

Bridging the Research to Practice Gap: A Systematic Scoping Review of Implementation of Interventions for Cancer-Related Fatigue Management

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Abstract

Background. Cancer-related fatigue (CRF) is one of the most common and distressing symptoms in people with cancer. Whilst efficacy of interventions for CRF have been extensively investigated, less has been done to ensure successful translation into routine clinical practice. The aim of this systematic scoping review was to synthesise knowledge surrounding the implementation of CRF interventions, summarise the processes and outcomes of implementation strategies used, and identify opportunities for further research.

Methods. PubMed, Cochrane CENTRAL, EMBASE and CINAHL databases were searched through to December 2020. The Cochrane Effective Practice and Organisation of Care (EPOC) Group taxonomy and the RE-AIM Framework were used to guide the evaluation of implementation strategies and outcomes, respectively.

Results. Six studies were included. Three used implementation frameworks (PARIHS, KTA, Cullens & Adams' Implementation Guide) to guide implementation. Overall, the implementation strategies used across all studies were reported to have directly resulted in immediate changes at the clinician level (e.g., increased clinician behaviours, self-efficacy, attitudes, knowledge of CRF management). No clear relationship was found between the use of implementation models and the number or type of implementation strategies used. For outcomes, Effectiveness and Implementation were the most highly reported RE-AIM measures followed by Reach then Maintenance. Adoption was the least reported.

Conclusions. Despite the high prevalence of CRF and evidence-based interventions for managing CRF, there is limited evidence informing the sustainable implementation of these interventions. There was an absence of external indicator reporting (e.g., start-up and ongoing intervention costs) in included studies, limiting the transability of study findings. Further, factors such as lack of clinician time, insufficient program funding, and unsustainable maintenance costs, were highlighted as key implementation barriers of CRF programs. This scoping systematic review emphasises the lack of quality CRF implementation studies presently available in the literature leading to a disconnect between effective CRF interventions, routine clinical care, and cancer survivors at present. Further, this review also highlights the need for robust study designs guided by established frameworks to methodically design and evaluate the implementation of CRF management interventions in the future.

1.0 Background

Cancer-related fatigue (CRF) is experienced by over 60% of cancer survivors depending on their cancer diagnosis and associated treatments, with two-thirds reporting severe CRF extending beyond 6 months, and one-third reporting persistent CRF over many years [1]. While CRF is known as one of the most distressing and prevalent symptoms experienced by people with cancer [2, 3], it has no current universal definition, with the National Comprehensive Cancer Network (NCCN) describing it as "a persistent, subjective sense of physical, emotional and/or cognitive exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" [4]. CRF greatly diminishes patients' physical, mental, occupational, emotional and social wellbeing during and after treatment [2, 5, 6]. Other than reduced quality of life, CRF can also lead to difficulties in decision making, daily living disruption and an increased dependency on others [7]. Such impacts on quality of life (QoL) have been widely reported by a broad range of cancer survivor populations [4, 6–13].

Various interventions for managing CRF have been investigated. These include physical activity and exercise (e.g. aerobic, resistance), pharmacological interventions (e.g. erythropoietin, methylphenidate, modafinil), psychological interventions (e.g. cognitive behaviour therapy), and complementary and alternatives medicine (CAM) therapies (e.g. acupuncture, massage). There is level one evidence [14–18] supporting the benefits of physical activity, exercise and psychological interventions for managing CRF. In a recent meta-analysis, Mustian and colleagues [16] identified that exercise (weighted effect size [WES], 0.30; 95% CI, 0.25–0.36; $P < .001$) and psychological interventions (WES, 0.27; 95% CI, 0.21–0.33; $P < .001$) produced significant moderate positive effects on CRF improvement, with authors suggesting that both management strategies be prescribed as first line therapy. While a plethora of research has focused on the efficacy of CRF interventions, there is much to learn about how these interventions can be incorporated into healthcare and 'real-world' settings.

While the discipline of implementation science is gaining momentum, less than half of interventions found to be effective in disease management and prevention are ever adopted into clinical use and routine practice [19–21]. Over recent years, cancer care and health service leaders are increasingly concentrating their efforts on facilitating the systematic uptake of research findings into routine care to improve service and patient outcomes [22]. Whilst there are numerous systematic reviews on the clinical efficacy of CRF interventions, to our knowledge there is no comprehensive review focussing on the implementation of CRF management interventions and programs. To address this gap, this systematic scoping review of the CRF literature was conducted to answer the following key questions: (1) What current efforts have been made to implement CRF interventions in clinical care?; (2) What implementation frameworks, strategies, theories or models have been used when implementing CRF interventions in clinical care?; and (3) What were the outcomes (reach, effectiveness, adoption, implementation, maintenance) of the implementation strategies used for CRF interventions?

2.0 Methods

This review sought to examine implementation in CRF literature and identify possible knowledge gaps, thus a scoping methodology was adopted [23]. This systematic scoping review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines [24] (See Additional File 1).

Eligibility Criteria

The population for this review were cancer survivors (regardless of age, gender, tumour and treatment type) at any stage of their cancer trajectory that have experienced fatigue as a result of their cancer or cancer treatment. The taxonomy of implementation strategies developed by the Cochrane Effective Practice

and Organisation of Care (EPOC) Group [25] were used to determine the definition and inclusion of implementation studies in the review (see Additional File 2). These EPOC implementation strategies were developed for interventions that targeted and produced changes at the healthcare organisation level, healthcare professional level and the health service level and thus were considered relevant for this review.

For inclusion, studies were required to meet the following criteria: 1) have the implementation of an intervention/program/guideline as a primary goal; 2) have cancer-related fatigue as a primary symptom of interest; 3) incorporate at least one of the EPOC implementation strategies; 4) be published in English; and 5) have full-text available.

No restrictions were placed on types of study designs eligible for inclusion. As the key interest of our systematic scoping review is to describe implementation outcomes of CRF management interventions, we included original research articles (i.e. randomised controlled trials, observational studies, qualitative studies, mixed methods, abstracts, program evaluations) and other grey literature (e.g. evaluations of modules, online programs and institutional/government interventions). Descriptive articles (i.e. commentaries, editorials, recommendation reports/articles) were excluded.

