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# BMJ Open

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

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3 9 **Title Page**  
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7 11 **Title**  
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9 12 Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of  
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11 13 Health Care Interventions.  
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15 15 **Author Names and Affiliations**  
16

17 16 I.A.A. Perfors<sup>1</sup>, A.M. May<sup>1</sup>, J.A. Boeijen<sup>1</sup>, N.J. de Wit<sup>1</sup>, E. van der Wall<sup>2</sup>, C.W. Helsper<sup>1</sup>  
18  
19

20 17 1. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht,  
21  
22 18 Utrecht University, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.

23 19 2. UMC Utrecht Cancer Center, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
24  
25

26 20

27 21 **Corresponding Author**  
28

29 22 Ietje A.A. Perfors  
30

31 23 E-mail address: I.A.A.Perfors@umcutrecht.nl.  
32

33 24 Permanent address: Julius Center for Health Sciences and Primary Care, University Medical  
34  
35 25 Centre Utrecht, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
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27 **Second Title Page**

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29 **Title**

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

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3 33 **Abstract**

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5 34 **Words:** 300/300

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7 35 **Objective:** The role of primary care providers (PCP) in the cancer care continuum is  
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9 36 expanding. In the post-treatment phase, this role is increasingly recognized by policy makers  
10  
11 37 and health care professionals. During treatment, however, the role of PCP remains largely  
12  
13 38 undefined. This systematic review aims to map the content and effect of interventions aiming  
14  
15 39 to actively involve the General Practitioner (GP) during cancer treatment with a curative  
16  
17 40 intent.

18 41 **Study design** Systematic review

19 42 **Participants** Cancer patients treated with curative intent

20 43 **Data sources** Randomized controlled trials (RCTs), controlled clinical trials (CCT),  
21  
22 44 controlled before and after studies and interrupted time series focusing on interventions  
23  
24 45 designed to involve the GP during curative cancer treatment were systematically identified  
25  
26 46 from PubMed and EMBASE and subsequently reviewed. Risk of bias was scored according  
27  
28 47 to the EPOC risk of bias criteria.

29 48 **Results** Five RCTs and one CCT were included. Interventions and effects were heterogeneous  
30  
31 49 across studies. Four studies implemented interventions focussing on information transfer to  
32  
33 50 the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-  
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35 51 medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on  
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37 52 patient satisfaction with care was found in three studies. Subgroup analysis suggest a  
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39 53 reduction of health care use in elderly patients and reduction of clinical anxiety in those with  
40  
41 54 higher mental distress. No effects are reported on patients' quality of life (QoL).

42 55 **Conclusion** Interventions designed to actively involve the GP during curative cancer  
43  
44 56 treatment are scarce and diverse. Even though uptake of interventions is generally low, results  
45  
46 57 suggests a positive effect of GP involvement on patient satisfaction with care, but not on QoL.  
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48 58 Additional effects for vulnerable subgroups were found. More robust evidence for tailored  
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50 59 interventions is needed to enable the efficient and effective involvement of the GP during  
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52 60 curative cancer treatment.

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62 **PROSPERO registration number: CRD42018102253**

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3 **63 Strengths and Limitations of this study**

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6 65 • This is the first review that systematically reviews evidence based interventions,  
7 66 aiming at general practitioner involvement during the curative treatment phase of the  
8 67 cancer care continuum.

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11 68 • The electronic database search was performed without restriction on languages and  
12 69 period.

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14 70 • We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate  
15 71 tool to assess bias for complex interventions.

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18 72 • The title/abstract screening is done by single reviewer, two authors screened the full-  
19 73 text and the search was complemented with reference check of relevant articles.

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22 74 • The included studies are heterogeneous in intervention and outcome and therefore  
23 75 strong conclusions could not be made.

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76 **Keywords**

77 - Primary care

78 - General Practitioners

79 - Shared care

80 - Cancer patient

81 - Curative treatment

82 - Patient satisfaction

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## 84 **Background**

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

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

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

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

114

## 115 **Methods**

### 116 *Data source and search*

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

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

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### 135 *Study selection*

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

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### 144 *Data extraction and management*

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3 145 To determine relevance, the records were divided and screened on title and abstract by two  
4 146 single reviewers (IP,JB) and discussed with three additional reviewers in case of doubt  
5 147 (AM,CH and JB or IP). Two authors (IP,JB) performed full-text screening. Disagreements on  
6 148 eligibility were resolved in group discussion with researchers and clinicians (IP,JB,AM,CH).  
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9 149 If possible, a meta-analysis was planned to be conducted.

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### 12 13 14 151 *Patient and public involvement*

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16 152 Patients and public were not involved in the design of the current study.

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### 19 20 154 *Quality assessment*

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22 155 Risk of bias for individual studies was scored by two authors (JB,IP) with the EPOC risk of  
23 156 bias criteria [13]. In case outcomes of homogeneous study designs could be merged we rated  
24 157 the body of the evidence following the Grades of Recommendation, Assessment,  
25 158 Development and Evaluation approach (GRADE) [14] from the Cochrane collaboration.  
26 159 Present systematic review is reported following the PRISMA 2009 checklist [14].

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## 32 33 161 **Results**

### 34 35 162 *Study selection*

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37 163 As shown in Figure 1, 9727 records were eligible for inclusion after removal of duplicates.  
38 164 Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text  
39 165 screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP  
40 166 involvement started after completion of primary cancer treatment, (3) or no RCT, CCT,  
41 167 controlled before and after study or interrupted time series design was used. Two studies  
42 168 published multiple articles based on the same data [15–20]. As a result, five RCTs and one  
43 169 CCT were considered eligible for inclusion, which were described in ten articles. No  
44 170 additional eligible studies were identified in the reference lists of selected studies. Figure 2,  
45 171 Table 1, and 2 show a detailed account of the risk of bias, patient population, interventions,  
46 172 outcomes assessed and observed results for each study. Given the various research questions,  
47 173 interventions and heterogeneity of outcome measures, pooling of data, and GRADE  
48 174 assessment was not feasible.

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5 176 *Quality of studies*

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7 177 The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et  
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9 178 al. (2003) show a high risk of bias, resulting from high risk of selection and information bias  
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11 179 [15,16,21]. Drury et al. (2000) scored a medium risk of bias [22]. And the studies of Johnson  
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13 180 et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk  
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15 181 of bias [17–19,23,24]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several  
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17 182 limitations should be kept in mind. The randomization produced an imbalance, which  
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19 183 influenced comparability of outcomes between study groups without corresponding correction  
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21 184 in the analyses. Furthermore, it was not reported whether a baseline measurement was  
22  
23 185 performed and the exact timing of the first measurement (Table 2). Also, the percentage of  
24  
25 186 missing data was 33% in the intervention and 26% in the control group [15].

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28 188 *Study populations*

29 189 The six eligible studies were conducted in Europe (five) and Australia (one) among different  
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31 190 cancer patient populations over the past two decades. Breast cancer patients were the most  
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33 191 commonly studied group (between 33-100% of the study populations). Five RCTs included  
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35 192 patients with more than one type of cancer, in different stages. Three studies included patients  
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37 193 treated palliatively (<25% of total study population). In two RCT's cancer stage was not  
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39 194 specified.

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42 196 *Type of interventions*

43 197 The interventions in the studies (Table 1) were heterogeneous, but can be divided in mainly  
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45 198 information transfer to the GP (n=4) [15,16,21–23] and tailored primary care interventions  
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47 199 (n=2) [17–20,24].

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49 200 Interventions focusing on information transfer, provided additional, disease specific  
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51 201 educational, and practical information concerning treatment and care directly to the GP or via  
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53 202 the patient. Interventions were either directed at enhancing communication between GP and  
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55 203 other party (i.e. secondary care or patient), or directed at improving patient's attitude towards  
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57 204 the healthcare system (i.e. healthcare in general or intervention), physical- and psychological

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3 205 complains. Three interventions provided patients with information, which was to be  
4 206 transferred to the GP. In one CCT [21], informational cards were provided to the patients for  
5 207 use in primary care. Two other RCTs described an intervention with a Patient Held Record  
6 208 (PHR) [22,23] aimed to facilitate intersectoral communication, to provide patients with an  
7 209 aide memoire, and with the opportunity to stay actively involved in their treatment. One RCT  
8 210 supplied the GP with patient specific discharge summaries by secondary care, aiming to  
9 211 enhance GP knowledge of chemotherapy treatment and expected adverse effects [15,16].

14 212 The tailored primary care interventions aimed to support patients in managing their disease  
15 213 and treatment [17,18,20,24]. The interventions are too diverse to be merged and therefore  
16 214 described separately. In Johansson et al. (2001) [24] primary care was intensified by means of  
17 215 recruitment of a home care nurse, psychologist, dietician and training of the GP. The home  
18 216 care nurse initiated contact. The GP was regularly medically informed by the specialist and  
19 217 educated on management of cancer patients. In the one RCT from Hansen et al. (2011) and  
20 218 Bergholdt et al. (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on  
21 219 different aspects of rehabilitation. Afterwards the GP was informed on patient specific  
22 220 rehabilitation needs and encouraged to pro-actively contact the patient to support the patient  
23 221 in his/her needs.

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### 34 223 *Study outcomes*

36 224 Most often measured primary outcomes were health care utilization [15,16,21,22,24] and  
37 225 quality of life [15–17,22], as presented in Table 2. Other outcomes were patient and GP  
38 226 perceptions of care, symptoms, coping, and empowerment. The following outcomes were not  
39 227 measured in found articles: healthcare experience by informal caregivers, and disease specific  
40 228 outcomes (i.e. progress, mortality). Outcomes are described in more detail below.

44 229

### 47 230 *Intervention fidelity/compliance and health care use*

49 231 Health care use is related to the uptake of the intervention. For example, if the intervention  
50 232 aims at more GP involvement, health care use is likely to increase. Although all interventions  
51 233 aimed at increased involvement of primary care, four interventions did not show a significant  
52 234 increase of GP consultations [15,18,21,22]. Correspondingly, the uptake of interventions  
53 235 appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al. [18] an

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3 236 “active involvement” intervention, in which GP pro-activity was comparable to GP  
4 237 proactivity in the control group (52 to 60%) [18]. In two studies, information transfer to the  
5 238 GP by the patients was hardly used or remembered by the majority of the GPs [21,22].  
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8 239 Five studies, evaluated the effect of the intervention on hospital and/or primary care resource  
9 240 use. These studies showed no significant effect on secondary care health care use [21,22,24].  
11 241 Only the subgroup of older patients ( $\geq 70$  years of age) had a significantly lower use of  
12 242 secondary care [24] when primary care was actively involved. The studies reported no  
13 243 difference in the number of GP consultations in the intervention group compared to the  
14 244 control group [15,16,21–23], although GP consultations were part of the interventions.  
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#### 21 246 *Patient perception*

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23 247 Positive effects on patients’ satisfaction with care were indicated by three studies. Extended  
24 248 information by PHR or discharge summary improved patient perceived intersectoral  
25 249 cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that  
26 249 ‘the GP could help in the way a specialist could not’ [23]. Regardless of the uptake of the  
27 250 intervention, one study showed an improved satisfaction with communication and  
28 251 participation with care [22]. The significantly higher levels of perceived GP support in  
29 252 Nielsen et al.(2003) shortly after the intervention, declined to non-significant levels at six  
30 253 months after start of intervention. The authors did not present a mean difference overtime.  
31 254 One study with a low uptake of intervention showed no significant effect on patients  
32 255 satisfaction [20].  
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#### 41 258 *Quality of life and psychological outcomes*

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43 259 No study found a significant effect on quality of life [15,17,22]. Johnson et al (2001) [23],  
44 260 showed a significant difference in change of depression scores ( $p=0.04$ ). In the intervention  
45 261 group depression scores remained unchanged, whereas scores in the control group  
46 262 deteriorated significantly. Also, using a PHR combined with routinely visits to the GP led to a  
47 263 significantly higher reduction of the number of clinically anxiousness patients compared to  
48 264 usual care [23].  
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3 266 *GPs perceptions of care*  
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5 267 Four out of five studies evaluating effects on GPs perceptions of care, did not find relevant  
6 268 effects on GP's confidence in disease management and knowledge nor in the communication  
7 269 with the specialist [16,20,21,23]. Studies in which information was carried by the patient (a  
8 270 PHR or informational cards) showed little impact on GP satisfaction with care mostly due to  
9 271 low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant  
10 272 positive effects on GP perceived intersectoral cooperation and GP satisfaction with  
11 273 information.  
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277 Figure 1: Flow diagram for selection of studies, based on Preferred Reporting Items for  
278 Systematic Reviews and Meta-Analyses (PRISMA) [14].

