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Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

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Second Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Abstract

Words: 300/300

Objective: The role of primary care providers (PCP) in the cancer care continuum is expanding. In the post-treatment phase, this role is increasingly recognized by policy makers and health care professionals. During treatment, however, the role of PCP remains largely undefined. This systematic review aims to map the content and effect of interventions aiming to actively involve the General Practitioner (GP) during cancer treatment with a curative intent.

Study design Systematic review

Participants Cancer patients treated with curative intent

Data sources Randomized controlled trials (RCTs), controlled clinical trials (CCT), controlled before and after studies and interrupted time series focusing on interventions designed to involve the GP during curative cancer treatment were systematically identified from PubMed and EMBASE and subsequently reviewed. Risk of bias was scored according to the EPOC risk of bias criteria.

Results Five RCTs and one CCT were included. Interventions and effects were heterogeneous across studies. Four studies implemented interventions focussing on information transfer to the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on patient satisfaction with care was found in three studies. Subgroup analysis suggest a reduction of health care use in elderly patients and reduction of clinical anxiety in those with higher mental distress. No effects are reported on patients' quality of life (QoL).

Conclusion Interventions designed to actively involve the GP during curative cancer treatment are scarce and diverse. Even though uptake of interventions is generally low, results suggests a positive effect of GP involvement on patient satisfaction with care, but not on QoL. Additional effects for vulnerable subgroups were found. More robust evidence for tailored interventions is needed to enable the efficient and effective involvement of the GP during curative cancer treatment**.**

PROSPERO registration number: CRD42018102253

Strengths and Limitations of this study

- This is the first review that systematically reviews evidence based interventions, aiming at general practitioner involvement during the curative treatment phase of the cancer care continuum.
- The electronic database search was performed without restriction on languages and period.
- We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate tool to assess bias for complex interventions.
- The title/abstract screening is done by single reviewer, two authors screened the full-text and the search was complemented with reference check of relevant articles.
- The included studies are heterogeneous in intervention and outcome and therefore strong conclusions could not be made.

Keywords

- Primary care
- General Practitioners
- Shared care
- Cancer patient
- Curative treatment
- Patient satisfaction

Background

Cancer incidence and prevalence is increasing as a result of the aging population combined with expanding diagnostic and treatment possibilities. Due to improved outcome following cancer treatment, the nature of cancer treatment is changing toward more chronic disease management. Health policy makers and health care professionals therefore call for a change in the way cancer care is provided, to focus on more integrated and personalized cancer care during and after treatment [1,2]. In countries with gatekeeper health care systems such as The Netherlands, primary care is increasingly promoted as the preferred setting to provide integrated support during and after active cancer treatment, both to meet patient preference and to stabilize costs [2,3]. The concept of shared care has been suggested as the way forward in the organization of integrated cancer care [2,3]. Shared care is an organisational model involving both general practitioners (GPs) and specialists in a formal, explicit manner. Shared care models enhance the optimal access of patients to both hospital care and community based supportive care along the entire cancer care continuum [4]. In shared care models, GPs, along with other primary care professionals, add their competence to balance the biomedical aspects of cancer care with the psychosocial context and preferences of the individual patient [5], ensuring personalized, integrated care.

Traditionally, the role of primary care in palliative and end-of-life care is well established [6]. In addition, evidence suggests a solid role for primary care in cancer follow-up after treatment and survivorship care [7–9]. Less well appreciated, however, is primary care involvement during cancer treatment, particularly for patients treated with a curative intent. It is well established that in this phase patients frequently experience psychosocial distress and treatment-related side effects that negatively affect their quality of life [10]. Several studies suggest primary care involvement during active treatment, to improve patient outcomes and to ensure continuity in guidance from primary care [3,11].

So far, the most effective approach to involve primary care during cancer treatment remains unclear.

This systematic review aims to provide a comprehensive overview of the content and effect of interventions aiming at active involvement of the general practitioner during cancer treatment with curative intent compared to usual care.

Methods

Data source and search

A literature search was conducted in PubMed and EMBASE for articles describing randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies, and interrupted time series published in any language until the 3rd of July 2018. We used a search strategy that was previously applied in a review assessing continuity of care in the follow-up of patients with cancer [12]. Subsequently, this strategy was adapted for completeness and relevance based on sequential testing of search strategies to develop our final search strategy. The details of the sequential and final search strategies are listed in appendix A. The search terms include keywords and controlled vocabulary terms surrounding the central themes "general practitioner", "primary care", "oncology", and "care". Outcome measures and comparing study arm were not included in the selection criteria to widen the scope of the review. Instead of a database integrated filter, a tailored methodological search filter was used to limit retrieval to appropriate study design [12]. We reviewed references of selected articles for additional papers.

Outcomes will include any measure related to the quality of healthcare (e.g. healthcare use), the healthcare experience of: healthcare professionals, informal caregivers, and patients, outcomes at the patient-level, with a focus on, e.g., disease, quality of life, and psychosocial impact.

Study selection

Articles were selected if they described an intervention; (1) for cancer patients, (2) starting during curative treatment, (3) evaluating involvement of the GP, and (4) tested in a randomized controlled setting, CCT, controlled before and after studies or interrupted time series. Studies with a majority (>75%) of curative patients were included. In case the proportion of curative patients was unclear, the original authors were contacted. Without response, the inclusion of the trial was based on >75% percentage patient survival during the trial.

Data extraction and management

To determine relevance, the records were divided and screened on title and abstract by two single reviewers (IP,JB) and discussed with three additional reviewers in case of doubt (AM,CH and JB or IP). Two authors (IP,JB) performed full-text screening. Disagreements on eligibility were resolved in group discussion with researchers and clinicians (IP,JB,AM,CH). If possible, a meta-analysis was planned to be conducted.

Patient and public involvement

Patients and public were not involved in the design of the current study.

Quality assessment

Risk of bias for individual studies was scored by two authors (JB,IP) with the EPOC risk of bias criteria [13]. In case outcomes of homogeneous study designs could be merged we rated the body of the evidence following the Grades of Recommendation, Assessment, Development and Evaluation approach (GRADE) [14] from the Cochrane collaboration. Present systematic review is reported following the PRISMA 2009 checklist [14].

Results

Study selection

As shown in Figure 1, 9727 records were eligible for inclusion after removal of duplicates. Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP involvement started after completion of primary cancer treatment, (3) or no RCT, CCT, controlled before and after study or interrupted time series design was used. Two studies published multiple articles based on the same data [15–20]. As a result, five RCTs and one CCT were considered eligible for inclusion, which were described in ten articles. No additional eligible studies were identified in the reference lists of selected studies. Figure 2, Table 1, and 2 show a detailed account of the risk of bias, patient population, interventions, outcomes assessed and observed results for each study. Given the various research questions, interventions and heterogeneity of outcome measures, pooling of data, and GRADE assessment was not feasible.

Quality of studies

The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et al. (2003) show a high risk of bias, resulting from high risk of selection and information bias [15,16,21]. Drury et al. (2000) scored a medium risk of bias [22]. And the studies of Johnson et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk of bias [17–19,23,24]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several limitations should be kept in mind. The randomization produced an imbalance, which influenced comparability of outcomes between study groups without corresponding correction in the analyses. Furthermore, it was not reported whether a baseline measurement was performed and the exact timing of the first measurement (Table 2). Also, the percentage of missing data was 33% in the intervention and 26% in the control group [15].

Study populations

The six eligible studies were conducted in Europe (five) and Australia (one) among different cancer patient populations over the past two decades. Breast cancer patients were the most commonly studied group (between 33-100% of the study populations). Five RCTs included patients with more than one type of cancer, in different stages. Three studies included patients treated palliatively (<25% of total study population). In two RCT's cancer stage was not specified.

Type of interventions

The interventions in the studies (Table 1) were heterogeneous, but can be divided in mainly information transfer to the GP (n=4) [15,16,21–23] and tailored primary care interventions (n=2) [17–20,24].

Interventions focusing on information transfer, provided additional, disease specific educational, and practical information concerning treatment and care directly to the GP or via the patient. Interventions were either directed at enhancing communication between GP and other party (i.e. secondary care or patient), or directed at improving patient's attitude towards the healthcare system (i.e. healthcare in general or intervention), physical- and psychological

complains. Three interventions provided patients with information, which was to be transferred to the GP. In one CCT [21], informational cards were provided to the patients for use in primary care. Two other RCTs described an intervention with a Patient Held Record (PHR) [22,23] aimed to facilitate intersectoral communication, to provide patients with an aide memoire, and with the opportunity to stay actively involved in their treatment. One RCT supplied the GP with patient specific discharge summaries by secondary care, aiming to enhance GP knowledge of chemotherapy treatment and expected adverse effects [15,16].

The tailored primary care interventions aimed to support patients in managing their disease and treatment [17,18,20,24]. The interventions are to diverse to be merged and therefore described separately. In Johansson et al. (2001) [24] primary care was intensified by means of recruitment of a home care nurse, psychologist, dietician and training of the GP. The home care nurse initiated contact. The GP was regularly medically informed by the specialist and educated on management of cancer patients. In the one RCT from Hansen et al. (2011) and Bergholdt et al. (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on different aspects of rehabilitation. Afterwards the GP was informed on patient specific rehabilitation needs and encouraged to pro-actively contact the patient to support the patient in his/her needs.

Study outcomes

Most often measured primary outcomes were health care utilization [15,16,21,22,24] and quality of life [15–17,22], as presented in Table 2. Other outcomes were patient and GP perceptions of care, symptoms, coping, and empowerment. The following outcomes were not measured in found articles: healthcare experience by informal caregivers, and disease specific outcomes (i.e. progress, mortality). Outcomes are described in more detail below.

Intervention fidelity/compliance and health care use

Health care use is related to the uptake of the intervention. For example, if the intervention aims at more GP involvement, health care use is likely to increase. Although all interventions aimed at increased involvement of primary care, four interventions did not show a significant increase of GP consultations [15,18,21,22]. Correspondingly, the uptake of interventions appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al. [18] an

"active involvement" intervention, in which GP pro-activity was comparable to GP proactivity in the control group (52 to 60%) [18]. In two studies, information transfer to the GP by the patients was hardly used or remembered by the majority of the GPs [21,22].

Five studies, evaluated the effect of the intervention on hospital and/or primary care resource use. These studies showed no significant effect on secondary care health care use [21,22,24]. Only the subgroup of older patients (≥70 years of age) had a significantly lower use of secondary care [24] when primary care was actively involved. The studies reported no difference in the number of GP consultations in the intervention group compared to the control group [15,16,21–23], although GP consultations where part of the interventions.

Patient perception

Positive effects on patients' satisfaction with care were indicated by three studies. Extended information by PHR or discharge summary improved patient perceived intersectoral cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that 'the GP could help in the way a specialist could not' [23]. Regardless of the uptake of the intervention, one study showed an improved satisfaction with communication and participation with care [22]. The significantly higher levels of perceived GP support in Nielsen et al.(2003) shortly after the intervention, declined to non-significant levels at six months after start of intervention. The authors did not present a mean difference overtime. One study with a low uptake of intervention showed no significant effect on patients satisfaction [20].

Quality of life and psychological outcomes

No study found a significant effect on quality of life [15,17,22]. Johnson et al (2001) [23], showed a significant difference in change of depression scores (p0.04). In the intervention group depression scores remained unchanged, whereas scores in the control group deteriorated significantly. Also, using a PHR combined with routinely visits to the GP led to a significantly higher reduction of the number of clinically anxiousness patients compared to usual care [23].

GPs perceptions of care

Four out of five studies evaluating effects on GPs perceptions of care, did not find relevant effects on GP's confidence in disease management and knowledge nor in the communication with the specialist [16,20,21,23]. Studies in which information was carried by the patient (a PHR or informational cards) showed little impact on GP satisfaction with care mostly due to low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant positive effects on GP perceived intersectoral cooperation and GP satisfaction with information.

Figure 1: Flow diagram for selection of studies, based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14].

Abbreviations: GP: General practitioner

Figure 2. Risk of bias measured according to the EPOC criteria.

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Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
Drury et al. (2000)[22]	N = 650	*Inclusion*	UC and intervention vs UC
		During any RT clinic visit	Patients received a PHR
	60% ♀	Time after diagnosis not specified	Initiative GP contact: Patient
UK	MAM (33%), LUN, GI, GYN, URO, H&N, other (13%);	*Intervention*	PHR: A4 size plastic wallet content:
		Upon enrolment	- Communication sheets for use by patient, family care givers, and health care professionals
			- Medication records and appointment and contact details
	Cancer stage not specified	*Follow up*	- An explicit invite to caregivers to use the PHR
	59 patients died ≤ 3 months from baseline, which may reflect inclusion of patients with advanced disease	3 months	Patients were instructed to:
			- Use the PHR as an aide memoire and means of communication
			- Show it to anyone involved in their care
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20] Denmark	N = 955	*Inclusion*	Intervention vs UC
		Cancer diagnosis <3 months	Rehabilitation primary care program
	72% ♀		Initiative GP contact: Healthcare worker
		Intervention	
	MAM (43%), LUN, GI, other (19%), MEL	Upon enrolment	Rehabilitation primary care program consisting of:
			- Patient interview by rehabilitation coordinator (nurses) on physical, psychological, sexual, social, work-related and economy related rehabilitation needs
		Follow up	
	Cancer stage unknown, no deceased	14 months	- RC presents patient individual and general cancer patients rehabilitation needs to GP
			- RC encouraged GP to pro-active contact patient to facilitate a rehabilitation process
Johansson et al. (2001)[24]	N = 463	*Inclusion*	Intervention vs UC
		Newly diagnosed patients (<3 months after diagnosis)	Intensified primary care program
	57% ♀		Initiative GP contact: Healthcare worker
Sweden	MAM (47%), GI, PRO	*Intervention*	Individual Support intervention consisting of:

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
		Upon enrolment	- Intensified primary health care by means of recruitment of a home care nurse
	22% with advanced disease		- Education and supervision in cancer care for both GP and home care nurse
		Follow up	- Active involvement of dietician and psychologist care
		3 months	
Johnson et al. (2015)[23]	N = 97 86% ♀	*Inclusion* During first course of CT *Intervention*	UC and intervention vs UC (discharge summary) Shared Care program + PHR Initiative GP contact: Patient
Australia	MAM (76%), HEM, GYN, GI	First through last course of CT	PHR content: - Chemo schedule, appointments and medication information
	Cancer stage 3.3% palliative	*Follow up* 6 cycles of CT	- Communication pages for specialist and GP
	Stopped early (slow accrual); underpowered for the main analysis		Patients received: - A PHR - Instruction to visit their GP routinely after every course of CT (patient initiative) GPs received: - Educational resources about adverse treatment effects and apt solutions - Encouragement to use the communication page in PHR A project coordinator (a trial nurse) was appointed to facilitate communication between patient, GP, specialist and researchers
Luker et al. (2000)[21]	N = 79 100% ♀	*Inclusion* <4 weeks after diagnosis *Intervention*	UC and intervention vs UC Patients received information cards Initiative GP contact: Patient
UK	MAM (100%)	At start of treatment	Information card content: - Rationale for patient specific treatment; Prognostic indicators, complications, side effects and
	Cancer stage 100% curative	*Follow up* 4 months	referral indicators

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
			Patients received: -Informational cards to provide rapid access to treatment-specific information for members of the primary health care team - Encouragement to contact their primary health care team and show the Information cards
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16] Denmark	N = 248 64% ♀ MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL Cancer stage 15% palliative	*Inclusion* Newly diagnosed patients *Intervention* From referral onwards; during treatment *Follow up* 6 months	UC and intervention vs UC Shared care program Initiative GP contact: Patient Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment - Expected role of the GP - Contact information of all involved medical personnel Patients received: - Oral and written notification about the information provided to their GP - Encouragement to contact their GP when facing problems they assumed could be solved in this setting

Table 1 – Details of the interventions

Abbreviations: CT = Chemotherapy; GER = germinal cell; GI = gastrointestinal tract; GP = General Practitioner; GYN = gynaecological; HEM = haematological; H&N = head and neck; LUN = lung; MAM = mamma; MEL = melanoma; PHR = Patient Held Record; PRO = prostate; RC = Rehabilitation Coordinator; RT = Radiotherapy; UC = Usual Care; UK= United Kingdom; URO = urogenital; vs = versus.

