Behavior change techniques for increasing physical activity in cancer survivors: a systematic review and meta-analysis of randomized controlled trials

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Purpose: The purpose of this systematic review and meta-analysis is to investigate how physical activity (PA) can be effectively promoted in cancer survivors. The effect of PA-promoting interventions in general, behavior change techniques (BCTs), and further variables as moderators in particular are evaluated.

Methods: This study included randomized controlled trials of lifestyle interventions aiming at an increase in PA that can be carried out independently at home, published by December 2016, for adults diagnosed with cancer after completion of the main treatment. Primary outcomes were subjective and objective measures of PA prior to and immediately after the intervention. Metaanalysis and meta-regression were used to estimate effect sizes (ES) in terms of standardized mean differences, variation between ES in terms of heterogeneity indices (I2), and moderator effects in terms of regression coefficients.

Results: This study included 30 studies containing 45 ES with an overall significant small positive effect size of 0.28 (95% confidence interval=0.18-0.37) on PA, and I²=54.29%. The BCTs Prompts, Reduce prompts, Graded tasks, Non-specific reward, and Social reward were significantly related to larger effects, while Information about health consequences and Information about emotional consequences, as well as Social comparison were related to smaller ES. The number of BCTs per intervention did not predict PA effects. Interventions based on the Theory of Planned Behavior were associated with smaller ES, and interventions with a home-based setting component were associated with larger ES. Neither the duration of the intervention nor the methodological quality explained differences in ES.

Conclusion: Certain BCTs were associated with an increase of PA in cancer survivors. Interventions relying on BCTs congruent with (social) learning theory such as using prompts and rewards could be especially successful in this target group. However, large parts of between-study heterogeneity in ES remained unexplained. Further primary studies should directly compare specific BCTs and their combinations.

Keywords: exercise, lifestyle, intervention methods, behavior change, moderator effects, tumor

Background

About 14.1 million new cancer cases and 8.2 million cancer-related deaths were recorded worldwide in 2012.1 A person is defined as a cancer survivor from the moment of cancer diagnosis throughout life.² Early detection, improved diagnostics, and treatment have resulted in increased survival rates, 3,4 leading to almost 32.6 million cancer survivors worldwide with a diagnosis in the previous 5 years. Numerous disease- or treatment-related adverse effects, such as secondary cancers, fatigue, or depression, can decrease the length and quality of life.5

Correspondence: Emily Finne School of Public Health, Bielefeld University, Universitätsstrasse 25, Bielefeld, 33615, Germany Tel +49 521 106 3882 Fax +49 521 106 6433 Email emily.finne@uni-bielefeld.de In the last two decades it has been demonstrated that physical activity (PA) plays an important role not only in cancer prevention but also during and after cancer treatment. 6.7 PA increases physical functioning among cancer survivors and provides physiological and psychological benefits. 8-11 It is recommended that cancer survivors should become or stay physically active as soon as possible after diagnosis. They should engage in at least 150 minutes per week of moderately intense or 75 minutes per week of vigorous intense aerobic PA and should perform muscle-strengthening activities at least twice per week. 12 Despite this evidence, cancer survivors show low levels of PA 13-15 and a decline during cancer treatment without returning to PA levels prior to diagnosis. 16,17

Changing behavior from a mainly sedentary to a physically active lifestyle poses a challenge to most people but particularly to those with chronic diseases such as cancer. ^{18,19} PA that is easily performed at home (for example aerobics, walking, biking) is more convenient and accessible for patients and can play an important role in developing an active lifestyle. ²⁰

Various interventions have been developed in recent years, aiming at promoting PA in cancer survivors.^{21–24} Although reviews show beneficial effects in terms of PA increases^{23,25,26} and exercise tolerance,²⁴ substantial variance in effect sizes indicates a moderating effect of intervention characteristics such as study design, theoretical foundation, and content.

Regarding study design as a moderator, a recent metaanalysis on PA promoting interventions in different target groups found a strong methodological quality to be related to smaller intervention effects.²⁷ This finding suggests that, by including methodologically weak studies with larger effects in previous meta-analyses, overall effects may potentially have been overestimated.

Theories most commonly used as a basis of behavior change interventions are the Transtheoretical Model (TTM), Social Cognitive Theory (SCT), Health Belief Model, and Theory of Planned Behavior (TPB).²⁸ It is expected that interventions are more effective when built on a theoretical foundation.²⁹ However, studies show ambiguous results.^{30,31}

Examining intervention content as a potential moderator is challenging, since behavior change interventions are usually built out of multiple components. To facilitate consistent classification of intervention content by researchers and clinicians, Michie et al³² developed a taxonomy of behavior change techniques (BCTs) by employing a systematic expert consensus approach.³² A BCT is defined as "an observable, replicable and irreducible component of an intervention designed to alter or redirect causal processes that regulate

behavior".³³ The taxonomy of Michie et al³³ (BCTT v1) consists of standardized definitions of 93 different BCTs. No consistent matching of BCT definitions from BCTT v1 with theories or theory-based determinants of PA behavior is available yet. Studies that analyzed effective BCTs in interventions to increase PA^{30,31,34–38} showed equivocal results. Regarding cancer survivors, so far neither the amount of PA nor BCTs were compared between more or less successful trials.²⁴

The purpose of the present review and meta-analysis is to summarize the efficacy of interventions that aim at increasing overall PA that can be carried out independently at home in cancer survivors after completion of main cancer treatment and, particularly, to analyze which BCTs are most effective in this target group. Additional intervention features such as intervention duration, number of applied BCTs, and theoretical foundation as well as patient characteristics are analyzed as possible moderators of treatment effects.

Methods

To ensure correct proceedings along the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a PRISMA checklist was created and PRISMA review guidelines were followed (Figure S1).³⁹ Every study and intervention feature was extracted by two reviewers independently and ambiguity in this process was resolved by consulting with a third reviewer. Since only published results were analyzed and no individual data gathered, no ethical approval was obtained.

Search strategy

The electronic database MEDLINE was searched for articles from the earliest possible year to December 2016. The search strategy included medical subheadings and text word terms in different combinations, for example: neoplasms, cancer survivor, exercise, PA, physical fitness, muscle strength, health promotion, health education, behavior therapy, and randomized controlled trial (RCT). The complete search strategy is shown in Figure S2. Additionally, reference lists of retrieved articles and published reviews and meta-analyses on PA interventions in cancer survivors were screened.

