of the evidence when this was the case. We did not downgrade for publication bias; however, our evaluation of this was limited to effect estimates with more than ten studies. We generated a funnel plot for outcomes with more than ten studies; whilst we noted some outlying data, we were not concerned by this as these data were from very small studies and had limited impact on the overall effect estimate (see supplementary files 22 and 23). Because some outcome measurements included only few, small studies, we could not confidently rule out the possibility of publication bias or small study effects. All studies met our review eligibility criteria, and we did not downgrade any of the evidence for indirectness.

Discussion

Our analysis of 57 RCTs or quasi-RCTs (8548 adults) found moderate-certainty evidence that, when compared with usual care, interventions given during the perioperative pathway may slightly increase amount of PA, engagement of PA, and health-related quality of life of participants. There was a wide range of surgical groups, intervention types, and duration of interventions. While effects generally favoured interventions, we found low-certainty evidence for physical fitness and pain. Few studies reported adherence and adverse events, and certainty of these findings was very low. Participants

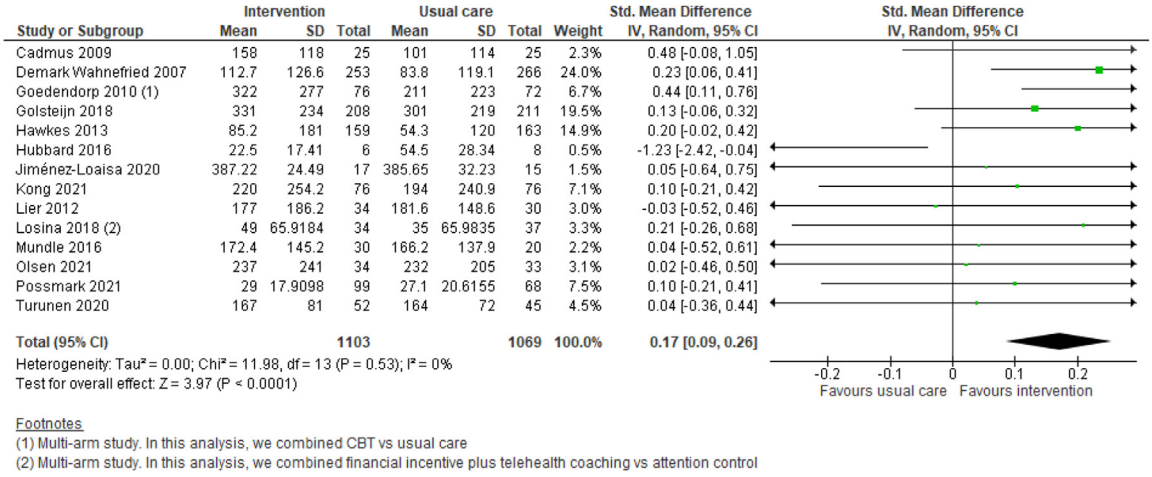

Fig. 3: Forest plot of combined data comparing PA interventions with usual care: Amount of PA at end of follow-up measured as minutes per day or week.

generally provided positive feedback about the interventions, although this was infrequently reported.

The effect sizes were modest. However, the mean differences and risk ratios offer a simplistic account of a complex picture which stems from numerous factors. Firstly, as 'usual care' is not standardised between studies, this will affect the pooled differences between groups in ways that are unpredictable in both size and direction of effect. Secondly, many trials included more than one type of intervention component (education/advice; behavioural mechanisms; and direct PA instruction). As one component might be more or less effective than another (or indeed, might worsen rather than improve intended outcomes), the net effect of this is also hard to predict. And lastly, there were generally moderate recruitment rates into the studies. We do not know if there are random or systematic differences between the types of patients who are likely to participate in studies and those who do not; if there are differences, they are likely to have more influence the further recruitment rates drop below 100%. We used rigorous methods to search and independently assess study eligibility, extract data and assess risk of bias in the included RCTs. We developed more specific inclusion criteria during the review process to manage the large number of studies that met our broad criteria but did not fit with our review objectives; this provided more direct evidence whilst also accounting for the wide range of possible interventions. We also established our choice of subgroup analyses posthoc, based on criteria thought to reveal differences in findings. Potentially, other relevant subgroups remain unexplored, as well as differences between studies such as those that included sites using enhanced recovery strategies after surgeries. Conducting multiple subgroup analyses, however, can be misleading[28] and we therefore limited our choice of these additional analyses.