Reference **Country**	**Primary and secondary outcome measures (instrument used)** **Timing of measurement**	**Findings if applicable to study:** **1. Uptake of intervention** **2. Health care use** **3. Patient related outcomes** **4. GP related outcomes**
Drury et al. (2000)[22]	*Primary* - Health care use (patient reported) - Patient satisfaction with communication and participation in care (SDQ) - Quality of life (EORTC QLQ-C30) *Secondary* - GP views on PHR (SDQ) *Measurements* Single measurement at 3 months	**Uptake of intervention** 27.3% of 202 responding GPs had seen the PHR **Health care use** (*intervention vs. controls)* Contact with care providers in 3 months follow-up; • Visit GP 78% vs. 85% • Visited secondary care clinics 95% vs. 95% **Patient related outcomes** *(intervention vs control)* - Satisfaction communication and participation in care mean ± SD (scale 1-5): 3.83±0.59 vs. 3.80±0.59, (95% CI 0.09- 0.15) - Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05 - Quality of life mean global scores: 66.8±24.2 vs. 65.3±23.7 **GP related outcome** *(seen PHR vs. not seen PHR)* - GP agrees that patients should have full access to their records 57% vs. 57%
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	*Primary* Quality of life (EORTC QLQ-C30) *Secondary* -Psychological distress (POMS) -Symptoms (scale of the EORTC QLQ-C30) -Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth) -GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth) -GP's satisfaction with their contribution to the patient's	**Uptake of intervention** pro-activity of GP intervention vs control: GP reported 61.2% vs 55.2% p=0.10, patient reported 60.1% vs51.9% p=0.15 **Patient related outcomes** *(intervention vs control)* -Quality of life; mean difference [95%CI]; • at 6 months 1.25 [-2.4-4.9] • at 14 months -0.71 [-4.3-2.8] - Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0] - Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5] - Patient satisfaction with, • GP on five dimensions, OR adj [95%CI] All NS; Doctor–patient relationship 0.94 [0.35-2.47], Medical care 1.2 [0.5-3.0], Information and support 1.6 [0.6-

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	rehabilitation course (two ad hoc questions, likert scale, at 14 mth) *Measurements* At 6 and 14 months	4.1], Organization of care 1.3 [0.8-2.1], GP's accessibility 1.2 [0.6-2.3] • GP support during the cancer course, OR adj [95%CI]; 1.14 [0.7-1.8] - Pro-activity GP and rehabilitation activity patient, OR adj [95%CI]; 1.96 [1.2-3.3] **GP related outcomes** *(intervention vs control)* - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[24]	*Primary* Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing) *Measurements* Single measurement at 3 months	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* Subgroup analysis for age (year) hospital admissions mean number of admissions ± SD, 3 months follow-up; • ≥70y: 0.4±0.6 vs. 0.9±1.0 (Student T test p = 0.0002) • <70y: 1.0±1.0 vs. 0.9±0.8 (Student T test p= 0.38) - Days of hospitalization; • ≥70y: 3.8±8.8 vs. 8.9±18.8 (Tukey HSD, p <0.01) • <70y: 4.4±5.9 vs. 3.6±4.9 (Student T test p = 0.24) - Mean number of outpatient care visits per patient; • ≥70y: 6.8±8.8 vs. 6.0±7.0 (Student T test p = 0.53) • <70y: 13.4±11.2 vs.12.9±11.5 (Student T test p = 0.7257) - Acute visits; • ≥70y: in 5% vs. 15% of patients (χ^2 p = 0.034) • <70y: in 11% vs. 10% of patients (χ^2 p = 0.80)
Johnson et al. (2015)[23]	*Primary* - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC) - Empowerment (PES)	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* - Emergency department presentations: no significant between-group differences were observed - Average number of GP visits 2.79 vs 1.61, p < 0.001

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	Secondary - Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits) - Patient perception of care (SDQ) - GP perception of care (SDQ) *Measurements* - before treatment - midway through treatment - after treatment	**Patient related outcomes** *(intervention vs control)* Patient perception of care; - GP could help in ways specialist could not: 57% vs. 19% ($\chi^2 = 11.5$; p = 0.002) - Patient opinion concerning PHR/GP visit after CT course: • 81% considered PHR useful • 35% considered visit inconvenient Depression; Geometric mean score [95%CI] • at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40] • after treatment: 4.04 [3.25 to 4.83] vs 4.72 [3.72 to 5.72] p = 0.04 for comparison of groups over time Anxiety; Geometric mean score [95%CI] • at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32 • after treatment: 5.49 [4.54 to 6.43] vs 5.24 [4.26 to 6.22] p = 0.80 for comparison of groups over time - Subgroup analysis for number of clinically anxious patients • at baseline: 14 CA patients vs 11 CA patients • after treatment: 3 CA patients vs 5 CA patients Decline intervention p=0.002; control p=0.014 Coping; Geometric mean difference over time -0.7 vs 0.1 p=0.35 Empowerment; Geometric mean difference over time 0.9 vs 0.9 p=0.47 **GP related outcome** *(intervention vs control)* - GPs satisfied with communication: 82% vs. 95% - GP confidence in managing: • side effects 85% vs. 71% (p =0.45) • psychological issues 97% vs. 81% (p= 0.04)
Luker	*Primary*	**Uptake of intervention** 8 of the 31 interviewed GPs recall seeing the Information Card

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
et al. (2000)[21]	- Patient utilization of the primary health care team (interview) - GP views after study (interview) *Measurements* - at baseline (preoperative) - 4 months after diagnosis	**Health care use** (*intervention vs. controls)* - Patient initiated contact • with GP ≥1 contact in 71% vs. 73%, p = 0.95 • district nurses no contact in 24% in both groups **GP related outcome** *(intervention)* - Recommending information card 7 of 8 GPs who recall intervention

Reference **Country**	**Primary and secondary outcome measures (instrument used)** **Timing of measurement**	**Findings if applicable to study:** **1. Uptake of intervention** **2. Health care use** **3. Patient related outcomes** **4. GP related outcomes**
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16]	*Primary* - Patient attitude towards the health care system (intersectoral cooperation and 'not feeling left in limbo' (SDQ) - Patient GP global assessment (one question) - Quality of life (EORTC QLQ-C30) - Performance status of function and self-care (ECOG) - Health care use: GP consultations (patient and GP reported SDQ) - GP assessment (SDQ) of: • Discharge information value • Own knowledge (patients confidence) • Own wishes to receive further information • Intersectoral cooperation *Measurements* Patient: - First measurement "Soon after the introduction of the intervention."(0 month) - 6 months GP assessment: timing unknown	**Uptake of intervention** Not reported **Patient related outcomes** *(intervention vs control)* - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055 - At 6 months 'Not feeling left in limbo'; 65.49 vs 55.58, p=0.055 - Patient GP global assessment; • at 0 months: 71.0 vs 58.68 (p = 0.04) • at 6 months: 68.9 vs 64.02 (p = 0.44) Quality of life and performance status: nor relevant or significant differences described **Health care use** (*intervention vs. controls)* - GPs reported regular contact; 75% vs. 75% - Patient reported GP consultation; • at 0 months: 67.8% vs 74.8% (p = 0.583) • at 6 months: 38.0% vs 31.5% (p = 0.046) **GP related outcome** *(intervention vs. control)* - Discharge information value GP on; • Psychosocial conditions 60% vs. 26% (p <0.001) • Information their patient had received 84% vs 49%, (p <0.001) - GP knowledge 94.8% vs 96.6% (NS) - GP wish more information 21% vs. 38% (p = 0.009) - GP rate intersectoral cooperation 'satisfactory' 85% vs. 73%, (p = 0.033) -Intersectoral contacts: 25/100 vs. 17/97 GPs had ≥1 contact, p = 0.23

289 Table 2. Study outcomes.

Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FACT-G = Functional Assessment of Cancer Therapy – General; GP = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs Assessment for Advanced Cancer Patient; NS = not significant, no p-value or confidence interval was provided nor could be calculated; OR adj = Odds ratio adjusted for confounders sex and age; PACIC = Patient Assessment of Chronic Illness Care; PES = Patient Empowerment Scale; PHR = Patient Held Record; POMS= Profile of Mood States; SD = Standard Deviation; SDQ = Self Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus; χ^2= Chi-square distribution.

Discussion

This systematic review shows that research evaluating the effect of interventions designed to involve the GP during curative cancer treatment is scarce. The six studies that were published evaluate either additional information transfer to the GP or tailored primary care. In general, the intervention uptake was low, and the risk of bias was low to moderate. Results indicate a positive effect of increased GP involvement in cancer care on patient satisfaction with care but not on quality of life. In subgroups, it may lower health care use and anxiety.

Even though active involvement of the GP during cancer treatment might have positive effects, implementation appears to be difficult to realize. This is seen for all interventions, irrespective whether the GP contact is initiated by the patient or by the healthcare provider. Drury et al (2000) suggested that a reason for the low uptake might be that GPs are not motivated to participate in the care of patients with curative disease as they do not feel closely involved in this stage [22]. This may explain why no studies were found where the GP was the initiator of involvement in care during cancer treatment. Another reason for the low uptake provided by the authors in the original articles include the difficulty to promote proactivity to GPs [17,18]. Johnson et al. (2015) showed that using a coordinator results in higher uptake of intervention [23].

Specific subgroups may benefit more from involvement of primary care. A stronger decrease in anxiety was reported in patients with elevated levels of anxiety and [23] the GP involvement led to a reduction in secondary care use among older patients [24]. It has been suggested that different cancer diagnoses bring different psychological burdens and care needs [25], but this could not be concluded from the present studies.

This review has several limitations. To provide a comprehensive overview we used a broad research question and search strategy. Consequently, we included heterogeneous studies. Due to this heterogeneity and the low number of available studies, data pooling was not possible, the estimate of effect could not be assessed according to the GRADE approach, and strong conclusions could not been drawn and. Furthermore, title and abstract were screened by one researcher, possibly leading to missing studies. However, since screening of references did not provide additional studies, we expect this limitation to be without effect. Moreover, to be complete, we included studies that also included palliatively treated patients. Some publications did not show separate results for the curatively- and palliatively treated population. We used a threshold for the minimum proportion of curatively treated patients

(i.e., 75%), but we cannot exclude that the observed effects were influenced the inclusion of palliative patients. Finally, the review relied solely on published studies, so we cannot exclude publication bias.

Our review shows that further large studies with a robust design are needed, which should focus on the effect of primary care involvement for various populations, including specifications for cancer types and vulnerable populations (e.g. elderly, and patients with physical or mental comorbidity). These studies should provide us with a definite answer on the effect of GP involvement in the cancer care path, addressing the questions when and how to organize the role of primary care and specifically for whom. In addition, this knowledge should facilitate primary care workers to appropriately implement their role, making full use of their specific expertise by consideration of the patients' context and values, provided in a trusted environment. To improve uptake of intervention we used only existing health care facilities in the intervention design of a RCT involving the GP and a homecare oncology nurse after diagnosis and during curative cancer treatment. Results of this study will be published in 2018/2019. [26]

Conclusion

Literature addressing the effects of interventions designed to actively involve the GP during curative cancer treatment is scarce and the results are diverse. Even though uptake of interventions is generally low, these studies suggest positive effects of increased primary care involvement on patient satisfaction. Other positive effects were seen, particularly for vulnerable populations. In view of various health care strategies which aim to transfer parts of the cancer care paths from secondary to the primary care, it is adamant to gather more robust evidence for customized interventions to enable the efficient and effective involvement of the GP during cancer treatment.

Data sharing statement

For the current study we did not generate new data. Therefore, sharing new data is not possible.

Declaration of Interest

Conflicts of interest: none

Role of the Funding Source

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Contributors

Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP); analysis and interpretation of data (IP, JB, AM, CW). Drafting the article or revising it critically for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the version to be submitted (IP, JB, AM, NW, EW, CH).

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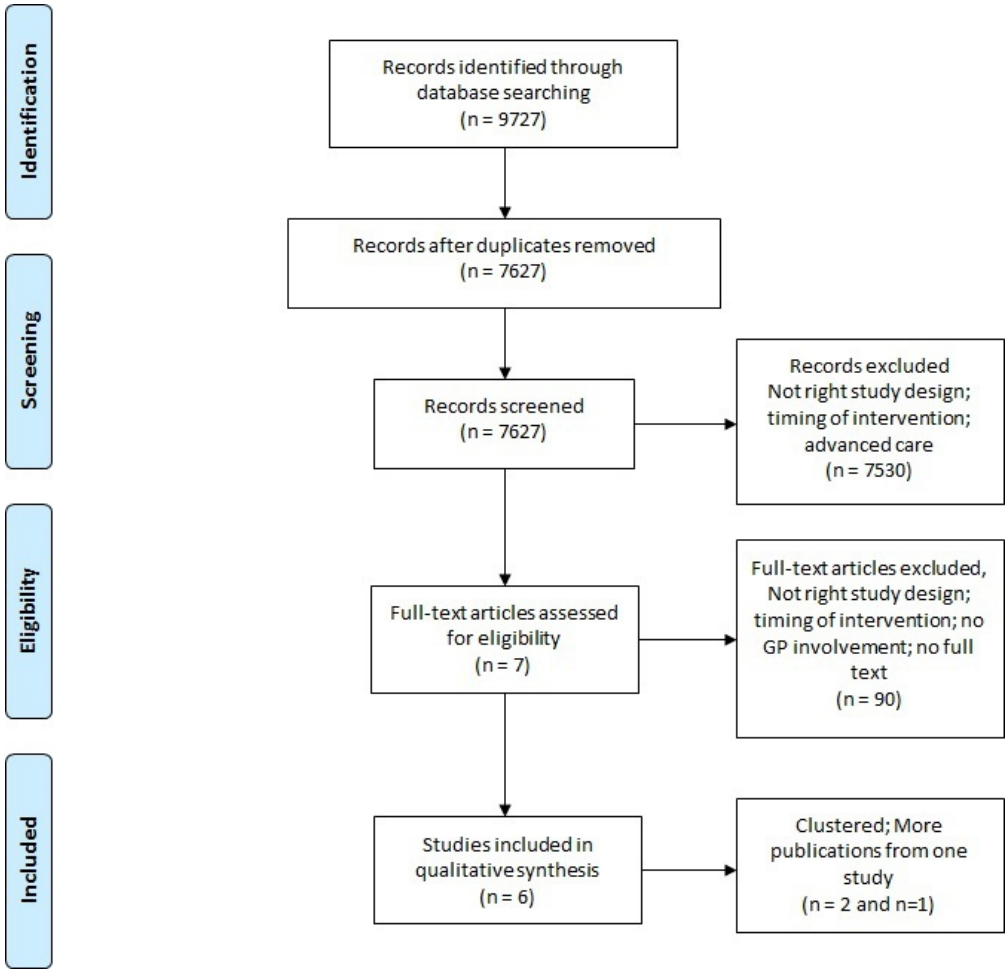

Figure 1. PRISMA flow diagram.

56x54mm (300 x 300 DPI)

Figure 2. Risk of bias measured according to the EPOC criteria.