Study inclusion criteria

For eligibility, studies had to meet the following conditions:

- 1. Type of study: RCT. Exclusion: RCT-pilot study subsequently evaluated in a main study.
- 2. Type of participants: Adult patients (18 years of age or older) diagnosed with cancer. Exclusion: Current active

- 3. Type of intervention: Lifestyle intervention aiming at an increase in PA behavior including exercise intervention and multicomponent program focusing on PA and further lifestyle factors; interventions that aim at increasing PA that can be easily carried out independently at home. Exclusion: Interventions aiming at PA that requires professional guidance, specific equipment or facilities (eg, fitness machines).
- 4. Type of control group: Usual care or wait-list control group.
- Type of outcome measure: PA (self-reported or objectively measured) prior to and immediately after the intervention. PA is defined as any bodily movement produced by skeletal muscles resulting in energy expenditure.

Follow-up measurements were not taken into account, since these were reported only for a subset of interventions and were of varying duration. Only full-text articles written in English and German were included. To identify studies meeting the inclusion criteria, titles and/or abstracts of studies retrieved with the search strategy were screened. The full texts of these studies were retrieved and assessed for eligibility.

Data extraction

Extracted information of study details included author, year, research question, the country where the study was carried out, recruitment source, inclusion and exclusion criteria, study design, and description of the control group (CG) vs intervention group (IG). Regarding participant characteristics, cancer type, age, gender, and time since diagnosis or treatment were extracted. Furthermore, the following intervention details were recorded: name, frequency and total duration of the intervention, setting, type of delivery, theoretical basis, and BCTs used. Regarding PA outcome, the method of measuring PA, the number of participants randomly assigned and assessed, as well as the PA level were extracted.

Coding of methodological quality

Methodological quality was assessed according to the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies (EPHPP-Tool).⁴⁰ The tool consists of questions to help with assessing the quality concerning the six criteria selection bias, study design, confounders, blinding, data collection methods, as well as withdrawals and dropouts, which are combined to a global rating of methodological quality. Additionally, intervention integrity and

statistical analyses (including intention-to-treat approach) are evaluated.

Coding of behavior change techniques

The BCT taxonomy v132 was used to identify and code the BCTs reported in each IG. The most comprehensive published description of the intervention content (eg, from study protocols) was used. Coding was carried out by MG and EF independently after completing the BCT taxonomy v1 Online Training⁴¹ using the given BCT definitions and coding rules. BCTs were coded as present or absent, and only the BCTs exclusively applied in the IG were extracted. After coding the first interventions, definitions and coding rules were discussed and additional coding rules established to interpret ambiguities. To quantify intercoder agreement, Cohen's kappa⁴² was calculated for BCTs and studies (Table S1) based on the semi-final coding after this discussion. Prevalenceadjusted bias-adjusted kappa (PABAK)42 values are additionally reported. These are kappa values adjusted for a potential bias by the overall proportion of "yes"-responses as well as by differences in this proportion between the coders. Remaining disagreements in coding were then solved by discussion and consulting with a third reviewer (AE).

Data synthesis (meta-analysis and meta-regression)

Since the majority of studies reported means and standard deviations (SD or equivalents) as outcome and only a few studies reported change scores, Hedge's g was computed as an effect size from the PA scores immediately after the intervention. Since only RCTs were included, possible baseline differences between groups should be random. For calculating SDs from other measures, formulae from the Cochrane Handbook were used.⁴³

Effect sizes and variances were calculated within the package "metafor"⁴⁴ for the Software R⁴⁵ and, where effect sizes had to be calculated from F-values, *P*-values or proportions, these calculations were performed with the package "compute.es", ⁴⁶ using conversion formulas from Cooper et al.⁴⁷ If required, SDs of PA outcomes following the intervention were estimated by regressing the log SDs on the log means following the Cochrane Handbook.⁴³

Available objective and self-reported measures were included, since both measure slightly different aspects of PA behavior and are only moderately correlated. 48,49 Within-study dependencies of effect sizes were accounted for.

For studies that provided multiple self-report measures, only one effect size regarding these measures was included. Scores of total moderate to vigorous physical activity were prioritized over scores solely including low-intensity activities or those limited to only moderate or vigorous intensity activities. Overall PA was preferred over measures of sport or exercise, and measures related to total volume (ie, combining intensity, frequency, and duration) were favored over the duration of PA. Validated self-report instruments were given priority. One study did not report any measure of PA volume or frequency, but instead gave a "relative treatment effect" and the corresponding SD for both groups. This study was included in the meta-analysis, since this outcome measure seemed directly related to overall PA, and sensitivity analysis excluding this study did not change our results meaningfully.

For studies which included different treatment conditions compared to the same CG, dependencies between effect sizes were also taken into account in the models.

Within-study covariances were estimated following Gleser and Olkin⁵¹ and Pustejovsky⁵² for multiple outcomes, multiple treatment conditions, or both. In cases without a reported correlation, the estimation of covariances was based on a correlation between self-reported and objective outcomes of r=0.51, as reported for cancer survivors.⁴⁹ Significance tests and CIs were based on robust estimation methods to adjust for a potentially misspecified variance—covariance matrix, since all but one covariance could only be estimated.

First, a multivariate mixed effects meta-analysis (a random effects meta-analysis that allows for effect sizes of different outcomes to be correlated within a study) with the function "rma.mv" within the "metafor" package was conducted to estimate the overall effect size and between-study heterogeneity for self-reported and objective PA outcomes using the restricted maximum likelihood estimation method. Heterogeneity due to differences between the true effects was estimated by calculating a variant of I² for multivariate meta-analysis based on a multivariate generalization of H², as suggested by Jackson et al.⁵³ Publication bias was examined by visual inspection of the funnel plot and testing the association of study sampling variances with effect sizes within the multivariate mixed model (similar to Egger's regression test).

To determine effects of individual BCTs, separate meta-regression models were then calculated with each BCT (coded as absent or present) as moderator. Only BCTs that were coded as being present for at least five comparisons were included. Additional models with further intervention characteristics as moderators followed the same approach.

Results

From a database search and reference checking of recent systematic reviews, 795 records were identified (Figure 1). After screening, 44 articles reporting on 30 trials met the inclusion criteria. ^{54–96} Of these articles, all 30 trials provided sufficient data for inclusion into the meta-analysis.

Description of included trials

Three of the 30 RCTs included compared more than one IG to an untreated CG, resulting in the investigation of a total of 34 comparisons for self-reported PA outcomes and 11 comparisons for objectively measured PA outcomes. All studies were published between 2006 and 2016.