279 Abbreviations: GP: General practitioner

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	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	+	+	-	-	-	?	+	+	+

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282 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 60% ♀	<i>Inclusion</i> 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	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 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)	N = 955 72% ♀	<i>Inclusion</i> Cancer diagnosis <3 months	Intervention vs UC Rehabilitation primary care program Initiative GP contact: Healthcare worker
Hansen et al. (2011) [17–20]	MAM (43%), LUN, GI, other (19%), MEL	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 14 months	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
Denmark	Cancer stage unknown, no deceased		
Johansson et al. (2001)[24]	N = 463 57% ♀	<i>Inclusion</i> Newly diagnosed patients (<3 months after diagnosis)	Intervention vs UC Intensified primary care program Initiative GP contact: Healthcare worker
Sweden	MAM (47%), GI, PRO	<i>Intervention</i>	Individual Support intervention consisting of:

Reference	Population N=number, Country cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
	22% with advanced disease	Upon enrolment  <i>Follow up</i> 3 months	- 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 - Active involvement of dietician and psychologist care
Johnson et al. (2015)[23]	N = 97 86% ♀	<i>Inclusion</i> During first course of CT  <i>Intervention</i> First through last course of CT  <i>Follow up</i> 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
Australia	MAM (76%), HEM, GYN, GI  Cancer stage 3.3% palliative  Stopped early (slow accrual); underpowered for the main analysis		
Luker et al. (2000)[21]	N = 79 100% ♀	<i>Inclusion</i> <4 weeks after diagnosis  <i>Intervention</i> At start of treatment  <i>Follow up</i> 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
UK	MAM (100%)  Cancer stage 100% curative		

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Reference	Population N=number, Country 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]	N = 248 64% ♀	<i>Inclusion</i> Newly diagnosed patients	UC and intervention vs UC Shared care program Initiative GP contact: Patient
Kousgaard et al. (2003) [16]	MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL	<i>Intervention</i> From referral onwards; during treatment	Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment
Denmark	Cancer stage 15% palliative	<i>Follow up</i> 6 months	- 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

284 Table 1 – Details of the interventions

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

Reference	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]	<p><i>Primary</i></p> <ul style="list-style-type: none"> <li>- Health care use (patient reported)</li> <li>- Patient satisfaction with communication and participation in care (SDQ)</li> <li>- Quality of life (EORTC QLQ-C30)</li> </ul> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>- GP views on PHR (SDQ)</li> </ul> <p><i>Measurements</i></p> <p>Single measurement at 3 months</p>	<p><b>Uptake of intervention</b> 27.3% of 202 responding GPs had seen the PHR</p> <p><b>Health care use</b> (<i>intervention vs. controls</i>)</p> <p>Contact with care providers in 3 months follow-up;</p> <ul style="list-style-type: none"> <li>• Visit GP 78% vs. 85%</li> <li>• Visited secondary care clinics 95% vs. 95%</li> </ul> <p><b>Patient related outcomes</b> (<i>intervention vs control</i>)</p> <ul style="list-style-type: none"> <li>- Satisfaction communication and participation in care mean <math>\pm</math> SD (scale 1-5): 3.83<math>\pm</math>0.59 vs. 3.80<math>\pm</math>0.59, (95% CI 0.09- 0.15)</li> <li>- Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05</li> <li>- Quality of life mean global scores: 66.8<math>\pm</math>24.2 vs. 65.3<math>\pm</math>23.7</li> </ul> <p><b>GP related outcome</b> (<i>seen PHR vs. not seen PHR</i>)</p> <ul style="list-style-type: none"> <li>- GP agrees that patients should have full access to their records 57% vs. 57%</li> </ul>
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	<p><i>Primary</i></p> <p>Quality of life (EORTC QLQ-C30)</p> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>-Psychological distress (POMS)</li> <li>-Symptoms (scale of the EORTC QLQ-C30)</li> <li>-Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth)</li> <li>-GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth)</li> <li>-GP's satisfaction with their contribution to the patient's</li> </ul>	<p><b>Uptake of intervention</b> pro-activity of GP intervention vs control: GP reported 61.2% vs 55.2% p=0.10, patient reported 60.1% vs 51.9% p=0.15</p> <p><b>Patient related outcomes</b> (<i>intervention vs control</i>)</p> <p>-Quality of life; mean difference [95%CI];</p> <ul style="list-style-type: none"> <li>• at 6 months 1.25 [-2.4-4.9]</li> <li>• at 14 months -0.71 [-4.3-2.8]</li> </ul> <p>- Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0]</p> <p>- Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5]</p> <p>- Patient satisfaction with,</p> <ul style="list-style-type: none"> <li>• GP on five dimensions, OR adj [95%CI] All NS;</li> </ul> <p>Doctor–patient relationship 0.94 [0.35-2.47], Medical care 1.2 [0.5-3.0], Information and support 1.6 [0.6-</p>

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Reference	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)  <i>Measurements</i> 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]  <b>GP related outcomes (intervention vs control)</b> - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[24]	<i>Primary</i> Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing)  <i>Measurements</i> Single measurement at 3 months	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> 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 (χ² p = 0.034) • <70y: in 11% vs. 10% of patients (χ² p = 0.80)
Johnson et al. (2015)[23]	<i>Primary</i> - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC) - Empowerment (PES)	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> - Emergency department presentations: no significant between-group differences were observed - Average number of GP visits 2.79 vs 1.61, p < 0.001

Reference	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
	<p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>- Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits )</li> <li>- Patient perception of care (SDQ)</li> <li>- GP perception of care (SDQ)</li> </ul> <p><i>Measurements</i></p> <ul style="list-style-type: none"> <li>- before treatment</li> <li>- midway through treatment</li> <li>- after treatment</li> </ul>	<p><b>Patient related outcomes</b> (<i>intervention vs control</i>)</p> <p>Patient perception of care;</p> <ul style="list-style-type: none"> <li>- GP could help in ways specialist could not: 57% vs. 19% (<math>\chi^2 = 11.5</math>; <math>p = 0.002</math>)</li> <li>- Patient opinion concerning PHR/GP visit after CT course: <ul style="list-style-type: none"> <li>• 81% considered PHR useful</li> <li>• 35% considered visit inconvenient</li> </ul> </li> </ul> <p>Depression; Geometric mean score [95%CI]</p> <ul style="list-style-type: none"> <li>• at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40]</li> <li>• after treatment: 4.04 [3.25 to 4.83] vs 4.72 [3.72 to 5.72] <math>p = 0.04</math> for comparison of groups over time</li> </ul> <p>Anxiety; Geometric mean score [95%CI]</p> <ul style="list-style-type: none"> <li>• at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32]</li> <li>• after treatment: 5.49 [4.54 to 6.43] vs 5.24 [4.26 to 6.22] <math>p = 0.80</math> for comparison of groups over time</li> </ul> <ul style="list-style-type: none"> <li>- Subgroup analysis for number of clinically anxious patients <ul style="list-style-type: none"> <li>• at baseline: 14 CA patients vs 11 CA patients</li> <li>• after treatment: 3 CA patients vs 5 CA patients</li> </ul> </li> </ul> <p>Decline intervention <math>p=0.002</math>; control <math>p=0.014</math></p> <p>Coping; Geometric mean difference over time -0.7 vs 0.1 <math>p=0.35</math></p> <p>Empowerment; Geometric mean difference over time 0.9 vs 0.9 <math>p=0.47</math></p> <p><b>GP related outcome</b> (<i>intervention vs control</i>)</p> <ul style="list-style-type: none"> <li>- GPs satisfied with communication: 82% vs. 95%</li> <li>- GP confidence in managing: <ul style="list-style-type: none"> <li>• side effects 85% vs. 71% (<math>p=0.45</math>)</li> <li>• psychological issues 97% vs. 81% (<math>p=0.04</math>)</li> </ul> </li> </ul>
Luker	<i>Primary</i>	<b>Uptake of intervention</b> 8 of the 31 interviewed GPs recall seeing the Information Card

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

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Reference	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]	<i>Primary</i> - Patient attitude towards the health care system (intersectoral cooperation and 'not feeling left in limbo' (SDQ)	<b>Uptake of intervention</b> Not reported  <b>Patient related outcomes (intervention vs control)</b> - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055
Kousgaard et al. (2003) [16]	- 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	- 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  <b>Health care use (intervention vs. controls)</b> - 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)
	<i>Measurements</i> Patient: - First measurement "Soon after the introduction of the intervention."(0 month) - 6 months GP assessment: timing unknown	<b>GP related outcome (intervention vs. control)</b> - 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.



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290 Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group;  
291 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  
292 = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs  
293 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  
294 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 =  
295 Self Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus;  $\chi^2$ = Chi-square distribution.

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## 297 Discussion

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

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

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

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

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3 329 (i.e., 75%), but we cannot exclude that the observed effects were influenced the inclusion of  
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6 331 publication bias.  
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10 333 Our review shows that further large studies with a robust design are needed, which should  
11 334 focus on the effect of primary care involvement for various populations, including  
12 335 specifications for cancer types and vulnerable populations (e.g. elderly, and patients with  
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14 336 physical or mental comorbidity). These studies should provide us with a definite answer on  
15 337 the effect of GP involvement in the cancer care path, addressing the questions when and how  
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17 338 to organize the role of primary care and specifically for whom. In addition, this knowledge  
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19 339 should facilitate primary care workers to appropriately implement their role, making full use  
20 340 of their specific expertise by consideration of the patients' context and values, provided in a  
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22 341 trusted environment. To improve uptake of intervention we used only existing health care  
23 342 facilities in the intervention design of a RCT involving the GP and a homecare oncology  
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25 343 nurse after diagnosis and during curative cancer treatment. Results of this study will be  
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27 344 published in 2018/2019. [26]  
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## 32 346 **Conclusion**

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35 347 Literature addressing the effects of interventions designed to actively involve the GP during  
36 348 curative cancer treatment is scarce and the results are diverse. Even though uptake of  
37 349 interventions is generally low, these studies suggest positive effects of increased primary care  
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39 350 involvement on patient satisfaction. Other positive effects were seen, particularly for  
40 351 vulnerable populations. In view of various health care strategies which aim to transfer parts of  
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42 352 the cancer care paths from secondary to the primary care, it is adamant to gather more robust  
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44 353 evidence for customized interventions to enable the efficient and effective involvement of the  
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46 354 GP during cancer treatment.  
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3 356 **Data sharing statement**  
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5 357 For the current study we did not generate new data. Therefore, sharing new data is not  
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7 358 possible.  
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11 360 **Declaration of Interest**  
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13 361 Conflicts of interest: none  
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18 363 **Role of the Funding Source**  
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20 364 This research did not receive any specific grant from funding agencies in the public,  
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22 365 commercial or not-for-profit sectors.  
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26 367 **Contributors**  
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28 368 Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP);  
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30 369 analysis and interpretation of data (IP, JB, AM, CW). Drafting the article or revising it  
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32 370 critically for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the  
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34 371 version to be submitted (IP, JB, AM, NW, EW, CH).  
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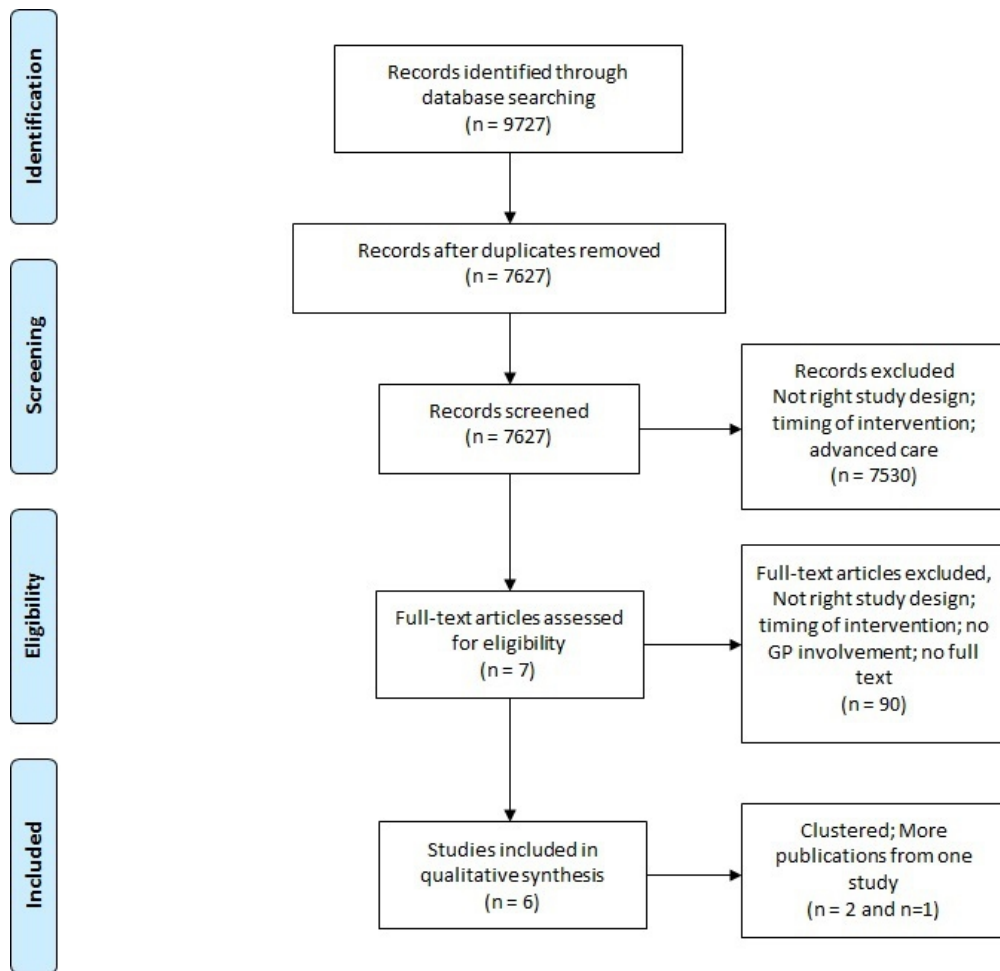


Figure 1. PRISMA flow diagram.

