



Review: Effectiveness of implementation strategies to increase physical activity uptake during and after cancer treatment



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ABSTRACT

Background: The purpose of this review was to assess the effectiveness of different strategies to implement physical activity during and after cancer treatment.

Design: We searched for studies containing strategies to implement physical activity in cancer care that meet the inclusion criteria of the Cochrane EPOC group. The primary outcome was physical activity uptake. We expressed the effectiveness of the strategies as the percentage of studies with improvement.

Results: Nine studies met the inclusion criteria. Patient groups doing physical activities via an implementation strategy had better outcomes than those receiving usual care: 83% of the studies showed improvement. Strategies showing significant improvement compared to usual care employed healthcare professionals to provide individual counselling or advice for exercise or interactive elements such as audit and feedback systems. When comparing the different strategies 1) interactive elements or 2) elements tailored to the needs of the patients had better physical activity uptake.

Conclusions: Implementation strategies containing individual and interactive elements, tailored to the individual needs of patients, are more successful in improving physical activity uptake.

1. Introduction

An increase in the relative cancer survival rate is expected in Europe in the coming 15 years (Meulepas et al., 2011; Verdecchia et al., 2007; Berrino and Capocaccia, 2008), resulting in an estimated doubling of cancer survivors (De werkgroep, 2004). These survivors will create unique societal challenges to counteract the detrimental and persistent adverse effects of cancer and its treatment (Hewitt et al., 2006). Symptoms such as loss of quality of life (QoL) (Yang et al., 2012), diminished cardiopulmonary fitness, (Jones et al., 2012) and cancer-related fatigue (Servaes et al., 2002; Bower et al., 2000; Fossa et al., 2003; Hjermstad et al., 2005; Loge et al., 2000; Vistad et al., 2007; Serveas, 2003; Gielissen, 2007) usually evolve during treatment and may persist

long after therapy completion (Courneya, 2001; Courneya and Friedenreich, 1999; Argiles et al., 2005; Dimeo et al., 2004; Wagner and Cella, 2004). In view of this, it is important to find ways of either preventing or addressing these symptoms, not only to relieve individual symptoms, but also in view of the societal impact, prolonged medical follow-up, and loss of work opportunities.

Studies have shown positive results of physical activity (PA) in counteracting symptoms related to cancer (Mishra et al., 2012; Cramp and Byron-Daniel, 2012; Markes et al., 2006; van Waart et al., 2015; Kampshoff et al., 2015), such as cardiopulmonary fitness (Schmitz et al., 2010), QoL (Schmitz et al., 2010; Knols et al., 2005; Courneya et al., 2012; Courneya, 2003; Young-McCaughan and Sexton, 1991; Schwartz, 1999; Courneya and Friedenreich, 1997; Kolden et al., 2002;

Abbreviations: EPOC, Effective Practice and Organization of Care; HCP, healthcare professional; IMS, implementation strategy; ITS, interrupted time series; NRCT, non-randomized controlled trial; PA, physical activity; PAU, physical activity uptake; PSI, percentage of studies with improvement; QoL, quality of life; RCT, randomized controlled trial

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Galvao and Newton, 2005), and fatigue (Cramp and Byron-Daniel, 2012; Schmitz et al., 2010; Schwartz, 1999; Kolden et al., 2002; McNeely et al., 2006; Schwartz et al., 2001; Schwartz, 2000; Dimeo et al., 1997; Winningham, 2001; Anon, 2003; Dimeo, 2001). Improvement of muscular strength (Mello et al., 2003), lean body mass, body fat levels (Winningham et al., 1989), self-esteem, and even better chemotherapy completion rates have been reported (van Waart et al., 2015). Evidence-based guidelines recommend implementing physical cancer rehabilitation programmes or other initiatives to improve PA uptake (PAU) in cancer care. However, it appears that current PAU is low (Stevinson and Fox, 2006; Courneya et al., 2003; Segal et al., 2001; Segal et al., 2003). This may be because (just as other new treatment approaches) PA programmes need active implementation strategies (IMSS) tailored to barriers and facilitators that prevent or promote successful implementation (Grimshaw et al., 2004).