In total, 4,507 cancer survivors were included (M=150, range=22–641) with a mean age of 57.1 years (median (Md)=56.7, SD=7.71, range=33.6–73.1), and an overall percentage of females of M=74.14% (Md=90.93, SD=35.25, range=0%–100%). Most samples were survivors of breast cancer (k=13 trials) or mixed types of cancer (k=11). The majority of trials were from the US (k=19) and mostly used standard care as control comparison (k=21, eight wait-list control, and one not stated).

The duration of interventions ranged from one-time recommendation (zero months) to 12 months (M=4.26, Md=3, SD=2.87), and treatment took place at home (k=16), at different treatment facilities (k=4) or both combined (k=10). Study characteristics are depicted in Table 1.

Methodological quality

Results of the methodological quality assessment are presented in Figure 2 (for details see also Table S2). Overall, nine of the 30 studies were rated as methodologically strong, 16 as moderate, and five as weak. Regarding patient selection bias, many of the studies were rated weak (k=18), while the remaining were rated moderate. Confounders were controlled for in most of the studies (k=26). For blinding, only two of the studies were ranked strong. In the remaining studies, the blinding process was either not explained, the outcome assessors were aware of the exposure status of the participant, or the participants were aware of the research question. Reliable and valid outcome measures were used in most of the studies (k=26). Regarding drop-outs, 21 studies had a rate of less than 20%, and were, therefore, rated as strong. Nine studies had 60%-79% drop-outs, and one study did not report on drop-outs. Half of the studies (k=15) reported a sample-size calculation. Many of the studies had small sample sizes, suggesting difficulties in providing adequate statistical power to detect between-group differences, even if they were pres-

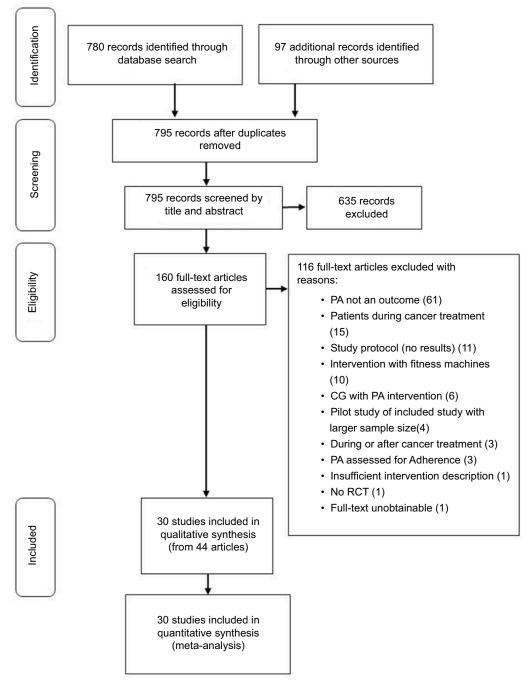


Figure 1 PRISMA flow chart of literature search for PA interventions in cancer survivors.

Abbreviations: CG, Control group; PA, physical activity; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial.

ent. Intention-to-treat analyses were used in 20 studies. The remaining studies used either per-protocol analysis (k=7) or analyses were not explained (k=3).

Regarding intervention integrity (ie, the degree to which an intervention is implemented as intended), three studies reported that more than 80% of participants of the IG received

the intervention, in two studies 60%–79% of participants received the intervention, while the remaining 25 studies did not communicate the information. Four studies measured the consistency of the intervention (ie, if all individuals receive the same intervention). Unfortunately, 26 studies did not report on the consistency of the intervention.

Table I Characteristics of participants and PA interventions

Reference	Cancer	Sample	Con-	Age	Gender	Time since	Intervention					Theory
	type	size	trol	(mean	(women)	diagnosis	Components	Setting	Duration	Types of	Intervention	•
		(u)	group	years)		(mean years)		9	(weeks)	PA	provided by	
Bantum et al, 2014 ⁵⁴	Diverse	352	ML	51.0	82.1%	8.1	Six sessions, web- based educational material	Home- based	9	MVPA	Trained peer facilitators	I
Basen- Engquist	Breast	09	SC	55.1	%001	3.2	21 Group sessions, educational	Facility- based	24	MVPA	I	SCT, TTM
Bennett et al, 2007 ⁵⁶	Breast, others	26	SC	57.8	89.3%	3.5°	Four counseling sessions (three phone sessions)	Home- based	24	Moderate intensity	Exercise specialist	Σ
Bloom et al, 2008 ⁵⁷	Breast	404	W.	I	%00I	1	Three workshops	Facility- based	12	Stretching, walking, others	Medical oncologist, others	Social support
Carmack Taylor et al, 2004,	Prostate	134	S	69.2	%0	I	21 Group sessions, educational material	Facility- based	24	Moderate	Group	SCT, TTM
Culos-Reed et al, 2010 ⁶⁰	Prostate	001	¥	67.4	%0	I	16 Group sessions, tailored exercise program	Combined	91	Walking, light resistance	Exercise specialist	ToPB
Demark- Wahnefried et al, 2003 and 2007; Ottenbacher et al,	Breast, prostate	543	S	57.0	56.4%	I	Tailored educational material (two workbooks), eight newsletters	Home- based	04	MVPA	Mail-based material	SCT, TTM
Hatchett et al. 2013 ⁶⁴	Breast	82	W _K	I	%001	I	Eight emails, access to e-counselor	Home- based	12	MVPA	Exercise specialist	SCT
Hébert et al, 2012 ⁶⁵	Prostate	42	¥	70.4	%0	I	One individual session, 13 group sessions, progress phone calls	Combined	24	MVPA	-	I
lbfelt et al, 2011; Høybye et al, 2008 ^{66,68}	Breast, prostate, colorectal	507	SC	0.13	35.3%	1.2	Retreat with lectures, patient group work, training, access to counselor	Facility- based	_	I	Medical doctor, others	I