Search Strategy

Four databases (PubMed, Cochrane CENTRAL, EMBASE and CINAHL) were searched (through to December 2020) as outlined in Additional File 3. Free text terms and relevant subject headings (i.e. MeSH, Emtree) for “cancer-related fatigue” (cancer fatigue, fatigue) and “interventions” were used. These terms were also combined with implementation study terms (e.g. “implementation”, “translation”, “program development”, etc.) using the Boolean logic operators (or, and). Reference and citation lists of relevant articles were also hand searched for eligible studies that met the inclusion criteria. Titles and abstracts of articles retrieved from the search strategy were independently screened by two authors (CS, OAA). The same two authors then assessed the eligibility of relevant full-text articles for inclusion in the review. Disagreements were resolved through consensus among the two authors, with a third author (RC) as arbiter where required.

Data Extraction

Data extraction was conducted by one author (OAA) and checked for accuracy by a second author (RC). Key information extracted included: study characteristics (i.e. author, publication year, study design, purpose, participants, sample size); intervention characteristics (i.e. setting, context, model of care, resources used, intervention description); implementation framework or theory used; implementation strategies used; and implementation outcomes. A model or framework was considered specific to implementation if it described the process of translating research into practice, explained the influences of implementation outcomes, or evaluated implementation processes [26]. Implementation strategies were categorised using the components from the EPOC taxonomy (see Additional File 2).

The RE-AIM framework [27] was used to assess implementation outcomes. RE-AIM was initially developed to balance emphasis on internal and external validity and to expand on assessments of interventions beyond efficacy [28-30]. It has been shown beneficial for evaluating behavioural change interventions and assessing implementation impact [28-30]. The RE-AIM framework has been widely used in reviews of literature to evaluate several behaviour change and public health interventions including (but not limited to) interventions directed at health literacy [31], physical activity [32, 33], community health [34] and nutrition [35]. In our review, data were extracted using a widely used [28, 30] RE-AIM coding sheet for systematic reviews published on the RE-AIM website (<http://www.re-aim.org/resources-and-tools/measures-and-checklists/> - Additional File 4). The coding sheet includes a set of indicators that, when reported, are indicative for reach of participants, program effectiveness, organisational adoption, implementation, and the maintenance of intervention programs [30]. For each RE-AIM indicator, it was recorded whether the indicator had been reported (yes or no), and if reported, specific outcome data were extracted. Due to the heterogeneity of included studies, a narrative synthesis was conducted. As the purpose of this review was to provide an overview of existing evidence regardless of methodological quality or risk of bias, no quality assessment was conducted, consistent with the PRISMA-ScR guidelines.

3.0 Results

Database searches resulted in 561 potentially eligible records. Of these, eight articles representing six implementation studies [36-41] met the inclusion criteria and were included in the review (See PRISMA Flow Chart: Figure 1).

Characteristics of Included Studies and Programs

Included studies are described in Table 1. Study design varied across studies, consisting of one clinical audit implementation study [36], one qualitative program evaluation [41], three pre-test, post-test single group observation studies [37, 39, 40], and one longitudinal 3-group quasi-experimental comparative study [38]. Of these, three [36, 37, 39] had the sole intent to examine the impact of implementation efforts (strategies, methods or techniques designed to change behaviours) on the adoption of CRF evidenced-based practice and guidelines (but did not investigate the efficacy of a CRF intervention), of which two [36, 37] reported the impact of implementation strategies at the organisational and health professional level, and one [39] described the impact of implementation efforts on oncology nurses and patients. The remaining three studies [38, 40, 41] investigated the efficacy of CRF interventions implemented at the patient level. Participants in each of the three efficacy studies [38, 40, 41] had mixed tumour types (i.e. breast, colon, lung, gastrointestinal, prostate, ovarian, uterine, myeloma, non-Hodgkin and Hodgkin lymphoma cancers). CRF interventions described in these three studies were physical activity and exercise [40], clinician and patient education [38], or combined exercise and education [41]. Of the two studies with education components [38, 41], only ‘information giving’ education strategies were described (e.g. information sessions on fatigue assessment and management, relaxation, spirituality, healing arts, communication exercise; and printed material on nutrition, sleep disturbance, emotional issues, and exercise). Types of physical activity described were aerobic exercise (e.g. walking, treadmill, Nu-Step), resistance training (e.g. resistance bands), balance and stretching, yoga and aquatic exercises [40, 41]. Of

the three studies that implemented CRF interventions [38, 40, 41], two [38, 40] reported the impact of CRF interventions on patient fatigue outcomes (e.g. reduced fatigue). Of the six studies included, three were conducted in the USA [38, 40, 41], two in China [36, 39], and one in Canada [37].

Implementation Models and Frameworks

Only three of the six studies were informed by an implementation framework or model. Huether and colleagues [40] utilised Cullens and Adams' Implementation Strategies for Best Practice Guide. Jones and colleagues [37] used the Knowledge to Action (KTA) implementation framework; and Tian and colleagues [39] used the Promoting Action on Research Implementation in Health Services (PARiHS) framework to guide dissemination and implementation of CRF guidelines into clinical practice.

Implementation Strategies

Distinct EPOC implementation strategies used by all included studies are recorded in Table 1.

Educational Meetings and Materials

Coaching and training strategies (i.e. educational meetings and educational materials) were the most used strategies (five of six studies) [36-40] to promote uptake of CRF interventions. Education was delivered in the form of regular staff meetings, staff training sessions and workshops, formal presentations, unit in-services, role-play sessions (i.e. participation in mock fatigue assessments & patient education sessions) and print materials (i.e. 'pocket' fatigue guidelines & tip sheets, flipcharts, newsletters, education booklets). Education content across each study varied but generally included background information on fatigue, fatigue management, fatigue assessment procedures and tools, and referral processes.

Local Opinion Leaders and Stakeholder Engagement

Stakeholder engagement were used in five of six studies [36, 37, 39-41]. Stakeholder groups commonly included clinicians (i.e. psychiatrists, radiation and medical oncologists, physical therapists, surgeons, professors, specialist nurses), cancer survivors, research staff (i.e. research assistants, postdoctoral fellows), and community support professionals. The use of a key opinion leader was described in only one study [39], engaging a nurse who trained and persuaded fellow clinicians to accept implementation efforts.

Use of Clinical Guidelines and Local Consensus Processes

Three studies [36-38] focused efforts on implementing existing clinical fatigue guidelines, including the National Comprehensive Cancer Network (NCCN) Fatigue Guidelines [36, 38] and the Canadian Association of Psychosocial Oncology (CAPO) guidelines for CRF [37]. Tian and colleagues developed and implemented the Clinical Practice Guideline: Nursing Care of Cancer-Related Fatigue in Adults with Cancers [39], whereas Jones and colleagues specifically described the adaptation of guidelines to the local context after stakeholder consensus [37].