The types of measures for our outcomes (particularly for amount of PA and physical fitness) were not consistent across studies which prevented overall pooling of some data and meant that meta-analysis often included only a few small studies. Because of numbers of studies, our subgroup analyses were limited to two outcomes: amount of PA measured as min/day or week, and HRQoL, for which we found no evidence of subgroup differences. However, we could not be confident whether this reflected no real difference between subgroups or no evidence of a difference because of insufficient studies in each subgroup. It is likely that services responsible for PA interventions had different motivators depending on the surgical indication which we could not explore because we had insufficient studies for all the clinical indications. We were similarly unable to explore the effect of the different intervention components in subgroup analysis, often because of large overlap or because of lack of information in published reports.

We did not limit our studies to those that specifically aimed to evaluate whether interventions enabled people to engage in PA in the long-term. Limitations in reporting standards in many studies meant that the study objectives were not always clear. Our evidence, therefore, included some studies that did not measure outcomes longitudinally, and many did not include a delay between end of the intervention and measurement; this delay allows us to establish if the intervention has been effective at changing self-regulated behaviour. The lack of long-term follow-up in these studies could be explained by funding/resource limitations that mean that most studies have a short-term research period.

Subgroups	No. of studies	Sample size		Effect size (95% CI)	Test for subgroup differences
		Intervention group	Control group		
Sub-grouped by duration of intervention					
<6 months[52,58,65,74,78]	5	419	383	SMD 0.08 (−0.09 to 0.25); I^2 = 19%; P = 0.34	P = 0.20
≥6 months[39,46,51,55,61,70,72,75,85]	9	684	686	SMD 0.22 (0.05–0.25); I^2 = 0%; P < 0.0001	
Sub-grouped by time of intervention commencement					
Pre-surgery[51,70]	2	110	102	SMD 0.24 (−0.21 to 0.69); I^2 = 58%; P = 0.29	P = 0.72
Post-surgery[39,46,52,55,58,61,65,72,74,75,78,85]	12	993	967	SMD 0.16 (0.07–0.25); I^2 = 0%; P = 0.0005	
Sub-grouped by type of surgery					
For various types of cancer[39,46,51,52,55,58,65]	7	803	821	SMD 0.21 (0.07–0.34); I^2 = 37%; P = 0.003	P = 0.22
For other conditions[61,70,74,75,78,85]	7	300	248	SMD 0.07 (−0.10 to 0.24); I^2 = 0%; P = 0.41	
Sub-grouped by age					
Mean age <60 years[39,46,51,61,65,70,75,78]	8	614	585	SMD 0.20 (0.09–0.32); I^2 = 30%; P 0.18	P = 0.67
Mean age ≥60 years[52,55,58,72,85]	5	459	464	SMD 0.12 (−0.05 to 0.30); I^2 = 30%; P = 0.18	
Unknown[74]	1	30	20	SMD 0.04 (−0.52 to 0.61); P = 0.88	

CI = confidence interval; SMD = standardised mean difference.

Table 4: **Amount of PA (minutes per day or week) | Subgroup analysis | Intervention vs control.**

We are not aware of any other systematic reviews that have included such a broad surgical population or have considered such a range of interventions to promote PA. Similar to our findings for HRQoL, Coenen et al.[147] also found a slight improvement in quality life when 'integrated programmes' were used in orthopaedic surgical patients. Their systematic review included services that were additional to usual care provision, and also evaluated whether these programmes improved participation in PA; because of the smaller number of studies and the wider differences between intervention, data were not pooled for PA. The work by Steffens and colleagues, for people undergoing cancer surgery, demonstrates an improvement in quality of life when there are higher levels of pre-operative PA.[148] Our own subgroup analysis, which included all indications for