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	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	+	+	-	-	-	?	+	+	+

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

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13 care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case  
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15 "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient  
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41 Combining search terms: #1 AND #2 AND #3 AND #4  
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## 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

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'randomized controlled trial'/exp OR random\*:ab,ti OR control\*:ab,ti OR  
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Combining search terms: #1 AND #2 AND #3 AND #4

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# PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

Page 1 of 2

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.
<b>RESULTS</b>			
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.
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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

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# PRISMA 2009 Checklist

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# BMJ Open

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

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

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5     General and Supportive Care; Systematic review.

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

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10 12 Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of  
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17 15 **Author Names and Affiliations**  
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19 16 I.A.A. Perfors<sup>1</sup>, A.M. May<sup>1</sup>, J.A. Boeijen<sup>1</sup>, N.J. de Wit<sup>1</sup>, E. van der Wall<sup>2</sup>, C.W. Helsper<sup>1</sup>  
20

21 17 1. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht,  
22 18 Utrecht University, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
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25 19 2. UMC Utrecht Cancer Center, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
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29 21 **Corresponding Author**  
30

31 22 Charles W. Helsper  
32

33 23 E-mail address: C.W.Helsper-2 @umcutrecht.nl.  
34

35 24 Permanent address: Julius Center for Health Sciences and Primary Care, University Medical  
36 25 Centre Utrecht, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
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27 **Second Title Page**

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29 **Title**

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

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3 **33 Abstract**  
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5 **34 Words:** 300/300  
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8 **35 Objective:** The role of primary care providers (PCP) in the cancer care continuum is expanding.  
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10 **36** In the post-treatment phase, this role is increasingly recognized by policy makers and health  
11 **37** care professionals. During treatment, however, the role of PCP remains largely undefined. This  
12 **38** systematic review aims to map the content and effect of interventions aiming to actively involve  
13 **39** the General Practitioner (GP) during cancer treatment with a curative intent.  
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17 **40 Study design** Systematic review  
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19 **41 Participants** Cancer patients treated with curative intent  
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21 **42 Data sources** Randomized controlled trials (RCTs), controlled clinical trials (CCT),  
22 **43** controlled before and after studies and interrupted time series focusing on interventions  
23 **44** designed to involve the GP during curative cancer treatment were systematically identified  
24 **45** from PubMed and EMBASE and were subsequently reviewed. Risk of bias was scored  
25 **46** according to the EPOC risk of bias criteria.  
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29 **47 Results** Five RCTs and one CCT were included. Interventions and effects were heterogeneous  
30 **48** across studies. Four studies implemented interventions focussing on information transfer to  
31 **49** the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-  
32 **50** medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on  
33 **51** patient satisfaction with care was found in three studies. Subgroup analysis suggest a  
34 **52** reduction of health care use in elderly patients and reduction of clinical anxiety in those with  
35 **53** higher mental distress. No effects are reported on patients' quality of life (QoL).  
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38 **54 Conclusion** Interventions designed to actively involve the GP during curative cancer  
39 **55** treatment are scarce and diverse. Even though uptake of interventions is low, results suggests  
40 **56** a positive effect of GP involvement on patient satisfaction with care, but not on QoL.  
41 **57** Additional effects for vulnerable subgroups were found. More robust evidence for tailored  
42 **58** interventions is needed to enable the efficient and effective involvement of the GP during  
43 **59** curative cancer treatment.  
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53 **61 PROSPERO registration number: CRD42018102253**  
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## 62 **Strengths and Limitations of this study**

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64 • This is the first review that systematically reviews evidence based interventions,  
65 aiming at general practitioner involvement during the curative treatment phase of the  
66 cancer care continuum.

67 • The electronic database search was performed without restriction on languages and  
68 period.

69 • We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate  
70 tool to assess bias for complex interventions.

71 • The title/abstract screening is done by single reviewer, two authors screened the full-  
72 text and the search was complemented with reference checks of relevant articles.

73 • The included studies are heterogeneous in intervention and outcome and therefore  
74 strong conclusions could not be made.

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3 75 **Keywords**  
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5 76 - Primary care  
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## 83 **Background**

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

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



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3 115 This systematic review aims to provide a comprehensive overview of the content and effect of  
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5 116 interventions aiming at active involvement of the general practitioner during cancer treatment  
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7 117 with curative intent compared to usual care.  
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## 11 119 **Methods**

### 13 120 *Data source and search*

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16 121 A literature search was conducted in PubMed and EMBASE for articles describing randomized  
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18 122 controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies,  
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20 123 and interrupted time series published in any language until the 3<sup>rd</sup> of July 2018. We used a  
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22 124 search strategy that was previously applied in a review assessing continuity of care in the  
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24 125 follow-up of patients with cancer [12]. Subsequently, this strategy was adapted for  
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26 126 completeness and relevance based on sequential testing of search strategies to develop our final  
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28 127 search strategy. The details of the sequential and final search strategies are listed in appendix  
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30 128 A. The search terms include keywords and controlled vocabulary terms surrounding the central  
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32 129 themes “general practitioner”, “primary care”, “oncology”, and “care”. Outcome measures and  
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34 130 comparing study arm were not included in the selection criteria to widen the scope of the review.  
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36 131 Instead of a database integrated filter, a tailored methodological search filter was used to limit  
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38 132 retrieval to appropriate study design [12]. We reviewed references of selected articles for  
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40 133 additional papers.

41 134 Outcomes are included if they are related to the quality of healthcare (e.g. healthcare use), the  
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43 135 healthcare experience of: healthcare professionals, informal caregivers, and patients, or  
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45 136 outcomes at the patient-level, with a focus on, e.g., disease, quality of life, and psychosocial  
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47 137 impact.  
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### 50 139 *Study selection*

51 140 Articles were selected if they described an intervention; (1) for cancer patients, (2) starting  
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53 141 during curative treatment, (3) evaluating involvement of the GP, and (4) tested in a randomized  
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55 142 controlled setting, CCT, controlled before and after studies or interrupted time series. Studies  
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57 143 with a majority (>75%) of curative patients were included. In case the proportion of curative  
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59 144 patients was unclear, the original authors were contacted. Without response, the inclusion of  
60  
145 the trial was based on >75% percentage patient survival during the trial.

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### 147 *Data extraction and management*

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

153

### 154 *Patient and public involvement*

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

156

### 157 *Quality assessment*

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

164

## 165 **Results**

### 166 *Study selection*

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

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3 175 2 show a detailed account of the risk of bias, patient population, interventions, outcomes  
4 176 assessed and observed results for each study. Given the various research questions,  
5 177 interventions and heterogeneity of outcome measures, pooling of data, and GRADE assessment  
6 178 was not feasible.  
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### 12 13 180 *Quality of studies*

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15 181 The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et  
16 182 al. (2003) show a high risk of bias, resulting from high risk of selection and information bias  
17 183 [15,16,23]. Drury et al. (2000) scored a medium risk of bias [24]. And the studies of Johnson  
18 184 et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk of  
19 185 bias [17–19,22,25]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several limitations  
20 186 should be kept in mind. The randomization produced an imbalance, which influenced  
21 187 comparability of outcomes between study groups without corresponding correction in the  
22 188 analyses. Furthermore, it was not reported whether a baseline measurement was performed and  
23 189 the exact timing of the first measurement (Table 2). Also, the percentage of missing data was  
24 190 33% in the intervention and 26% in the control group [15].  
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### 34 35 192 *Study populations*

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37 193 The six eligible studies were conducted in Europe (five) and Australia (one) among different  
38 194 cancer patient populations over the past two decades. Breast cancer patients were the most  
39 195 commonly studied group (between 33-100% of the study populations). Five RCTs included  
40 196 patients with more than one type of cancer, in different stages. Three studies included  
41 197 palliatively treated patients (<25% of total study population). In two RCT's cancer stage was  
42 198 not specified.  
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### 50 51 200 *Usual care*

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53 201 In most studies, usual care was not described in detail. Only Luker et al. [23] described the  
54 202 structured care that usual care patients received, which included home visits from a breast care  
55 203 nurse and written patient information on treatments. In general, the patient's GP received a  
56 204 discharge summary [15–17,19,20,25] at the end of the treatment period [15,16] or after each  
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3 205 visit [25]. Other types of transferred information to the GP included an extract of the hospital  
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5 206 record [15,16] or communication by telephone [25]. Two studies did not describe what usual  
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7 207 care entailed [21,22,24].  
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11 209 *Type of interventions*  
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14 210 All participants received usual care, which was extended when the participant was appointed to  
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16 211 the intervention. The interventions in the studies (Table 1) were heterogeneous, but can be  
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18 212 divided in mainly information transfer to the GP (n=4) [15,16,23–25] and tailored primary care  
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20 213 interventions (n=2) [17–20,22].

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22 214 Interventions focusing on information transfer, provided additional, disease specific  
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24 215 educational, and practical information concerning treatment and care directly to the GP or via  
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26 216 the patient. Interventions were either directed at enhancing communication between GP and  
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28 217 another party (i.e. secondary care or patient), or directed at improving patient's attitude towards  
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30 218 the healthcare system (i.e. healthcare in general or intervention), physical- or psychological  
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32 219 complains. Three interventions provided patients with information, which was to be transferred  
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34 220 to the GP. In one CCT [23], informational cards were provided to the patients for use in primary  
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36 221 care. Two other RCTs described an intervention with a Patient Held Record (PHR) [24,25]  
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38 222 aimed to facilitate intersectoral communication, to provide patients with an aide memoire, and  
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40 223 with the opportunity to stay actively involved in their treatment. One RCT supplied the GP with  
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42 224 patient specific discharge summaries by secondary care, aiming to enhance GP knowledge of  
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44 225 chemotherapy treatment and expected adverse effects [15,16].

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46 226 The tailored primary care interventions aimed to support patients in managing their disease and  
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48 227 treatment [17,18,20,22]. The interventions were to diverse to be merged and they are therefore  
49  
50 228 described separately. In Johansson et al. (2001) [22] primary care was intensified by means of  
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52 229 recruitment of a home care nurse, psychologist, dietician and training of the GP. The home care  
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54 230 nurse initiated contact. The GP was regularly informed by the specialist and educated on  
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56 231 management of cancer patients. In the one RCT from Hansen et al. (2011) and Bergholdt et al.  
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58 232 (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on different aspects of  
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60 233 rehabilitation. Afterwards the GP was informed on patient specific rehabilitation needs and  
234 encouraged to pro-actively contact the patient to support the patient in his/her needs.

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3 236 *Study outcomes*  
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5 237 The most often measured primary outcomes were health care utilization [15,16,22–24] and  
6 238 quality of life [15–17,24], as presented in Table 2. Other outcomes were patient and GP  
7 239 perceptions of care, symptoms, coping, and empowerment. The following outcomes were not  
8 240 presented in the included articles: healthcare experience by informal caregivers, and disease  
9 241 specific outcomes (i.e. progress, mortality). Outcomes are described in more detail below.  
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17 243 *Intervention fidelity/compliance and health care use*  
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19 244 Health care use is related to the uptake of the intervention. For example, if the intervention aims  
20 245 at more GP involvement, health care use is likely to increase. Although all interventions aimed  
21 246 at increased involvement of primary care, four interventions did not show a significant increase  
22 247 of GP consultations [15,18,23,24]. Correspondingly, the uptake of interventions appeared to be  
23 248 low in the majority of the studies. This is illustrated by Bergholdt et al. [18] which describes an  
24 249 “active involvement” intervention, in which GP pro-activity was comparable to GP proactivity  
25 250 in the control group (52 to 60%) [18]. In two studies, information transfer to the GP by their  
26 251 patients was hardly used or remembered by the majority of the GPs [23,24].  
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34 252 Five studies, evaluated the effect of the intervention on hospital and/or primary care resource  
35 253 use. These studies showed no significant effect on secondary care health care use [22–24]. Only  
36 254 the subgroup of older patients ( $\geq 70$  years of age) had a significantly lower use of secondary  
37 255 care [22] when primary care was actively involved. Even though GP consultations were part  
38 256 of the interventions several studies reported no difference in the number of GP consultations in  
39 257 the intervention group compared to the control group [15,16,23–25].  
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47 259 *Patient perception*  
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49 260 Positive effects on patients’ satisfaction with care were indicated by three studies. Extended  
50 261 information by PHR or discharge summary improved patient perceived intersectoral  
51 262 cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that ‘the  
52 263 GP could help in the way a specialist could not’ [25]. Regardless of the uptake of the  
53 264 intervention, one study showed an improved satisfaction with communication and participation  
54 265 with care [24]. The significantly higher levels of perceived GP support shortly after the  
55 266 intervention described in Nielsen et al.(2003) declined to non-significant levels at six months  
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3 267 after start of intervention. The authors did not present a mean difference overtime. One study  
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5 268 with a low uptake of intervention showed no significant effect on patients satisfaction [20].  
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10 270 *Quality of life and psychological outcomes*