Audit and Feedback

Specific audit and feedback strategies were described in two studies [36, 39]. One study [39] described periodic audit completion rounds on nursing units, and routine discussions with staff to gather concerns, challenges, suggestions and distribute feedback; however, study authors did not report the specific details of audit content. The second study [36] described health professional training; fatigue screening at patient admission; fatigue screening at regular intervals throughout care; delivery of comprehensive fatigue assessments; and the provision of management strategies (i.e. physical activity and other strategies) to patients as components that were audited. In addition, interviews with patients and reviewed patient records were used to measure clinician compliance with audit components. A third study did [40] report the use of audit and feedback strategies, however they did not specify processes in further detail.

Managerial Supervision and Managing Performance

Managerial supervision and monitoring of performance strategies were utilised in two studies [36, 40] in the form of regular reporting to senior leaders, routine communication with nurses, and ongoing monitoring of staff to ensure program compliance. Wang and colleagues [36] reported that intervention leaders worked within the nursing unit to monitor nursing practice to ensure adequate nurse education on CRF, nurse provision of CRF assessment upon patient admission, and nurse delivery of patient education for CRF management strategies (i.e. physical activity, and other strategies). Unfortunately, Huether and colleagues [40] did not provide specific detail on performance outcomes of interest despite reporting the use of managerial supervision and monitoring of performance strategies.

Continuous Quality Improvement

Continuous quality improvement strategies were described by three studies [39-41] and generally involved protocol revisions and program modification based on clinician or patient feedback. Of these studies, the 'Energy Through Motion' CRF program [40] reported the formation of a dedicated quality improvement program; however, details of this quality improvement program were not provided.

Tailored Interventions

Four studies [36-39], described tailored interventions that were based on assessments of barriers to change. Wang and colleagues [36] conducted a clinical audit to determine CRF management barriers; Borneman and colleagues [38] identified barriers at the patient, professional and system level during the first phase of their quasi-experimental study; Tian and colleagues [37] identified barriers and facilitators through focus group discussions, surveys and observation; and Jones and colleagues [37] conducted semi-structured focus group interviews with stakeholder groups. Common barriers identified were lack of CRF

knowledge, inconsistent application of CRF guidelines, insufficient knowledge of CRF screening and assessment, resistant attitudes towards program adoption, busy environments, heavy workloads, and time restrictions.

Reminders

Only one study [40] reported the regular use of practice reminders to reinforce the intervention to staff members. Reminders were distributed by the project leader through intervention 'tips of the week'; however, the distribution method used (e.g. newsletter, text, email) remains unclear.

Organisational Culture

Efforts to change organisational culture were reported across all studies [36-41] using practical methods including the formation of fatigue specific referral and clinical feedback systems, creation and incorporation of CRF assessment flowcharts and assessment tools, addition of fatigue management processes to organisation protocol, and the development of CRF information documentation for both staff and patients.

Implementation (RE-AIM) Outcomes

Implementation outcomes of the included studies are outlined in Tables 1 and 2, and Additional File 5. Overall, Effectiveness and Implementation were the most highly reported dimensions followed by Reach. Adoption and Maintenance were the least reported dimensions.

Reach

Descriptions of target population (including demographic information), inclusion criteria and sample size were reported in five [37-41] of six studies. Only one study [39] reported the representativeness or characteristics of participants and non-participants by comparing the sample with broader populations. Program participation rate was reported by two of six studies.

Effectiveness

Fatigue and behavioural outcome measures were reported in four of six studies [38-41]. Of these studies, all reported reduced CRF severity as a result of the intervention. The 'Energy Through Motion' CRF intervention [40] resulted in decreased fatigue severity by an average of two points compared to an increase of 0.69 points in the usual care arm ($p=0.0006$). Improvements were also seen in activity levels [increase of 2.59 points ($p=0.0016$) in the intervention group vs. a decrease of 1.07 points in the usual care group] and overall quality of life [increase of 1.24-2.41 across QOL domains in intervention vs. a decrease of 0.69-1.41 in the usual care group]. Pre- and post-program scores from Van Gerpen and Becker's 'LifeSpring' CRF intervention [41] demonstrated statistically significant improvements in fatigue [5.58 (2.11) vs. 3.55 (1.86); $p < 0.0001$] and sleep [4.77 (2.5) vs. 3.26 (2.27); $p < 0.0001$], while Tian and colleagues' [39] also produced lower patient CRF scores after their CRF intervention [post: 5.59 (2.09) vs. pre: 6.50 (1.90); $t = 2.22$, $p = 0.04$]. Lastly, the 'Passport to Comfort' CRF intervention [38] produced significant and beneficial effects on fatigue barriers ($p=0.001$) and patient fatigue management knowledge ($p=0.002$). No studies reported on cost-effectiveness.

Adoption (setting and staff level)

Indicators for adoption were the least reported outcomes in the included studies. Descriptions of intervention location were reported by five studies [36-40], and descriptions of expertise of the delivery agent (staff) were reported by five studies [36-38, 40, 41]. Interventions and implementation efforts were delivered and led by a range of staff including specialist nurses [38-40], nursing students [40], clinical psychologists and clinical psychology students [37], and physical therapists and exercise physiologists [41]. Indicators such as the description of targeted locations, inclusion/exclusion criteria of settings and staff, method to identify settings and staff, setting and staff participation rate, representativeness of staff and settings, number of staff participating in intervention delivery, and measures of intervention cost were not reported by any study.