In recent years, many initiatives have been launched to implement PA in daily cancer care, sometimes in clinical trials. The effectiveness and experiences of the strategies were positive overall, but a systematic overview is lacking, particularly one showing which strategies help patients and healthcare professionals (HCPs) in successfully implementing PA in daily cancer care.

Therefore, the purpose of this review was to systematically assess the effectiveness of different strategies for implementing PA during and after cancer treatment.

2. Design

Since the word ‘intervention’ has multiple meanings, we will use the word ‘IMS’ instead of ‘intervention’, for the remainder of this article.

2.1. Search strategy

We searched the MEDLINE, EMBASE, and CINAHL databases from January 2000 to November 2016. The search was limited to studies of human beings written in English. The search terms included the methodological filters of the Cochrane Effective Practice and Organization of Care (EPOC) Group combined with selected MeSH terms and free text terms. The search strategies used are outlined in Supplement S1. We also searched all references of articles selected for inclusion for further relevant trials. Supplement S2 shows the inclusion criteria.

2.2. Selection of articles

Two reviewers (CIJ and NO) independently reviewed the search-generated titles and abstracts to see whether they fulfilled the selection criteria. Differences in the selection of titles and abstracts were discussed and resolved through consultation with a third reviewer (RH). If doubt remained, the full article was acquired for further inspection. The full articles of selected studies were also reassessed and carefully inspected for a final decision about inclusion. The names of the authors, institutions, or journals of publication were not anonymised for the reviewers. The characteristics of each included study (narrative synthesis) were evaluated; for the quantitative synthesis, only the studies with an randomized controlled trial (RCT), non-randomized controlled trial (NRCT), controlled before after (CBA), or interrupted times series (ITS) study design were included, in accordance with the inclusion criteria of Cochrane EPOC Group.

2.3. Data extraction

Two reviewers (CIJ and MTD) independently extracted data from the studies (the study details of which had not been anonymised) using a data extraction form based on the Cochrane EPOC Group Data Abstraction Form 2002, the Cochrane EPOC Group Data Collection Checklist 2002, and the revised EPOC Taxonomy 2015.

We extracted the following information: participant characteristics (number and description of participants), setting characteristics, characteristics of the implementation strategy (including format, deliverer, timing, frequency, and duration), control, outcomes, and study quality characteristics. The reviewers compared the data extracted and resolved disagreement by discussion until consensus was reached. If there was no consensus, a third reviewer settled the matter (RH).

2.4. Quality assessment: assessing the risk of bias

Two reviewers (CIJ and MTD) independently assessed the quality of each study included in the quantitative synthesis using the Cochrane EPOC group’s suggested ‘risk of bias criteria’. Disagreement was resolved by consultation with a third reviewer (RH).

2.5. Data analysis for quantitative synthesis

We performed two analyses to assess the effectiveness of strategies for improving PAU during and after cancer treatment:

Analysis 1: an IMS group compared to a control group. The effectiveness of the IMS group compared to the control group was expressed in terms of the percentage of studies with improvement (PSI). We calculated the PSI both at the study level and at the IMS group level, since some studies had compared two or more IMS groups to the control group. We calculated the PSI of the primary outcome. Moreover, we calculated the PSIs of the secondary outcomes. We analysed outcomes evaluated for 6 months from the start of follow-up and after the first 6 months from the start of follow-up. We also analysed the PSI of studies using IMSs during treatment and of studies using them after treatment. We intended to perform a random-effect meta-analysis if the different IMS groups and outcomes did not show too much heterogeneity.

Analysis 2: IMS groups compared to each other: We analysed the primary and secondary outcomes. We intended to perform a random-effect meta-analysis if the various IMS groups and outcomes did not show too much heterogeneity. We analysed outcomes evaluated for 6 months from the start of follow-up and after the first 6 months from the start of follow-up. We also analysed the PSI of in studies using IMSs during treatment and of studies using them after treatment.