48x62mm (300 x 300 DPI)

Search terms

Syntax PUBMED

#1

((((((((((((((((((((((“primary care”[Title/Abstract]) OR “primary health care”[Title/Abstract]) OR “primary medical care”[Title/Abstract]) OR “first-contact medical care”[Title/Abstract]) OR “first line care”[Title/Abstract]) OR “primary care physician”[Title/Abstract]) OR “primary care physicians”[Title/Abstract]) OR “general practitioner”[Title/Abstract]) OR “general practitioners”[Title/Abstract]) OR GP[Title/Abstract]) OR GPs[Title/Abstract]) OR G.P.[Title/Abstract]) OR GP-organised[Title/Abstract]) OR “family doctor*”[Title/Abstract]) OR “family practice*”[Title/Abstract]) OR "primary health care"[MeSH Terms]) OR "physicians, primary care"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "primary care nursing"[MeSH Terms]) OR "nursing care"[MeSH Terms]) OR "general practitioners"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "family practice"[MeSH Terms])

#2

(((((((oncolog*[Title/Abstract]) OR cancer*[Title/Abstract]) OR malignancy[Title/Abstract]) OR carcinoma[Title/Abstract]) OR ((tumor[Title/Abstract] AND malignant[Title/Abstract]))) OR “medical oncology”[MeSH Terms]) OR carcinoma[MeSH Terms]) OR ((neoplasms[MeSH Terms] AND malignant[Title/Abstract])))

#3

((((((((((((((((((((((((((((((((((care[Title/Abstract]) OR continu*[Title/Abstract]) OR follow-up[Title/Abstract]) OR surveillance[Title/Abstract])) OR “patient discharge”[Title/Abstract]) OR “hospital discharge”[Title/Abstract]) OR transmural[Title/Abstract]) OR collaborative[Title/Abstract]) OR

interdisciplinary[Title/Abstract]) OR multidisciplinary[Title/Abstract]) OR "liaison nurse*"[Title/Abstract]) OR "health care planning"[Title/Abstract]) OR "health care management"[Title/Abstract]) OR "community health planning"[Title/Abstract]) OR "service integration"[Title/Abstract]) OR "services integration"[Title/Abstract]) OR "professional-patient relations"[Title/Abstract]) OR "professional-family relations"[Title/Abstract]) OR "shared services"[Title/Abstract])) OR "multi professional working"[Title/Abstract]) OR interprofessional[Title/Abstract]) OR "multi agency working"[Title/Abstract]) OR "inter agency working"[Title/Abstract]) OR "case management"[Title/Abstract]) OR "patient discharge"[MeSH Terms]) OR "patient care planning"[MeSH Terms]) OR "patient care team"[MeSH Terms]) OR "continuity of patient care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case management"[MeSH Terms]) OR "community health planning"[MeSH Terms]) OR "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient relations"[MeSH Terms]) OR "interprofessional relations"[MeSH Terms]) OR "professional-family relations"[MeSH Terms]) OR "cooperative behavior"[MeSH Terms])

#4 (((((("randomized controlled trial"[Publication Type]) OR random*[Title/Abstract]) OR control*[Title/Abstract]) OR intervention*[Title/Abstract]))

Combining search terms: #1 AND #2 AND #3 AND #4

Syntax EMBASE

#1

'primary care':ab,ti OR 'primary health care':ab,ti OR 'primary medical care':ab,ti OR 'first-contact medical care':ab,ti OR 'first line care':ab,ti OR 'primary care physician':ab,ti OR 'primary care physicians':ab,ti OR 'general practitioner':ab,ti OR 'general practitioners':ab,ti OR gp:ab,ti OR gps:ab,ti OR g.p.:ab,ti OR 'gp organised':ab,ti OR 'gp organized':ab,ti OR 'family doctor':ab,ti OR 'family doctors':ab,ti OR 'family practice':ab,ti OR 'family practices':ab,ti OR 'primary health care'/exp OR 'primary health care' OR 'general practice'/exp OR 'general practice'

#2

oncology:ab,ti OR cancer:ab,ti OR malignancy:ab,ti OR carcinoma:ab,ti OR (tumor:ab,ti AND malignant:ab,ti) OR ('neoplasm'/exp OR neoplasm AND malignant:ab,ti) OR 'malignant neoplastic disease'/exp OR 'malignant neoplastic disease'

#3

care:ab,ti OR continu*:ab,ti OR 'follow up':ab,ti OR surveillance:ab,ti OR 'discharging plan':ab,ti OR 'discharge plan':ab,ti OR 'discharge planning':ab,ti OR 'patient discharge':ab,ti OR 'hospital discharge':ab,ti OR transmural:ab,ti OR collaborative:ab,ti OR interdisciplinary:ab,ti OR multidisciplinary:ab,ti OR 'liaison nurse':ab,ti OR 'health care planning':ab,ti OR 'health care management':ab,ti OR 'community health planning':ab,ti OR 'service integration':ab,ti OR 'services integration':ab,ti OR 'professional-patient relations':ab,ti OR 'professional-family relations':ab,ti OR 'shared services':ab,ti OR 'shared notes':ab,ti OR 'multi professional working':ab,ti OR interprofessional:ab,ti OR 'multi agency working':ab,ti OR 'inter agency working':ab,ti OR 'case management':ab,ti OR 'patient care'/exp OR 'integrated health care system' OR 'health care planning'/exp

#4

'randomized controlled trial'/exp OR random*:ab,ti OR control*:ab,ti OR intervention*:ab,ti

Combining search terms: #1 AND #2 AND #3 AND #4

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n.a.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n.a.
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n.a.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No pooling of data not assessed.
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n.a.
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 and figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	15 – 17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	18 - 22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n.a.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n.a.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n.a.
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	25

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

PRISMA 2009 Checklist

BMJ Open

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-026383.R1
Article Type:	Research
Date Submitted by the Author:	04-Dec-2018
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Primary Subject Heading:	Oncology
Secondary Subject Heading:	General practice / Family practice, Patient-centred medicine
Keywords:	PRIMARY CARE, Shared care, Curative treatment, Patient satisfaction, General Practitioner, Cancer

Journal

BMJ Open

Type of Contribution

General and Supportive Care; Systematic review.

Word Count (excluding title page, abstract, tables, acknowledgements, contributions and references): 3431/4000 words, 5/5 tables or figures, 29/100 references.

Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

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Second Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Abstract

Words: 300/300

Objective: The role of primary care providers (PCP) in the cancer care continuum is expanding. In the post-treatment phase, this role is increasingly recognized by policy makers and health care professionals. During treatment, however, the role of PCP remains largely undefined. This systematic review aims to map the content and effect of interventions aiming to actively involve the General Practitioner (GP) during cancer treatment with a curative intent.

Study design Systematic review

Participants Cancer patients treated with curative intent

Data sources Randomized controlled trials (RCTs), controlled clinical trials (CCT), controlled before and after studies and interrupted time series focusing on interventions designed to involve the GP during curative cancer treatment were systematically identified from PubMed and EMBASE and were subsequently reviewed. Risk of bias was scored according to the EPOC risk of bias criteria.

Results Five RCTs and one CCT were included. Interventions and effects were heterogeneous across studies. Four studies implemented interventions focussing on information transfer to the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on patient satisfaction with care was found in three studies. Subgroup analysis suggest a reduction of health care use in elderly patients and reduction of clinical anxiety in those with higher mental distress. No effects are reported on patients' quality of life (QoL).

Conclusion Interventions designed to actively involve the GP during curative cancer treatment are scarce and diverse. Even though uptake of interventions is low, results suggests a positive effect of GP involvement on patient satisfaction with care, but not on QoL. Additional effects for vulnerable subgroups were found. More robust evidence for tailored interventions is needed to enable the efficient and effective involvement of the GP during curative cancer treatment**.**

PROSPERO registration number: CRD42018102253

Strengths and Limitations of this study

- This is the first review that systematically reviews evidence based interventions, aiming at general practitioner involvement during the curative treatment phase of the cancer care continuum.
- The electronic database search was performed without restriction on languages and period.
- We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate tool to assess bias for complex interventions.
- The title/abstract screening is done by single reviewer, two authors screened the full-text and the search was complemented with reference checks of relevant articles.
- The included studies are heterogeneous in intervention and outcome and therefore strong conclusions could not be made.

Keywords

- Primary care
- General Practitioner
- Shared care
- Cancer
- Curative treatment
- Patient satisfaction

Background

Cancer incidence and prevalence is increasing as a result of the aging population combined with expanding diagnostic and treatment possibilities. Due to improved outcome following cancer treatment, the nature of cancer treatment is changing toward more chronic disease management. Health policy makers and health care professionals therefore call for a change in the way cancer care is provided, to focus on more integrated and personalized cancer care during and after treatment [1,2]. In countries with gatekeeper health care systems, such as The Netherlands, GPs are generally the coordinators of care, who have a longstanding and personal relationship with their patients. This enables knowledge of both the medical and personal situation of the patient and care, which is provided in a trusted environment with a familiar health care worker. Therefore, primary care is increasingly promoted as the preferred setting to provide integrated support during and after active cancer treatment, both to meet patient preference and to stabilize costs [2,3]. The concept of shared care has been suggested as the way forward in the organization of integrated cancer care [2,3]. Shared care is an organisational model involving both general practitioners (GPs) and specialists in a formal, explicit manner. Shared care models enhance the optimal access of patients to both hospital care and community based supportive care along the entire cancer care continuum [4]. In shared care models, GPs, along with other primary care professionals, add their competence to balance the biomedical aspects of cancer care with the psychosocial context and preferences of the individual patient [5], ensuring personalized, integrated care.

Traditionally, the role of primary care in palliative and end-of-life care is well established [6]. In addition, evidence suggests a solid role for primary care in cancer follow-up after treatment and survivorship care [7–9]. Less well appreciated, however, is primary care involvement during cancer treatment, particularly for patients treated with a curative intent. It is well established that in this phase patients frequently experience psychosocial distress and treatment-related side effects that negatively affect their quality of life [10]. Several studies suggest primary care involvement during active treatment, to improve patient outcomes and to ensure continuity in guidance from primary care [3,11]. In the near future the GP might even be involved in treatments in primary care such as chemo- or hormone therapy. Currently however, involvement of primary care is generally restricted to supportive care during cancer treatment.

So far, the most effective approach to involve primary care during cancer treatment remains unclear.

This systematic review aims to provide a comprehensive overview of the content and effect of interventions aiming at active involvement of the general practitioner during cancer treatment with curative intent compared to usual care.

Methods

Data source and search

A literature search was conducted in PubMed and EMBASE for articles describing randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies, and interrupted time series published in any language until the 3rd of July 2018. We used a search strategy that was previously applied in a review assessing continuity of care in the follow-up of patients with cancer [12]. Subsequently, this strategy was adapted for completeness and relevance based on sequential testing of search strategies to develop our final search strategy. The details of the sequential and final search strategies are listed in appendix A. The search terms include keywords and controlled vocabulary terms surrounding the central themes "general practitioner", "primary care", "oncology", and "care". Outcome measures and comparing study arm were not included in the selection criteria to widen the scope of the review. Instead of a database integrated filter, a tailored methodological search filter was used to limit retrieval to appropriate study design [12]. We reviewed references of selected articles for additional papers.

Outcomes are included if they are related to the quality of healthcare (e.g. healthcare use), the healthcare experience of: healthcare professionals, informal caregivers, and patients, or outcomes at the patient-level, with a focus on, e.g., disease, quality of life, and psychosocial impact.

Study selection

Articles were selected if they described an intervention; (1) for cancer patients, (2) starting during curative treatment, (3) evaluating involvement of the GP, and (4) tested in a randomized controlled setting, CCT, controlled before and after studies or interrupted time series. Studies with a majority (>75%) of curative patients were included. In case the proportion of curative patients was unclear, the original authors were contacted. Without response, the inclusion of the trial was based on >75% percentage patient survival during the trial.

Data extraction and management

To determine relevance, the records were divided and screened on title and abstract by two single reviewers (IP,JB) and discussed with three additional reviewers in case of doubt (AM,CH and JB or IP). Two authors (IP,JB) performed full-text screening. Disagreements on eligibility were resolved in group discussion with researchers and clinicians (IP,JB,AM,CH).A meta-analysis was planned to be conducted if possible.

Patient and public involvement

Patients and public were not involved in the design of the current study.

Quality assessment

Risk of bias for individual studies was scored by two authors (JB,IP) with the risk of bias criteria from the "Effective Practice and Organisation of Care Group (EPOC), which is a Cochrane review group [13]. In case outcomes of homogeneous study designs could be merged we rated the body of the evidence following the Grades of Recommendation, Assessment, Development and Evaluation approach (GRADE) [14] from the Cochrane collaboration. This systematic review is reported following the PRISMA 2009 checklist [14].

Results

Study selection

As shown in Figure 1, 9,727 records were eligible for inclusion after removal of duplicates. Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP involvement started after completion of primary cancer treatment, or (3) no RCT, CCT, controlled before and after study or interrupted time series design was used. Three studies published multiple articles based on the same data [15–22]. As a result, five RCTs and one CCT were considered eligible for inclusion, which were described in ten articles. No additional eligible studies were identified in the reference lists of selected studies. Figure 2, Table 1, and

2 show a detailed account of the risk of bias, patient population, interventions, outcomes assessed and observed results for each study. Given the various research questions, interventions and heterogeneity of outcome measures, pooling of data, and GRADE assessment was not feasible.

Quality of studies

The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et al. (2003) show a high risk of bias, resulting from high risk of selection and information bias [15,16,23]. Drury et al. (2000) scored a medium risk of bias [24]. And the studies of Johnson et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk of bias [17–19,22,25]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several limitations should be kept in mind. The randomization produced an imbalance, which influenced comparability of outcomes between study groups without corresponding correction in the analyses. Furthermore, it was not reported whether a baseline measurement was performed and the exact timing of the first measurement (Table 2). Also, the percentage of missing data was 33% in the intervention and 26% in the control group [15].

Study populations

The six eligible studies were conducted in Europe (five) and Australia (one) among different cancer patient populations over the past two decades. Breast cancer patients were the most commonly studied group (between 33-100% of the study populations). Five RCTs included patients with more than one type of cancer, in different stages. Three studies included palliatively treated patients (<25% of total study population). In two RCT's cancer stage was not specified.

Usual care

In most studies, usual care was not described in detail. Only Luker et al. [23] described the structured care that usual care patients received, which included home visits from a breast care nurse and written patient information on treatments. In general, the patient's GP received a discharge summary [15–17,19,20,25] at the end of the treatment period [15,16] or after each

visit [25]. Other types of transferred information to the GP included an extract of the hospital record [15,16] or communication by telephone [25]. Two studies did not describe what usual care entailed [21,22,24].

Type of interventions

All participants received usual care, which was extended when the participant was appointed to the intervention. The interventions in the studies (Table 1) were heterogeneous, but can be divided in mainly information transfer to the GP (n=4) [15,16,23–25] and tailored primary care interventions (n=2) [17–20,22].

Interventions focusing on information transfer, provided additional, disease specific educational, and practical information concerning treatment and care directly to the GP or via the patient. Interventions were either directed at enhancing communication between GP and another party (i.e. secondary care or patient), or directed at improving patient's attitude towards the healthcare system (i.e. healthcare in general or intervention), physical- or psychological complains. Three interventions provided patients with information, which was to be transferred to the GP. In one CCT [23], informational cards were provided to the patients for use in primary care. Two other RCTs described an intervention with a Patient Held Record (PHR) [24,25] aimed to facilitate intersectoral communication, to provide patients with an aide memoire, and with the opportunity to stay actively involved in their treatment. One RCT supplied the GP with patient specific discharge summaries by secondary care, aiming to enhance GP knowledge of chemotherapy treatment and expected adverse effects [15,16].

The tailored primary care interventions aimed to support patients in managing their disease and treatment [17,18,20,22]. The interventions were to diverse to be merged and they are therefore described separately. In Johansson et al. (2001) [22] primary care was intensified by means of recruitment of a home care nurse, psychologist, dietician and training of the GP. The home care nurse initiated contact. The GP was regularly informed by the specialist and educated on management of cancer patients. In the one RCT from Hansen et al. (2011) and Bergholdt et al. (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on different aspects of rehabilitation. Afterwards the GP was informed on patient specific rehabilitation needs and encouraged to pro-actively contact the patient to support the patient in his/her needs.