Implementation

Intervention completion rates were reported by four studies [36, 37, 40, 41] and ranged from 80 to 90%. No study described methods to ensure fidelity of the intervention. Additionally, only the 'Energy Through Motion' CRF program [40] detailed the ongoing implementation cost of the intervention (intervention kits valued at \$21.75 USD per patient). Results of implementation efforts varied across all studies. Implementation strategies utilised in Wang and colleagues [36] resulted in a 97% increase in nurse CRF education, 86% increase in nurse CRF patient assessment upon admission and at regular intervals throughout treatment, 75% increase in nurse provision of patient education on exercise management strategies for CRF, and 83% increase in nurse provision of patient education on other CRF management strategies. Jones and colleagues [37] reported that their two-hour health and community professional training session resulted in large to very large increases in clinician CRF knowledge ($d=0.98$), self-efficacy in CRF assessment ($d=0.88$), self-efficacy to intervene for CRF ($d=1.13$), and intent to apply CRF guidelines ($d=1.35$). Tian and colleagues [39] dissemination of CRF guidelines led to increased clinician knowledge, attitude and CRF management behaviours, and the increased adoption of effective CRF management strategies amongst patients. Borneman and colleagues [40] strategies resulted in the reduction of patient barriers to fatigue, with their specific strategies to address professional and system barriers (e.g. formal fatigue presentations to staff, monthly newsletters, ongoing meetings with nurse practitioners) resulting in organisational change (e.g. routine fatigue assessment added to outpatient clinic sheet, increased supportive care referrals). Although Huether and colleagues [40] and Van Gerpen and Becker [41] described the use of implementation strategies in their respective programs, outcomes of their implementation efforts were not reported.

Maintenance

Maintenance indicators at both the individual and setting level were not fully reported in any study and only partially reported across four of the six studies [38-41]. Borneman and colleagues [38] reported individual follow-up and attrition (three months) after program completion; however, did not provide follow-up data at ≥ 6 months post-intervention. All four studies provided explicit information on the status of the intervention at completion. Tian and colleagues [39] stated that innovations and strategies developed from their implementation efforts were maintained for two months after project completion, but were discontinued due to lack of staff time and funding. Borneman and colleagues [38] noted their dissemination of the intervention was conducted at the study institution and that plans were underway to disseminate the intervention into other community centres. Van Gerpen and Becker [41] provided an evaluation of a pre-existing program and thus it was assumed the program was still in place at publication of their article. Lastly, Heuther and colleagues who developed the 'Energy Through Motion' CRF intervention [40] indicated their program was continued after the project completion.

At the time of writing this review, the 'LifeSpring' CRF intervention described in Van Gerpen and Becker's evaluation [41] is currently maintained and institutionalised at the US Bryan Health Medical Center. Moreover, Van Gerpen and Becker detail that various adaptations to the original program were made (e.g. program expanded to include all cancer types, removal of education classes specific to breast cancer, addition of strength training, etc.). Additionally, the 'Energy Through Motion' CRF intervention [40] appears to be institutionalised at survivorship clinics offered by the University of Iowa Holden Comprehensive Cancer Centre in the United States; however, little detail of the current program and its integration can be found. None of the studies provided details on costs associated with maintenance, however Van Gerpen and colleagues [41] state that ongoing funding for the program was provided by the medical centre's foundation, and Huether and colleagues report that after project completion of the 'Energy Through Motion' CRF intervention, "continuation of funding for patient supplies was obtained through requests from a regular benefactor of the cancer centre" [40].

4.0 Discussion

Efforts to sustainably implement evidenced-based CRF management strategies into routine clinical care are urgently needed, owing to the high incidence, prevalence and burden of CRF in cancer survivors severely impacting health-related quality of life [1]. Despite established CRF management strategies [1, 16], sustainable models of care connecting cancer survivors to effective CRF interventions have yet to be satisfactorily investigated [42]. Indeed, our systematic scoping review was able to identify only six studies evaluating the implementation of interventions designed for individuals experiencing CRF, all of which had limited external validity and lacked methodological rigor (e.g. poor reporting of exclusion criteria, study design, data analysis; limited to no follow-up periods; absence of frameworks and theories to guide implementation, etc).

Only three studies used specific implementation models to guide the dissemination process, and not all models were used to their full capacity. While Tian and colleagues [37] evaluated the effectiveness of facilitation strategies to improve uptake of their newly formed CRF clinical guidelines, their application of the PARIHS framework to guide translation was partially consistent with the framework's standards as they did not incorporate patient preferences or representation in guideline formulation [43]. When applied accurately, implementation theories and frameworks have been shown to enhance dissemination into practice through improving interpretability of study findings and increasing the use of essential implementation strategies, subsequently making the spread of evidence-based interventions more likely [27]. Given only three studies adopted an implementation framework in our review, it is difficult to establish which model is the most helpful for future CRF implementation.

Despite limited use of implementation models, a range of implementation strategies were used across included studies. Training and education of healthcare professionals and the utilisation of stakeholder engagement were the most used strategies to implement CRF interventions and promote behaviour change in clinical practice; a representative reflection of trends identified in implementation and health intervention literature [44-48]. Although the majority of studies in this review demonstrated their use of various implementation strategies resulted in immediate changes at the clinician, organisational and patient level (e.g. increased clinician knowledge and self-efficacy in CRF assessment and management strategies, addition of fatigue management processes and referral systems to organisation protocols; reduced CRF severity in cancer survivors); it was difficult to determine the impact (and impact strength) of individual strategies on implementation outcomes. Only Wang and colleagues [36] described the effect of each implementation strategy and the impact each specific strategy had on distinct identified barriers to CRF guideline adoption. Aside from this, impacts of specific strategies were only reported across studies on the odd occasion. For example, Tian and colleagues [39] explicitly concluded that the role of an opinion leader was integral to the successful implementation of their CRF guidelines into clinical practice. The same study also reported that the integration of nursing unit leaders from the nursing department into the facilitation team - a process described as the conversion of external causes (i.e. university investigators) into internal causes (i.e. nurse leaders) - directly increased staff confidence in providing care for individuals experiencing CRF, and directly enabled program sustainability. While it is challenging to determine the impact of individual implementation strategies, and the likelihood of multiple implementation strategies being used concomitantly, further research to identify the preferred strategy from clinicians, patients and other stakeholders in CRF interventions are likely to be helpful in ascertaining the usefulness, relevance and effectiveness of specific implementations strategies that will improve implementation efforts [49].

Maintenance and Adoption were the least reported RE-AIM indicators, while Reach, Effectiveness, and Implementation were highly reported across the studies. Further, across all domain indicators, reporting was exceptionally higher for aspects of internal validity (e.g. inclusion criteria, sample size) than for external validity (e.g. representativeness of participants, description of settings and staff, intervention fidelity). This is consistent with previous reviews of health interventions across a variety of populations [30, 32, 50-52]. Of note was the level of reporting on Adoption, with indicators at the staff and setting level amongst the lowest reported. Details of intervention settings and delivery staff are critical as they allow for the assessment of intervention applicability (and its effect) to different conditions [52]. In five of six included studies, intervention facilitators were employed solely to deliver the CRF intervention or implementation effort, and often had high levels of specific training and supervision, a situation which is not indicative of "real-life practice". Thus, to assist the replication and translation of CRF guidelines and management interventions to routine practice; information regarding intervention setting and staff characteristics, and level of staff skill and training is vital.