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12 271 No study found a significant effect on quality of life [15,17,24]. Johnson et al (2001) [23],  
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14 272 showed a significant difference in change of depression scores (p0.04). In the intervention  
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16 273 group depression scores remained unchanged, whereas scores in the control group deteriorated  
17  
18 274 significantly. Also, using a PHR combined with routine visits to the GP led to a significantly  
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20 275 higher reduction of the number of clinically anxiousness patients compared to usual care [25].  
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24 277 *GPs perceptions of care*

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26 278 Four out of five studies evaluating effects on GPs perceptions of care did not find relevant  
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28 279 effects on GP's confidence in disease management and knowledge nor in the communication  
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30 280 with the specialist [16,20,23,25]. Studies in which information was carried by the patient (a  
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32 281 PHR or informational cards) showed little impact on GP satisfaction with care mostly due to  
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34 282 low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant  
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36 283 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  60% ♀	<i>Inclusion</i> 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	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 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)	N = 955  72% ♀	<i>Inclusion</i> Cancer diagnosis <3 months	Intervention vs UC Rehabilitation primary care program Initiative GP contact: Healthcare worker
Hansen et al. (2011) [17–20]	MAM (43%), LUN, GI, other (19%), MEL	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 14 months	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
Denmark	Cancer stage unknown, no deceased		
Johansson et al. (2001)[22]	N = 463  57% ♀	<i>Inclusion</i> Newly diagnosed patients (<3 months after diagnosis)	Intervention vs UC Intensified primary care program Initiative GP contact: Healthcare worker
Sweden	MAM (47%), GI, PRO	<i>Intervention</i>	Individual Support intervention consisting of:

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Reference	Population N=number, cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
	22% with advanced disease	Upon enrolment  <i>Follow up</i> 3 months	- 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 - Active involvement of dietician and psychologist care
Johnson et al. (2015)[25]	N = 97  86% ♀	<i>Inclusion</i> During first course of CT  <i>Intervention</i> First through last course of CT  <i>Follow up</i> 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
Australia	MAM (76%), HEM, GYN, GI  Cancer stage 3.3% palliative  Stopped early (slow accrual); underpowered for the main analysis		
Luker et al. (2000)[23]	N = 79  100% ♀	<i>Inclusion</i> <4 weeks after diagnosis  <i>Intervention</i> At start of treatment  <i>Follow up</i> 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
UK	MAM (100%)  Cancer stage 100% curative		



Reference	Population N=number, Country 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]	N = 248 64% ♀	<i>Inclusion</i> Newly diagnosed patients	UC and intervention vs UC Shared care program Initiative GP contact: Patient
Kousgaard et al. (2003) [16]	MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL	<i>Intervention</i> From referral onwards; during treatment	Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment
Denmark	Cancer stage 15% palliative	<i>Follow up</i> 6 months	- 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

287 Table 1 – Details of the interventions

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

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Reference	Primary and secondary outcome measures (instrument used)	Findings if applicable to study:
	<b>Timing of measurement</b>	<ol style="list-style-type: none"> <li><b>Uptake of intervention</b></li> <li><b>Health care use</b></li> <li><b>Patient related outcomes</b></li> <li><b>GP related outcomes</b></li> </ol>
Drury et al. (2000)[24]	<p><i>Primary</i></p> <ul style="list-style-type: none"> <li>- Health care use (patient reported)</li> <li>- Patient satisfaction with communication and participation in care (SDQ)</li> <li>- Quality of life (EORTC QLQ-C30)</li> </ul> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>- GP views on PHR (SDQ)</li> </ul> <p><i>Measurements</i></p> <p>Single measurement at 3 months</p>	<p><b>Uptake of intervention</b> 27.3% of 202 responding GPs had seen the PHR</p> <p><b>Health care use (intervention vs. controls)</b></p> <p>Contact with care providers in 3 months follow-up;</p> <ul style="list-style-type: none"> <li>• Visit GP 78% vs. 85%</li> <li>• Visited secondary care clinics 95% vs. 95%</li> </ul> <p><b>Patient related outcomes (intervention vs control)</b></p> <ul style="list-style-type: none"> <li>- 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)</li> <li>- Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05</li> <li>- Quality of life mean global scores: 66.8±24.2 vs. 65.3±23.7</li> </ul> <p><b>GP related outcome (seen PHR vs. not seen PHR)</b></p> <ul style="list-style-type: none"> <li>- GP agrees that patients should have full access to their records 57% vs. 57%</li> </ul>
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	<p><i>Primary</i></p> <p>Quality of life (EORTC QLQ-C30)</p> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>-Psychological distress (POMS)</li> <li>-Symptoms (scale of the EORTC QLQ-C30)</li> <li>-Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth)</li> <li>-GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth)</li> </ul>	<p><b>Uptake of intervention</b> 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</p> <p><b>Patient related outcomes (intervention vs control)</b></p> <ul style="list-style-type: none"> <li>-Quality of life; mean difference [95%CI]; <ul style="list-style-type: none"> <li>• at 6 months 1.25 [-2.4-4.9]</li> <li>• at 14 months -0.71 [-4.3-2.8]</li> </ul> </li> <li>- Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0]</li> <li>- Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5]</li> <li>- Patient satisfaction with, <ul style="list-style-type: none"> <li>• GP on five dimensions, OR adj [95%CI] All NS;</li> </ul> </li> </ul>

Reference	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)  <i>Measurements</i> 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]  <b>GP related outcomes (intervention vs control)</b> - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[22]	<i>Primary</i> Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing)  <i>Measurements</i> Single measurement at 3 months	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> Subgroup analysis for age (year) hospital admissions mean number of admissions $\pm$ SD, 3 months follow-up; • $\geq 70$ y: 0.4 $\pm$ 0.6 vs. 0.9 $\pm$ 1.0 (Student T test p = 0.0002) • $< 70$ y: 1.0 $\pm$ 1.0 vs. 0.9 $\pm$ 0.8 (Student T test p = 0.38) - Days of hospitalization; • $\geq 70$ y: 3.8 $\pm$ 8.8 vs. 8.9 $\pm$ 18.8 (Tukey HSD, p <0.01) • $< 70$ y: 4.4 $\pm$ 5.9 vs. 3.6 $\pm$ 4.9 (Student T test p = 0.24) - Mean number of outpatient care visits per patient; • $\geq 70$ y: 6.8 $\pm$ 8.8 vs. 6.0 $\pm$ 7.0 (Student T test p = 0.53) • $< 70$ y: 13.4 $\pm$ 11.2 vs. 12.9 $\pm$ 11.5 (Student T test p = 0.7257) - Acute visits; • $\geq 70$ y: in 5% vs. 15% of patients ( $\chi^2$ p = 0.034) • $< 70$ y: in 11% vs. 10% of patients ( $\chi^2$ p = 0.80)
Johnson et al. (2015)[25]	<i>Primary</i> - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC)	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> - Emergency department presentations: no significant between-group differences were observed

Reference	Primary and secondary outcome measures	Findings if applicable to study:
Country	(instrument used) Timing of measurement	<ol style="list-style-type: none"> <li>Uptake of intervention</li> <li>Health care use</li> <li>Patient related outcomes</li> <li>GP related outcomes</li> </ol>
	- Empowerment (PES)	- Average number of GP visits 2.79 vs 1.61, p < 0.001
	<i>Secondary</i>	<b>Patient related outcomes (intervention vs control)</b>
	- Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits )	Patient perception of care; - GP could help in ways specialist could not: 57% vs. 19% ( $\chi^2 = 11.5$ ; p = 0.002)
	- Patient perception of care (SDQ)	- Patient opinion concerning PHR/GP visit after CT course:
	- GP perception of care (SDQ)	<ul style="list-style-type: none"> <li>81% considered PHR useful</li> <li>35% considered visit inconvenient</li> </ul>
	<i>Measurements</i>	Depression; Geometric mean score [95%CI]
	- before treatment	<ul style="list-style-type: none"> <li>at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40]</li> </ul>
	- midway through treatment	<ul style="list-style-type: none"> <li>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</li> </ul>
	- after treatment	Anxiety; Geometric mean score [95%CI]
		<ul style="list-style-type: none"> <li>at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32]</li> <li>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</li> </ul>
		- Subgroup analysis for number of clinically anxious patients
		<ul style="list-style-type: none"> <li>at baseline: 14 CA patients vs 11 CA patients</li> <li>after treatment: 3 CA patients vs 5 CA patients</li> </ul>
		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
		<b>GP related outcome (intervention vs control)</b>
		- GPs satisfied with communication: 82% vs. 95%
		- GP confidence in managing:
		<ul style="list-style-type: none"> <li>side effects 85% vs. 71% (p =0.45)</li> <li>psychological issues 97% vs. 81% (p= 0.04)</li> </ul>

Reference	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]	<i>Primary</i> - Patient utilization of the primary health care team (interview) - GP views after study (interview)  <i>Measurements</i> - at baseline (preoperative) - 4 months after diagnosis	<b>Uptake of intervention</b> 8 of the 31 interviewed GPs recall seeing the Information Card  <b>Health care use</b> ( <i>intervention vs. controls</i> ) - Patient initiated contact <ul style="list-style-type: none"> <li>• with GP <math>\geq 1</math> contact in 71% vs. 73%, <math>p = 0.95</math></li> <li>• district nurses no contact in 24% in both groups</li> </ul> <b>GP related outcome</b> ( <i>intervention</i> ) - Recommending information card 7 of 8 GPs who recall intervention

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Reference	Primary and secondary outcome measures (instrument used)	Findings if applicable to study:
	<b>Timing of measurement</b>	<ol style="list-style-type: none"> <li><b>Uptake of intervention</b></li> <li><b>Health care use</b></li> <li><b>Patient related outcomes</b></li> <li><b>GP related outcomes</b></li> </ol>
Nielsen et al. (2003) [15]	<i>Primary</i> - Patient attitude towards the health care system (intersectoral cooperation and 'not feeling left in limbo' (SDQ)	<b>Uptake of intervention</b> Not reported  <b>Patient related outcomes (intervention vs control)</b> - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055
Kousgaard et al. (2003) [16]	- 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	- 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  <b>Health care use (intervention vs. controls)</b> - 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)
	<i>Measurements</i> Patient: - First measurement "Soon after the introduction of the intervention."(0 month) - 6 months GP assessment: timing unknown	<b>GP related outcome (intervention vs. control)</b> - 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

292 Table 2. Study outcomes.

1 293 Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group;  
2 294 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  
3 295 = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs  
4 296 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;  
5 297 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  
6 298 Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus;  $\chi^2$ = Chi-square distribution.  
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For peer review only

## 300 Discussion

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

307 Even though active involvement of the GP during cancer treatment might have positive effects,  
308 implementation appears to be difficult to realize. This is seen for all interventions, irrespective  
309 whether the GP contact is initiated by the patient or by the healthcare provider. This shows that  
310 finding a feasible intervention is challenging. Drury et al (2000) suggested that a reason for the  
311 low uptake might be that GPs are not motivated to participate in the care of patients with  
312 curative disease as they do not feel closely involved in this stage [24]. This may explain why  
313 no studies were found where the GP was the initiator of involvement in care during cancer  
314 treatment. Low GP motivation is in contrast to what Dossett et al. (2017) show in their review  
315 on communication of specialist and GP during the cancer care continuum, they state that GPs  
316 desire involvement but think that specialist and patient prefer a specialist-based instead of  
317 shared-based cancer care [26]. Dossett et al (2017) confirms a preference of a specialist based  
318 model of care by specialists, which may result in a low motivation to activate the patient to see  
319 the GP [26]. Another reason for low uptake may be the difficulty to promote proactivity by GPs  
320 [17,18]. Dossett et al (2017) suggest that an adequate relationship and communication between  
321 the specialist and GP are important elements for the success of an intervention [26]. These  
322 findings suggest that, when designing an intervention, raising support of both primary and  
323 secondary health care workers is vital. The fact that healthcare system have different challenges  
324 and needs (e.g. communication between caregiver or distance to healthcare services),  
325 strengthens the need to tailor the potential solutions to local needs.

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



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3 331 This review has several limitations. To provide a comprehensive overview we used a broad  
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5 332 research question and search strategy. Consequently, we included heterogeneous studies. Due  
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7 333 to this heterogeneity and the low number of available studies, data pooling was not possible and  
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9 334 the estimate of effect could not be assessed according to the GRADE approach. To add to the  
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11 335 difficulty of reviewing heterogeneous studies, most studies addressed complex interventions.  
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13 336 The challenge of providing an overview of such studies could partly be countered by the limited  
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15 337 availability of process measures (e.g. uptake of intervention), but still strong conclusions could  
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17 338 not been drawn. Another potential limitation is that two databases were used to screen on title  
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19 339 and abstract by one researcher, possibly leading to missing studies. However, since screening  
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21 340 of references did not provide additional studies, we expect this limitation to be without effect.  
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23 341 In addition, to be complete, we included studies that also included palliatively treated patients.  
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25 342 Some publications did not show separate results for the curatively- and palliatively treated  
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27 343 population. We used a threshold for the minimum proportion of curatively treated patients (i.e.,  
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29 344 75%), but we cannot exclude that the observed effects were influenced the inclusion of  
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31 345 palliative patients. Finally, the review relied solely on published studies, so we cannot exclude  
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33 346 publication bias.