Study outcomes

The most often measured primary outcomes were health care utilization [15,16,22–24] and quality of life [15–17,24], as presented in Table 2. Other outcomes were patient and GP perceptions of care, symptoms, coping, and empowerment. The following outcomes were not presented in the included articles: healthcare experience by informal caregivers, and disease specific outcomes (i.e. progress, mortality). Outcomes are described in more detail below.

Intervention fidelity/compliance and health care use

Health care use is related to the uptake of the intervention. For example, if the intervention aims at more GP involvement, health care use is likely to increase. Although all interventions aimed at increased involvement of primary care, four interventions did not show a significant increase of GP consultations [15,18,23,24]. Correspondingly, the uptake of interventions appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al. [18] which describes an "active involvement" intervention, in which GP pro-activity was comparable to GP proactivity in the control group (52 to 60%) [18]. In two studies, information transfer to the GP by their patients was hardly used or remembered by the majority of the GPs [23,24].

Five studies, evaluated the effect of the intervention on hospital and/or primary care resource use. These studies showed no significant effect on secondary care health care use [22–24]. Only the subgroup of older patients (≥70 years of age) had a significantly lower use of secondary care [22] when primary care was actively involved. Even though GP consultations where part of the interventions several studies reported no difference in the number of GP consultations in the intervention group compared to the control group [15,16,23–25]..

Patient perception

Positive effects on patients' satisfaction with care were indicated by three studies. Extended information by PHR or discharge summary improved patient perceived intersectoral cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that 'the GP could help in the way a specialist could not' [25]. Regardless of the uptake of the intervention, one study showed an improved satisfaction with communication and participation with care [24]. The significantly higher levels of perceived GP support shortly after the intervention described in Nielsen et al.(2003) declined to non-significant levels at six months

after start of intervention. The authors did not present a mean difference overtime. One study with a low uptake of intervention showed no significant effect on patients satisfaction [20].

Quality of life and psychological outcomes

No study found a significant effect on quality of life [15,17,24]. Johnson et al (2001) [23], showed a significant difference in change of depression scores (p0.04). In the intervention group depression scores remained unchanged, whereas scores in the control group deteriorated significantly. Also, using a PHR combined with routine visits to the GP led to a significantly higher reduction of the number of clinically anxiousness patients compared to usual care [25].

GPs perceptions of care

Four out of five studies evaluating effects on GPs perceptions of care did not find relevant effects on GP's confidence in disease management and knowledge nor in the communication with the specialist [16,20,23,25]. Studies in which information was carried by the patient (a PHR or informational cards) showed little impact on GP satisfaction with care mostly due to low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant positive effects on GP perceived intersectoral cooperation and GP satisfaction with information.

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Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
Drury et al. (2000)[24]	N = 650	*Inclusion*	UC and intervention vs UC
		During any RT clinic visit	Patients received a PHR
	60% ♀	Time after diagnosis not specified	Initiative GP contact: Patient
UK	MAM (33%), LUN, GI, GYN, URO, H&N, other (13%);	*Intervention*	PHR: A4 size plastic wallet content:
		Upon enrolment	- Communication sheets for use by patient, family care givers, and health care professionals
			- Medication records and appointment and contact details
	Cancer stage not specified	*Follow up*	- An explicit invite to caregivers to use the PHR
	59 patients died ≤ 3 months from baseline, which may reflect inclusion of patients with advanced disease	3 months	Patients were instructed to:
			- Use the PHR as an aide memoire and means of communication
			- Show it to anyone involved in their care
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	N = 955	*Inclusion*	Intervention vs UC
		Cancer diagnosis <3 months	Rehabilitation primary care program
	72% ♀		Initiative GP contact: Healthcare worker
		Intervention	
	MAM (43%), LUN, GI, other (19%), MEL	Upon enrolment	Rehabilitation primary care program consisting of:
			- Patient interview by rehabilitation coordinator (nurses) on physical, psychological, sexual, social, work-related and economy related rehabilitation needs
		Follow up	
Denmark	Cancer stage unknown, no deceased	14 months	- RC presents patient individual and general cancer patients rehabilitation needs to GP
			- RC encouraged GP to pro-active contact patient to facilitate a rehabilitation process
Johansson et al. (2001)[22]	N = 463	*Inclusion*	Intervention vs UC
		Newly diagnosed patients (<3 months after diagnosis)	Intensified primary care program
	57% ♀		Initiative GP contact: Healthcare worker
Sweden	MAM (47%), GI, PRO	*Intervention*	Individual Support intervention consisting of:

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
		Upon enrolment	- Intensified primary health care by means of recruitment of a home care nurse
	22% with advanced disease		- Education and supervision in cancer care for both GP and home care nurse
		Follow up	- Active involvement of dietician and psychologist care
		3 months	
Johnson et al. (2015)[25]	N = 97	*Inclusion*	UC and intervention vs UC (discharge summary)
		During first course of CT	Shared Care program + PHR
	86% ♀		Initiative GP contact: Patient
		Intervention	
Australia	MAM (76%), HEM, GYN, GI	First through last course of CT	PHR content:
			- Chemo schedule, appointments and medication information
	Cancer stage	*Follow up*	- Communication pages for specialist and GP
	3.3% palliative	6 cycles of CT	
			Patients received:
	Stopped early (slow accrual);		- A PHR
	underpowered for the main		- Instruction to visit their GP routinely after every course of CT (patient initiative)
	analysis		GPs received:
			- Educational resources about adverse treatment effects and apt solutions
			- Encouragement to use the communication page in PHR
			A project coordinator (a trial nurse) was appointed to facilitate communication between patient, GP, specialist and researchers
Luker et al. (2000)[23]	N = 79	*Inclusion*	UC and intervention vs UC
		<4 weeks after diagnosis	Patients received information cards
	100% ♀		Initiative GP contact: Patient
		Intervention	
UK	MAM (100%)	At start of treatment	Information card content:
			- Rationale for patient specific treatment; Prognostic indicators, complications, side effects and
	Cancer stage	*Follow up*	referral indicators
	100% curative	4 months	

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
			Patients received: -Informational cards to provide rapid access to treatment-specific information for members of the primary health care team - Encouragement to contact their primary health care team and show the Information cards
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16] Denmark	N = 248 64% ♀ MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL Cancer stage 15% palliative	*Inclusion* Newly diagnosed patients *Intervention* From referral onwards; during treatment *Follow up* 6 months	UC and intervention vs UC Shared care program Initiative GP contact: Patient Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment - Expected role of the GP - Contact information of all involved medical personnel Patients received: - Oral and written notification about the information provided to their GP - Encouragement to contact their GP when facing problems they assumed could be solved in this setting

Table 1 – Details of the interventions

Abbreviations: CT = Chemotherapy; GER = germinal cell; GI = gastrointestinal tract; GP = General Practitioner; GYN = gynaecological; HEM = haematological; H&N = head and neck; LUN = lung; MAM = mamma; MEL = melanoma; PHR = Patient Held Record; PRO = prostate; RC = Rehabilitation Coordinator; RT = Radiotherapy; UC = Usual Care; UK= United Kingdom; URO = urogenital; vs = versus.

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
Drury et al. (2000)[24]	*Primary* - Health care use (patient reported) - Patient satisfaction with communication and participation in care (SDQ) - Quality of life (EORTC QLQ-C30) *Secondary* - GP views on PHR (SDQ) *Measurements* Single measurement at 3 months	**Uptake of intervention** 27.3% of 202 responding GPs had seen the PHR **Health care use** (*intervention vs. controls)* Contact with care providers in 3 months follow-up; • Visit GP 78% vs. 85% • Visited secondary care clinics 95% vs. 95% **Patient related outcomes** *(intervention vs control)* - Satisfaction communication and participation in care mean ± SD (scale 1-5): 3.83±0.59 vs. 3.80±0.59, (95% CI 0.09- 0.15) - Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05 - Quality of life mean global scores: 66.8±24.2 vs. 65.3±23.7 **GP related outcome** *(seen PHR vs. not seen PHR)* - GP agrees that patients should have full access to their records 57% vs. 57%
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	*Primary* Quality of life (EORTC QLQ-C30) *Secondary* -Psychological distress (POMS) -Symptoms (scale of the EORTC QLQ-C30) -Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth) -GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth)	**Uptake of intervention** pro-activity of GP intervention vs control: GP reported 61.2% vs 55.2% p=0.10, patient reported 60.1% vs51.9% p=0.15 **Patient related outcomes** *(intervention vs control)* -Quality of life; mean difference [95%CI]; • at 6 months 1.25 [-2.4-4.9] • at 14 months -0.71 [-4.3-2.8] - Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0] - Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5] - Patient satisfaction with, • GP on five dimensions, OR adj [95%CI] All NS;

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	-GP's satisfaction with their contribution to the patient's rehabilitation course (two ad hoc questions, likert scale, at 14 mth) *Measurements* At 6 and 14 months	Doctor–patient relationship 0.94 [0.35-2.47], Medical care 1.2 [0.5-3.0], Information and support 1.6 [0.6-4.1], Organization of care 1.3 [0.8-2.1], GP's accessibility 1.2 [0.6-2.3] • GP support during the cancer course, OR adj [95%CI]; 1.14 [0.7-1.8] - Pro-activity GP and rehabilitation activity patient, OR adj [95%CI]; 1.96 [1.2-3.3] **GP related outcomes** *(intervention vs control)* - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[22]	*Primary* Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing) *Measurements* Single measurement at 3 months	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* Subgroup analysis for age (year) hospital admissions mean number of admissions ± SD, 3 months follow-up; • ≥70y: 0.4±0.6 vs. 0.9±1.0 (Student T test p = 0.0002) • <70y: 1.0±1.0 vs. 0.9±0.8 (Student T test p= 0.38) - Days of hospitalization; • ≥70y: 3.8±8.8 vs. 8.9±18.8 (Tukey HSD, p <0.01) • <70y: 4.4±5.9 vs. 3.6±4.9 (Student T test p = 0.24) - Mean number of outpatient care visits per patient; • ≥70y: 6.8±8.8 vs. 6.0±7.0 (Student T test p = 0.53) • <70y: 13.4±11.2 vs.12.9±11.5 (Student T test p = 0.7257) - Acute visits; • ≥70y: in 5% vs. 15% of patients (χ^2 p = 0.034) • <70y: in 11% vs. 10% of patients (χ^2 p = 0.80)
Johnson et al. (2015)[25]	*Primary* - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC)	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* - Emergency department presentations: no significant between-group differences were observed

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	- Empowerment (PES)	- Average number of GP visits 2.79 vs 1.61, p < 0.001
	Secondary - Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits) - Patient perception of care (SDQ) - GP perception of care (SDQ)	**Patient related outcomes** *(intervention vs control)* Patient perception of care; - GP could help in ways specialist could not: 57% vs. 19% (χ^2 = 11.5; p = 0.002) - Patient opinion concerning PHR/GP visit after CT course: • 81% considered PHR useful • 35% considered visit inconvenient
	Measurements - before treatment - midway through treatment - after treatment	Depression; Geometric mean score [95%CI] • at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40] • after treatment: 4.04 [3.25 to 4.83] vs 4.72 [3.72 to 5.72] p = 0.04 for comparison of groups over time Anxiety; Geometric mean score [95%CI] • at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32 • after treatment: 5.49 [4.54 to 6.43] vs 5.24 [4.26 to 6.22] p = 0.80 for comparison of groups over time - Subgroup analysis for number of clinically anxious patients • at baseline: 14 CA patients vs 11 CA patients • after treatment: 3 CA patients vs 5 CA patients Decline intervention p=0.002; control p=0.014 Coping; Geometric mean difference over time -0.7 vs 0.1 p=0.35 Empowerment; Geometric mean difference over time 0.9 vs 0.9 p=0.47
		GP related outcome *(intervention vs control)* - GPs satisfied with communication: 82% vs. 95% - GP confidence in managing: • side effects 85% vs. 71% (p =0.45) • psychological issues 97% vs. 81% (p= 0.04)

Reference **Country**	**Primary and secondary outcome measures (instrument used)** **Timing of measurement**	**Findings if applicable to study:** **1. Uptake of intervention** **2. Health care use** **3. Patient related outcomes** **4. GP related outcomes**
Luker et al. (2000)[23]	*Primary* - Patient utilization of the primary health care team (interview) - GP views after study (interview) *Measurements* - at baseline (preoperative) - 4 months after diagnosis	**Uptake of intervention** 8 of the 31 interviewed GPs recall seeing the Information Card **Health care use** (*intervention vs. controls)* - Patient initiated contact • with GP ≥1 contact in 71% vs. 73%, p = 0.95 • district nurses no contact in 24% in both groups **GP related outcome** *(intervention)* - Recommending information card 7 of 8 GPs who recall intervention

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16]	*Primary* - Patient attitude towards the health care system (intersectoral cooperation and 'not feeling left in limbo' (SDQ) - Patient GP global assessment (one question) - Quality of life (EORTC QLQ-C30) - Performance status of function and self-care (ECOG) - Health care use: GP consultations (patient and GP reported SDQ) - GP assessment (SDQ) of: • Discharge information value • Own knowledge (patients confidence) • Own wishes to receive further information • Intersectoral cooperation *Measurements* Patient: - First measurement "Soon after the introduction of the intervention."(0 month) - 6 months GP assessment: timing unknown	**Uptake of intervention** Not reported **Patient related outcomes** *(intervention vs control)* - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055 - At 6 months 'Not feeling left in limbo'; 65.49 vs 55.58, p=0.055 - Patient GP global assessment; • at 0 months: 71.0 vs 58.68 (p = 0.04) • at 6 months: 68.9 vs 64.02 (p = 0.44) Quality of life and performance status: nor relevant or significant differences described **Health care use** (*intervention vs. controls)* - GPs reported regular contact; 75% vs. 75% - Patient reported GP consultation; • at 0 months: 67.8% vs 74.8% (p = 0.583) • at 6 months: 38.0% vs 31.5% (p = 0.046) **GP related outcome** *(intervention vs. control)* - Discharge information value GP on; • Psychosocial conditions 60% vs. 26% (p <0.001) • Information their patient had received 84% vs 49%, (p <0.001) - GP knowledge 94.8% vs 96.6% (NS) - GP wish more information 21% vs. 38% (p = 0.009) - GP rate intersectoral cooperation 'satisfactory' 85% vs. 73%, (p = 0.033) -Intersectoral contacts: 25/100 vs. 17/97 GPs had ≥1 contact, p = 0.23

Table 2. Study outcomes.

Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FACT-G = Functional Assessment of Cancer Therapy – General; GP = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs Assessment for Advanced Cancer Patient; NS = not significant, no p-value or confidence interval was provided nor could be calculated; OR adj = Odds ratio adjusted for confounders sex and age; PACIC = Patient Assessment of Chronic Illness Care; PES = Patient Empowerment Scale; PHR = Patient Held Record; POMS= Profile of Mood States; SD = Standard Deviation; SDQ = Self Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus; χ^2= Chi-square distribution.

Discussion

This systematic review shows that published research describing the effect of interventions designed to involve the GP during curative cancer treatment is scarce. The six studies that were published evaluate either additional information transfer to the GP or tailored primary care. In general, the intervention uptake was low, and the risk of bias was low to moderate. Results indicate a positive effect of increased GP involvement in cancer care on patient satisfaction with care but not on quality of life. In subgroups, it may lower health care use and anxiety.

Even though active involvement of the GP during cancer treatment might have positive effects, implementation appears to be difficult to realize. This is seen for all interventions, irrespective whether the GP contact is initiated by the patient or by the healthcare provider. This shows that finding a feasible intervention is challenging. Drury et al (2000) suggested that a reason for the low uptake might be that GPs are not motivated to participate in the care of patients with curative disease as they do not feel closely involved in this stage [24]. This may explain why no studies were found where the GP was the initiator of involvement in care during cancer treatment. Low GP motivation is in contrast to what Dossett et al. (2017) show in their review on communication of specialist and GP during the cancer care continuum, they state that GPs desire involvement but think that specialist and patient prefer a specialist-based instead of shared-based cancer care [26]. Dossett et al (2017) confirms a preference of a specialist based model of care by specialists, which may result in a low motivation to activate the patient to see the GP [26]. Another reason for low uptake may be the difficulty to promote proactivity by GPs [17,18]. Dossett et al (2017) suggest that an adequate relationship and communication between the specialist and GP are important elements for the success of an intervention [26]. These findings suggest that, when designing an intervention, raising support of both primary and secondary health care workers is vital. The fact that healthcare system have different challenges and needs (e.g. communication between caregiver or distance to healthcare services), strengthens the need to tailor the potential solutions to local needs.