Cost was another notable implementation outcome that was under-reported, yet is essential when establishing sustainable models of care for cancer survivors. Cost effectiveness, including start-up and ongoing costs of intervention delivery, have been identified as key factors in determining the translation of research findings into practice [53]. However, these costs as notable financial barriers for sustainability were rarely reported, with only the 'Energy Through Motion' CRF intervention providing an explicit cost of intervention materials (\$21.75 USD per patient) [40]. Cost concerns have been shown to be associated with reduced stakeholder willingness to implement evidenced-based interventions and has emerged as the most significant barrier to evidenced-based practice implementation and program sustainability [54-56], making its reporting in future implementation efforts for CRF management critical.

Assessment of intervention maintenance and sustainability has been identified as a neglected area in clinical research [30, 32, 50-52, 57], with results of this review indicating no different. Our review found evidence of only two settings continuing their CRF intervention program (either in part or whole) beyond the study duration. Across all studies, the same common barriers to program continuation were reported: lack of clinician knowledge and skills in the management of CRF, shortage of clinician human resources, lack of program and staff funding, and lack of clinician time. A clear example of this was seen in Tian and colleagues [39] which found clinician acceptance, knowledge and attitude to providing CRF management was considerably lower in the nursing unit with the higher workload. In fact, Tian and colleagues concluded that sufficient nurse human capital in the second unit (with the lower workload) had effectively ensured successful implementation. Additionally Wang and colleagues [36] also noted that time restrictions and heavy workloads affected the capacity of staff to complete routine CRF assessment and patient education. These barriers to the sustainability of intervention and guideline implementation efforts have been repeatedly highlighted across the CRF literature [58-60]. Berger and Mooney [61] provide an accurate summary, explaining that a lack of access to, and re-imbursement for, integrated supportive cancer programs and services is the largest challenge to effectively implementing CRF guidelines into routine practice [61]. They concluded that without additional time and reimbursement, clinicians cannot be expected to adequately provide effective or targeted care to individuals experiencing CRF.

Implications for Future Research and Practice

Implementation research in CRF management is severely lacking, highlighting a real need for focussed implementation science research in cancer care. Although feasibility, acceptability and effectiveness outcomes are widely reported across CRF literature, a greater focus on other pertinent implementation outcomes such as adoption and program maintenance are paramount to translate CRF guidelines and interventions into real-world settings. Future studies need to put greater emphasis on reporting aspects of external validity such as representativeness, setting characteristics, staff level characteristics, and implementation cost. For implementation costs, Cidav and colleagues [53] present a pragmatic approach for costing specific components of implementation strategies, which may serve as a potential solution to common burdens associated with implementation costing and economic evaluations. Additionally, to ensure program maintenance, investigators should consider sources of ongoing funding and endeavour to use existing resources (staff, equipment, infrastructure, etc.) to deliver implementation efforts.

Inconsistencies in implementation study design, definitions, and terminology across already scarce CRF literature were also identified by our systematic scoping review. Pearson and colleagues [58] suggest that CRF implementation studies incorporate several iterative phases, to provide opportunities to trial, assess and refine elements; determine resource needs and costs; and gather evidence of implementation impact [58]. Moreover, future CRF implementation research should be underpinned or guided by an implementation framework to facilitate dissemination of evidence-based CRF management strategies; utilise the most appropriate and most rigorous pragmatic designs with adequately powered samples and longer follow-up periods; and report the impact of implementation at the system, health professional and cancer survivor level.

CRF remains one of the most prevalent symptoms and unmet needs in cancer survivors. Although our review could not determine the impact of specific strategies on implementation outcomes of CRF management programs – in order to address this pertinent unmet need, we posit that clinical leaders endeavour to build clinician awareness and knowledge of evidenced-based CRF management and assessment strategies through the provision of educational training and resources (e.g. printed materials, training sessions, department in-services, meetings, online resources, distribution of established CRF clinical practice guidelines). Clinical leaders should seek regular engagement with clinical staff and relevant stakeholder groups to identify potential/existing enablers or barriers to clinical change and to tailor implementation efforts to specific contexts. To address common barriers to implementation, emphasis should be placed on the allocation of clinician resources within settings, the provision of time management support to clinicians (e.g. reallocation of work tasks, adjustment of procedures to fit clinician schedule, adjustment of clinician schedule to fit procedures) and the identification of 'clinical champions' or opinion leaders, to encourage peer behaviour change and compliance with the recommended CRF management and assessment practices.

Limitations

This review has two limitations. First, the inconsistencies of what constitutes an implementation study (e.g. implementation processes, terminologies, and definitions, intention to treat, inclusion/exclusion criteria) made it difficult to detect a distinct relationship between the use of implementation models and strategies, and implementation outcomes. However, this was not unique to our review, with similar inconsistencies being frequently reported across implementation science literature [62-64]. Second, our review was also limited to studies in English, potentially resulting in publication bias limiting the generalisability of results.

5.0 Conclusion

This systematic scoping review is the first to examine models, strategies and outcomes of studies reporting on the implementation of interventions for individuals experiencing cancer-related fatigue. Our review found that various implementation strategies have been used to promote uptake of CRF management interventions and guidelines in practice. Despite certain strategies resulting in immediate changes at the organisational, clinician and patient level; lack of consistent reporting of external indicators (e.g. ongoing and start-up costs of intervention, setting and staff representativeness) and factors such as lack of clinician time, insufficient clinician and intervention funding, and unsustainable maintenance costs are potential barriers to study translatability and

CRF program implementation. This review emphasises the absence of quality CRF implementation studies and highlights the pertinent need for more robust, theory driven implementation studies to bridge this important knowledge-practice gap.