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Reference	Cancer	Sample	Co	Age	Gender	Time since	Intervention					Theory
	type	size (n)	trol group	(mean years)	(women)	diagnosis (mean years)	Components	Setting	Duration (weeks)	Types of PA	Intervention provided by	
Irwin et al, 2008 ⁶⁷	Breast	75	S	55.8	%001	3.5	Three supervised group training sessions and two home-based training sessions per week, educational material	Combined	54	Walking, others	Medical doctor, others	1
James et al, 2011 and 2015 ^{69,70}	Diverse	133	⊼	57.2	77.4%	3.5	Six group sessions, home-based training program, educational material	Combined	ω	Resistance training, MVPA	Exercise specialist, others	SCT
Kim et al, 2011™	Breast	45	I	45.6	%00I	<u> </u>	12 Tailored phone sessions, educational material	Home- based	2	Moderate intensity	Nurses	Σ
Lahart et al, 2016 ⁷²	Breast	88	SC	53.6	%00 1	0.7	One individual session, three phone sessions, educational material	Home- based	24	MVPA	Researcher	Σ
Ligibel et al, 2012 ⁷³	Breast, colorectal	121	SC	54.3	%9.76	1	Ten phone sessions, educational material	Home- based	91	Moderate intensity	Behavioral counselor	SCT
Livingston et al, 2011 and 2015 ⁷⁴⁷⁵	Prostate	147	S	65.6	%0	0.5°	One individual session, 24 supervised training sessions, unsupervised training	Combined	12	MVPA, resistance training, others	Exercise specialist	ŠCI
Matthews et al, 2007 ⁷⁶	Breast	36	SC	54.1	%00I	0.8	One counseling visit, five phone sessions	Home- based	13	Walking	Health counselor	SCT
												(Conditions)

type Breast, prostate, colorectal	danipic oito)			Time since	Intervention					Theory
	azie (u)	trol	(mean years)	(women)	diagnosis (mean years)	Components	Setting	Duration (weeks)	Types of	Intervention	600
	149	.	73.1	54.5%	. . .	Tailored	Home-	48	Resistance	Health	SCT, TTM
						educational material	based		training, mvpa	counselor	
						(workbook),					
						phone sessions.					
						eight automated					
						phone prompts					
	162	SS	51.8	87.2%	6:1	Exercise	Home-	4	Moderate	Exercise	1
colorectal						recommendation	based		intensity	specialist	
						or exercise					
						recommendation					
						plus educational					
						material, and					
						pedometer					
~	98	SC (+	53.1	%00I	8:	One individual	Combined	12	Moderate	Researcher	SCT, TTM
		phone				session, 15 phone			intensity (eg,		
		calls)				sessions, mailed			biking)		
						educational			ì		
						material, and					
						feedback					
Breast	192	SC (+	0.09	%00I	3.0	One individual	Combined	12	Moderate	Researcher	SCT, TTM
		phone				session, 11 phone			intensity		
		calls)				sessions, mailed			aerobic (eg,		
						educational			biking)		
						material, and					
, [0,000	74	Ç	7 7 2	62.5%	C	reedback		2	N C	20000	N F F C S
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						sessions mailed			perobic (eq		
		calls)				educational			hiking)		
						material, and			/9 		
						feedback					
Diverse	35	M۲	33.6	82.9%	2.5	One individual	Home-	12	Moderate	Researcher	SCT, TTM
						session, 15 phone	based		intensity		
						sessions, access to			aerobic		
						monitored online					
						peer forum					

Table I (Continued)

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Reference	Cancer	Sample	Con-	Age	Gender	Time since	Intervention					Theory
	type	size (n)	trol group	(mean years)	(women)	diagnosis (mean years)	Components	Setting	Duration (weeks)	Types of PA	Intervention provided by	
Rau et al, 2009 ⁵⁰	Diverse	811	SC (+ phone calls)	56.4	38.5%	I	Three phone sessions	Home- based	24	MVPA	I	TTM, MI
Reif et al, 2010 and 2013 ^{86,87}	Breast, others	261	SC	57.7	71.7%	1	Eight group sessions, educational material	Combined	24	I	Nurse, others	Self- management
Rogers et al, 2012 and 2015 ⁸⁸⁸⁹	Breast	222	SC	4. 4.	%001	4.5	Six discussion group sessions, 12 supervised exercise sessions, home-based training, three counseling sessions	Combined	2	Moderate- intensity (eg. walking)	Exercise specialist, others	SCT
Sheppard et al, 2016%	Breast	3.	SC	54.7	%00I	₂ .	Six group sessions with supervised training and education, 12 phone sessions	Facility- based	12	Moderate intensity (walking)	Exercise specialist, others	TPB, SCT, MI
Short et al, 2012, 2013, and 2015 ^{91–93}	Breast	330	SC	55.0	%00I	4.	Three tailored newsletters or targeted PA guidebook ^c	Home- based	12	Moderate intensity (aerobic, resistance training)	Mail-based	SCT, TPB°
Vallance et al, 2007 and 2008 ⁹⁴⁹⁵	Breast	377	SC	58.0	%00I	3.3	PA recommendation plus PA guidebook or plus pedometer and step calendar or plus both ^c	Home- based	2	MVPA	Print-based	TPB
von Gruenigen et al, 2012%	Uterine	75	SC	58.0	%00I	<u>8</u>	l 6 group sessions, three counseling visits, PA guidebook, newsletters, phone sessions, emails	Combined	84	Moderate intensity (eg, walking)	Physician, others	SCT
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Notes: "Time since treatment. "Theory mentioned as basis of intervention. For several intervention groups.

Abbreviations: MI, Motivational Interviewing; MVPA, moderate to vigorous physical activity; PA, physical activity; SC, standard care; SCT, Social Cognitive Theory; TPB, Theory of Planned Behavior; TTM, Transtheoretical Model of Behavior Change; WL, wait-list control group; —, not reported.

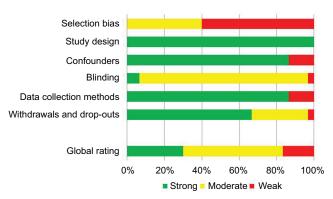


Figure 2 Quality assessment results presented as percentages across all included studies (k=30).

Behavior change technique coding

Overall, 41 of the 93 BCTs were coded at least once in the semi-final and 37 in the final coding. For the individual BCTs, based on the semi-final coding, Cohen's kappa ranged from 0.30 (BCT *Reduce prompts*) to 1.0, with the exception of four BCTs that were coded only once or twice by one reviewer but not the other, resulting in κ =0. Including these values, mean κ was 0.76 and reflects substantial agreement. PABAK values ranged from 0.65–1.0 (M=0.93) for the different BCTs. Regarding the different trials, Cohen's κ ranged from 0.67–1.0 (M=0.91) and PABAK from 0.74–1.0 (M=0.94) (see Table S1). Overall, a substantial agreement could be reached.