Specific subgroups may benefit more from involvement of primary care. A stronger decrease in anxiety was reported in patients with elevated levels of anxiety and [25] the GP involvement led to a reduction in secondary care use among older patients [22]. It has been suggested that different cancer diagnoses bring different psychological burdens and care needs [27], but this could not be concluded from this review.

This review has several limitations. To provide a comprehensive overview we used a broad research question and search strategy. Consequently, we included heterogeneous studies. Due to this heterogeneity and the low number of available studies, data pooling was not possible and the estimate of effect could not be assessed according to the GRADE approach. To add to the difficulty of reviewing heterogeneous studies, most studies addressed complex interventions. The challenge of providing an overview of such studies could partly be countered by the limited availability of process measures (e.g. uptake of intervention), but still strong conclusions could not been drawn. Another potential limitation is that two databases were used to screen on title and abstract by one researcher, possibly leading to missing studies. However, since screening of references did not provide additional studies, we expect this limitation to be without effect. In addition, to be complete, we included studies that also included palliatively treated patients. Some publications did not show separate results for the curatively- and palliatively treated population. We used a threshold for the minimum proportion of curatively treated patients (i.e., 75%), but we cannot exclude that the observed effects were influenced the inclusion of palliative patients. Finally, the review relied solely on published studies, so we cannot exclude publication bias.

Current literature shows several important challenges for designing and studying interventions which effectively involve GPs in cancer care. First, finding a feasible intervention seems challenging. Second, when designing an intervention, raising support of primary and secondary health care workers seems vital. Third, challenges and solutions may be setting and population specific. For these reasons, exploratory research seems necessary to design feasible and effective interventions and meaningful studies. Fourth, large studies with a robust design are needed, which should focus on the effect of primary care involvement for various populations, including specifications for cancer types and vulnerable populations (e.g. elderly, and patients with physical or mental comorbidity).

Based on the findings in this review and guidelines for developing and evaluating complex interventions [28] and feasibility studies [29], we developed a framework, which describes consecutive steps that can guide the future development of effective interventions (Figure 3). In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care. This framework should provide us with a definitive answer on the effects of GP involvement in the cancer care pathway in different health care settings, for a variety of populations.

Interventions based on the framework should optimally facilitate primary care workers to appropriately implement their role in shared care, by making full use of their specific expertise by consideration of the patients' context and values, provided in a trusted environment.

Conclusion

Literature addressing the effects of interventions designed to actively involve the GP during curative cancer treatment is scarce and the results are diverse. Even though uptake of interventions is generally low, these studies suggest positive effects of increased primary care involvement on patient satisfaction. Other positive effects were seen, particularly for vulnerable populations. In view of various health care strategies, which aim to transfer parts of the cancer care paths from secondary to the primary care, it is adamant to gather more robust evidence for customized interventions to enable the efficient and effective involvement of the GP during cancer treatment.

Data sharing statement

For the current study we did not generate new data. Therefore, sharing new data is not possible.

Declaration of Interest

Conflicts of interest: none

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Contributors

Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP); analysis and interpretation of data (IP, JB, AM, CH). Drafting the article or revising it critically for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the version to be submitted (IP, JB, AM, NW, EW, CH).

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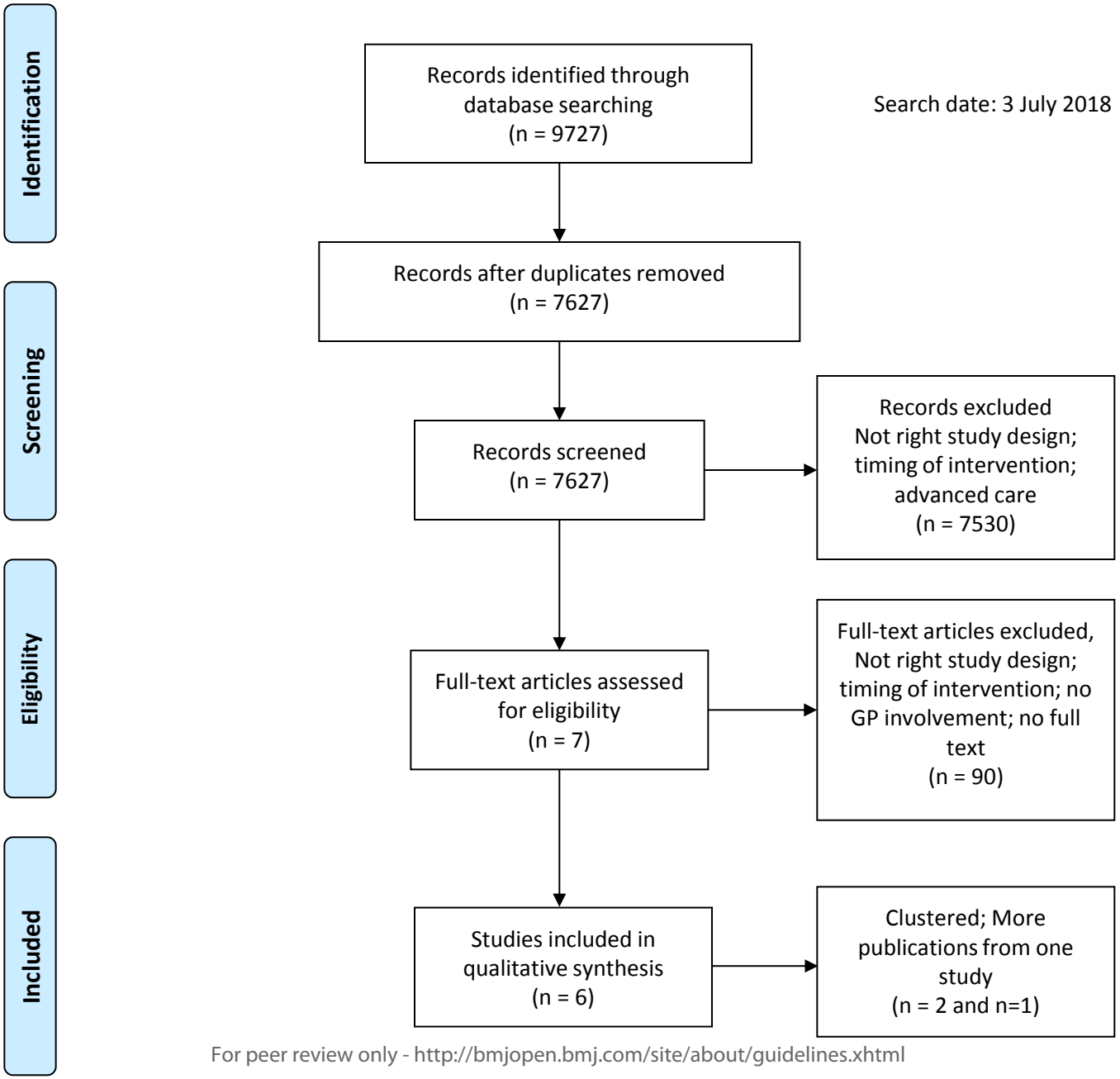
Figure 1. Flow diagram for selection of studies, based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14].

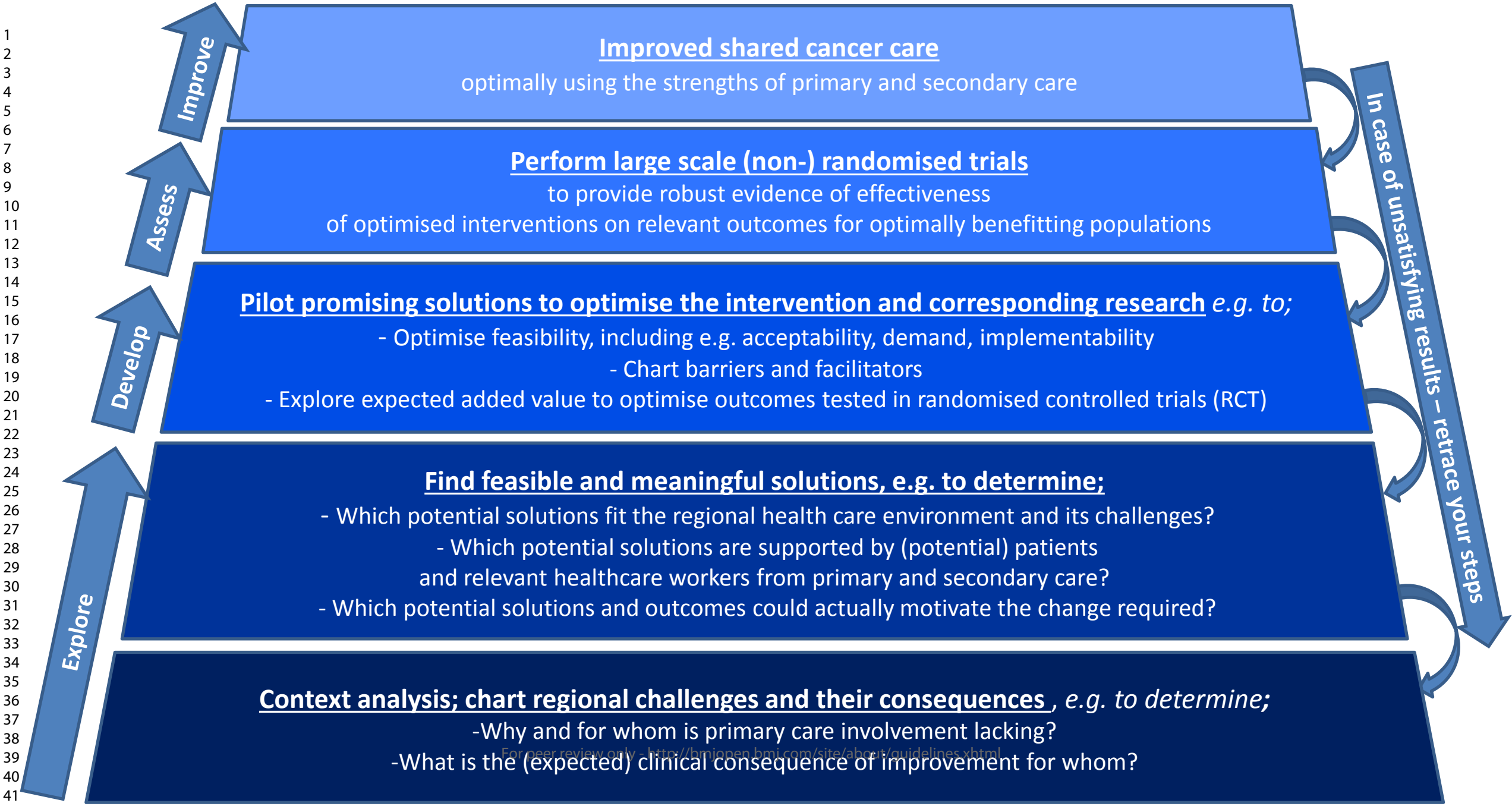
Abbreviations: GP: General practitioner

Figure 2. Risk of bias measured according to the EPOC criteria

Figure 3. Framework for development of interventions aimed to effectively involve the GP in cancer care. In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 9727)
Search date: 3 July 2018
Records after duplicates removed (n = 7627)
Records screened (n = 7627)
Records excluded Not right study design; timing of intervention; advanced care (n = 7530)
Full-text articles assessed for eligibility (n = 7)
Full-text articles excluded, Not right study design; timing of intervention; no GP involvement; no full text (n = 90)
Studies included in qualitative synthesis (n = 6)
Clustered; More publications from one study (n = 2 and n=1)


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Baseline outcome measurements similar (selection bias)
Baseline characteristics similar (selection bias)
Incomplete outcome data (attrition bias)
Knowledge of the allocated interventions adequately prevented during the study (performance bias)
Protection against contamination (performance bias)
Selective reporting (reporting bias)
Other bias
Drury et al. 2000
Hansen et al. 2011/Bergholdt et al. 2012/2013/2013
Johansson et al. 2001
Johnson et al. 2015
Luker et al. 2000
Nielsen et al. 2003/Kousgaard et al. 2003



Search terms

Syntax PUBMED

#1

((((((((((((((((((((((“primary care”[Title/Abstract]) OR “primary health care”[Title/Abstract]) OR “primary medical care”[Title/Abstract]) OR “first-contact medical care”[Title/Abstract]) OR “first line care”[Title/Abstract]) OR “primary care physician”[Title/Abstract]) OR “primary care physicians”[Title/Abstract]) OR “general practitioner”[Title/Abstract]) OR “general practitioners”[Title/Abstract]) OR GP[Title/Abstract]) OR GPs[Title/Abstract]) OR G.P.[Title/Abstract]) OR GP-organised[Title/Abstract]) OR “family doctor*”[Title/Abstract]) OR “family practice*”[Title/Abstract]) OR "primary health care"[MeSH Terms]) OR "physicians, primary care"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "primary care nursing"[MeSH Terms]) OR "nursing care"[MeSH Terms]) OR "general practitioners"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "family practice"[MeSH Terms])

#2

(((((((oncolog*[Title/Abstract]) OR cancer*[Title/Abstract]) OR malignancy[Title/Abstract]) OR carcinoma[Title/Abstract]) OR ((tumor[Title/Abstract] AND malignant[Title/Abstract]))) OR “medical oncology”[MeSH Terms]) OR carcinoma[MeSH Terms]) OR ((neoplasms[MeSH Terms] AND malignant[Title/Abstract])))

#3

((((((((((((((((((((((((((((((((((care[Title/Abstract]) OR continu*[Title/Abstract]) OR follow-up[Title/Abstract]) OR surveillance[Title/Abstract])) OR “patient discharge”[Title/Abstract]) OR “hospital discharge”[Title/Abstract]) OR transmural[Title/Abstract]) OR collaborative[Title/Abstract]) OR

interdisciplinary[Title/Abstract]) OR multidisciplinary[Title/Abstract]) OR "liaison nurse*"[Title/Abstract]) OR "health care planning"[Title/Abstract]) OR "health care management"[Title/Abstract]) OR "community health planning"[Title/Abstract]) OR "service integration"[Title/Abstract]) OR "services integration"[Title/Abstract]) OR "professional-patient relations"[Title/Abstract]) OR "professional-family relations"[Title/Abstract]) OR "shared services"[Title/Abstract])) OR "multi professional working"[Title/Abstract]) OR interprofessional[Title/Abstract]) OR "multi agency working"[Title/Abstract]) OR "inter agency working"[Title/Abstract]) OR "case management"[Title/Abstract]) OR "patient discharge"[MeSH Terms]) OR "patient care planning"[MeSH Terms]) OR "patient care team"[MeSH Terms]) OR "continuity of patient care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case management"[MeSH Terms]) OR "community health planning"[MeSH Terms]) OR "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient relations"[MeSH Terms]) OR "interprofessional relations"[MeSH Terms]) OR "professional-family relations"[MeSH Terms]) OR "cooperative behavior"[MeSH Terms])

#4 (((((("randomized controlled trial"[Publication Type]) OR random*[Title/Abstract]) OR control*[Title/Abstract]) OR intervention*[Title/Abstract]))