Abbreviations

CAM – Complementary and Alternative Medicines

CAPO – Canadian Association of Psychosocial Oncology

CRF – Cancer-related fatigue

EPOC – Effective Practice and Organisation of Care Group

KTA – Knowledge to Action Implementation Framework

NCCN – National Comprehensive Cancer Network

PARIHS - Promoting Action on Research Implementation in Health Services Framework

PRISMA-ScR – Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews

QOL – Quality of Life

RE-AIM – Reach Effectiveness Adoption Implementation Maintenance

WES – Weighted effect size

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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Tables

Table 1: Summary of Included Articles							
Author, year [Program name], country	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
Abbott et al. 2017 [65] & Huether et al., 2016 [40] / Energy Through Motion ©/Iowa United States	Pre-, post-test single group/ Ambulatory / (n=39) Pre-, post-test single group / 2 Survivorship clinics/ (n=50)	Feasibility (Abbott et al., 2017) Effectiveness (Huether et al., 2016)	Adult Cancer Survivors	Nurse-led survivorship clinics Home-based exercise	Activity trackers, Resistance Bands, Verbal instruction, Printed material (i.e., exercise & calorie guides), Pedometers, Activity logs, Bottle	3-month physical activity program that incorporated education, a specialised kit (including info on PA benefits, exercise equipment, sleep strategies logbook, home workouts) and ongoing patient support. The program also included an intricate text message system provide information and encouragement and promote adherence.	(Cullen & Adams, 2010) Implement: Strategies 1 Best Practi Guide
Implementation Strategies						Outcomes	
<u>System/health professional level</u>						<u>Effectiveness</u>	
<p>Reminders: update practice reminders provided by project leader to regularly reinforce the program. Local Opinion leaders: DNP student, clinical nurse specialist, nurse practitioners informed content and development.</p> <p>Continuous Quality Improvement: Senior leaders, existing and new team members were regularly updated on intervention progress. ● Dedicated quality improvement program. ● Protocol revisions based on feedback from clinicians, patients, or family.</p> <p>Managerial supervision & Monitoring Performance: Regular reports to senior leaders.</p> <p>Interprofessional Education & Educational meetings: Presentations on evidence on CRF, physical activity and the Energy Through Motion program at staff meetings, unit in-services, Educational materials: pocket guides provided for clinicians</p>						<ul style="list-style-type: none"> · Results o Fatigue: Decreased by an average of 2 points compared to an increase of 0.69 in usual care arm (p=0.0006) o Activity Levels: Increased activity levels by a mean of 2.59 points (p=0.0016) compared to usual care (decreased levels by a mean of 1.07) o QOL: Improved in all measured areas from 1.24-2.41 points (0-10 scale) compared to decrease (0.69 – 1.14 points) in usual care. o Program evaluation: Participants reported that the program was helpful and beneficial. Connecting activity trackers to the computer and follow-along activity videos considered least helpful (Information videos also report as not used regularly). · Percent attrition: 10% 	
						<u>Adoption</u>	
						<ul style="list-style-type: none"> · Setting Participation rate: 100% (out of 2 eligible settings) 	
						<u>Implementation</u>	
						<ul style="list-style-type: none"> · Completion rate: 90% 	
						<u>Maintenance (Setting Level)</u>	
						Program still maintained at the University of Iowa Holden Comprehensive Cancer Centre	
<hr/>							
Author, year [Program name], country	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
Borneman et al., 2010 [66] & 2011 [38] / [Passport to Comfort]/ California, United States	Quasi-experimental comparative study/Ambulatory/ (Phase 1 [usual care] n=83, Phase 2 [intervention] n=104, Phase 3 [Dissemination] n=93)	Phase 1 & 2: Effectiveness Phase 3: Dissemination	Patients with breast, colon, lung and prostate cancer (at least 1 month after diagnosis).	Nurse-led	Teaching Packet consisting of written educational materials.	Phase 1, 2: Psycho-educational intervention. Each patient received 4 (approx. 60min) educational sessions as well as written information material or 'tip' sheets in a 'teaching packet'. Tip sheets provided education on exercise, nutrition, emotional issues and sleep disturbance. During sessions, information on pain assessment, fatigue	None Desc

assessment and fatigue management was provided. A month after last educational session participants received bi-weekly follow-up phone calls every 2 weeks for 3 months.

Implementation Strategies:

System/ Health Professional Level

Local Consensus Processes & Clinical Guidelines: Intervention informed by the National Comprehensive Cancer Network (NCCN). A 'Patient Pain Knowledge Tool' was created based on NCCN pain guidelines.

Educational Meetings & Material: Regular meetings with nurses. ● Pain and fatigue presentations by national experts to oncologists and nurse practitioners. ● Monthly newsletter to practitioners for ongoing education and communication. ● Internal Advisory Board met quarterly to gain clinician input from researchers involved in the intervention.

Organisational Culture (Phase 3): Pain and fatigue education provided to all clinicians at a total of 38 in-services. ● Pain and fatigue information provided at key meetings. ● Routine fatigue assessment added to outpatient clinic vital sign flow sheet. ● Increased referrals to supportive care departments for pain and fatigue. ● Patient education materials were translated into Spanish. ● Patient education materials made available on employee Intranet. ● Advocacy posters placed around clinic to remind staff and patients to discuss fatigue. ● **Audit and feedback:** Clinical feedback reports completed for patients and provided to MDs and NPs based on chart audits with specific feedback for pain and fatigue management.

Tailored interventions: Strategies created to address identified patient, professional and system barriers.

Outcomes

Reach

· **Participation rate** (Phase 3): 93%

Effectiveness

· Phase 1 & 2: **Fatigue** - fatigue management barriers were significantly higher in the usual care group than in intervention group. The usual care group had significantly more fatigue (beta = -0.155).

· Phase 3: **Fatigue** - Significant immediate and sustained effects were shown on the Fatigue Barriers Scale (FBS) for the intervention group. The intervention group demonstrated a significant delayed effect in Physical Quality of Life - maintained baseline levels of QOL throughout the study when we would normally expect a decrease in QOL. Statistically significant differences between QOL measures were small.

Maintenance (Individual).

· (2-month follow-up) Attrition rate: 32.5%

Author, year [Program name], country	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
Jones et al., 2020 [37]/ Canada	Prospective Cohort/(n=18)	Implementation Intervention Acceptability and Feasibility	Healthcare professional and community support workers	N/A	Flipchart/Checklist– summarised guidelines, screening and assessment information.	A one-time in person 2-hour training session offered to health care practitioners and community support providers about the CAPO CRF guidelines. First hour provided information on practice gaps reported in literature, CAPO CRF guidelines, communication skills and motivational interviewing principles. Second hour involved role-play and group discussions.	Knowledge Action (KT) Model

Implementation Strategies

Clinical Guidelines: Canadian Association of Psychosocial Oncology (CAPO) guidelines for CRF used to inform education sessions.