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37 348 Current literature shows several important challenges for designing and studying interventions  
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39 349 which effectively involve GPs in cancer care. First, finding a feasible intervention seems  
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41 350 challenging. Second, when designing an intervention, raising support of primary and secondary  
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43 351 health care workers seems vital. Third, challenges and solutions may be setting and population  
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45 352 specific. For these reasons, exploratory research seems necessary to design feasible and  
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47 353 effective interventions and meaningful studies. Fourth, large studies with a robust design are  
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49 354 needed, which should focus on the effect of primary care involvement for various populations,  
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51 355 including specifications for cancer types and vulnerable populations (e.g. elderly, and patients  
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53 356 with physical or mental comorbidity).

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55 357 Based on the findings in this review and guidelines for developing and evaluating complex  
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57 358 interventions [28] and feasibility studies [29], we developed a framework, which describes  
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59 359 consecutive steps that can guide the future development of effective interventions (Figure 3).  
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360 In this framework, each step is aimed to provide a foundation for the next step, thereby  
361 providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care.  
362 This framework should provide us with a definitive answer on the effects of GP involvement  
363 in the cancer care pathway in different health care settings, for a variety of populations.

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3 364 Interventions based on the framework should optimally facilitate primary care workers to  
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5 365 appropriately implement their role in shared care, by making full use of their specific expertise  
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7 366 by consideration of the patients' context and values, provided in a trusted environment.  
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## 10 11 368 **Conclusion**

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14 369 Literature addressing the effects of interventions designed to actively involve the GP during  
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16 370 curative cancer treatment is scarce and the results are diverse. Even though uptake of  
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18 371 interventions is generally low, these studies suggest positive effects of increased primary care  
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20 372 involvement on patient satisfaction. Other positive effects were seen, particularly for vulnerable  
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22 373 populations. In view of various health care strategies, which aim to transfer parts of the cancer  
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24 374 care paths from secondary to the primary care, it is adamant to gather more robust evidence for  
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26 375 customized interventions to enable the efficient and effective involvement of the GP during  
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3 378 **Data sharing statement**  
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5 379 For the current study we did not generate new data. Therefore, sharing new data is not possible.  
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10 381 **Declaration of Interest**  
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12 382 Conflicts of interest: none  
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17 384 **Role of the Funding Source**  
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20 385 This research did not receive any specific grant from funding agencies in the public, commercial  
21 386 or not-for-profit sectors.  
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26 388 **Contributors**  
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28 389 Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP);  
29 390 analysis and interpretation of data (IP, JB, AM, CH). Drafting the article or revising it critically  
30 391 for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the version to  
31 392 be submitted (IP, JB, AM, NW, EW, CH).  
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3 481 Figure 1. Flow diagram for selection of studies, based on Preferred Reporting Items for  
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5 482 Systematic Reviews and Meta-Analyses (PRISMA) [14].  
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7 483 Abbreviations: GP: General practitioner  
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13 486 Figure 2. Risk of bias measured according to the EPOC criteria  
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20 489 Figure 3. Framework for development of interventions aimed to effectively involve the GP in  
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22 490 cancer care. In this framework, each step is aimed to provide a foundation for the next step,  
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24 491 thereby providing a stepwise approach to feasible and meaningful involvement of the GP in  
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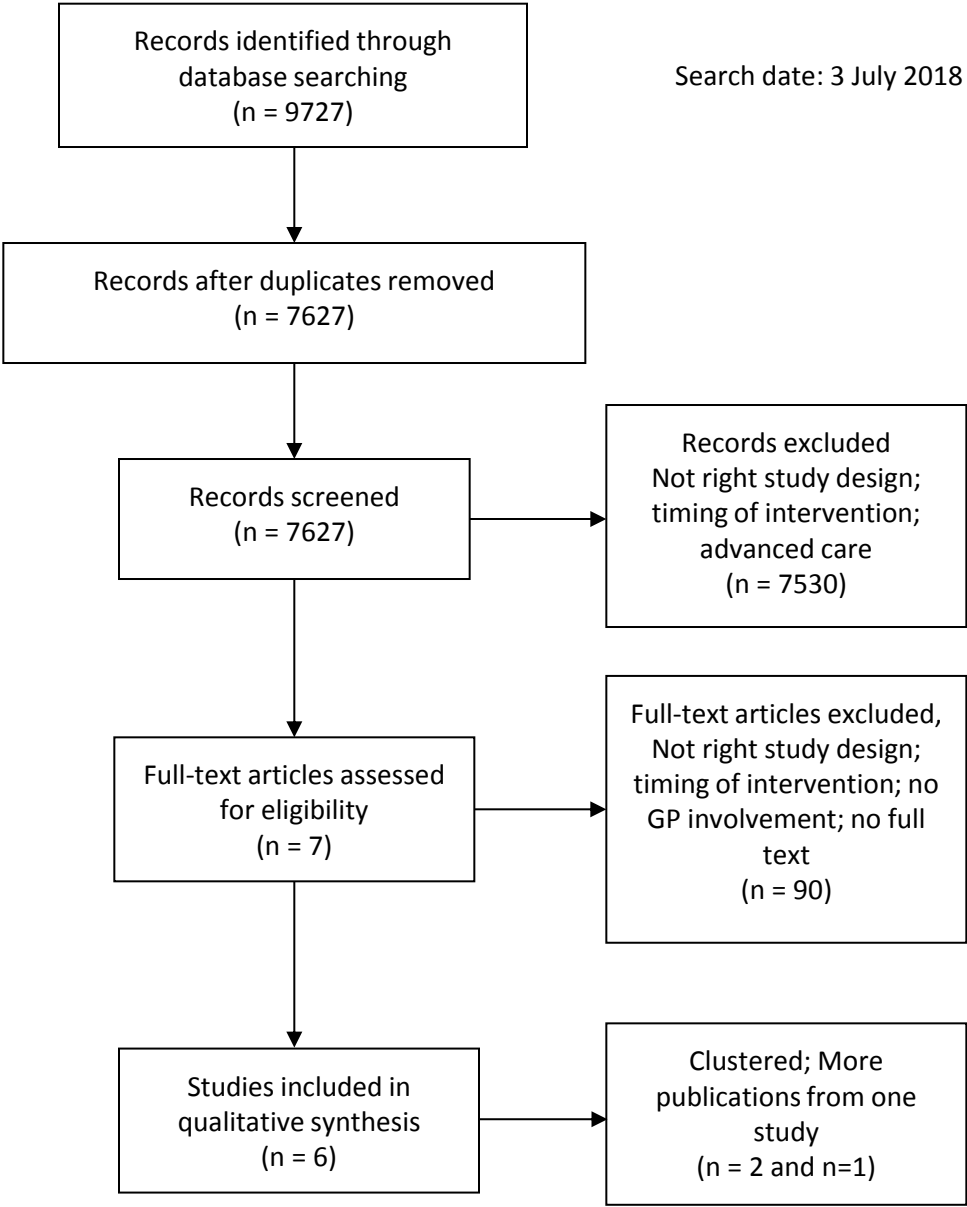
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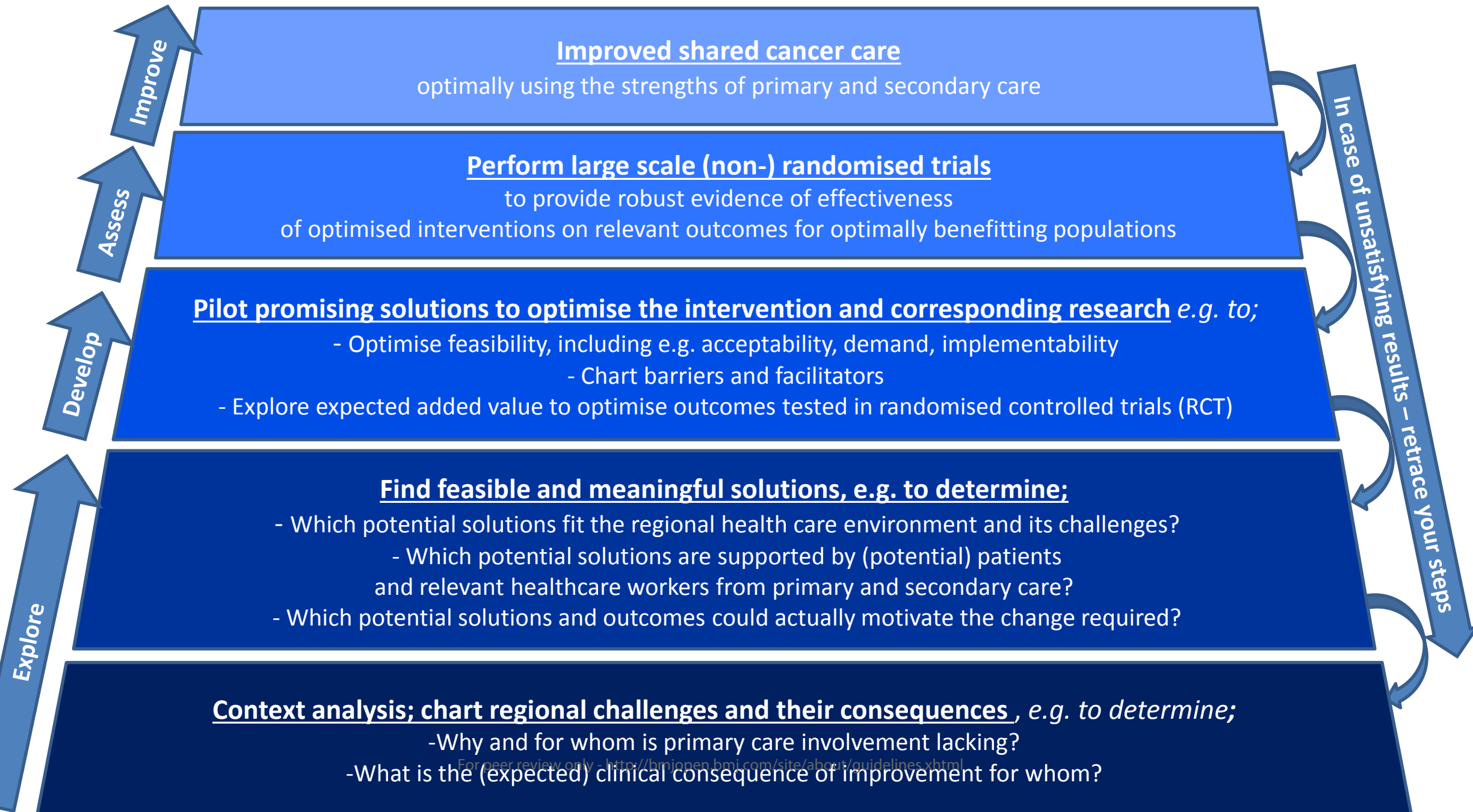
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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Baseline outcome measurements similar (selection bias)	Baseline characteristics similar (selection bias)	Incomplete outcome data (attrition bias)	Knowledge of the 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	+	+	-	-	-	?	+	+	+

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6 "service integration"[Title/Abstract]) OR "services integration"[Title/Abstract]) OR  
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12 planning"[MeSH Terms]) OR "patient care team"[MeSH Terms]) OR "continuity of patient  
13 care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case  
14 management"[MeSH Terms]) OR "community health planning"[MeSH Terms]) OR  
15 "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient  
16 relations"[MeSH Terms]) OR "interprofessional relations"[MeSH Terms]) OR  
17 "professional-family relations"[MeSH Terms]) OR "cooperative behavior"[MeSH Terms])  
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41 Combining search terms: #1 AND #2 AND #3 AND #4  
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## 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

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3 'randomized controlled trial'/exp OR random\*:ab,ti OR control\*:ab,ti OR  
4 intervention\*:ab,ti  
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10 Combining search terms: #1 AND #2 AND #3 AND #4  
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# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

Page 1 of 2

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.
<b>RESULTS</b>			
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.
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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

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# PRISMA 2009 Checklist

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# BMJ Open

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

Journal:	<i>BMJ Open</i>
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
<b>Primary Subject Heading</b>:	Oncology
Secondary Subject Heading:	General practice / Family practice, Patient-centred medicine
Keywords:	PRIMARY CARE, Shared care, Curative treatment, Patient satisfaction, General Practitioner, Cancer

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1     **Journal**

2     BMJ Open

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4     **Type of Contribution**

5     General and Supportive Care; Systematic review.

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

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3 9 **Title Page**  
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8 11 **Title**  
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10 12 Involving the General Practitioner during Curative Cancer Treatment: a Systematic Review of  
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12 13 Health Care Interventions.  
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16  
17 15 **Author Names and Affiliations**  
18

19 16 I.A.A. Perfors<sup>1</sup>, A.M. May<sup>1</sup>, J.A. Boeijen<sup>1</sup>, N.J. de Wit<sup>1</sup>, E. van der Wall<sup>2</sup>, C.W. Helsper<sup>1</sup>  
20

21 17 1. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht,  
22  
23 18 Utrecht University, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
24

25 19 2. UMC Utrecht Cancer Center, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
26  
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28 20

29 21 **Corresponding Author**  
30

31 22 Charles W. Helsper  
32

33 23 E-mail address: C.W.Helsper-2@umcutrecht.nl.  
34

35 24 Permanent address: Julius Center for Health Sciences and Primary Care, University Medical  
36  
37 25 Centre Utrecht, P.O. Box 85500, 3508 GA Utrecht, the Netherlands.  
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27 **Second Title Page**

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29 **Title**

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

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1  
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3 **33 Abstract**

4  
5 **34 Words:** 300/300

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8 **35 Objective:** The role of primary care providers (PCP) in the cancer care continuum is  
9  
10 **36** expanding. In the post-treatment phase, this role is increasingly recognized by policy makers  
11  
12 **37** and health care professionals. During treatment, however, the role of PCP remains largely  
13  
14 **38** undefined. This systematic review aims to map the content and effect of interventions aiming  
15  
16 **39** to actively involve the General Practitioner (GP) during cancer treatment with a curative  
17  
18 **40** intent.