Combining search terms: #1 AND #2 AND #3 AND #4

Syntax EMBASE

#1

'primary care':ab,ti OR 'primary health care':ab,ti OR 'primary medical care':ab,ti OR 'first-contact medical care':ab,ti OR 'first line care':ab,ti OR 'primary care physician':ab,ti OR 'primary care physicians':ab,ti OR 'general practitioner':ab,ti OR 'general practitioners':ab,ti OR gp:ab,ti OR gps:ab,ti OR g.p.:ab,ti OR 'gp organised':ab,ti OR 'gp organized':ab,ti OR 'family doctor':ab,ti OR 'family doctors':ab,ti OR 'family practice':ab,ti OR 'family practices':ab,ti OR 'primary health care'/exp OR 'primary health care' OR 'general practice'/exp OR 'general practice'

#2

oncology:ab,ti OR cancer:ab,ti OR malignancy:ab,ti OR carcinoma:ab,ti OR (tumor:ab,ti AND malignant:ab,ti) OR ('neoplasm'/exp OR neoplasm AND malignant:ab,ti) OR 'malignant neoplastic disease'/exp OR 'malignant neoplastic disease'

#3

care:ab,ti OR continu*:ab,ti OR 'follow up':ab,ti OR surveillance:ab,ti OR 'discharging plan':ab,ti OR 'discharge plan':ab,ti OR 'discharge planning':ab,ti OR 'patient discharge':ab,ti OR 'hospital discharge':ab,ti OR transmural:ab,ti OR collaborative:ab,ti OR interdisciplinary:ab,ti OR multidisciplinary:ab,ti OR 'liaison nurse':ab,ti OR 'health care planning':ab,ti OR 'health care management':ab,ti OR 'community health planning':ab,ti OR 'service integration':ab,ti OR 'services integration':ab,ti OR 'professional-patient relations':ab,ti OR 'professional-family relations':ab,ti OR 'shared services':ab,ti OR 'shared notes':ab,ti OR 'multi professional working':ab,ti OR interprofessional:ab,ti OR 'multi agency working':ab,ti OR 'inter agency working':ab,ti OR 'case management':ab,ti OR 'patient care'/exp OR 'integrated health care system' OR 'health care planning'/exp

#4

'randomized controlled trial'/exp OR random*:ab,ti OR control*:ab,ti OR intervention*:ab,ti

Combining search terms: #1 AND #2 AND #3 AND #4

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n.a.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n.a.
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n.a.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No pooling of data not assessed.
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n.a.
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 and figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	15 – 17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	18 - 22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n.a.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n.a.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n.a.
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	25

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

PRISMA 2009 Checklist

BMJ Open

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-026383.R2
Article Type:	Research
Date Submitted by the Author:	24-Jan-2019
Complete List of Authors:	Perfors, Ietje; University Medical Center Utrecht, Julius Center May, Anne; University Medical Center Utrecht, Julius Center Boeijen, Josi; University Medical Center Utrecht, Julius Center de Wit, Niek; University Medical Center Utrecht, Julius Center for Primary Care van der Wall, Elsken Helsper, Charles; University Medical Centre Utrecht, 1Julius Centre for Health Sciences and Primary Care
Primary Subject Heading:	Oncology
Secondary Subject Heading:	General practice / Family practice, Patient-centred medicine
Keywords:	PRIMARY CARE, Shared care, Curative treatment, Patient satisfaction, General Practitioner, Cancer

Journal

BMJ Open

Type of Contribution

General and Supportive Care; Systematic review.

Word Count (excluding title page, abstract, tables, acknowledgements, contributions and references): 3421/4000 words, 5/5 tables or figures, 29/100 references.

Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Author Names and Affiliations

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Second Title Page

Title

Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of Health Care Interventions.

Abstract

Words: 300/300

Objective: The role of primary care providers (PCP) in the cancer care continuum is expanding. In the post-treatment phase, this role is increasingly recognized by policy makers and health care professionals. During treatment, however, the role of PCP remains largely undefined. This systematic review aims to map the content and effect of interventions aiming to actively involve the General Practitioner (GP) during cancer treatment with a curative intent.

Study design Systematic review

Participants Cancer patients treated with curative intent

Data sources Randomized controlled trials (RCTs), controlled clinical trials (CCT), controlled before and after studies and interrupted time series focusing on interventions designed to involve the GP during curative cancer treatment were systematically identified from PubMed and EMBASE and were subsequently reviewed. Risk of bias was scored according to the EPOC risk of bias criteria.

Results Five RCTs and one CCT were included. Interventions and effects were heterogeneous across studies. Four studies implemented interventions focussing on information transfer to the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on patient satisfaction with care was found in three studies. Subgroup analysis suggest a reduction of health care use in elderly patients and reduction of clinical anxiety in those with higher mental distress. No effects are reported on patients' quality of life (QoL).

Conclusion Interventions designed to actively involve the GP during curative cancer treatment are scarce and diverse. Even though uptake of interventions is low, results suggests a positive effect of GP involvement on patient satisfaction with care, but not on QoL. Additional effects for vulnerable subgroups were found. More robust evidence for tailored interventions is needed to enable the efficient and effective involvement of the GP during curative cancer treatment**.**

PROSPERO registration number: CRD42018102253

Strengths and Limitations of this study

- This is the first review that systematically reviews evidence based interventions, aiming at general practitioner involvement during the curative treatment phase of the cancer care continuum.
- The electronic database search was performed without restriction on languages and period.
- We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate tool to assess bias for complex interventions.
- The title/abstract screening is done by single reviewer, two authors screened the full-text and the search was complemented with reference checks of relevant articles.
- The included studies are heterogeneous in intervention and outcome and therefore strong conclusions could not be made.

Keywords

- Primary care
- General Practitioner
- Shared care
- Cancer
- Curative treatment
- Patient satisfaction

Background

Cancer incidence and prevalence is increasing as a result of the aging population combined with expanding diagnostic and treatment possibilities. Due to improved outcome following cancer treatment, the nature of cancer treatment is changing toward more chronic disease management. Health policy makers and health care professionals therefore call for a change in the way cancer care is provided, to focus on more integrated and personalized cancer care during and after treatment [1,2]. In countries with gatekeeper health care systems, such as The Netherlands, GPs are generally the coordinators of care, who have a longstanding and personal relationship with their patients. This enables knowledge of both the medical and personal situation of the patient and care, which is provided in a trusted environment with a familiar health care worker. Therefore, primary care is increasingly promoted as the preferred setting to provide integrated support during and after active cancer treatment, both to meet patient preference and to stabilize costs [2,3]. The concept of shared care has been suggested as the way forward in the organization of integrated cancer care [2,3]. This shared care model is an organisational model involving both general practitioners (GPs) and specialists in a formal, explicit manner. Shared care models enhance the optimal access of patients to both hospital care and community based supportive care along the entire cancer care continuum [4]. In shared care models, GPs, along with other primary care professionals, add their competence to balance the biomedical aspects of cancer care with the psychosocial context and preferences of the individual patient [5], ensuring personalized, integrated care. To achieve shared care the GP should be involved in the organisation of care during cancer treatment.

Traditionally, the role of primary care in palliative and end-of-life care is well established [6]. In addition, evidence suggests a solid role for primary care in cancer follow-up after treatment and survivorship care [7–9]. Less well appreciated, however, is primary care involvement during cancer treatment, particularly for patients treated with a curative intent. It is well established that in this phase patients frequently experience psychosocial distress and treatment-related side effects that negatively affect their quality of life [10]. Several studies suggest primary care involvement during active treatment, to improve patient outcomes and to ensure continuity in guidance from primary care [3,11]. In the near future the GP might even be involved in treatments in primary care such as chemo- or hormone therapy. Currently however, involvement of primary care is generally restricted to supportive care during cancer treatment.

So far, the most effective approach to involve primary care during cancer treatment remains unclear.

This systematic review aims to provide a comprehensive overview of the content and effect of interventions aiming at active involvement of the general practitioner during cancer treatment with curative intent compared to usual care.

Methods

Data source and search

A literature search was conducted in PubMed and EMBASE for articles describing randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies, and interrupted time series published in any language until the 3rd of July 2018. We used a search strategy that was previously applied in a review assessing continuity of care in the follow-up of patients with cancer [12]. Subsequently, this strategy was adapted for completeness and relevance based on sequential testing of search strategies to develop our final search strategy. The details of the sequential and final search strategies are listed in appendix A. The search terms include keywords and controlled vocabulary terms surrounding the central themes "general practitioner", "primary care", "oncology", and "care". Outcome measures and comparing study arm were not included in the selection criteria to widen the scope of the review. Instead of a database integrated filter, a tailored methodological search filter was used to limit retrieval to appropriate study design [12]. We reviewed references of selected articles for additional papers.

Outcomes are included if they are related to the quality of healthcare (e.g. healthcare use), the healthcare experience of: healthcare professionals, informal caregivers, and patients, or outcomes at the patient-level, with a focus on, e.g., disease, quality of life, and psychosocial impact.

Study selection

Articles were selected if they described an intervention; (1) for cancer patients, (2) starting during curative treatment, (3) evaluating involvement of the GP, and (4) tested in a randomized controlled setting, CCT, controlled before and after studies or interrupted time

series. Studies with a majority (>75%) of curative patients were included. In case the proportion of curative patients was unclear, the original authors were contacted. Without response, the inclusion of the trial was based on >75% percentage patient survival during the trial.

Data extraction and management

To determine relevance, the records were divided and screened on title and abstract by two single reviewers (IP,JB) and discussed with three additional reviewers in case of doubt (AM,CH and JB or IP). Two authors (IP,JB) performed full-text screening. Disagreements on eligibility were resolved in group discussion with researchers and clinicians (IP,JB,AM,CH).A meta-analysis was planned to be conducted if possible.

Patient and public involvement

Patients and public were not involved in the design of the current study.

Quality assessment

Risk of bias for individual studies was scored by two authors (JB,IP) with the risk of bias criteria from the "Effective Practice and Organisation of Care Group (EPOC), which is a Cochrane review group [13]. In case outcomes of homogeneous study designs could be merged we rated the body of the evidence following the Grades of Recommendation, Assessment, Development and Evaluation approach (GRADE) [14] from the Cochrane collaboration. This systematic review is reported following the PRISMA 2009 checklist [14].

Results

Study selection

As shown in Figure 1, 9,727 records were eligible for inclusion after removal of duplicates. Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP involvement started after completion of primary cancer treatment, or (3) no RCT, CCT,

controlled before and after study or interrupted time series design was used. Three studies published multiple articles based on the same data [15–22]. As a result, five RCTs and one CCT were considered eligible for inclusion, which were described in ten articles. No additional eligible studies were identified in the reference lists of selected studies. Figure 2, Table 1, and 2 show a detailed account of the risk of bias, patient population, interventions, outcomes assessed and observed results for each study. Given the various research questions, interventions and heterogeneity of outcome measures, pooling of data, and GRADE assessment was not feasible.

Quality of studies

The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et al. (2003) show a high risk of bias, resulting from high risk of selection and information bias [15,16,23]. Drury et al. (2000) scored a medium risk of bias [24]. And the studies of Johnson et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk of bias [17–19,22,25]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several limitations should be kept in mind. The randomization produced an imbalance, which influenced comparability of outcomes between study groups without corresponding correction in the analyses. Furthermore, it was not reported whether a baseline measurement was performed and the exact timing of the first measurement (Table 2). Also, the percentage of missing data was 33% in the intervention and 26% in the control group [15].

Study populations

The six eligible studies were conducted in Europe (five) and Australia (one) among different cancer patient populations over the past two decades. Breast cancer patients were the most commonly studied group (between 33-100% of the study populations). Five RCTs included patients with more than one type of cancer, in different stages. Three studies included palliatively treated patients (<25% of total study population). In two RCT's cancer stage was not specified.

Usual care

In most studies, usual care was not described in detail. Only Luker et al. [23] described the structured care that usual care patients received, which included home visits from a breast care nurse and written patient information on treatments. In general, the patient's GP received a discharge summary [15–17,19,20,25] at the end of the treatment period [15,16] or after each visit [25]. Other types of transferred information to the GP included an extract of the hospital record [15,16] or communication by telephone [25]. Two studies did not describe what usual care entailed [21,22,24].

Type of interventions

All participants received usual care, which was extended when the participant was appointed to the intervention. The interventions in the studies (Table 1) were heterogeneous, but can be divided in mainly information transfer to the GP (n=4) [15,16,23–25] and tailored primary care interventions (n=2) [17–20,22].

Interventions focusing on information transfer, provided additional, disease specific educational, and practical information concerning treatment and care directly to the GP or via the patient. Interventions were either directed at enhancing communication between GP and another party (i.e. secondary care or patient), or directed at improving patient's attitude towards the healthcare system (i.e. healthcare in general or intervention), physical- or psychological complains. Three interventions provided patients with information, which was to be transferred to the GP. In one CCT [23], informational cards were provided to the patients for use in primary care. Two other RCTs described an intervention with a Patient Held Record (PHR) [24,25] aimed to facilitate intersectoral communication, to provide patients with an aide memoire, and with the opportunity to stay actively involved in their treatment. One RCT supplied the GP with patient specific discharge summaries by secondary care, aiming to enhance GP knowledge of chemotherapy treatment and expected adverse effects [15,16].

The tailored primary care interventions aimed to support patients in managing their disease and treatment [17,18,20,22]. The interventions were to diverse to be merged and they are therefore described separately. In Johansson et al. (2001) [22] primary care was intensified by means of recruitment of a home care nurse, psychologist, dietician and training of the GP. The home care nurse initiated contact. The GP was regularly informed by the specialist and educated on management of cancer patients. In the one RCT from Hansen et al. (2011) and

Bergholdt et al. (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on different aspects of rehabilitation. Afterwards the GP was informed on patient specific rehabilitation needs and encouraged to pro-actively contact the patient to support the patient in his/her needs.

Study outcomes

The most often measured primary outcomes were health care utilization [15,16,22–24] and quality of life [15–17,24], as presented in Table 2. Other outcomes were patient and GP perceptions of care, symptoms, coping, and empowerment. The following outcomes were not presented in the included articles: healthcare experience by informal caregivers, and disease specific outcomes (i.e. progress, mortality). Outcomes are described in more detail below.

Intervention fidelity/compliance and health care use

Health care use is related to the uptake of the intervention. For example, if the intervention aims at more GP involvement, health care use is likely to increase. Although all interventions aimed at increased involvement of primary care, four interventions did not show a significant increase of GP consultations [15,18,23,24]. Correspondingly, the uptake of interventions appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al. [18] which describes an "active involvement" intervention, in which GP pro-activity was comparable to GP proactivity in the control group (52 to 60%) [18]. In two studies, information transfer to the GP by their patients was hardly used or remembered by the majority of the GPs [23,24].

Five studies, evaluated the effect of the intervention on hospital and/or primary care resource use. These studies showed no significant effect on secondary care health care use [22–24]. Only the subgroup of older patients (≥70 years of age) had a significantly lower use of secondary care [22] when primary care was actively involved. Even though GP consultations where part of the interventions several studies reported no difference in the number of GP consultations in the intervention group compared to the control group [15,16,23–25]..

Patient perception

Positive effects on patients' satisfaction with care were indicated by three studies. Extended information by PHR or discharge summary improved patient perceived intersectoral cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that 'the GP could help in the way a specialist could not' [25]. Regardless of the uptake of the intervention, one study showed an improved satisfaction with communication and participation with care [24]. The significantly higher levels of perceived GP support shortly after the intervention described in Nielsen et al.(2003) declined to non-significant levels at six months after start of intervention. The authors did not present a mean difference overtime. One study with a low uptake of intervention showed no significant effect on patients satisfaction [20].

Quality of life and psychological outcomes

No study found a significant effect on quality of life [15,17,24]. Johnson et al (2001) [23], showed a significant difference in change of depression scores (p0.04). In the intervention group depression scores remained unchanged, whereas scores in the control group deteriorated significantly. Also, using a PHR combined with routine visits to the GP led to a significantly higher reduction of the number of clinically anxiousness patients compared to usual care [25].