Local Consensus Processes: Clinical guidelines adapted to the Ottawa context after consensus amongst stakeholders.

Local opinion leaders & Tailored Intervention: Focus interviews and program development with stakeholder groups (patients, health care professionals and community support professionals, pedagogy expert) to identify barriers to change; subsequent strategies then created.

Educational materials: All participants provided with a flipchart that contains information on assessing and managing fatigue.

Outcomes

Reach

Participation Rate: 90%

Implementation Impact

· Program was effective in increasing knowledge, self-efficacy and intent to apply guidelines.

· **CRF Knowledge:** -3.959(14), p = 0.001) with a large effect size (d = 0.98).

· **Self-Efficacy in CRF Assessment** (t = 2.621(13), p = 0.021) with a large effect size (d = 0.88).

· **Self-efficacy to intervene for CRF** (t = 2.924(13), p = 0.012) with a large effect size (d = 1.13).

· **Intent to apply Clinical Guidelines in Practice:** t = 4.786(13), p = 0.000) with a large effect size (d = 1.35).

· **Feasibility:** mean satisfaction score (52.27 ± 6.97 of 60 points maximum).

Implementation

Completion Rate: 88.9%

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Author, year [Program name], country	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
Tian et. al 2017 [39]/ China	Pre-test, post-test/ Radiotherapy Unit & Medical Oncology Unit/N/A	Implementation – Intervention Translating guidelines into practice	Nursing Staff	N/A	Nursing record chart, CRF education booklet, CRF quality control checklist	Study outlined the creation of a 'CRF Nursing Guideline' using a steering group (consisting of clinical experts). The resulting guidelines were implemented into practice through an evidenced-based project utilising training and education for nurses, changes to nursing procedures (screening and assessment and quality review) and the provision of staff resources. Impact of the project was measured at the organisational, staff and patient level.	The Promo Action on Research Implementation in Health Services (PARIHS) framework

Implementation Strategies:

System/health professional level

Continuous Quality Improvement & Audit and Feedback: Feedback and suggestions periodically collected to determine whether further specific training or modification (to nursing procedure) was required.

Educational materials: CRF Education booklet and other training print materials given to nursing staff.

Educational meetings: Training courses on CRF nursing care were established, including elementary training on evidence-based nursing practice and specific training on CRF nursing care. Seminars on evidence-based practice concerning CRF management.

Clinical Practice Guidelines/ Local Consensus Processes: The "Clinical Practice Guideline: Nursing Care of Cancer-Related Fatigue in Adults with Cancer" was developed by interventionists.

Local opinion leaders: Creation of a steering group (six directors from nursing, medical oncology, radiotherapy, Traditional Chinese Medicine, Psychiatry departments). ● Opinion leader identified to change nurse negative opinion of the project, train other nurses and act as a role model for fellow clinicians. ● Integration of existing staff into facilitation team.

Tailored Intervention: Initial focus groups and discussions conducted to identify barriers to change. Subsequent strategies then created.

Outcomes

Implementation Impact

- Nurse Outcomes: After implementation of the project, knowledge, attitudes, and behaviour scores were all higher than at baseline.

- Patient Outcomes:

- o No differences were detected between the baseline and final scores of the "self-efficacy questionnaire for CRF management" (SQFM) scale.

- o Patients adopted more effective CRF management strategies (previously just rested to alleviate fatigue)

- o CRF scores lower after intervention than prior to intervention [5.59(2.09) vs. 6.50 (1.90); t = 2.22, p = 0.04]

Author, year [Program name]	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
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name], country	Size						Framework Theories
Van Gerpen & Becker, 2013 [41]/ [LifeSpring]/ United States	Program Evaluation Article /Wellness Centre/N/A	Program Evaluation	Adult Cancer Survivors	Physical therapist and exercise physiologist led	Resistance Bands T-shirts w/LifeSpring logo Written Hand out materials Snacks Balloons (for release at graduation) Exercise equipment (dumbbells, machines)	Exercise and education program. 12-week program consisting of a bi-weekly exercise session and a weekly education session. Exercise component consists of: 20-30-minutes of aerobic exercise (5-min intervals of stationary bike, treadmill, walking on the indoor track, recumbent stepper (Nu-SteP), or upper-body ergometer) and 20-30-minutes of group exercises (resistance training, balance/flexibility/stretching exercises, aquatic exercises and relaxation, Pilates or BODYFLOW™ exercises). Educational sessions are led by content experts and include topics such as exercise and cancer, healing, communication and coping, spirituality sleep.	None Desc
Implementation Strategies: <u>System/Health Professional Level</u> Local Opinion leaders: Program development by physical therapist, medical and radiation oncologists, general surgeons, nurses, cancer survivors. ● Phone interviews with intervention leaders from other programs to provide additional insight on recruitment, retention, program design education session topics, screening tools, etc. Continuous Quality Improvement: Program was modified to include all cancer types (originally only breast cancer survivors) after results from initial program evaluation. Sessions were limited to 12 participants after previous larger class sizes caused challenges in providing individualised support. -					Outcomes <u>Effectiveness/ Efficacy</u> Participants reported improvements in their fatigue, pain, sleep disturbances, depression, and quality of life, (demonstrated from their pre-, mid-, and post program scores). · Fatigue: [5.58 (2.11) vs. 3.55 (1.86); p < 0.0001] · Sleep [4.77 (2.5) vs. 3.26 (2.27); p < 0.0001], · Quality of life [3.63 (2.27) vs. 2.08 (1.86); p < 0.00 · Pain [2.52 (2.31) vs. 1.85 (1.85); p < 0.001], · Depression [2.72 (2.21) vs. 1.65 (1.49); p < 0.0001 - <u>Implementation</u> Participation/Attendance Rates: 80%. From 2007 to ap 2013: 182 participated in program and 152 completed t program <u>Maintenance (Setting Level)</u> Program still maintained at the Bryan Health Medical C		
Author, year [Program name], country	Study design /Setting/ Sample Size	Purpose	Participants	Models of Care	Resources Used/ Described	Intervention/ Program Description	Implement Model/ Framework Theories
Wang et al., 2018 [36]/ China	Clinical Audit/ Hospital/ N/A	Implementation Project	Nursing Staff	N/A	Educational materials	This article first determined the current state of CRF management in the oncology department by undertaking an initial audit. Strategies (listed below) were then implemented to improve practice and address the barriers identified. A follow-up audit was conducted to evaluate the impact of changes made.	None described. Researchers used the JF Getting Research in Practice (G tool to iden barriers and practice ga
Implementation Strategies					Outcomes		

Local Opinion Leaders: Routine communication with stakeholders to inform strategy development and promote good clinical practice.