Subgroups	No. of studies	Sample size		Effect size (95% CI)	Test for subgroup differences
		Intervention group	Control Group		
Sub-grouped by duration of intervention					
<6 months[32,34,39,44,52,56,58,77–79,81,86]	12	869	724	SMD 0.03 (−0.11 to 0.17); I^2 = 42%; P = 0.67	P = 0.10
≥6 months[33,40,46,55,61,76]	6	521	524	SMD 0.32 (0.01–0.62); I^2 = 75%; P = 0.04	
Sub-grouped by time of intervention commencement					
Pre-surgery[33,34,79,86]	4	118	185	SMD -0.05 (−0.56 to 0.46); I^2 = 80%; P = 0.84	P = 0.49
Post-surgery[32,39,40,44,46,52,55,56,58,61,76–78,81]	14	1202	1063	SMD 0.13 (0.00–0.26); I^2 = 45%; P = −0.04	
Sub-grouped by type of surgery					
For various types of cancer[40,44,46,52,55,58,79]	7	773	771	SMD 0.11 (−0.14 to 0.37); I^2 = 79%; P = 0.39	P = 0.91
For other conditions[32–34,39,56,61,76–78,81,86]	11	617	477	SMD 0.10 (−0.04 to 0.24); I^2 = 13%; P = 0.32	
Sub-grouped by BMI					
Mean value < 30 kg/m^2 [39,40,44,46,52,55,56,76,79,86]	10	943	933	SMD 0.05 (−0.14 to 0.24); I^2 = 72%; P = 0.61	P = 0.09
Mean value ≥ 30 kg/m^2 [61,77,78,81]	4	339	213	SMD 0.07 (−0.10 to 0.24); I^2 = 0%; P = 0.41	
Unknown[32–34,58]	4	108	102	SMD 0.40 (0.13–0.68); I^2 = 0%; P = 0.004	
Sub-grouped by age					
Mean age <60 years[33,40,44,46,61,76,78]	7	550	504	SMD 0.25 (−0.02 to 0.52); I^2 = 70%: P = 0.07	P = 0.19
Mean age ≥60 years[32,34,39,52,55,56,58,77,79,81,86]	11	840	744	SMD 0.04 (−0.12 to 0.20); I^2 = 51%; P = 0.59	

CI = confidence interval; SMD = standardised mean difference; BMI = body mass index.

Table 5: **HRQoL (using various components) | Subgroup analysis | Intervention vs control.**

Outcome	No. of studies	Sample size		Effect size (95% CI)
Amount of PA using energy expenditure measures[37]	1	Objective/subjective: 25	Self-regulation: 23	MD: 723.00 (−409.33 to 1855.33)
Amount of PA measured as activity counts per minute[31]	1	CBPT: 98	Education: 100	MD: −6.13 (−66.77 to 54.51)
Amount of PA using the Godin score[63]	1	Centre-based: 233	Home-based: 228	MD: (−0.86 to 0.62)
Amount of PA using PAL score[66]	1	Home-based: 37	Centre-based: 41	MD: 0.01 (−0.45 to 0.47)
Engagement in PA (clinic vs home)[62]	1	Centre-based: 28	Home-based: 29	RR: 1.25 (1.03–1.52)
Engagement in PA (home vs hospital)[80]	1	Home-based: 48	Centre-based: 60	RR: 1.30 (0.90–1.87)
Physical fitness using VO_2 peak[66,80]	2	Home-based: 107	Centre-based: 115	SMD: 0.21 (−0.07 to 0.50); I^2 = 11%; P = 0.14
Physical fitness using the incremental shuttle walking test[63]	1	Centre-based: 163	Home-based: 179	MD: −8.20 (−43.85 to 27.45)
Physical fitness using an exercise tolerance test (METSs max)[80]	1	Home-based: 70	Hospital-based: 74	MD: 0.50 (0.09–0.91)
HRQoL (PCS of SF-36)[80]	1	Home-based: 74	Centre-based: 70	MD: −2.30 (−5.70 to 1.10)
HRQoL (EQ-5D)[63]	1	Centre-based: 231	Home-based: 223	MD: 0.02 (−0.03 to 0.07)
HRQoL (MacNew Questionnaire)[66]	1	Home-based: 37	Centre-based: 41	MD: 0.32 (0.27–0.37)
HRQoL (PCS of SF-12)[31]	1	CBPT: 114	Education: 115	MD: 1.82 (−1.44 to 5.08)
Pain using BPI[31]	1	CBPT: 114	Education: 115	Back pain (MD): 0.12 (−0.54 to 0.78) Leg pain (MD): −0.46 (−1.17 to 0.25)
Pain using self-reported chest pain on movement[63]	1	Centre-based: 163	Home-based: 179	MD: 0.09 (−0.09 to 0.27)