3. Results

3.1. Selection of studies

Supplement S3 illustrates the literature search and the study selection. Electronic searches and the snowball method identified 11,837 titles. After removing 2460 duplicates, we screened 9381 titles and excluded 8729 studies. We excluded 537 more during abstract screening. We obtained full-text screenings for the remaining 115 studies. Of these, 97 were excluded and 18 articles (van Waart et al., 2015; Bennett et al., 2007; Damush et al., 2006; Jones et al., 2004; Jones et al., 2005; Ligibel et al., 2010; McGuire et al., 2011; Ottenbacher et al., 2012; Pinto et al., 2013; Pinto et al., 2008a; Pinto et al., 2008b; Pinto and Trunzo, 2004; Purcell et al., 2011; Rabin et al., 2011; Vallance et al., 2008a; Vallance et al., 2008b; Vallance et al., 2007; Windsor et al., 2009) were included in the narrative synthesis. Reason for excluding 97 full-text articles is described in Supplement S3. The group of 18 included articles contained 14 original studies. The 9 studies that met the Cochrane EPOC group inclusion criteria were included in the quantitative synthesis (van Waart et al., 2015; Bennett et al., 2007; Jones et al., 2004; Jones et al., 2005; Ottenbacher et al., 2012; Pinto et al., 2013; Pinto et al., 2008b; Purcell et al., 2011; Rabin et al., 2011; Vallance et al., 2008a; Vallance et al., 2008b; Vallance et al., 2007; Pinto et al., 2005). We excluded 5 studies that did not meet the EPOC inclusion criteria (Damush et al., 2006; Ligibel et al., 2010; McGuire et al., 2011; Pinto et al., 2008a; Windsor et al., 2009).

3.2. Study characteristics of the included studies (narrative synthesis)

Supplement S4 briefly describes the characteristics of the studies included in the narrative synthesis. Eight studies took place in the United States, two in Canada, two in Europe (one in the United Kingdom, and one in the Netherlands), one in Australia, and one in New Zealand. All the studies focused on outpatient care and took place in a practice university based setting or teaching setting. Nine studies had an RCT design and five had a non-controlled cohort design. No study with an NRCT, CBA, or ITS design was identified.

The study populations consisted of patients only in 12 studies and a mix of patients and professionals in 2 studies. The numbers of participants ranged from 18 to 450. The most frequently targeted patient populations were those with breast cancer (9 studies), followed by mixed or unspecified populations (5 studies). The mean ages of the patient participants ranged from 32 to 63 years old, and the mean ages of the healthcare professionals (HCPs) ranged from 51 to 57 years old.

Six studies focused on sedentary patients only and eight studies focused on sedentary and non-sedentary patients together. In four studies, the physical cancer rehabilitation programmes was applied during the primary treatment of cancer, while in ten studies it was applied after the treatment of cancer. The IMSs were directed at ten individuals and at groups combined with an individually delivered component in four studies. The IMSs were delivered by professionals from different disciplines: there were four researchers, two physicians, one exercise counsellor, a computer in one study and in five studies multiple professionals from different disciplines. It was unclear who delivered the strategy in one study. Eleven articles contained IMSs that were delivered person-to-person, 8 were on paper, 7 were delivered by means of a computer, and 1 strategy was delivered as an audio recording.

3.3. Quality characteristics of the studies included in the quantitative synthesis

We included nine studies meeting the Cochrane EPOC Group criteria and containing the primary outcome PAU in our quantitative synthesis. All the included studies had RCT designs.

Supplement S5 shows the results of the qualitative assessment using the risk of bias criteria suggested by the Cochrane EPOC Group.

Most RCTs concealed the allocation (6 of 9 studies; 67%). In all the studies, it was unclear whether the professionals had been correctly followed up (9 of 9 studies; 100%). The patients were followed up in 7 of 9 studies (78%).

It was unclear in most articles whether blinding had been assessed correctly; only 2 of the 9 studies (22%) clearly reported correct blinding. Five of the 9 studies (55%) described a baseline measurement. The quality criteria 'reliable primary outcome measures' and 'protection against contamination' were less well described in 0% (0 of 9) and 11% (1 of 9) of the studies.

3.4. Outcomes

The planned meta-analysis was not performed due to the heterogeneity of the IMSs and the evaluated outcomes. The analyses of effectiveness included six original studies and ten IMS groups (van Waart et al., 2015; Bennett et al., 2007; Jones et al., 2004; Jones et al., 2005; Pinto et al., 2013; Pinto et al., 2008b; Purcell et al., 2011; Pinto et al., 2005). Overall, the IMS groups had better outcomes than the control groups.