Clinical Guidelines: Content of all educational materials derived from the NCCN CRF guidelines.
Organisational Culture & Educational materials: Information brochures and posters about CRF management strategies developed for patients and staff. ● Flow chart detailing CRF assessment steps created and displayed in nursing unit. ● Paper-based CRF assessment tools (including BFI) created and distributed for use.

Educational meetings: Formal 2-hr education sessions on CRF background, management and assessment delivered to all nurses. ● 'Practice fatigue assessments' and patient education sessions completed by nurses (under supervision).

Monitoring Performance & Managerial Supervision: Ongoing discussions, communication and monitoring of nurses to ensure compliance.

Tailored interventions: Clinical audit conducted to address barriers to change. ● Procedures adjusted to account for changes in environment, workload and time restrictions (i.e. reallocation of work tasks, management support, time management via prioritisation of work tasks, balancing resources).

Implementation Impact

Compliance with best practice audit criteria (compliance rates) -

- Health professional received education and training
Baseline audit – **0%** Follow up audit - **97%**

- CRF assessment upon admission and at regular intervals throughout care: Baseline audit – **0%** Follow up audit - **86%**

- Focused assessment of fatigue undertaken in patients who screen positively: Baseline audit – **0%** Follow up audit - **64%**

- Patient education about physical activities: Baseline audit – **3%**, Follow up audit - **78%**

- Patient informed about the strategies to manage cancer related fatigue: Baseline audit – **0%** Follow up audit - **83%**

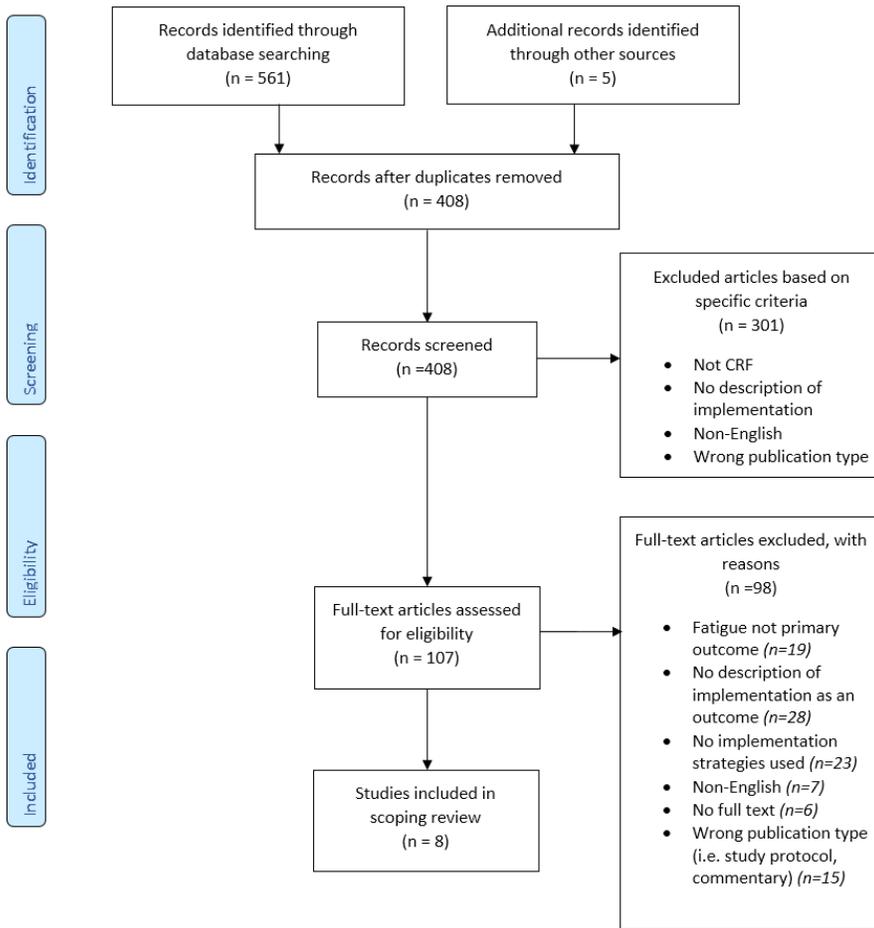
Abbreviations: **BFI** = Brief Fatigue Inventory; **CAPO** = Canadian Association for Psychosocial Oncology; **CRF** = Cancer-related Fatigue; **DNP** = Doctor of Nursing Practice; **JBI** = Joanna Briggs Institute; **MD** = Doctor of Medicine; **NCCN** = National Comprehensive Cancer Network; **N/A**= Not applicable; **NP** = nurse practitioner; **PA**=physical activity; **QOL** = Quality of Life

Table 2: Use and reporting of RE-AIM indicators across included studies

Dimension	Indicators	Percentage of studies reporting indicators
Reach	Participation rate	(n=2) 33.3%
	Comparisons between participants and non-participants (Representativeness)	(n=1) 16.7%
Effectiveness	Measure of fatigue outcome	(n=4) 66.7%
Adoption	Setting Participation Rate	(n=0) 0%
	Comparisons between participating sites compared with nonparticipating	(n=0) 0%
	Staff Participation Rate	(n=0) 0%
	Characteristics of staff participants vs nonparticipating staff or typical staff	(n=0) 0%
Implementation	Measure of implementation fidelity	(n=0) 0%
	Cost of implementation—money	(n=1) 16.7%
Maintenance (Individual Level)	Measure of primary outcome ≥6 months post-treatment	(n=0) 0%
Maintenance (Setting) ¹	Reported if program is still ongoing at ≥6 months post-treatment	(n=0) 0%

1. Maintenance (setting) was not explicitly reported across any included studies, however 2 programs currently institutionalised are still running as at September 2020.

Figures



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Figure 1

Prisma Flow Diagram

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalFile3.docx](#)
- [AdditionalFile1PRISMAScRChecklist2019.docx](#)
- [AdditionalFile2.docx](#)
- [AdditionalFile4.docx](#)
- [AdditionalFile5.docx](#)