19 **41 Study design** Systematic review

20 **42 Participants** Cancer patients treated with curative intent

21  
22 **43 Data sources** Randomized controlled trials (RCTs), controlled clinical trials (CCT),  
23  
24 **44** controlled before and after studies and interrupted time series focusing on interventions  
25  
26 **45** designed to involve the GP during curative cancer treatment were systematically identified  
27  
28 **46** from PubMed and EMBASE and were subsequently reviewed. Risk of bias was scored  
29  
30 **47** according to the EPOC risk of bias criteria.

31 **48 Results** Five RCTs and one CCT were included. Interventions and effects were heterogeneous  
32  
33 **49** across studies. Four studies implemented interventions focussing on information transfer to  
34  
35 **50** the GP and two RCTs implemented patient tailored GP interventions. The studies have a low-  
36  
37 **51** medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on  
38  
39 **52** patient satisfaction with care was found in three studies. Subgroup analysis suggest a  
40  
41 **53** reduction of health care use in elderly patients and reduction of clinical anxiety in those with  
42  
43 **54** higher mental distress. No effects are reported on patients' quality of life (QoL).

44 **55 Conclusion** Interventions designed to actively involve the GP during curative cancer  
45  
46 **56** treatment are scarce and diverse. Even though uptake of interventions is low, results suggests  
47  
48 **57** a positive effect of GP involvement on patient satisfaction with care, but not on QoL.  
49  
50 **58** Additional effects for vulnerable subgroups were found. More robust evidence for tailored  
51  
52 **59** interventions is needed to enable the efficient and effective involvement of the GP during  
53  
54 **60** curative cancer treatment.

55 **62 PROSPERO registration number: CRD42018102253**

### 63 **Strengths and Limitations of this study**

64

65 • This is the first review that systematically reviews evidence based interventions,  
66 aiming at general practitioner involvement during the curative treatment phase of the  
67 cancer care continuum.

68 • The electronic database search was performed without restriction on languages and  
69 period.

70 • We evaluate the studies with the EPOC risk of bias tool, which is the most appropriate  
71 tool to assess bias for complex interventions.

72 • The title/abstract screening is done by single reviewer, two authors screened the full-  
73 text and the search was complemented with reference checks of relevant articles.

74 • The included studies are heterogeneous in intervention and outcome and therefore  
75 strong conclusions could not be made.

1  
2  
3 76 **Keywords**  
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5 77 - Primary care  
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8 78 - General Practitioner  
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10 79 - Shared care  
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13 80 - Cancer  
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15 81 - Curative treatment  
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17 82 - Patient satisfaction  
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## 84 **Background**

85 Cancer incidence and prevalence is increasing as a result of the aging population combined  
86 with expanding diagnostic and treatment possibilities. Due to improved outcome following  
87 cancer treatment, the nature of cancer treatment is changing toward more chronic disease  
88 management. Health policy makers and health care professionals therefore call for a change in  
89 the way cancer care is provided, to focus on more integrated and personalized cancer care  
90 during and after treatment [1,2]. In countries with gatekeeper health care systems, such as The  
91 Netherlands, GPs are generally the coordinators of care, who have a longstanding and  
92 personal relationship with their patients. This enables knowledge of both the medical and  
93 personal situation of the patient and care, which is provided in a trusted environment with a  
94 familiar health care worker. Therefore, primary care is increasingly promoted as the preferred  
95 setting to provide integrated support during and after active cancer treatment, both to meet  
96 patient preference and to stabilize costs [2,3]. The concept of shared care has been suggested  
97 as the way forward in the organization of integrated cancer care [2,3]. This shared care model  
98 is an organisational model involving both general practitioners (GPs) and specialists in a  
99 formal, explicit manner. Shared care models enhance the optimal access of patients to both  
100 hospital care and community based supportive care along the entire cancer care continuum  
101 [4]. In shared care models, GPs, along with other primary care professionals, add their  
102 competence to balance the biomedical aspects of cancer care with the psychosocial context  
103 and preferences of the individual patient [5], ensuring personalized, integrated care. To  
104 achieve shared care the GP should be involved in the organisation of care during cancer  
105 treatment.

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

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2  
3 117 So far, the most effective approach to involve primary care during cancer treatment remains  
4  
5 118 unclear.

6  
7 119 This systematic review aims to provide a comprehensive overview of the content and effect of  
8  
9 120 interventions aiming at active involvement of the general practitioner during cancer treatment  
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11 121 with curative intent compared to usual care.

12  
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## 15 123 **Methods**

### 18 124 *Data source and search*

19  
20 125 A literature search was conducted in PubMed and EMBASE for articles describing  
21  
22 126 randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and  
23  
24 127 after studies, and interrupted time series published in any language until the 3<sup>rd</sup> of July 2018.  
25  
26 128 We used a search strategy that was previously applied in a review assessing continuity of care  
27  
28 129 in the follow-up of patients with cancer [12]. Subsequently, this strategy was adapted for  
29  
30 130 completeness and relevance based on sequential testing of search strategies to develop our  
31  
32 131 final search strategy. The details of the sequential and final search strategies are listed in  
33  
34 132 appendix A. The search terms include keywords and controlled vocabulary terms surrounding  
35  
36 133 the central themes “general practitioner”, “primary care”, “oncology”, and “care”. Outcome  
37  
38 134 measures and comparing study arm were not included in the selection criteria to widen the  
39  
40 135 scope of the review. Instead of a database integrated filter, a tailored methodological search  
41  
42 136 filter was used to limit retrieval to appropriate study design [12]. We reviewed references of  
43  
44 137 selected articles for additional papers.

45  
46 138 Outcomes are included if they are related to the quality of healthcare (e.g. healthcare use), the  
47  
48 139 healthcare experience of: healthcare professionals, informal caregivers, and patients, or  
49  
50 140 outcomes at the patient-level, with a focus on, e.g., disease, quality of life, and psychosocial  
51  
52 141 impact.

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54 142

### 53 143 *Study selection*

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56 144 Articles were selected if they described an intervention; (1) for cancer patients, (2) starting  
57  
58 145 during curative treatment, (3) evaluating involvement of the GP, and (4) tested in a  
59  
60 146 randomized controlled setting, CCT, controlled before and after studies or interrupted time

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3 147 series. Studies with a majority (>75%) of curative patients were included. In case the  
4  
5 148 proportion of curative patients was unclear, the original authors were contacted. Without  
6  
7 149 response, the inclusion of the trial was based on >75% percentage patient survival during the  
8  
9 150 trial.

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11 151

### 12 13 152 *Data extraction and management*

14  
15 153 To determine relevance, the records were divided and screened on title and abstract by two  
16  
17 154 single reviewers (IP,JB) and discussed with three additional reviewers in case of doubt  
18  
19 155 (AM,CH and JB or IP). Two authors (IP,JB) performed full-text screening. Disagreements on  
20  
21 156 eligibility were resolved in group discussion with researchers and clinicians  
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23 157 (IP,JB,AM,CH).A meta-analysis was planned to be conducted if possible.

24  
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### 26 27 159 *Patient and public involvement*

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29 160 Patients and public were not involved in the design of the current study.

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31 161

### 32 33 162 *Quality assessment*

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35 163 Risk of bias for individual studies was scored by two authors (JB,IP) with the risk of bias  
36  
37 164 criteria from the “Effective Practice and Organisation of Care Group (EPOC), which is a  
38  
39 165 Cochrane review group [13]. In case outcomes of homogeneous study designs could be  
40  
41 166 merged we rated the body of the evidence following the Grades of Recommendation,  
42  
43 167 Assessment, Development and Evaluation approach (GRADE) [14] from the Cochrane  
44  
45 168 collaboration. This systematic review is reported following the PRISMA 2009 checklist [14].

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## 48 49 170 **Results**

### 50 51 171 *Study selection*

52  
53 172 As shown in Figure 1, 9,727 records were eligible for inclusion after removal of duplicates.  
54  
55 173 Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text  
56  
57 174 screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP  
58  
59 175 involvement started after completion of primary cancer treatment, or (3) no RCT, CCT,

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2  
3 176 controlled before and after study or interrupted time series design was used. Three studies  
4  
5 177 published multiple articles based on the same data [15–22]. As a result, five RCTs and one  
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7 178 CCT were considered eligible for inclusion, which were described in ten articles. No  
8  
9 179 additional eligible studies were identified in the reference lists of selected studies. Figure 2,  
10  
11 180 Table 1, and 2 show a detailed account of the risk of bias, patient population, interventions,  
12  
13 181 outcomes assessed and observed results for each study. Given the various research questions,  
14  
15 182 interventions and heterogeneity of outcome measures, pooling of data, and GRADE  
16  
17 183 assessment was not feasible.

184

### 185 *Quality of studies*

186 The EPOC risk of bias is presented in Figure 2. Luker et al. (2000) and Nielsen/Kousgaard et  
187 al. (2003) show a high risk of bias, resulting from high risk of selection and information bias  
188 [15,16,23]. Drury et al. (2000) scored a medium risk of bias [24]. And the studies of Johnson  
189 et al. (2015), Johansson et al. (2001) and Bergholdt et al. (2012/2013/2013) show a low risk  
190 of bias [17–19,22,25]. Regarding the RCT by Nielsen/Kousgaard et al. (2003) several  
191 limitations should be kept in mind. The randomization produced an imbalance, which  
192 influenced comparability of outcomes between study groups without corresponding correction  
193 in the analyses. Furthermore, it was not reported whether a baseline measurement was  
194 performed and the exact timing of the first measurement (Table 2). Also, the percentage of  
195 missing data was 33% in the intervention and 26% in the control group [15].

196

### 197 *Study populations*

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

204

### 205 *Usual care*

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3 206 In most studies, usual care was not described in detail. Only Luker et al. [23] described the  
4  
5 207 structured care that usual care patients received, which included home visits from a breast  
6  
7 208 care nurse and written patient information on treatments. In general, the patient's GP received  
8  
9 209 a discharge summary [15–17,19,20,25] at the end of the treatment period [15,16] or after each  
10  
11 210 visit [25]. Other types of transferred information to the GP included an extract of the hospital  
12  
13 211 record [15,16] or communication by telephone [25]. Two studies did not describe what usual  
14  
15 212 care entailed [21,22,24].  
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17 213

### 18 214 *Type of interventions*

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21 215 All participants received usual care, which was extended when the participant was appointed  
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23 216 to the intervention. The interventions in the studies (Table 1) were heterogeneous, but can be  
24  
25 217 divided in mainly information transfer to the GP (n=4) [15,16,23–25] and tailored primary  
26  
27 218 care interventions (n=2) [17–20,22].

28  
29 219 Interventions focusing on information transfer, provided additional, disease specific  
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31 220 educational, and practical information concerning treatment and care directly to the GP or via  
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33 221 the patient. Interventions were either directed at enhancing communication between GP and  
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35 222 another party (i.e. secondary care or patient), or directed at improving patient's attitude  
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37 223 towards the healthcare system (i.e. healthcare in general or intervention), physical- or  
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39 224 psychological complains. Three interventions provided patients with information, which was  
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41 225 to be transferred to the GP. In one CCT [23], informational cards were provided to the  
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43 226 patients for use in primary care. Two other RCTs described an intervention with a Patient  
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45 227 Held Record (PHR) [24,25] aimed to facilitate intersectoral communication, to provide  
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47 228 patients with an aide memoire, and with the opportunity to stay actively involved in their  
48  
49 229 treatment. One RCT supplied the GP with patient specific discharge summaries by secondary  
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51 230 care, aiming to enhance GP knowledge of chemotherapy treatment and expected adverse  
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53 231 effects [15,16].

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55 232 The tailored primary care interventions aimed to support patients in managing their disease  
56  
57 233 and treatment [17,18,20,22]. The interventions were to diverse to be merged and they are  
58  
59 234 therefore described separately. In Johansson et al. (2001) [22] primary care was intensified by  
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235 means of recruitment of a home care nurse, psychologist, dietician and training of the GP. The  
236 home care nurse initiated contact. The GP was regularly informed by the specialist and  
237 educated on management of cancer patients. In the one RCT from Hansen et al. (2011) and

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3 238 Bergholdt et al. (2012/2013/2013)[17–20], a rehabilitation team interviewed all patients on  
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5 239 different aspects of rehabilitation. Afterwards the GP was informed on patient specific  
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7 240 rehabilitation needs and encouraged to pro-actively contact the patient to support the patient  
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9 241 in his/her needs.

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### 12 13 243 *Study outcomes*

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15 244 The most often measured primary outcomes were health care utilization [15,16,22–24] and  
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17 245 quality of life [15–17,24], as presented in Table 2. Other outcomes were patient and GP  
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19 246 perceptions of care, symptoms, coping, and empowerment. The following outcomes were not  
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21 247 presented in the included articles: healthcare experience by informal caregivers, and disease  
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23 248 specific outcomes (i.e. progress, mortality). Outcomes are described in more detail below.