3.4.1. Physical activity uptake

Supplement S6 shows an overview of the outcomes and supplements S7A en S7B show measured PSIs for the analysis 'IMS groups versus control groups'. The analysis of our primary outcome, PAU, included six studies and ten IMS groups.

The analyses of the total six studies showed that in five of six

studies, the PAU improved in the IMS groups significantly more than in the control groups, resulting in an PSI of 83% (5 of 6 studies). We divided the analyses into outcomes measured for 6 months of follow up and outcomes measured after 6 months of follow-up. In the first 6 months of follow-up, the improvement was 67% (4 of 6 studies) and after 6 months of follow-up, it was 50% (1 of 2 studies). We found a total PSI of PAU of 50% (1 of 2 studies) during treatment and 100% (4 of 4 studies) after treatment.

The analyses of the ten IMS groups showed that they had significantly better PAUs than the control groups resulting in an PSI of 70% (7 of 10 groups). We also divided this analysis into outcomes measured for the first 6 months of follow-up and outcomes measured thereafter. The improvements were 60% (6 of 10 groups) and 50% (1 of 2 groups), respectively. We found a total PSI of PAU of 25% (1 of 4 groups) during treatment and 100% (6 of 6 groups) after treatment.

3.4.2. Secondary outcomes (Fitness, QoL, Fatigue and Mental health)

We also calculated the PSIs for our secondary outcomes of effectiveness. Supplement 6 shows an overview of the outcomes and supplements S7A en S7B show measured PSIs. The analysis of our secondary outcomes included six studies and ten IMS groups. It was possible to calculate the PSI for the outcomes Fitness, QoL, Fatigue, and Mental health. The analyses of the total six studies showed that one or more secondary outcomes in the IMS groups improved significantly more than in the control groups, a PSI of 33% (2 of 6 studies). We divided the analyses into outcomes measured for the first 6 months of follow-up and outcomes measured after the first 6 months. The improvement of all the secondary outcomes at the study level for the first 6 months of follow-up was 33% (2 of 6 studies). After the first 6 months of follow-up, the improvement was 50% (1 of 2 studies).

The analyses of the ten IMS groups showed that one or more secondary outcomes improved significantly in these groups compared with the control groups – a PSI of 30% (3 of 10 IMS groups). We also divided this analysis into outcomes measured for the first 6 months of follow-up and outcomes measured after 6 months. The improvement was 20% for the first 6 months of follow-up (2 of 10 IMS groups), while after 6 months follow-up, it increased to 50% (1 of 2 IMS groups). Because of the small number of studies and the heterogeneity of the secondary outcomes, we did not perform the planned analyses of IMSs during and after treatment.

3.4.3. Characteristics of effective IMSs

IMSs targeting patients were used in all IMS groups with effects that were significantly positive compared to the effects in the control groups. With the exception of three IMS groups (Purcell et al., 2011), the IMS groups received individually delivered IMSs.

3.4.3.1. The primary outcome (PAU). The IMS groups that significantly improved the PAU in the first 6 months of follow-up included: 1) five cases of individual counselling or advice for exercise given by HCPs (Bennett et al., 2007; Jones et al., 2004; Jones et al., 2005; Pinto et al., 2013; Purcell et al., 2011) and 2) one case of interactive elements using motivational interviewing with audit and feedback (Bennett et al., 2007).

One IMS group showed significant effects on the PAU after more than 6 months. This IMS group received tailored individual person-to-person counselling. The IMSs that showed significantly improved PAU compared with controls used a wide variety of formats: person-to-person contact (face to face or phone) as well as paper-, computer- and audio-based materials.

3.4.3.2. The secondary outcomes. Fitness. The IMS groups that showed a significant effect for fitness after 6 months included a person-to-person individual counselling strategy (Pinto et al., 2008b; Pinto et al., 2005).

Fatigue. The IMS groups that showed an effect on fatigue after 6 months had individual counselling strategies (Pinto et al., 2008b; Pinto

et al., 2005).

Mental health outcomes. The IMS groups that found positive effects on mental health used educational material and a recommendation to exercise (Jones et al., 2004; Jones et al., 2005).