The included interventions used an average of 10.44 BCTs (Md=11, SD=4.44), ranging from 1–17. The BCTs most commonly used were Goal setting (behavior) and Social support (unspecified) (in k=27 IGs), followed by Problem solving and Self-monitoring of behavior (k=26), Instructions on how to perform the behavior (k=24), Behavioral practice/rehearsal (k=23), and Adding objects to the environment (k=21, often related to the use of pedometers).

Overall meta-analysis

The meta-analysis included k=45 effect sizes (34 for self-reported, 11 for objective PA outcomes) within 30 trials. All trials used self-reported PA as an outcome and eight trials (effect sizes from 10 IGs) additionally used objectively measured PA. Raw means and SDs for the PA outcomes immediately after the intervention were extracted for 33 effects. The SD had to be estimated in eight studies (10 comparisons overall). For the prediction of SDs from log means the values R²=0.946 for the IG and R²=0.918 for the CG were detected. The estimated SDs were controlled for plausibility. In two cases the effect size was estimated based on available data,

comparing group proportions by converting effect sizes to the standardized mean difference.

The funnel plot (Figure S3) and regression of effect size on sampling variance (β =3.65, $t_{(df=28)}$ =2.273, P=0.031) indicated a significant asymmetry in the distribution of standard errors related to observed study outcomes mainly caused by small studies with particularly large effect sizes. The estimated pooled effect size may, therefore, be slightly overestimated. However, with a fail-safe N (number of unpublished studies with nonsignificant findings that would have to exist for the overall effect to become insignificant) of 1,859 for a probability of error of alpha=5%, an overall positive effect seems likely.

The model resulted in an overall estimated effect size in terms of standardized mean difference of g=0.276 (95% CI=0.183–0.369 based on robust variance estimation), indicating a significant effect in favor of the IG (P<0.001; Figure 3). There was significant heterogeneity of effect sizes ($Q_{(df=44)}$ =94.081, P<0.001), with τ^2 =0.048 (95% CI=0.013–0.132) for subjective outcomes and τ^2 =0.007 (95% CI=0.000–0.097) for objective outcomes, respectively. About 54.29% of the total variation in effect sizes was estimated to be caused by heterogeneity of true effects (I^2). On average, effect sizes for self-reported PA were higher than for objective outcomes (g=0.316 as compared to 0.182, $F_{(1,28)}$ =4.642, P=0.040).

Meta-regression of PA outcomes on behavior change techniques and other potential moderators

Results of multivariate mixed effects models on BCTs

Number of BCTs

Figure 4 shows predicted and observed effect sizes of the included studies in relation to the number of BCTs used in the analyzed interventions. Effect sizes did not increase meaningfully with the number of BCTs per intervention (estimated increase per additional BCT, β =0.005, 95% CI=-0.007-0.017, P=0.408).

Moderator effects of specific BCTs

Of the final 37 BCTs exclusively applied in an IG, 27 were coded as being present for at least five effect sizes and were, therefore, analyzed as possible moderators in the metaregression models for self-reported and objectively measured PA outcomes (see Table 2). The BCTs Prompts/cues, Reduce prompts/cues, Graded tasks, Nonspecific reward, and Social reward were significantly related to larger effect sizes, while

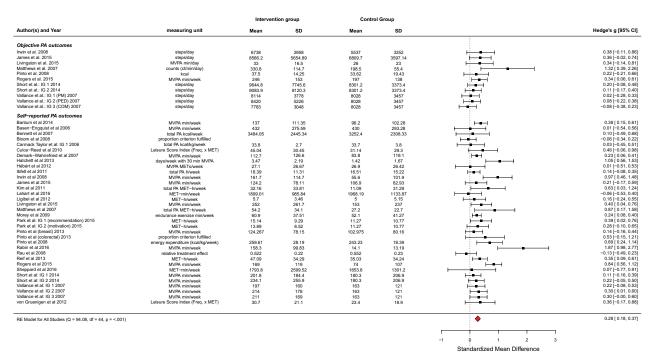


Figure 3 Forest plot of included studies.

Abbreviations: Cl, confidence interval; COM, combination of PM and PED; IG, intervention group; MET, metabolic equivalent; MVPA, moderate to vigorous physical activity; PA, physical activity; PED, step pedometer; PM, print materials; RE model, random-effects model.

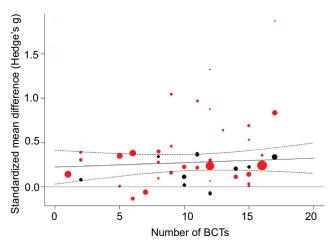


Figure 4 Prediction of effect sizes by number of BCTs.

Notes: Solid line: predicted effect size of mixed-effects model; dashed lines: 95% confidence bounds; dotted line: reference line for null effect; bubbles: individual study effect sizes with size relative to inverse variance weight; red: subjective PA outcome; black: objective PA outcome.

Abbreviations: BCTs, Behavior Change Techniques; PA, physical activity.

Information about health consequences and Information about emotional consequences as well as Social comparison were used in interventions with smaller treatment effects (P<0.05). The largest differences in effect sizes associated with the use of specific BCTs were comparable in size to the magnitude of the overall effect. With a borderline significant

trend, the potential moderator Self-monitoring of behavior was associated with larger effect sizes and the moderators Discrepancy between current behavior and goal and Information about social and environmental consequences with smaller effect sizes (P<0.10).

None of these individually tested BCTs reduced the unexplained heterogeneity in effects to a nonsignificant level. Overall, the amount of heterogeneity explained by the mentioned BCTs was higher for objective than for self-reported outcomes, although the heterogeneity estimates were rather imprecise due to the small number of effect sizes for objective outcomes.

Of the seven mentioned BCTs coded most often (see "BCT coding" above), only Self-monitoring of behavior had a trend to significance while the other six BCTs were clearly not significant.