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### 26 27 250 *Intervention fidelity/compliance and health care use*

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29 251 Health care use is related to the uptake of the intervention. For example, if the intervention  
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31 252 aims at more GP involvement, health care use is likely to increase. Although all interventions  
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33 253 aimed at increased involvement of primary care, four interventions did not show a significant  
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35 254 increase of GP consultations [15,18,23,24]. Correspondingly, the uptake of interventions  
36  
37 255 appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al. [18]  
38  
39 256 which describes an “active involvement” intervention, in which GP pro-activity was  
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41 257 comparable to GP proactivity in the control group (52 to 60%) [18]. In two studies,  
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43 258 information transfer to the GP by their patients was hardly used or remembered by the  
44  
45 259 majority of the GPs [23,24].

46 260 Five studies, evaluated the effect of the intervention on hospital and/or primary care resource  
47  
48 261 use. These studies showed no significant effect on secondary care health care use [22–24].  
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50 262 Only the subgroup of older patients ( $\geq 70$  years of age) had a significantly lower use of  
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52 263 secondary care [22] when primary care was actively involved. Even though GP consultations  
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54 264 were part of the interventions several studies reported no difference in the number of GP  
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56 265 consultations in the intervention group compared to the control group [15,16,23–25].

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### 58 59 267 *Patient perception*

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3 268 Positive effects on patients' satisfaction with care were indicated by three studies. Extended  
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5 269 information by PHR or discharge summary improved patient perceived intersectoral  
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7 270 cooperation [15,16]. GP consultations were evaluated as useful. Also patients reported that  
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9 271 'the GP could help in the way a specialist could not' [25]. Regardless of the uptake of the  
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11 272 intervention, one study showed an improved satisfaction with communication and  
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13 273 participation with care [24]. The significantly higher levels of perceived GP support shortly  
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15 274 after the intervention described in Nielsen et al.(2003) declined to non-significant levels at six  
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17 275 months after start of intervention. The authors did not present a mean difference overtime.  
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19 276 One study with a low uptake of intervention showed no significant effect on patients  
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21 277 satisfaction [20].  
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### 279 *Quality of life and psychological outcomes*

26 280 No study found a significant effect on quality of life [15,17,24]. Johnson et al (2001) [23],  
27  
28 281 showed a significant difference in change of depression scores (p0.04). In the intervention  
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30 282 group depression scores remained unchanged, whereas scores in the control group  
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32 283 deteriorated significantly. Also, using a PHR combined with routine visits to the GP led to a  
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34 284 significantly higher reduction of the number of clinically anxiousness patients compared to  
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36 285 usual care [25].  
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### 287 *GPs perceptions of care*

41 288 Four out of five studies evaluating effects on GPs perceptions of care did not find relevant  
42  
43 289 effects on GP's confidence in disease management and knowledge nor in the communication  
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45 290 with the specialist [16,20,23,25]. Studies in which information was carried by the patient (a  
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47 291 PHR or informational cards) showed little impact on GP satisfaction with care mostly due to  
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49 292 low uptake of intervention. Only Nielsen/Kousgaard et al. (2003) [15,16] found significant  
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51 293 positive effects on GP perceived intersectoral cooperation and GP satisfaction with  
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53 294 information.  
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Reference	Population N=number, Country cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
Drury et al. (2000)[24]	N = 650 60% ♀	<i>Inclusion</i> 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	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 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)	N = 955 72% ♀	<i>Inclusion</i> Cancer diagnosis <3 months	Intervention vs UC Rehabilitation primary care program Initiative GP contact: Healthcare worker
Hansen et al. (2011) [17–20]	MAM (43%), LUN, GI, other (19%), MEL	<i>Intervention</i> Upon enrolment  <i>Follow up</i> 14 months	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
Denmark	Cancer stage unknown, no deceased		
Johansson et al. (2001)[22]	N = 463 57% ♀	<i>Inclusion</i> 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	<i>Intervention</i> 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



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Reference	Population N=number, Country cancer origin, stage	Timing of inclusion, intervention Follow-up	Nature of the intervention and comparison groups
		<i>Follow up</i> 3 months	- Active involvement of dietician and psychologist care
Johnson et al. (2015)[25]	N = 97 86% ♀	<i>Inclusion</i> During first course of CT	UC and intervention vs UC (discharge summary) Shared Care program + PHR Initiative GP contact: Patient
Australia	MAM (76%), HEM, GYN, GI  Cancer stage 3.3% palliative  Stopped early (slow accrual); underpowered for the main analysis	<i>Intervention</i> First through last course of CT  <i>Follow up</i> 6 cycles of CT	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]	N = 79 100% ♀	<i>Inclusion</i> <4 weeks after diagnosis	UC and intervention vs UC Patients received information cards Initiative GP contact: Patient
UK	MAM (100%)  Cancer stage 100% curative	<i>Intervention</i> At start of treatment  <i>Follow up</i> 4 months	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	Population N=number, Country 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]	N = 248 64% ♀	<i>Inclusion</i> Newly diagnosed patients	UC and intervention vs UC Shared care program Initiative GP contact: Patient
Kousgaard et al. (2003) [16]	MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL	<i>Intervention</i> From referral onwards; during treatment  <i>Follow up</i> 6 months	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
Denmark	Cancer stage 15% palliative		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

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

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

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Reference	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]	<p><i>Primary</i></p> <ul style="list-style-type: none"> <li>- Health care use (patient reported)</li> <li>- Patient satisfaction with communication and participation in care (SDQ)</li> <li>- Quality of life (EORTC QLQ-C30)</li> </ul> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>- GP views on PHR (SDQ)</li> </ul> <p><i>Measurements</i></p> <p>Single measurement at 3 months</p>	<p><b>Uptake of intervention</b> 27.3% of 202 responding GPs had seen the PHR</p> <p><b>Health care use</b> (<i>intervention vs. controls</i>)</p> <p>Contact with care providers in 3 months follow-up;</p> <ul style="list-style-type: none"> <li>• Visit GP 78% vs. 85%</li> <li>• Visited secondary care clinics 95% vs. 95%</li> </ul> <p><b>Patient related outcomes</b> (<i>intervention vs control</i>)</p> <ul style="list-style-type: none"> <li>- Satisfaction communication and participation in care mean <math>\pm</math> SD (scale 1-5): 3.83<math>\pm</math>0.59 vs. 3.80<math>\pm</math>0.59, (95% CI 0.09- 0.15)</li> <li>- Confidence in facing future aspects of cancer: 62% vs. 71%, p = 0.05</li> <li>- Quality of life mean global scores: 66.8<math>\pm</math>24.2 vs. 65.3<math>\pm</math>23.7</li> </ul> <p><b>GP related outcome</b> (<i>seen PHR vs. not seen PHR</i>)</p> <ul style="list-style-type: none"> <li>- GP agrees that patients should have full access to their records 57% vs. 57%</li> </ul>
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [17–20]	<p><i>Primary</i></p> <p>Quality of life (EORTC QLQ-C30)</p> <p><i>Secondary</i></p> <ul style="list-style-type: none"> <li>-Psychological distress (POMS)</li> <li>-Symptoms (scale of the EORTC QLQ-C30)</li> <li>-Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 mth)</li> <li>-GP proactivity measured on GP and patient level. (one ad hoc question, at 14 mth)</li> <li>-GP's satisfaction with their contribution to the patient's</li> </ul>	<p><b>Uptake of intervention</b> pro-activity of GP intervention vs control: GP reported 61.2% vs 55.2% p=0.10, patient reported 60.1% vs 51.9% p=0.15</p> <p><b>Patient related outcomes</b> (<i>intervention vs control</i>)</p> <ul style="list-style-type: none"> <li>-Quality of life; mean difference [95%CI]; <ul style="list-style-type: none"> <li>• at 6 months 1.25 [-2.4-4.9]</li> <li>• at 14 months -0.71 [-4.3-2.8]</li> </ul> </li> <li>- Psychological distress, mean difference [95%CI]; -0.68 [-4.3-3.0]</li> <li>- Patient participation on rehabilitation services, OR adj [95%CI]; 1.0 [0.7-1.5]</li> <li>- Patient satisfaction with, <ul style="list-style-type: none"> <li>• GP on five dimensions, OR adj [95%CI] All NS;</li> </ul> </li> </ul> <p>Doctor–patient relationship 0.94 [0.35-2.47], Medical care 1.2 [0.5-3.0], Information and support 1.6 [0.6-</p>

Reference	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)  <i>Measurements</i> 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]  <b>GP related outcomes (intervention vs control)</b> - Overall satisfaction, OR adj [95% CI]; 1.10 [0.47-2.56]
Johansson et al. (2001)[22]	<i>Primary</i> Health care use: -Hospital admissions and days of hospitalization (with correction for weight loss and distress) (record reviewing) - Utilization of outpatient care (record reviewing)  <i>Measurements</i> Single measurement at 3 months	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> Subgroup analysis for age (year) hospital admissions mean number of admissions $\pm$ SD, 3 months follow-up; • $\geq 70y$ : $0.4 \pm 0.6$ vs. $0.9 \pm 1.0$ (Student T test $p = 0.0002$ ) • $< 70y$ : $1.0 \pm 1.0$ vs. $0.9 \pm 0.8$ (Student T test $p = 0.38$ ) - Days of hospitalization; • $\geq 70y$ : $3.8 \pm 8.8$ vs. $8.9 \pm 18.8$ (Tukey HSD, $p < 0.01$ ) • $< 70y$ : $4.4 \pm 5.9$ vs. $3.6 \pm 4.9$ (Student T test $p = 0.24$ ) - Mean number of outpatient care visits per patient; • $\geq 70y$ : $6.8 \pm 8.8$ vs. $6.0 \pm 7.0$ (Student T test $p = 0.53$ ) • $< 70y$ : $13.4 \pm 11.2$ vs. $12.9 \pm 11.5$ (Student T test $p = 0.7257$ ) - Acute visits; • $\geq 70y$ : in 5% vs. 15% of patients ( $\chi^2 p = 0.034$ ) • $< 70y$ : in 11% vs. 10% of patients ( $\chi^2 p = 0.80$ )
Johnson et al. (2015)[25]	<i>Primary</i> - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC) - Empowerment (PES)	<b>Uptake of intervention</b> Not reported  <b>Health care use (intervention vs. controls)</b> - Emergency department presentations: no significant between-group differences were observed - Average number of GP visits 2.79 vs 1.61, $p < 0.001$

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Reference	Primary and secondary outcome measures	Findings if applicable to study:
Country	(instrument used)	<ol style="list-style-type: none"> <li>1. Uptake of intervention</li> <li>2. Health care use</li> <li>3. Patient related outcomes</li> <li>4. GP related outcomes</li> </ol>
	Timing of measurement	
	<i>Secondary</i>	<b>Patient related outcomes</b> ( <i>intervention vs control</i> )
	- Health care use; hospital admission and emergency presentation ((Record viewing), number of GP visits )	Patient perception of care; - GP could help in ways specialist could not: 57% vs. 19% ( $\chi^2 = 11.5$ ; $p = 0.002$ )
	- Patient perception of care (SDQ)	- Patient opinion concerning PHR/GP visit after CT course:
	- GP perception of care (SDQ)	<ul style="list-style-type: none"> <li>• 81% considered PHR useful</li> <li>• 35% considered visit inconvenient</li> </ul>
	<i>Measurements</i>	Depression; Geometric mean score [95%CI]
	- before treatment	<ul style="list-style-type: none"> <li>• at baseline: 4.09 [3.31 to 4.86] vs 3.66 [2.92 to 4.40]</li> </ul>
	- midway through treatment	<ul style="list-style-type: none"> <li>• after treatment: 4.04 [3.25 to 4.83] vs 4.72 [3.72 to 5.72] <math>p = 0.04</math> for comparison of groups over time</li> </ul>
	- after treatment	Anxiety; Geometric mean score [95%CI]
		<ul style="list-style-type: none"> <li>• at baseline: 8.05 [6.71 to 9.40] vs 7.91 [6.50 to 9.32]</li> <li>• after treatment: 5.49 [4.54 to 6.43] vs 5.24 [4.26 to 6.22] <math>p = 0.80</math> for comparison of groups over time</li> </ul>
		- Subgroup analysis for number of clinically anxious patients
		<ul style="list-style-type: none"> <li>• at baseline: 14 CA patients vs 11 CA patients</li> <li>• after treatment: 3 CA patients vs 5 CA patients</li> </ul>
		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 $p=0.47$
		<b>GP related outcome</b> ( <i>intervention vs control</i> )
		- GPs satisfied with communication: 82% vs. 95%
		- GP confidence in managing:
		<ul style="list-style-type: none"> <li>• side effects 85% vs. 71% (<math>p=0.45</math>)</li> <li>• psychological issues 97% vs. 81% (<math>p= 0.04</math>)</li> </ul>
Luker	<i>Primary</i>	<b>Uptake of intervention</b> 8 of the 31 interviewed GPs recall seeing the Information Card