3.4.3.3. Comparing IMSs. Some of the studies compared different types of IMSs. The analysis included three original studies (Ottenbacher et al., 2012; Rabin et al., 2011; Vallance et al., 2008a; Vallance et al., 2008b; Vallance et al., 2007), each of which had a study population of patients who had finished their primary treatment.

One study compared advice to exercise with 1) distribution of educational material, 2) a pedometer (audit and feedback system), or 3) a combination of distribution of educational material with a pedometer. After 12 weeks of follow-up, the amount of PA and walking had increased significantly in the two groups using an interactive element (pedometer) compared with the group receiving only exercise advice. At the same time, the two groups receiving educational material had increased their walking significantly compared with the group receiving only advice. All significant effects were lost at a follow-up of 6 months or more (Vallance et al., 2008a; Vallance et al., 2008b; Vallance et al., 2007).

A study comparing the distribution of three informative website addresses with an interactive website (containing information, audit, feedback, reminders, and a forum) found a trend of increasing PA for the interactive website, but no significant effect (Rabin et al., 2006). A significant difference in fatigue was found in favour of the interactive website.

Another study comparing tailored mailing interacting on the patient's needs with mailings of standard educational material found a significant increase of PA for the tailored mailings up to 1 year of follow-up. The trend remained, but significance was lost at 2 years of follow-up (Ottenbacher et al., 2012).

4. Discussion

We identified IMSs and their elements aimed at implementing PA during and after cancer treatment. We included 18 studies in the narrative synthesis using the EPOC group inclusion criteria, while 9 studies were included in our quantitative synthesis. Our results showed that most IMS-targeted patients (most often with breast cancer, with strategies that were delivered individually and delivered person to person). IMSs used individual counselling and interactive elements that were tailored to the individual needs of patients, which resulted in the best improvement of the PAU. Our overall conclusion was that IMS groups had significantly better PAU than control groups. For our primary outcome, all the calculated total PSIs were between 50% and 83%. This shows that IMS groups had significantly more PAU than control groups. Our secondary outcome measures (Fitness, QoL, Fatigue, and Mental health) showed less significant effects, with calculated PSIs between 20% and 50%.

Recent progress in behavioural change suggests that, with appropriate support, survivors can be motivated to adopt long-term lifestyle changes (Courneya et al., 2008). We found only two studies that reported a follow-up after 6 months. It is questionable whether the PAU will be retained in the long run. For this reason, it is difficult to draw conclusions regarding consolidation from the studies currently included. More data are needed to study the importance of IMSs leading to sustained behavior change.

It is to be expected that well-implemented PA will have a positive effect on patients' fitness, QoL, fatigue, and mental health, since studies have shown positive results of PA in improving cardiopulmonary fitness (Schmitz et al., 2010) and QoL (Schmitz et al., 2010; Knols et al., 2005; Courneya et al., 2012; Courneya, 2003; Young-McCaughan and Sexton, 1991; Schwartz, 1999; Courneya and Friedenreich, 1997; Kolden et al., 2002; Galvao and Newton, 2005) and in decreasing fatigue (Cramp and Byron-Daniel, 2012; Schmitz et al., 2010; Schwartz, 1999; Kolden et al.,

2002; McNeely et al., 2006; Schwartz et al., 2001; Schwartz, 2000; Dimeo et al., 1997; Winningham, 2001; Anon, 2003; Dimeo, 2001).

In our review, the lower PSIs (20% and 33%), calculated for the secondary outcome measures, are for the first 6 months of follow-up, while the higher PSI (50%) is for the follow-up after 6 months. It could be hypothesised that the effects of the IMSs on patients' fitness, QoL, fatigue, and mental health take more time and therefore only become apparent after 6 months, especially since the PSI calculated in our review after 6 months is remarkably higher than the one calculated before 6 months. More studies performing follow-up after 6 months could help to clarify the long-term effects of IMSs on PAU, fitness, QoL, fatigue, and mental health.