Further study characteristics analyzed as potential moderators

Intervention features

Theories that were mentioned as the foundation of interventions were analyzed as further potential moderators concerning an increase in PA (see Table 3). Some interventions referred to more than one theory so that frequently mentioned theories were coded binary as absent or present

Table 2 Results of simple meta-regression analyses with BCTs and further study characteristics as predictors of 45 effect sizes from physical activity interventions

Moderator	k	β	95% CI	Percentage reduction in heterogeneity (I ²) ^b
Single BCT ^a				
I.I Goal setting	37	-0.050	(-0.160, 0.059)	0.00%
1.2 Problem solving	35	0.015	(-0.065, 0.095)	0.00%
1.3 Goal setting outcome	6	0.082	(-0.207, 0.372)	0.17%
1.4 Action planning	24	-0.034	(-0.147, 0.079)	0.00%
1.5 Review behavior goal(s)	14	0.090	(-0.098, 0.278)	0.61%
1.6 Discrepancy between current behavior and goal	6	-0.084#	(-0.174, 0.007)	1.17%
2.2 Feedback on behavior	16	0.042	(-0.087, 0.171)	0.31%
2.3 Self-monitoring of behavior	34	0.085#	(-0.013, 0.182)	5.15%
3.1 Social support (unspecified)	37	0.011	(-0.089, 0.110)	0.18%
3.2 Social support (practical)	5	-0.018	(-0.170, 0.134)	0.20%
4.1 Instruction on how to perform the behavior	34	-0.029	(-0.137, 0.079)	0.00%
5.1 Information about health consequences	11	-0.093*	(-0.183, -0.002)	1.92%
5.3 Information about social and environmental consequences	22	-0.092#	(-0.199, 0.015)	1.16%
5.6 Information about emotional consequences	7	-0.097*	(-0.184, -0.010)	0.92%
6.1 Demonstration of the behavior	19	-0.004	(-0.120, 0.111)	0.02%
6.2 Social comparison	9	-0.143***	(-0.203, -0.083)	1.83%
7.1 Prompts/cues	9	0.170*	(0.003, 0.336)	1.75%
7.3 Reduce prompts/cues	11	0.224*	(0.045, 0.404)	7.92%
8.1 Behavioral practice/rehearsal	32	-0.105	(-0.236, 0.026)	1.46%
8.7 Graded tasks	20	0.203**	(0.057, 0.348)	4.33%
9.1 Credible source	6	-0.014	(-0.092, 0.065)	0.01%
9.2 Pros and cons	6	-0.002	(-0.403, 0.399)	0.12%
10.3 Nonspecific reward	10	0.322***	(0.140, 0.504)	11.41%
10.4 Social reward	12	0.274**	(0.098, 0.450)	5.92%
10.9 Self-reward	6	0.325	(-0.231, 0.881)	2.06%
12.3 Avoidance/reducing exposure to cues for the behavior	6	0.220	(-0.107, 0.546)	1.95%
12.5 Adding objects to the environment	28	0.077	(-0.039, 0.193)	1.87%
Number of BCTs			,	
Overall number of BCTs uniquely applied in IG	45	0.005	(-0.007, 0.017)	1.29%
Number of BCTs applied from the group of those significantly associated with larger treatment effects ^c	45	0.066***	(0.032, 0.101)	8.59%
Number of BCTs applied from the group of those significantly associated with smaller treatment effects ^d	45	-0.042***	(-0.064, -0.021)	1.87%

Notes: 'Only results for BCTs involved in $k \ge 5$ effects sizes (or used in ≥ 5 IGs) are reported; bcompared to the model without moderator; BCTs 7.1, 7.3, 8.7, 10.3, 10.4; BCTs 5.3, 5.6, 6.2. " $P \le 0.10$, * $P \le 0.05$, ** $P \le 0.01$, *** $P \le 0.01$, *** $P \le 0.01$, *** $P \le 0.01$ (based on robust estimation). k, number of interventions where a specific BCT was present; b, estimated meta-regression coefficient for the comparison of effect size with BCT present vs absent; I^2 , percentage of residual heterogeneity, test for residual heterogeneity was significant ($P \le 0.001$) for all BCTs.

Abbreviations: BCT, Behavior Change Technique; CI, confidence interval; IG, intervention group.

for each study. The most frequently used theories were Social Cognitive Theory (SCT, in 25 IGs), the Transtheoretical Model (TTM, in 11), and Theory of Planned Behavior (TPB, in 7), whereas seven interventions used other theories and for eight interventions no theoretical foundation was mentioned. Interventions based on the SCT reported slightly but not significantly larger effect sizes. No difference was found for interventions based on the TTM. Interventions based on the TPB revealed significantly smaller effects (*P*<0.001). No significant moderating effects were found for interventions

that did not mention a theoretical foundation or those that were based on other theories when compared to the remaining interventions.

Effect sizes varied with the setting of the intervention (P<0.001). Interventions that included a home-based training component seemed more effective than those that only took place at facilities like clinics or gyms, and those that combined both settings showed the largest effect sizes.

The duration of the intervention did not explain differences in effects sizes. However, effect sizes for longer

Table 3 Moderating effects of study and patient characteristics

Moderator	k	β	95% CI	Percentage reduction in heterogeneity (I ²) ^a
Patient characteristics				
Mean age (years)	43	-0.016#	(-0.034, 0.002)	3.76%
Proportion of females	45	0.001	(-0.002, 0.004)	1.40%
Type of cancer: test of moderator effect: F _(2,27) =0.017				0.25%
Breast	25	0.272	(0.114, 0.430)	
Other	7	0.291	(0.139, 0.443)	
Various	13	0.277	(0.151, 0.404)	
Intervention features				
Duration of the intervention (months)	45	-0.012	(-0.031, 0.007)	0.62%
Theoretical foundation:				
SCT (used vs not used SCT)	25	0.149	(-0.030, 0.327)	2.52%
TTM (used vs not)	11	-0.006	(-0.212, 0.201)	0.51%
TPB (used vs not)	7	-0.126***	(-0.184, 0.067)	0.29%
Other theory (used vs not)	7	-0.151	(-0.354, 0.053)	2.19%
No theory mentioned (vs any theory)	8	0.039	(-0.050, 0.127)	0.06%
Intervention setting: test of moderator effect: $F_{(2,27)}=11.771***$				9.77%
At home	27	0.261	(0.135, 0.386)	
Facility	4	0.039	(-0.066, 0.143)	
Both combined	14	0.386	(0.281, 0.491)	
Further study characteristics				
Methodological quality: test of moderator effect: F _(2,27) =0.211				1.18%
Strong	15	0.303	(0.178, 0.427)	
Moderate	23	0.295	(0.136, 0.454)	
Weak	7	0.216	(-0.030, 0.463)	
Control group (wait-list vs standard care)	10 (vs 34)	0.144	(-0.103, 0.391)	0.00%
Year of publication	45	0.022#	(-0.004, 0.048)	5.72%

Notes: "Compared to the model without moderator. " $P \le 0.10$, *** $P \le 0.001$ (based on robust estimation). k, number of interventions where a specific BCT was present; β , moderator effect: coefficient from meta-regression model; confidence intervals (Cls) based on robust estimation, I2, percentage of residual (unaccounted for) heterogeneity; test for residual heterogeneity was significant (P<0.001) for all moderators.