GPs perceptions of care

Four out of five studies evaluating effects on GPs perceptions of care did not find relevant effects on GP's confidence in disease management and knowledge nor in the communication with the specialist [16,20,23,25]. Studies in which information was carried by the patient (a PHR or informational cards) showed little impact on GP satisfaction with care mostly due to low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant positive effects on GP perceived intersectoral cooperation and GP satisfaction with information.

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
Drury et al. (2000)[24]	N = 650 60% ♀	*Inclusion* During any RT clinic visit Time after diagnosis not specified	UC and intervention vs UC Patients received a PHR Initiative GP contact: Patient
UK	MAM (33%), LUN, GI, GYN, URO, H&N, other (13%); Cancer stage not specified 59 patients died ≤ 3 months from baseline, which may reflect inclusion of patients with advanced disease	*Intervention* Upon enrolment *Follow up* 3 months	PHR: A4 size plastic wallet content: - Communication sheets for use by patient, family care givers, and health care professionals - Medication records and appointment and contact details - An explicit invite to caregivers to use the PHR Patients were instructed to: - Use the PHR as an aide memoire and means of communication - Show it to anyone involved in their care
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20] Denmark	N = 955 72% ♀ MAM (43%), LUN, GI, other (19%), MEL Cancer stage unknown, no deceased	*Inclusion* Cancer diagnosis <3 months *Intervention* Upon enrolment *Follow up* 14 months	Intervention vs UC Rehabilitation primary care program Initiative GP contact: Healthcare worker Rehabilitation primary care program consisting of: - Patient interview by rehabilitation coordinator (nurses) on physical, psychological, sexual, social, work-related and economy related rehabilitation needs - RC presents patient individual and general cancer patients rehabilitation needs to GP - RC encouraged GP to pro-active contact patient to facilitate a rehabilitation process
Johansson et al. (2001)[22]	N = 463 57% ♀	*Inclusion* Newly diagnosed patients (<3 months after diagnosis)	Intervention vs UC Intensified primary care program Initiative GP contact: Healthcare worker
Sweden	MAM (47%), GI, PRO 22% with advanced disease	*Intervention* Upon enrolment	Individual Support intervention consisting of: - Intensified primary health care by means of recruitment of a home care nurse - Education and supervision in cancer care for both GP and home care nurse

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
		Follow up 3 months	- Active involvement of dietician and psychologist care
Johnson et al. (2015)[25] Australia	N = 97 86% ♀ MAM (76%), HEM, GYN, GI Cancer stage 3.3% palliative Stopped early (slow accrual); underpowered for the main analysis	*Inclusion* During first course of CT *Intervention* First through last course of CT *Follow up* 6 cycles of CT	UC and intervention vs UC (discharge summary) Shared Care program + PHR Initiative GP contact: Patient PHR content: - Chemo schedule, appointments and medication information - Communication pages for specialist and GP Patients received: - A PHR - Instruction to visit their GP routinely after every course of CT (patient initiative) GPs received: - Educational resources about adverse treatment effects and apt solutions - Encouragement to use the communication page in PHR A project coordinator (a trial nurse) was appointed to facilitate communication between patient, GP, specialist and researchers
Luker et al. (2000)[23] UK	N = 79 100% ♀ MAM (100%) Cancer stage 100% curative	*Inclusion* <4 weeks after diagnosis *Intervention* At start of treatment *Follow up* 4 months	UC and intervention vs UC Patients received information cards Initiative GP contact: Patient Information card content: - Rationale for patient specific treatment; Prognostic indicators, complications, side effects and referral indicators Patients received: -Informational cards to provide rapid access to treatment-specific information for members of the

Reference Country	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
			primary health care team - Encouragement to contact their primary health care team and show the Information cards
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16] Denmark	N = 248 64% ♀ MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL Cancer stage 15% palliative	*Inclusion* Newly diagnosed patients *Intervention* From referral onwards; during treatment *Follow up* 6 months	UC and intervention vs UC Shared care program Initiative GP contact: Patient Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment - Expected role of the GP - Contact information of all involved medical personnel Patients received: - Oral and written notification about the information provided to their GP - Encouragement to contact their GP when facing problems they assumed could be solved in this setting

Table 1 – Details of interventions aiming at active involvement of the general practitioner during treatment with curative intent.

Abbreviations: CT = Chemotherapy; GER = germinal cell; GI = gastrointestinal tract; GP = General Practitioner; GYN = gynaecological; HEM = haematological; H&N = head and neck; LUN = lung; MAM = mamma; MEL = melanoma; PHR = Patient Held Record; PRO = prostate; RC = Rehabilitation Coordinator; RT = Radiotherapy; UC = Usual Care; UK= United Kingdom; URO = urogenital; vs = versus.

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
Drury et al. (2000)[24]	*Primary* - Health care use (patient reported) - Patient satisfaction with communication and participation in care (SDQ) - Quality of life (EORTC QLQ-C30) *Secondary* - GP views on PHR (SDQ) *Measurements* Single measurement at 3 months	**Uptake of intervention** 27.3% of 202 responding GPs had seen the PHR **Health care use** (*intervention vs. controls)* Contact with care providers in 3 months follow-up; • Visit GP 78% vs. 85% • Visited secondary care clinics 95% vs. 95% **Patient related outcomes** *(intervention vs control)* - Satisfaction communication and participation in care mean ± SD (scale 1-5): 3.83±0.59 vs. 3.80±0.59, (95% CI 0.09- 0.15) - Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05 - Quality of life mean global scores: 66.8±24.2 vs. 65.3±23.7 **GP related outcome** *(seen PHR vs. not seen PHR)* - GP agrees that patients should have full access to their records 57% vs. 57%
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	*Primary* Quality of life (EORTC QLQ-C30) *Secondary* -Psychological distress (POMS) -Symptoms (scale of the EORTC QLQ-C30) -Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth) -GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth) -GP's satisfaction with their contribution to the patient's	**Uptake of intervention** pro-activity of GP intervention vs control: GP reported 61.2% vs 55.2% p=0.10, patient reported 60.1% vs51.9% p=0.15 **Patient related outcomes** *(intervention vs control)* -Quality of life; mean difference [95%CI]; • at 6 months 1.25 [-2.4-4.9] • at 14 months -0.71 [-4.3-2.8] - Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0] - Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5] - Patient satisfaction with, • GP on five dimensions, OR adj [95%CI] All NS; Doctor–patient relationship 0.94 [0.35-2.47], Medical care 1.2 [0.5-3.0], Information and support 1.6 [0.6-

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	rehabilitation course (two ad hoc questions, likert scale, at 14 mth) *Measurements* At 6 and 14 months	4.1], Organization of care 1.3 [0.8-2.1], GP's accessibility 1.2 [0.6-2.3] • GP support during the cancer course, OR adj [95%CI]; 1.14 [0.7-1.8] - Pro-activity GP and rehabilitation activity patient, OR adj [95%CI]; 1.96 [1.2-3.3] **GP related outcomes** *(intervention vs control)* - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[22]	*Primary* Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing) *Measurements* Single measurement at 3 months	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* Subgroup analysis for age (year) hospital admissions mean number of admissions ± SD, 3 months follow-up; • ≥70y: 0.4±0.6 vs. 0.9±1.0 (Student T test p = 0.0002) • <70y: 1.0±1.0 vs. 0.9±0.8 (Student T test p= 0.38) - Days of hospitalization; • ≥70y: 3.8±8.8 vs. 8.9±18.8 (Tukey HSD, p <0.01) • <70y: 4.4±5.9 vs. 3.6±4.9 (Student T test p = 0.24) - Mean number of outpatient care visits per patient; • ≥70y: 6.8±8.8 vs. 6.0±7.0 (Student T test p = 0.53) • <70y: 13.4±11.2 vs.12.9±11.5 (Student T test p = 0.7257) - Acute visits; • ≥70y: in 5% vs. 15% of patients (χ^2 p = 0.034) • <70y: in 11% vs. 10% of patients (χ^2 p = 0.80)
Johnson et al. (2015)[25]	*Primary* - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC) - Empowerment (PES)	**Uptake of intervention** Not reported **Health care use** (*intervention vs. controls)* - Emergency department presentations: no significant between-group differences were observed - Average number of GP visits 2.79 vs 1.61, p < 0.001

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
	Secondary - Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits) - Patient perception of care (SDQ) - GP perception of care (SDQ) *Measurements* - before treatment - midway through treatment - after treatment	**Patient related outcomes** *(intervention vs control)* Patient perception of care; - GP could help in ways specialist could not: 57% vs. 19% (χ^2 = 11.5; p = 0.002) - Patient opinion concerning PHR/GP visit after CT course: • 81% considered PHR useful • 35% considered visit inconvenient Depression; Geometric mean score [95%CI] • at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40] • after treatment: 4.04 [3.25 to 4.83] vs 4.72 [3.72 to 5.72] p = 0.04 for comparison of groups over time Anxiety; Geometric mean score [95%CI] • at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32 • after treatment: 5.49 [4.54 to 6.43] vs 5.24 [4.26 to 6.22] p = 0.80 for comparison of groups over time - Subgroup analysis for number of clinically anxious patients • at baseline: 14 CA patients vs 11 CA patients • after treatment: 3 CA patients vs 5 CA patients Decline intervention p=0.002; control p=0.014 Coping; Geometric mean difference over time -0.7 vs 0.1 p=0.35 Empowerment; Geometric mean difference over time 0.9 vs 0.9 p=0.47 **GP related outcome** *(intervention vs control)* - GPs satisfied with communication: 82% vs. 95% - GP confidence in managing: • side effects 85% vs. 71% (p =0.45) • psychological issues 97% vs. 81% (p= 0.04)
Luker	*Primary*	**Uptake of intervention** 8 of the 31 interviewed GPs recall seeing the Information Card

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
et al. (2000)[23]	- Patient utilization of the primary health care team (interview) - GP views after study (interview) *Measurements* - at baseline (preoperative) - 4 months after diagnosis	**Health care use** (*intervention vs. controls)* - Patient initiated contact • with GP ≥1 contact in 71% vs. 73%, p = 0.95 • district nurses no contact in 24% in both groups **GP related outcome** *(intervention)* - Recommending information card 7 of 8 GPs who recall intervention

Reference Country	Primary and secondary outcome measures (instrument used) Timing of measurement	Findings if applicable to study: 1. Uptake of intervention 2. Health care use 3. Patient related outcomes 4. GP related outcomes
Nielsen et al. (2003) [15] Kousgaard et al. (2003) [16]	*Primary* - Patient attitude towards the health care system (intersectoral cooperation and 'not feeling left in limbo' (SDQ) - Patient GP global assessment (one question) - Quality of life (EORTC QLQ-C30) - Performance status of function and self-care (ECOG) - Health care use: GP consultations (patient and GP reported SDQ) - GP assessment (SDQ) of: • Discharge information value • Own knowledge (patients confidence) • Own wishes to receive further information • Intersectoral cooperation *Measurements* Patient: - First measurement "Soon after the introduction of the intervention."(0 month) - 6 months GP assessment: timing unknown	**Uptake of intervention** Not reported **Patient related outcomes** *(intervention vs control)* - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055 - At 6 months 'Not feeling left in limbo'; 65.49 vs 55.58, p=0.055 - Patient GP global assessment; • at 0 months: 71.0 vs 58.68 (p = 0.04) • at 6 months: 68.9 vs 64.02 (p = 0.44) Quality of life and performance status: nor relevant or significant differences described **Health care use** (*intervention vs. controls)* - GPs reported regular contact; 75% vs. 75% - Patient reported GP consultation; • at 0 months: 67.8% vs 74.8% (p = 0.583) • at 6 months: 38.0% vs 31.5% (p = 0.046) **GP related outcome** *(intervention vs. control)* - Discharge information value GP on; • Psychosocial conditions 60% vs. 26% (p <0.001) • Information their patient had received 84% vs 49%, (p <0.001) - GP knowledge 94.8% vs 96.6% (NS) - GP wish more information 21% vs. 38% (p = 0.009) - GP rate intersectoral cooperation 'satisfactory' 85% vs. 73%, (p = 0.033) -Intersectoral contacts: 25/100 vs. 17/97 GPs had ≥1 contact, p = 0.23

Table 2. Study results for interventions aiming at active involvement of the general practitioner during curative intent.

Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FACT-G = Functional Assessment of Cancer Therapy – General; GP = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs Assessment for Advanced Cancer Patient; NS = not significant, no p-value or confidence interval was provided nor could be calculated; OR adj = Odds ratio adjusted for confounders sex and age; PACIC = Patient Assessment of Chronic Illness Care; PES = Patient Empowerment Scale; PHR = Patient Held Record; POMS= Profile of Mood States; SD = Standard Deviation; SDQ = Self Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus; χ^2= Chi-square distribution.

Discussion

This systematic review shows that published research describing the effect of interventions designed to involve the GP during curative cancer treatment is scarce. The six studies that were published evaluate either additional information transfer to the GP or tailored primary care. In general, the intervention uptake was low, and the risk of bias was low to moderate. Results indicate a positive effect of increased GP involvement in cancer care on patient satisfaction with care but not on quality of life. In subgroups, it may lower health care use and anxiety.

Even though active involvement of the GP during cancer treatment might have positive effects, implementation appears to be difficult to realize. This is seen for all interventions, irrespective whether the GP contact is initiated by the patient or by the healthcare provider. This shows that finding a feasible intervention is challenging. Drury et al (2000) suggested that a reason for the low uptake might be that GPs are not motivated to participate in the care of patients with curative disease as they do not feel closely involved in this stage [24]. This may explain why no studies were found where the GP was the initiator of involvement in care during cancer treatment. Low GP motivation is in contrast to what Dossett et al. (2017) show in their review on communication of specialist and GP during the cancer care continuum, they state that GPs desire involvement but think that specialist and patient prefer a specialist-based instead of shared-based cancer care [26]. Dossett et al (2017) confirms a preference of a specialist based model of care by specialists, which may result in a low motivation to activate the patient to see the GP [26]. Another reason for low uptake may be the difficulty to promote proactivity by GPs [17,18]. Dossett et al (2017) suggest that an adequate relationship and communication between the specialist and GP are important elements for the success of an intervention [26]. These findings suggest that, when designing an intervention, raising support of both primary and secondary health care workers is vital. The fact that healthcare system have different challenges and needs (e.g. communication between caregiver or distance to healthcare services), strengthens the need to tailor the potential solutions to local needs.

Specific subgroups may benefit more from involvement of primary care. A stronger decrease in anxiety was reported in patients with elevated levels of anxiety and [25] the GP involvement led to a reduction in secondary care use among older patients [22]. It has been suggested that different cancer diagnoses bring different psychological burdens and care needs [27], but this could not be concluded from this review.

This review has several limitations. To provide a comprehensive overview we used a broad research question and search strategy. Consequently, we included heterogeneous studies. Due to this heterogeneity and the low number of available studies, data pooling was not possible and the estimate of effect could not be assessed according to the GRADE approach. To add to the difficulty of reviewing heterogeneous studies, most studies addressed complex interventions. The challenge of providing an overview of such studies could partly be countered by the limited availability of process measures (e.g. uptake of intervention), but still strong conclusions could not been drawn. Another potential limitation is that two databases were used to screen on title and abstract by one researcher, possibly leading to missing studies. However, since screening of references did not provide additional studies, we expect this limitation to be without effect. In addition, to be complete, we included studies that also included palliatively treated patients. Some publications did not show separate results for the curatively- and palliatively treated population. We used a threshold for the minimum proportion of curatively treated patients (i.e., 75%), but we cannot exclude that the observed effects were influenced the inclusion of palliative patients. Finally, the review relied solely on published studies, so we cannot exclude publication bias.

Current literature shows several important challenges for designing and studying interventions which effectively involve GPs in cancer care. First, finding a feasible intervention seems challenging. Second, when designing an intervention, raising support of primary and secondary health care workers seems vital. Third, challenges and solutions may be setting and population specific. For these reasons, exploratory research seems necessary to design feasible and effective interventions and meaningful studies. Fourth, large studies with a robust design are needed, which should focus on the effect of primary care involvement for various populations, including specifications for cancer types and vulnerable populations (e.g. elderly, and patients with physical or mental comorbidity).