Most studies of IMSs for PA focused on patients with breast cancer. Because of this, more research is needed to assess the effects of IMSs on the PA of patients with other tumour types

Gastro-intestinal, reproductive, and urological cancers worldwide account for more than 50.5% of the incidence of all cancers, being more than four times the incidence of breast cancer (11.9%) (Ferlay et al., 2013; Ferlay et al., 2017). Patients with gastro-intestinal and gynaecological cancers judge their cancer care as less adequate than patients with other tumour types (Booij et al., 2013). Patients with gastro-intestinal cancers also rated the information after finishing their primary treatment as significantly poorer than patients with breast cancer did (Lievens et al., 2003). There are descriptions of study groups who intended to recruit patients with abdominal tumours, but have difficulties doing so (van Waart et al., 2015; Courneya and Gill et al., 2008). Some suggested reasons are that patients with abdominal tumours, such as pancreatic cancer, receive palliative rather than adjuvant treatment, and patients who had undergone major abdominal surgery were usually advised to refrain from intensive PA for 6 weeks after surgery. Clinicians were also more hesitant in referring patients with colon cancer to studies (van Waart et al., 2015). Therefore, it seems especially important to study the implementation of PA for patients treated in clinical pathways for gastro-intestinal, gynaecological, and urological oncology. Studies focussing on IMSs for these patients are urgently needed.

The studies included in our analysis "IMSs groups versus control groups" dealt mainly with IMSs after treatment. We redefined the analyses and calculated the PSIs of IMSs during and after treatment separately. Especially after primary treatment (PSI of 100%), IMSs seem promising in improving PAU. The studies included in the analysis "Comparing IMSs" only considered IMSs applied after primary treatment had been completed. Therefore, the conclusions of this analysis can only be drawn for IMSs applied after treatment. More research is needed to study the effects of IMSs applied at different times during treatment.

All the studies we included used statistical significance to measure the effects of the IMSs. Recently, the importance of clinical significance has grown in the medical literature. Clinical significance connects evidence-based effects with the clinical effects on patients. However, none of the included studies provided clinical significance calculations, and we cannot validly do these calculations ourselves with the available data. Including clinical significance in future studies can enrich the knowledge of effects of IMSs in daily practice.

IMSs that showed significantly improved PAU compared with controls used a wide variety of formats (person-to-person interaction as in face-to-face or phone contact, as well as paper-, computer- and audio-based materials). In the studies comparing multiple IMSs, we found no evidence about which format of delivery was the most effective, but we found increased PAU for the formats paper and computer. Remarkably, most IMSs that showed significantly improved PAU used a combination of formats. Although multiple educational activities for patients seem to be effective, much is still unknown; for example, which materials and which providers of the educational materials lead to the best PAU. However, more research is needed to find the best deliverer, format, and additional effect of combination formats compared with single

formats.

The assumption is that tailoring the IMSs to determinants and barriers of the targeted setting and population will prove to be successful. Researching determinants and barriers before starting the implementation is comparable with clinical practice, where a diagnosis is made in order to choose the right treatment (Baker et al., 2015). We found only one study evaluating the determinants or barriers for a successful implementation before designing the elements of the IMS (Rabin et al., 2011). Therefore, it is questionable whether the IMSs were tailored enough to be fit-for-purpose. Evidence of an additional effect of tailoring of the IMSs in cancer care needs further exploration. Examining the determinants and barriers of a successful implementation of PA in cancer care could be the first step towards the design of a successful and tailored IMS.

In most implementation literature, strategies attempting to reach successful implementation of healthcare programmes focus mainly on behavioural changes of HCPs and organisations (Grimshaw et al., 2001). In our review, we were surprised to find mainly strategies attempting to change the behavior of the patients. This may be due to the fact that strategies directed at patients tend to be easier to achieve than changing HCPs and healthcare systems themselves, since it requires less capacity and fewer financial and organisational changes. Consistent with our findings, implementation research done in other patient groups shows that the most frequently used elements of IMSs were education and interactive elements (Borgert et al., 2015; van Riet Paap et al., 2015). Individual and interactive elements, tailored to the individual needs of patients, were found to be most effective (Bourke et al., 2013).

However, strategies aimed at HCPs (educational outreach and audit and feedback), might have an additional effect on successful implementation regarding professional performance, patient outcomes, and costs (Wensing et al., 2006; Grol and Grimshaw, 2003). Strategies directed at the organisation could also support the implementation of physical cancer rehabilitation programmes mainly because contextual factors (such as workload, poor co-ordination, and management) can be important barriers to success.