CI = confidence interval; MD = mean difference; CBPT = cognitive behavioural physical therapy; PAL = physical activity level; RR = relative risk; VO_2 peak = peak oxygen uptake; SMD = standardised mean difference; METS = metabolic equivalent tasks; HRQoL = health-related quality of life; PCS = physical component score; SF-36/SF-12 = 36/12-Item Short-Form Health Survey; EQ-5D = five-dimensional EuroQol questionnaire; BPI=Brief Pain Inventory.

Table 6: | **Intervention vs intervention.**

surgery, showed no evidence of overall improvement in HRQoL for pre-operative interventions. In their meta-analysis of 24 studies of the effect of counselling about PA in primary care (not specific to surgical patients), van der Wardt et al.[149] found interventions showed a marginal effect on changing people's PA behaviour. In a related area of practice, Mishra et al.[150] (2012) conducted a Cochrane systematic review of exercise interventions and quality of life in cancer survivors. The review included 3694 participants in 40 trials, and found beneficial effects of exercise on global HRQoL in a smaller number of participants at 12 weeks (SMD 0.48, 95% CI 0.16–0.81); the effect was still evident at six months but data were available in only 115 participants, and are reflective of few clinical trials with long follow-up times. A recently published umbrella review of prehabilitation in adults undergoing surgery, which included 55 systematic reviews, found evidence of beneficial effects of prehabilitation in decreasing complications, reducing risk of non-home discharge, reducing length of stay, and improving functional recovery.[151] However, despite beneficial effects being identified for exercise interventions, the certainty of evidence for each intervention type was low or very low which, similar to our findings, was due to methodological variance and a lack of a core set of outcome measurements.

The evidence in our review broadly supports existing data interventions delivered in the perioperative setting for surgical patients.[152–154] As the interventions involved a variety of practitioners, with 23.9% delivered by a multidisciplinary team, our review broadly supports evidence that the effectiveness of perioperative interventions relies on the involvement of a multiprofessional team,[155–158] and supports preliminary work on the potential for collaborative care.[13,14] These data will inform the discussion around how to integrate models of care into a perioperative pathway which optimise not only surgical outcomes, but also the medium to long-term health benefits of increased PA.

In conclusion, we found moderate-certainty evidence that PA interventions delivered in the perioperative setting may have overall benefit. These interventions probably increase the amount of PA up to 12 months after surgery. In general, the findings for all outcomes showed a trend in favour of PA interventions; however, because of imprecision in some of the findings, we could not rule out the possibility of no change in PA. The broad range of measures used in the studies often limited our ability to combine data and the development of a core outcome set in this field would improve future quantitative synthesis.

Contributors

MP: screened references; completed full-text review; data extraction; synthesis of quantitative data; accessed and verified the underlying data; writing the final report. SL: prepared search strategies; screened references; completed full-text review; data extraction; provided advice and guidance on systematic review preparation; accessed and verified the underlying data; writing the final report. AR: screened references; completed full-text review; data extraction; accessed and verified the underlying data; writing the final report. SG: liaised with NIHR; prepared protocol for PROSPERO; prepared search strategies and ran

searches; screened references; completed full-text review; writing the final report. AC: provided guidance and advice throughout project; writing the final report. RC: provided guidance and advice throughout project; advised on the final report. EL: provided guidance and advice throughout project; advised on the final report. AS: writing the final report; guarantor.

Data sharing statement

Further data from the project are available on request from the corresponding author.

Declaration of interests

RC reports grants from Yorkshire Cancer Research. SG reports studentship grant from NIHR ARC NWC paid to the University of Central Lancashire. AS reports grants from European Society of Anaesthesiology; and consulting fees (personal payment for advice on new airway devices).

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2022.101806.

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