Abbreviations: CI, confidence interval; SCT, Social Cognitive Theory; TPB, Theory of Planned Behavior; TTM, Transtheoretical Model.

interventions had a tendency to be smaller (mean effect size=0.30 for duration <3 months, 0.36 for 3 months, and 0.19 for >3 months; $F_{(2,27)} = 1.452$, P = 0.252).

Study characteristics

Methodological quality had no significant effect on effect size (see Table 3). Particularly, studies with lower quality did not result in larger effect sizes. Studies published more currently reported slightly larger effect sizes with an estimated increase per year of β =0.022 (P<0.10). Effects for trials with a wait-list CG did not differ meaningfully from those with a standard care comparison.

Patient characteristics

Effect sizes had a tendency to be smaller in studies with older participants, with an estimated decrease in effect size of β =0.016 per year of mean age of the study population (P<0.10). No differential effects were found for cancer survivors with different types of cancer, neither did the proportion of females vs males have a significant effect on outcomes.

Discussion

Within this meta-analysis, treatment effects from 30 RCTs on interventions for cancer survivors following acute treatment and aiming at an increase in PA which can be carried out independently at home were analyzed. The results show an overall significant positive effect (Hedge's g=0.28; 95% CI=0.18–0.37) after the end of treatment, which is in line with the magnitude of effect sizes of other meta-analyses for PA interventions in cancer patients and survivors. 23,26,98 Therefore, the effect is of small magnitude in terms of established rules and typical for studies in this field.

Behavior change techniques

Our results show that some specific BCTs were associated with larger effects on PA increases. Namely, including

prompts or cues to perform PA behavior (eg, adding a pedometer to a workbook as a behavioral cue) or employing intermittent telephone calls as prompts⁷⁹ and gradually decreasing such prompts (or the frequency/intensity of interventions) over time were significantly associated with larger PA increases. The same was true for setting graded tasks that increase in difficulty (eg, increasing the frequency and/or duration of exercise sessions from week to week was a common strategy or progressing to more demanding exercises) and for delivering different kinds of rewards for effort or progress toward PA behavior (eg, immediate reinforcement via positive automated messaging for participants who attained their personal exercise goal, 99 praise for achievement of goals, or progress toward goal⁶¹). In general, interventions using a larger number of these specific BCTs showed larger PA increases.

In contrast, BCTs including information about the consequences of PA behavior in terms of health benefits or positive emotional effects were used in less successful interventions. Likewise, social comparison, ie, to draw attention to the performance of others compared to the patient her/himself, or emphasizing discrepancies between PA goals and actual behavior was associated with smaller intervention effects in our analysis. Combinations of more than two of these BCTs were associated with smaller PA increases.

In contrast, the overall number of BCTs used in an intervention had no significant impact on the achieved PA increase immediately after the intervention compared to standard care or wait-list controls in our study. This result is in line with meta-regressions that included BCTs to increase PA behavior in adults with obesity³⁷ or diabetes.³⁶ In contrast, Samdal et al¹⁰⁰ found more BCTs associated with larger intervention effects in overweight or obese adults.

Overall, results on the effectiveness of specific BCTs for increasing PA do not show a consistent pattern, and our analysis is only partly consistent with previous research. Rewards were associated with greater success, in line with other studies on healthy adults of the general population as well as older adults. However, a negative effect was found for Graded tasks in one study, while others found a positive effect of graded tasks only on long-term but not on immediate success. On the other hand, BCTs similar to Social comparison, which was associated with lower effect sizes in our study, showed a positive PA effect in healthy adults, In terms of Information on consequences of the behavior, we obtained a negative association with effect size, whereas others found no effect. One meta-analysis showed a positive effect.

None of the compared studies^{30,34–37,100,101} endorse the positive effects we found in relation to Prompts and cues.

Several authors came to the conclusion that a combination of BCTs fostering self-regulation, ie, Self-monitoring, Goal setting, Feedback on performance, and Reviewing goals are especially promising in increasing PA in different populations.31,34,38 Of these only Self-monitoring showed a marginally significant effect in our study, while no effects were found for other self-regulatory BCTs. One reason could be that cancer survivors as a specific target group react differentially to certain BCTs than other groups. This conclusion is backed by the results of French et al,35 who found these techniques were not successful in older adults in contrast to younger populations. A similar mechanism could apply to Social comparison.³⁵ Social comparison might be more important for younger people than for cancer survivors or the elderly, and, thus, might not be as effective when applied as BCT in these target groups.

In addition to potential target group effects, ¹⁰² reasons for the differences observed may lie in different taxonomies used for coding of BCTs (ie, CALO-RE taxonomy vs BCTT v1) or in the challenge of adequate translation of intervention methods into practical application, ^{103,104} as well as the varying numbers of included studies.

In our analysis, the most frequently used BCTs, including some of the self-regulatory techniques mentioned above, were not associated with a more successful PA increase. In other reviews and meta-analyses on different target groups, these or similarly defined BCTs were shown to be associated with larger PA effects (ie, Instructions on how to perform behavior, ³⁴ Problem solving, ^{30,35} Goal setting, ^{31,100} Behavioral practice³¹).

One possible explanation for this finding may be that some of these BCTs were used in too many interventions to enable meaningful comparisons in our analysis. Further studies should specifically test intervention effects of such frequently employed BCTs in different target groups alone and in combination with other techniques. 103

Further moderators

Overall, results on the use of specific theories in PA interventions are equivocal. Most studies did not find differences between specific theories reported as the basis of PA interventions^{101,105} or the use of theory in general.^{27,30,106}

Interventions that were described as based on the TPB showed lower effect sizes. Husebø et al,¹⁰⁷ on the other hand, reported that constructs of the TPB (ie, intention, perceived behavioral control) were weakly but significantly associated

with better exercise adherence in eight studies with cancer patients and survivors. The most frequently stated theory in our analysis was SCT and interventions based on SCT reported slightly but not significantly larger effect sizes. While some of the identified BCTs directly match SCT constructs (like Setting graded tasks to increase self-efficacy), other techniques fitting into the SCT framework (like Role modeling) were not associated with better success.