A multifaceted strategy, focusing on different levels (e.g. the patient, HCP, and/or organisational level of care), could be the most successful way of achieving implementation in healthcare (Grimshaw et al., 2004; Prior et al., 2008; Grol et al., 2005; Grol, 2013) mainly because determinants often arise at different levels. We found no multifaceted strategy as such in the studies in this review. Evidence of the additional effect of a multifaceted strategy to implement PA in cancer care is still questionable and needs further exploration.

5. Strengths and limitations

We used the EPOC criteria in a broad search strategy, which we completed with a manual search. It is possible that we missed some relevant studies, because different terms in literature are used for implementation strategies and PAU.

We used the suggested risk of bias criteria as defined by the Cochrane EPOC Group. However, we did not use a scale for assessing quality or risk of bias because there is no empirical evidence for such a scale (Emerson et al., 1990; Schulz et al., 1995). Calculating a summary score inevitably involves assigning weights to different items in the scale, and it is difficult to justify the weights assigned. Furthermore, scales have been shown to be unreliable assessments of validity (Juni et al., 1999), and they are less likely to be transparent to readers of the review.

Since we used the Cochrane EPOC Group's suggested risk of bias criteria, none of the included articles met all the quality criteria. However, it is known that studying IMSs and their elements is a challenging matter, for which one has to settle with less advanced study designs. Particularly 'the prevention of contamination' and 'keeping the strategies blinded' are major challenges. The risk of bias criterion

'correct follow-up of professionals' was not described in any of our included studies. Perhaps none of the included studies measured the effects of the IMSs on the HCPs, so follow-up of HCPs did not seem to be a prerequisite matter.

While calculating the PSI, we did not take into account the wide range (18–450) of the total numbers of participants in the different studies included in this review. The outcomes of the included studies would be interpreted differently if importance were attached to the reliability of the data. As a result, the outcome of this review might also be different. We did not take this into account because the number of participants was not an inclusion criterion for the EPOC rules, and it is also questionable how the number of participants should be calculated in relation to the total outcome.

The studies included in our review varied greatly during follow-up. Therefore, we classified the total number of outcomes in two groups: 1) outcomes for the first 6 months of follow-up and 2) outcomes after the first 6 months of follow-up. This gave us the opportunity to perform analyses on the effects of the IMSs within and beyond 6 months. However, these findings should be interpreted with caution, since merging follow-up times could present a distorted image of the actual situation.

We tried to specify the effects of timing related to treatment by redefining the analyses into studies during and after treatment. The total outcome of effects of our review should be interpreted with caution because IMSs during and after treatment can have different effects. Meanwhile, all outcomes in our review should be interpreted with caution due to the small number of studies in the analyses. More research is needed to explore the effects of IMSs and the effects of timing throughout the treatment.

6. Conclusion

IMSs seem effective in achieving implementation of PA in cancer care. Most IMSs targeted patients and were delivered individually as well as person-to-person. The IMSs containing individual and interactive elements that were tailored to the personal needs of patients seem most successful. Studies exploring PA IMSs for patient with tumour types other than breast cancer are rare yet this type of research needs to be encouraged. The findings of this review provide a solid base for enhancing the implementation of PA for all cancer survivors, and in doing so might improve the QoL of these patients.

Conflict of interests

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

Our study concerns the A-Care 2 program. The Committee on Research Involving Human Subjects, Arnhem–Nijmegen region of the Netherlands assessed the study and concluded that our study would be carried out in accordance with the applicable rules concerning the review of research ethics committees and informed consent [register number 2014/211].

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed in this study are included in this published article and its supplementary information files.

Authors' contribution

CIJ drafted the manuscript and conducted the systematic review.
 PO helped to draft the manuscript and helped to conduct the systematic review.
 MTD helped to conduct the systematic review.
 WRG helped to draft the manuscript.
 WH helped to draft the manuscript.
 RH helped to draft the manuscript and helped to conduct the systematic review.
 All authors read and approved the final manuscript.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.critrevonc.2017.09.005>.

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