Based on the findings in this review and guidelines for developing and evaluating complex interventions [28] and feasibility studies [29], we propose a framework, which describes consecutive steps that can guide the future development of effective interventions (Figure 3). In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care. This framework should support us in finding definitive answers on the effects of GP involvement in the cancer care pathway in different health care settings, for a variety of

populations. Interventions based on the framework should optimally facilitate primary care workers to appropriately implement their role in shared care, by making full use of their specific expertise by consideration of the patients' context and values, provided in a trusted environment.

Conclusion

Literature addressing the effects of interventions designed to actively involve the GP during curative cancer treatment is scarce and the results are diverse. Even though uptake of interventions is generally low, these studies suggest positive effects of increased primary care involvement on patient satisfaction. Other positive effects were seen, particularly for vulnerable populations. In view of various health care strategies, which aim to transfer parts of the cancer care paths from secondary to the primary care, it is adamant to gather more robust evidence for customized interventions to enable the efficient and effective involvement of the GP during cancer treatment.

Data sharing statement

For the current study we did not generate new data. Therefore, sharing new data is not possible.

Declaration of Interest

Conflicts of interest: none

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Contributors

Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP); analysis and interpretation of data (IP, JB, AM, CH). Drafting the article or revising it critically for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the version to be submitted (IP, JB, AM, NW, EW, CH).

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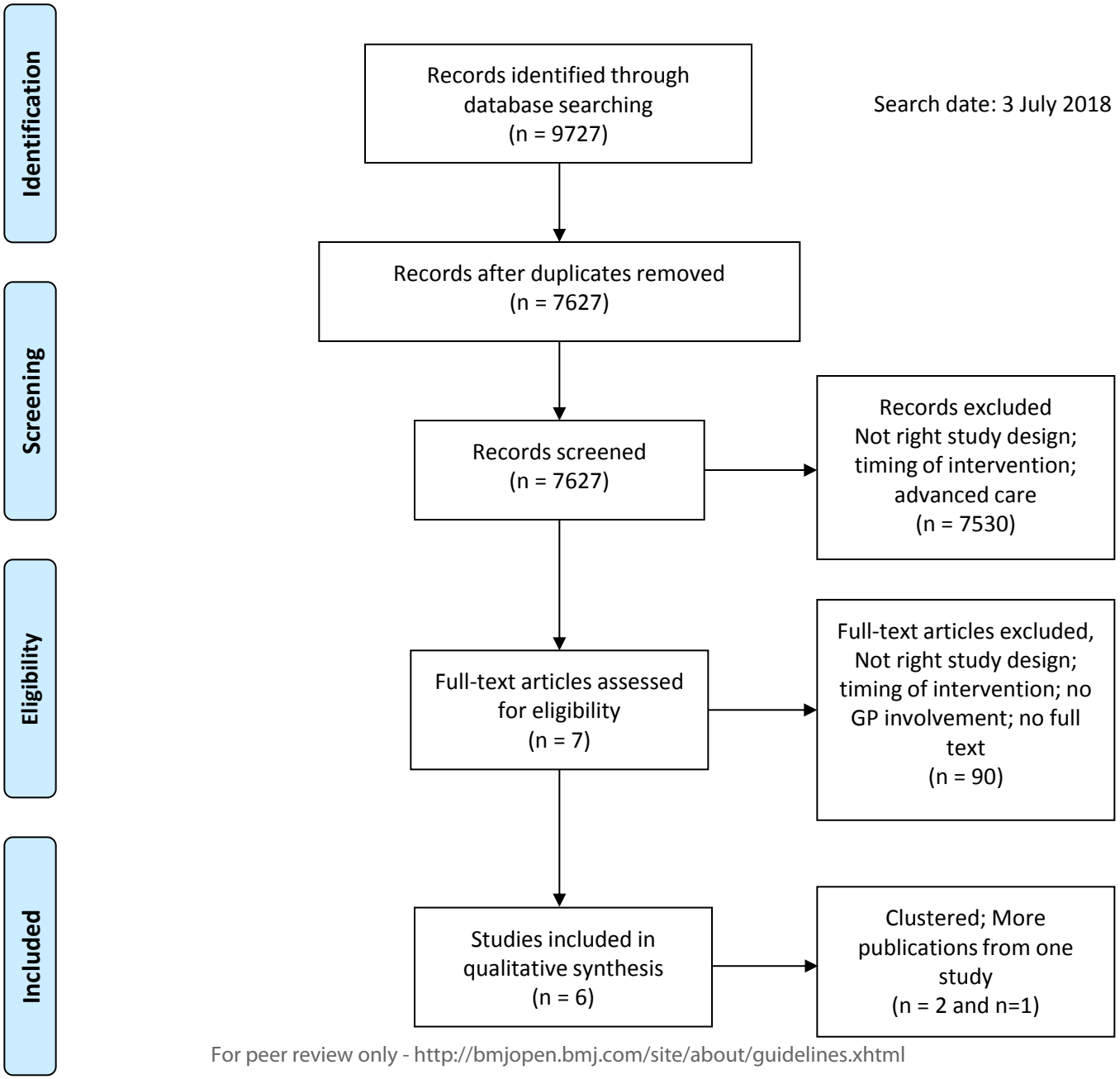
Figure 1. Flow diagram for selection of studies, based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14].

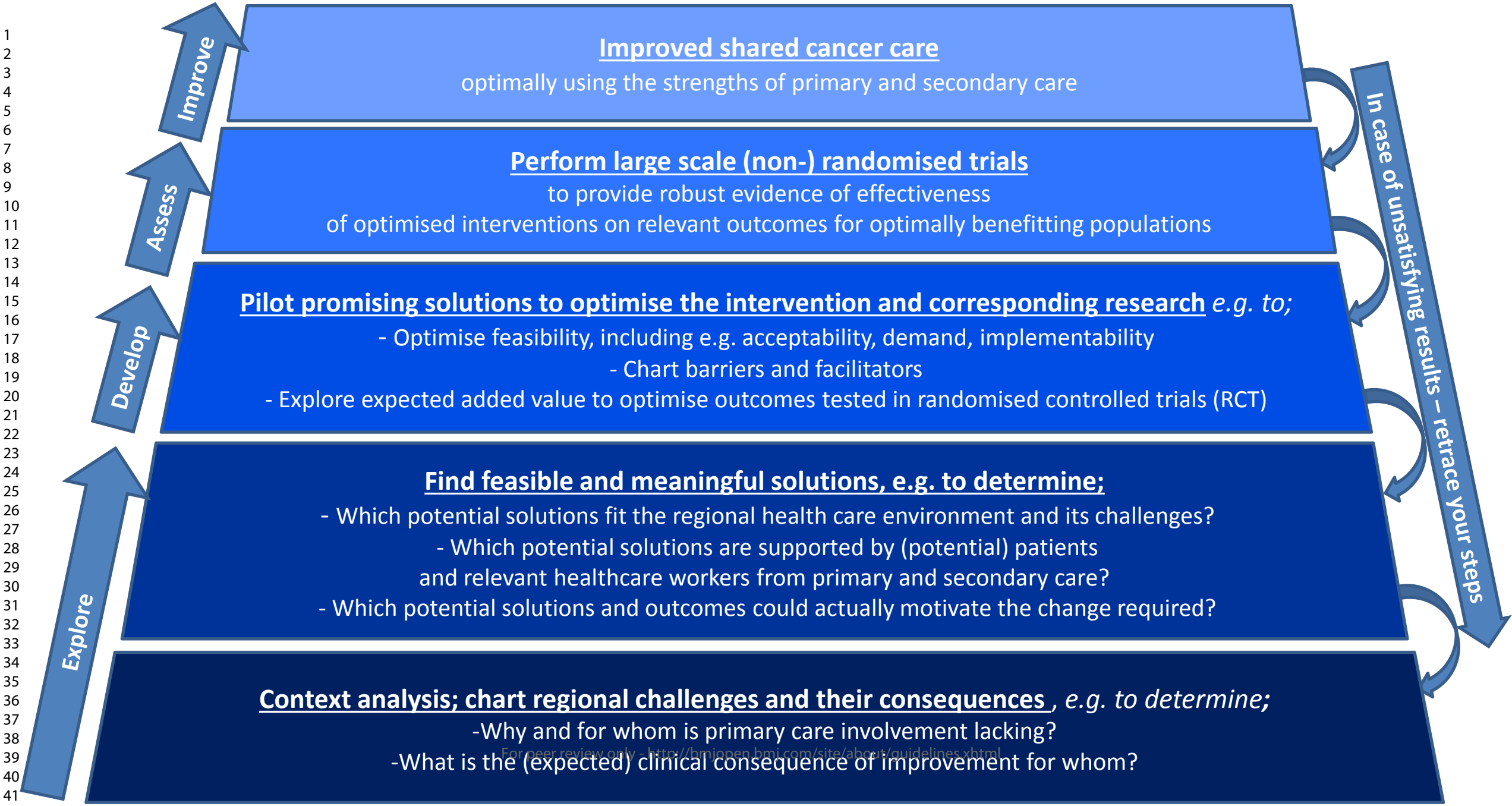
Abbreviations: GP: General practitioner

Figure 2. Risk of bias measured according to the EPOC criteria.

Figure 3. Framework for development of interventions aimed to effectively involve the GP in cancer care. In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 9727)
Search date: 3 July 2018
Records after duplicates removed (n = 7627)
Records screened (n = 7627)
Records excluded Not right study design; timing of intervention; advanced care (n = 7530)
Full-text articles assessed for eligibility (n = 7)
Full-text articles excluded, Not right study design; timing of intervention; no GP involvement; no full text (n = 90)
Studies included in qualitative synthesis (n = 6)
Clustered; More publications from one study (n = 2 and n=1)


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Baseline outcome measurements similar (selection bias)
Baseline characteristics similar (selection bias)
Incomplete outcome data (attrition bias)
Knowledge of the allocated interventions adequately prevented during the study (performance bias)
Protection against contamination (performance bias)
Selective reporting (reporting bias)
Other bias
Drury et al. 2000
Hansen et al. 2011/Bergholdt et al. 2012/2013/2013
Johansson et al. 2001
Johnson et al. 2015
Luker et al. 2000
Nielsen et al. 2003/Kousgaard et al. 2003



Search terms

Syntax PUBMED

#1

((((((((((((((((((((((“primary care”[Title/Abstract]) OR “primary health care”[Title/Abstract]) OR “primary medical care”[Title/Abstract]) OR “first-contact medical care”[Title/Abstract]) OR “first line care”[Title/Abstract]) OR “primary care physician”[Title/Abstract]) OR “primary care physicians”[Title/Abstract]) OR “general practitioner”[Title/Abstract]) OR “general practitioners”[Title/Abstract]) OR GP[Title/Abstract]) OR GPs[Title/Abstract]) OR G.P.[Title/Abstract]) OR GP-organised[Title/Abstract]) OR “family doctor*”[Title/Abstract]) OR “family practice*”[Title/Abstract]) OR "primary health care"[MeSH Terms]) OR "physicians, primary care"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "primary care nursing"[MeSH Terms]) OR "nursing care"[MeSH Terms]) OR "general practitioners"[MeSH Terms]) OR "physicians, family"[MeSH Terms]) OR "family practice"[MeSH Terms])

#2

(((((((oncolog*[Title/Abstract]) OR cancer*[Title/Abstract]) OR malignancy[Title/Abstract]) OR carcinoma[Title/Abstract]) OR ((tumor[Title/Abstract] AND malignant[Title/Abstract]))) OR “medical oncology”[MeSH Terms]) OR carcinoma[MeSH Terms]) OR ((neoplasms[MeSH Terms] AND malignant[Title/Abstract])))

#3

((((((((((((((((((((((((((((((((((care[Title/Abstract]) OR continu*[Title/Abstract]) OR follow-up[Title/Abstract]) OR surveillance[Title/Abstract])) OR “patient discharge”[Title/Abstract]) OR “hospital discharge”[Title/Abstract]) OR transmural[Title/Abstract]) OR collaborative[Title/Abstract]) OR

interdisciplinary[Title/Abstract]) OR multidisciplinary[Title/Abstract]) OR "liaison nurse*"[Title/Abstract]) OR "health care planning"[Title/Abstract]) OR "health care management"[Title/Abstract]) OR "community health planning"[Title/Abstract]) OR "service integration"[Title/Abstract]) OR "services integration"[Title/Abstract]) OR "professional-patient relations"[Title/Abstract]) OR "professional-family relations"[Title/Abstract]) OR "shared services"[Title/Abstract])) OR "multi professional working"[Title/Abstract]) OR interprofessional[Title/Abstract]) OR "multi agency working"[Title/Abstract]) OR "inter agency working"[Title/Abstract]) OR "case management"[Title/Abstract]) OR "patient discharge"[MeSH Terms]) OR "patient care planning"[MeSH Terms]) OR "patient care team"[MeSH Terms]) OR "continuity of patient care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case management"[MeSH Terms]) OR "community health planning"[MeSH Terms]) OR "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient relations"[MeSH Terms]) OR "interprofessional relations"[MeSH Terms]) OR "professional-family relations"[MeSH Terms]) OR "cooperative behavior"[MeSH Terms])

#4 (((((("randomized controlled trial"[Publication Type]) OR random*[Title/Abstract]) OR control*[Title/Abstract]) OR intervention*[Title/Abstract]))

Combining search terms: #1 AND #2 AND #3 AND #4

Syntax EMBASE

#1

'primary care':ab,ti OR 'primary health care':ab,ti OR 'primary medical care':ab,ti OR 'first-contact medical care':ab,ti OR 'first line care':ab,ti OR 'primary care physician':ab,ti OR 'primary care physicians':ab,ti OR 'general practitioner':ab,ti OR 'general practitioners':ab,ti OR gp:ab,ti OR gps:ab,ti OR g.p.:ab,ti OR 'gp organised':ab,ti OR 'gp organized':ab,ti OR 'family doctor':ab,ti OR 'family doctors':ab,ti OR 'family practice':ab,ti OR 'family practices':ab,ti OR 'primary health care'/exp OR 'primary health care' OR 'general practice'/exp OR 'general practice'

#2

oncology:ab,ti OR cancer:ab,ti OR malignancy:ab,ti OR carcinoma:ab,ti OR (tumor:ab,ti AND malignant:ab,ti) OR ('neoplasm'/exp OR neoplasm AND malignant:ab,ti) OR 'malignant neoplastic disease'/exp OR 'malignant neoplastic disease'

#3

care:ab,ti OR continu*:ab,ti OR 'follow up':ab,ti OR surveillance:ab,ti OR 'discharging plan':ab,ti OR 'discharge plan':ab,ti OR 'discharge planning':ab,ti OR 'patient discharge':ab,ti OR 'hospital discharge':ab,ti OR transmural:ab,ti OR collaborative:ab,ti OR interdisciplinary:ab,ti OR multidisciplinary:ab,ti OR 'liaison nurse':ab,ti OR 'health care planning':ab,ti OR 'health care management':ab,ti OR 'community health planning':ab,ti OR 'service integration':ab,ti OR 'services integration':ab,ti OR 'professional-patient relations':ab,ti OR 'professional-family relations':ab,ti OR 'shared services':ab,ti OR 'shared notes':ab,ti OR 'multi professional working':ab,ti OR interprofessional:ab,ti OR 'multi agency working':ab,ti OR 'inter agency working':ab,ti OR 'case management':ab,ti OR 'patient care'/exp OR 'integrated health care system' OR 'health care planning'/exp

#4

'randomized controlled trial'/exp OR random*:ab,ti OR control*:ab,ti OR intervention*:ab,ti

Combining search terms: #1 AND #2 AND #3 AND #4

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n.a.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n.a.
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n.a.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No pooling of data not assessed.
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n.a.
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 and figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	15 – 17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	18 - 22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n.a.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n.a.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n.a.
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	25

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

PRISMA 2009 Checklist