While the authors of the present study could not identify a cluster of BCTs that completely matches one specific theory of behavior change, BCTs that proved advantageous in our study seem mostly congruent with principles of (social) learning theory, ie, rewards, including sense of achievement and situational cues which are faded out gradually and may promote habit building. In contrast, those BCTs relying on knowledge and rational decision making (ie, setting goals, providing information, problem solving) seemed less successful in increasing PA in cancer survivors. The latter is consistent with smaller effect sizes for TPB-based interventions which often rely on information and rationality.

However, in many cases it remains unclear how exactly theory is implemented in interventions. An explicit methodology for linking BCTs to theories is currently being developed and will help to clarify relations between BCTs, mechanisms of action, and other variables such as modes of delivery, populations, settings, and types of behavior.³³ Further research should establish whether the results of the present study can be replicated for cancer survivors compared to other groups, since this would have theoretical implications for planning interventions for this target group.

In terms of intervention duration, we did not find a meaningful effect on PA increase. A study by Bernard et al²⁷ even reports a shorter duration of theory-based interventions designed to promote PA, ie, less than 14 weeks, to be associated with larger treatment effects in different target groups. Although not significant, our results point in the same direction with the lowest effect sizes for those interventions longer than 3 months. These findings underline that duration alone may not be the best measure of overall intervention intensity and that, in fact, more complex or longer interventions do not necessarily lead to greater success.

Methodological quality of included studies was also not associated with the magnitude of intervention effects indicating that the results are not contorted by differences in study quality. In contrast, two recent studies^{27,100} reported significant moderator effects suggesting overestimation of the efficacy of PA interventions due to methodological weaknesses. Both of these studies employed the Cochrane tool for assessing risk

of bias, ¹⁰⁸ while the present study used the EPHPP-Tool. ⁴⁰ As Armijo-Olivo et al ¹⁰⁹ demonstrated, ratings using the EPHPP-Tool may differ from those resulting from the Cochrane tool. This may explain the diverging results. However, it was also found that the EPHPP tool seems superior in terms of interrater reliability. ¹⁰⁹

Strengths and limitations

This is the first study that systematically analyzed the associations of BCTs with PA increases in cancer survivors after treatment employing a current BCT taxonomy, where two coders evaluated studies independently, arriving at good interrater reliabilities. Furthermore, self-reported as well as objectively measured PA outcomes were included while adjusting the analysis for intratrial correlations.

Some limitations must also be taken into account. As our search was limited to MEDLINE, missing studies may lead to publication bias. However, we also accounted for reference lists of other current reviews and meta-analyses.^{23,98}

Although the overall methodological quality of trials was not related to effect sizes, only a subset implemented an intention-to-treat analysis or reported on intervention integrity. As these criteria are not included in the overall quality rating, they may have biased the results.

Our meta-analysis is limited to outcomes measured directly after completion of interventions. Effects of specific BCTs might differ between immediate and long-term outcomes, as recently shown by Samdal et al. ¹⁰⁰ Further research on long-term effects is, therefore, desirable.

Eight trials added an objectively measured PA outcome to a self-report measure. Since these trials contained more effect size information than those relying only on self-report measures, this may have influenced our results. However, including all available information by using a multivariate model and adjusting for dependencies between outcomes seemed more appropriate than including only information on self-reported measures. The overall effect size was similar to other studies on cancer survivors. Due to the limited amount of data on objective outcomes, it was not suitable to distinguish the results of meta-regression models by subjective vs objective outcome.

Peters et al¹⁰³ described limitations of analyzing effectiveness of BCTs by meta-analytical techniques. Within the included studies, BCTs may not have been transferred to intervention strategies effectively or may not have been adapted to target groups and contexts adequately. A prerequisite for finding an effect of BCTs in a meta-regression is the exclusive use of a BCT in the IG, but not in the CG. Since

most of the included interventions only provided a very short description of the "standard care," it was impossible to code and, therefore, detect BCTs for the CG accurately.

Effects of different BCTs may have confounded each other or may have been confounded by other study characteristics such as the overall number of BCTs applied in an intervention. Due to a large number of analyzed potential moderators compared to the limited number of included studies, calculation of more complex models allowing analyses of confounding effects were not possible.

Since some BCTs were often used in combination in the same studies (see <u>Table S3</u>) we adjusted for within-study dependencies of effect sizes and show "dose-response" relations for the use of those BCTs associated with effect sizes, but we cannot rule out that trial characteristics other than these BCTs were responsible for differences in PA effects. Furthermore, many BCTs were tested as moderators in separate models without adjustment for multiple testing.

Furthermore, some BCTs were used in very many or very few interventions, reducing the power of tests for moderator effects of these BCTs. A nonsignificant effect may not be interpreted as a proof of lack of effectiveness. The results are, therefore, exploratory and do not allow definite or causal conclusions.

We found some BCT definitions and coding rules not being clearly outlined and, therefore, added more specific coding rules, attaining good intercoder reliabilities afterwards. Others report similar issues.¹⁰⁰ Cradock et al³⁶ also developed extensive additional coding rules, which we included in our discussion process.

Notwithstanding these limitations, meta-analyzing the effectiveness of BCTs for increasing PA in cancer survivors and comparing the results to other target groups can be seen as one constituent of further developing theory-based interventions aimed at health behavior change in this target group.¹⁰³

Conclusions

A growing body of evidence shows the positive effects of PA in cancer survivors. Thus, identifying the relevant characteristics of interventions is of great importance. The present meta-analysis shows significant effects for interventions aiming at an increase in PA that can be carried out independently by cancer survivors. The magnitude of PA increase seems neither to depend on the duration of the intervention nor on the number of BCTs used, but certain techniques were associated with significantly larger or smaller PA-increasing effects. Interventions relying on BCTs congruent with (social) learning

theory, such as using prompts and rewards and setting graded tasks, could be especially successful in this target group. However, large parts of between-study heterogeneity in effect sizes remained unexplained by single moderator variables. Other factors than those studied here may impact on the success of PA interventions in cancer survivors, or synergistic effects of moderators may exist that can only be revealed in more complex analyses which require larger meta-studies. To strengthen validity, the results should be replicated and in addition be complemented by the analysis of long-term effects and direct comparisons to other target groups. Further primary studies should directly test and compare specific BCTs and their combinations. Coding instruments should be more precise with an extension of definitions and anchor examples for different interventions goals.

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Disclosure

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