Reference	Primary and secondary outcome measures	Findings if applicable to study:
Country	(instrument used)	1. Uptake of intervention
	Timing of measurement	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)	<b>Health care use</b> ( <i>intervention vs. controls</i> )
	<i>Measurements</i>	- Patient initiated contact
	- at baseline (preoperative)	• with GP $\geq 1$ contact in 71% vs. 73%, $p = 0.95$
	- 4 months after diagnosis	• district nurses no contact in 24% in both groups
		<b>GP related outcome</b> ( <i>intervention</i> )
		- Recommending information card 7 of 8 GPs who recall intervention

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Reference	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]	<i>Primary</i> - Patient attitude towards the health care system (intersectoral cooperation and ‘not feeling left in limbo’ (SDQ)	<b>Uptake of intervention</b> Not reported  <b>Patient related outcomes (intervention vs control)</b> - At 6 months: attitude towards intersectoral cooperation; 59.22 vs. 51.71, p = 0.055
Kousgaard et al. (2003) [16]	- 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	- 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  <b>Health care use (intervention vs. controls)</b> - 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)
	<i>Measurements</i> Patient: - First measurement “Soon after the introduction of the intervention.”(0 month) - 6 months GP assessment: timing unknown	<b>GP related outcome (intervention vs. control)</b> - 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

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

1 302 Abbreviations: CA = clinically anxious; CI = Confidence Interval; CT = chemotherapy; Dan-PEP = Danish Patients Evaluate General Practice; ECOG = Eastern Cooperative Oncology Group;  
2 303 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  
3 304 = General Practitioner; GYN = gynaecological; HADS = Hospital Anxiety and Depression Scale; Mini-MAC = Mini Mental Adjustment to Cancer scale; mth = Months; NA-ACP = Needs  
4 305 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  
5 306 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 =  
6 307 Self Developed Questionnaire; SCNS-SF34 = Supportive Care Needs Survey Short Form 34; UC = Usual Care; vs = versus;  $\chi^2$ = Chi-square distribution.  
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For peer review only



## 309 Discussion

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

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

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

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3 341 This review has several limitations. To provide a comprehensive overview we used a broad  
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5 342 research question and search strategy. Consequently, we included heterogeneous studies. Due  
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7 343 to this heterogeneity and the low number of available studies, data pooling was not possible  
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9 344 and the estimate of effect could not be assessed according to the GRADE approach. To add to  
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11 345 the difficulty of reviewing heterogeneous studies, most studies addressed complex  
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13 346 interventions. The challenge of providing an overview of such studies could partly be  
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15 347 countered by the limited availability of process measures (e.g. uptake of intervention), but still  
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17 348 strong conclusions could not be drawn. Another potential limitation is that two databases  
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19 349 were used to screen on title and abstract by one researcher, possibly leading to missing  
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21 350 studies. However, since screening of references did not provide additional studies, we expect  
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23 351 this limitation to be without effect. In addition, to be complete, we included studies that also  
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25 352 included palliatively treated patients. Some publications did not show separate results for the  
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27 353 curatively- and palliatively treated population. We used a threshold for the minimum  
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29 354 proportion of curatively treated patients (i.e., 75%), but we cannot exclude that the observed  
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31 355 effects were influenced the inclusion of palliative patients. Finally, the review relied solely on  
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33 356 published studies, so we cannot exclude publication bias.

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38 358 Current literature shows several important challenges for designing and studying interventions  
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40 359 which effectively involve GPs in cancer care. First, finding a feasible intervention seems  
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42 360 challenging. Second, when designing an intervention, raising support of primary and  
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44 361 secondary health care workers seems vital. Third, challenges and solutions may be setting and  
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46 362 population specific. For these reasons, exploratory research seems necessary to design  
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48 363 feasible and effective interventions and meaningful studies. Fourth, large studies with a robust  
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50 364 design are needed, which should focus on the effect of primary care involvement for various  
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52 365 populations, including specifications for cancer types and vulnerable populations (e.g. elderly,  
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54 366 and patients with physical or mental comorbidity).

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56 367 Based on the findings in this review and guidelines for developing and evaluating complex  
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58 368 interventions [28] and feasibility studies [29], we propose a framework, which describes  
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60 369 consecutive steps that can guide the future development of effective interventions (Figure 3).  
370 In this framework, each step is aimed to provide a foundation for the next step, thereby  
371 providing a stepwise approach to feasible and meaningful involvement of the GP in cancer  
372 care. This framework should support us in finding definitive answers on the effects of GP  
373 involvement in the cancer care pathway in different health care settings, for a variety of

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3 374 populations. Interventions based on the framework should optimally facilitate primary care  
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5 375 workers to appropriately implement their role in shared care, by making full use of their  
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7 376 specific expertise by consideration of the patients' context and values, provided in a trusted  
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9 377 environment.

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## 12 13 379 **Conclusion**

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15 380 Literature addressing the effects of interventions designed to actively involve the GP during  
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17 381 curative cancer treatment is scarce and the results are diverse. Even though uptake of  
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19 382 interventions is generally low, these studies suggest positive effects of increased primary care  
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21 383 involvement on patient satisfaction. Other positive effects were seen, particularly for  
22  
23 384 vulnerable populations. In view of various health care strategies, which aim to transfer parts  
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25 385 of the cancer care paths from secondary to the primary care, it is adamant to gather more  
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27 386 robust evidence for customized interventions to enable the efficient and effective involvement  
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29 387 of the GP during cancer treatment.

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3 389 **Data sharing statement**  
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5 390 For the current study we did not generate new data. Therefore, sharing new data is not  
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7 391 possible.  
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12 393 **Declaration of Interest**  
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14 394 Conflicts of interest: none  
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19 396 **Role of the Funding Source**  
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21 397 This research did not receive any specific grant from funding agencies in the public,  
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23 398 commercial or not-for-profit sectors.  
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28 400 **Contributors**  
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30 401 Conception and design of the study (IP, JB, AM, NW, EW, CH). Acquisition of data (JB, IP);  
31  
32 402 analysis and interpretation of data (IP, JB, AM, CH). Drafting the article or revising it  
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34 403 critically for important intellectual content (IP, JB, AM, NW, EW, CH). Final approval of the  
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36 404 version to be submitted (IP, JB, AM, NW, EW, CH).  
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3 493 Figure 1. Flow diagram for selection of studies, based on Preferred Reporting Items for  
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5 494 Systematic Reviews and Meta-Analyses (PRISMA) [14].  
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7 495 Abbreviations: GP: General practitioner  
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13 498 Figure 2. Risk of bias measured according to the EPOC criteria.  
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20 501 Figure 3. Framework for development of interventions aimed to effectively involve the GP in  
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22 502 cancer care. In this framework, each step is aimed to provide a foundation for the next step,  
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24 503 thereby providing a stepwise approach to feasible and meaningful involvement of the GP in  
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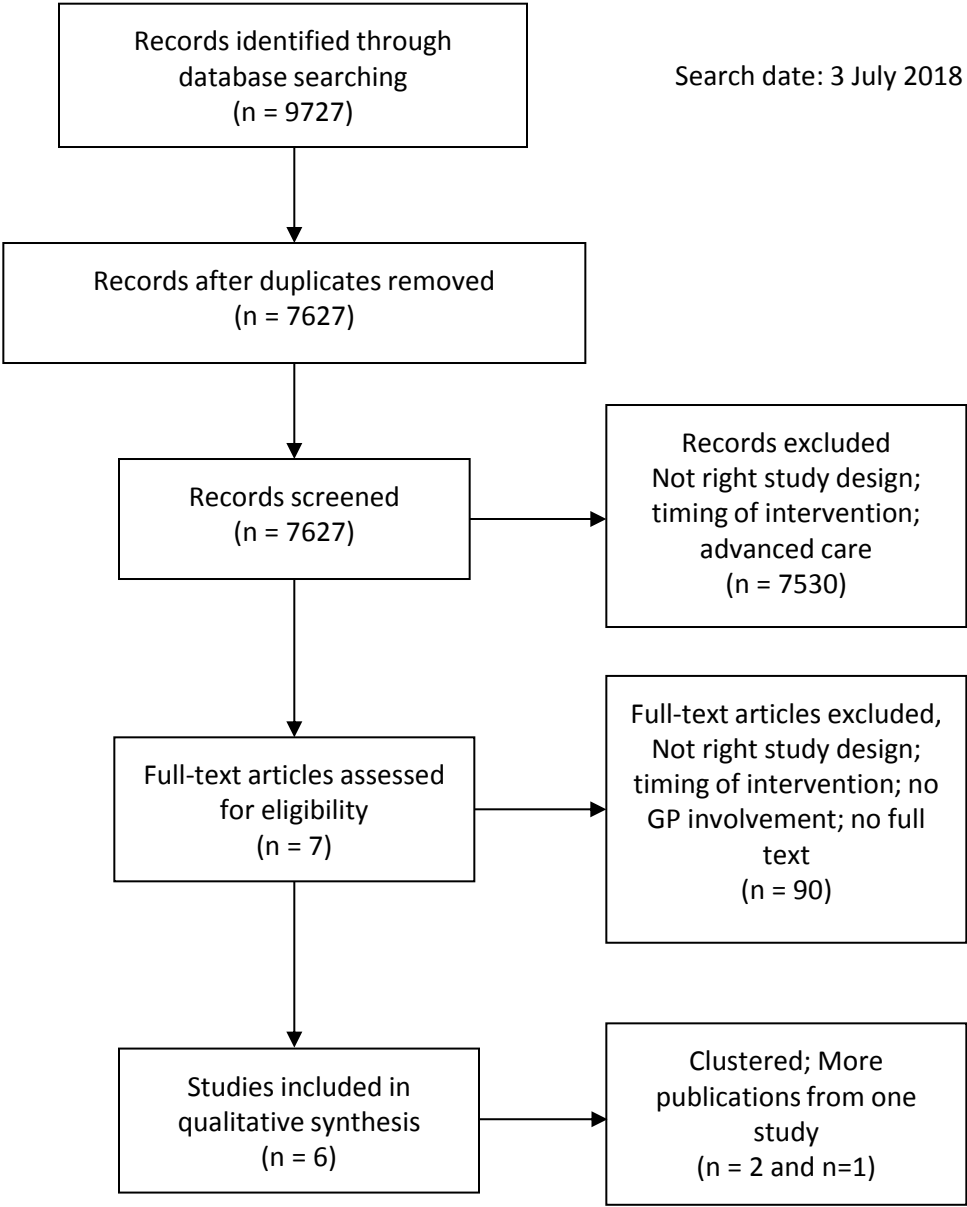
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Identification

Screening

Eligibility

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	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	+	+	-	-	-	?	+	+	+

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Improve

**Improved shared cancer care**  
optimally using the strengths of primary and secondary care

Assess

**Perform large scale (non-) randomised trials**  
to provide robust evidence of effectiveness  
of optimised interventions on relevant outcomes for optimally benefitting populations

Develop

**Pilot promising solutions to optimise the intervention and corresponding research e.g. to;**  
- Optimise feasibility, including e.g. acceptability, demand, implementability  
- Chart barriers and facilitators  
- Explore expected added value to optimise outcomes tested in randomised controlled trials (RCT)

Explore

**Find feasible and meaningful solutions, e.g. to determine;**  
- Which potential solutions fit the regional health care environment and its challenges?  
- Which potential solutions are supported by (potential) patients and relevant healthcare workers from primary and secondary care?  
- Which potential solutions and outcomes could actually motivate the change required?

**Context analysis; chart regional challenges and their consequences, e.g. to determine;**  
-Why and for whom is primary care involvement lacking?  
-What is the (expected) clinical consequence of improvement for whom?

In case of unsatisfying results – retrace your steps



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3 interdisciplinary[Title/Abstract]) OR multidisciplinary[Title/Abstract]) OR "liaison  
4 nurse\*[Title/Abstract]) OR "health care planning"[Title/Abstract]) OR "health care  
5 management"[Title/Abstract]) OR "community health planning"[Title/Abstract]) OR  
6 "service integration"[Title/Abstract]) OR "services integration"[Title/Abstract]) OR  
7 "professional-patient relations"[Title/Abstract]) OR "professional-family  
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9 working"[Title/Abstract]) OR interprofessional[Title/Abstract]) OR "multi agency  
10 working"[Title/Abstract]) OR "inter agency working"[Title/Abstract]) OR "case  
11 management"[Title/Abstract]) OR "patient discharge"[MeSH Terms]) OR "patient care  
12 planning"[MeSH Terms]) OR "patient care team"[MeSH Terms]) OR "continuity of patient  
13 care"[MeSH Terms]) OR "patient-centered care"[MeSH Terms]) OR "case  
14 management"[MeSH Terms]) OR "community health planning"[MeSH Terms]) OR  
15 "delivery of health care, integrated"[MeSH Terms]) OR "professional-patient  
16 relations"[MeSH Terms]) OR "interprofessional relations"[MeSH Terms]) OR  
17 "professional-family relations"[MeSH Terms]) OR "cooperative behavior"[MeSH Terms])  
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20 control\*[Title/Abstract]) OR intervention\*[Title/Abstract]))

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## 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

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3 'randomized controlled trial'/exp OR random\*:ab,ti OR control\*:ab,ti OR  
4 intervention\*:ab,ti  
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# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

Page 1 of 2

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.
<b>RESULTS</b>			
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.
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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

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For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org)



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