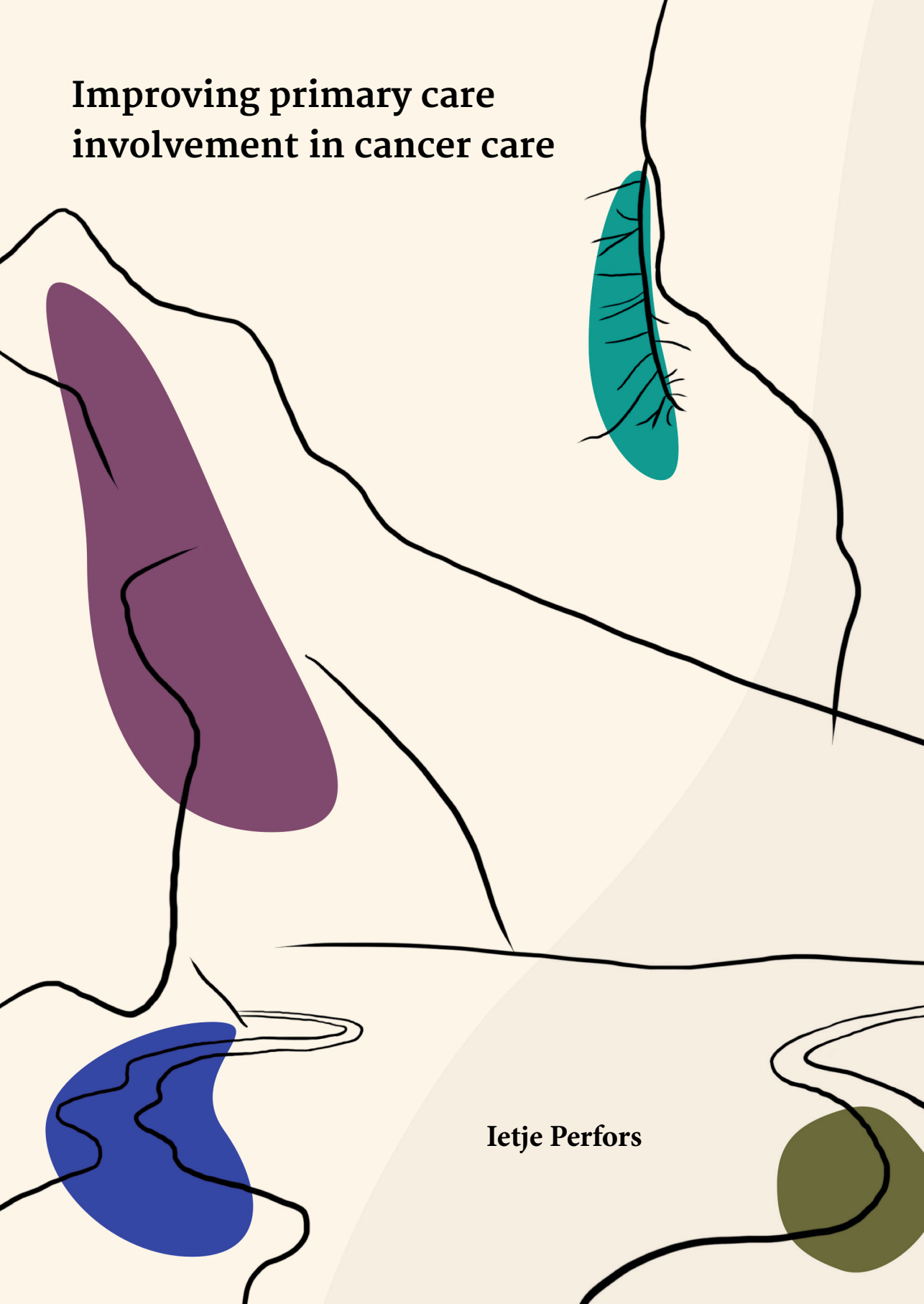
Improving primary care involvement in cancer care



Ietje Perfors

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Colofon
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Improving primary care involvement in cancer care

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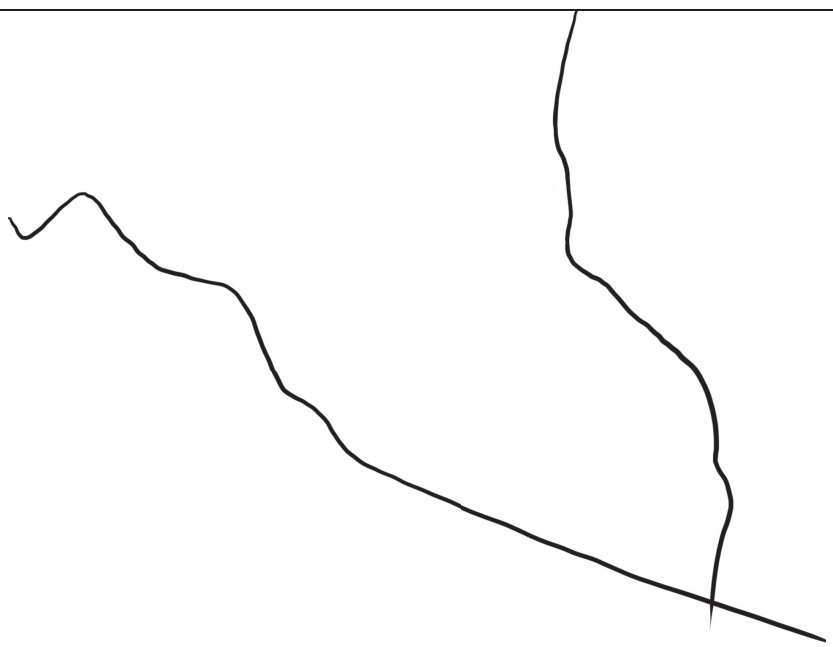

CHAPTER 1

General Introduction

Ietje Perfors

The changing perspective of cancer care

Due to improvements in healthcare, the number of people surviving into old age is steadily increasing. Since cancer is a disease that comes with age, currently over 18 million people are diagnosed with cancer worldwide.[1] It is estimated that in 2040 the number of newly diagnosed cancer patients will reach 30 million.[1] Due to improved diagnostics, an increasing number of patients is detected in an earlier stage of disease.[2] This early diagnosis, combined with therapeutic advances in cancer treatments, result in a higher number of patients with prolonged survival.[3] Even though the improved treatment regimens do benefit cancer outcome, they also result in side effects, sometimes long-lasting.[4–6] The acute and long-term burden of cancer are particularly challenging, since cancer patients are mostly elderly who frequently suffer from comorbidities.[7, 8] These changes transform the nature of cancer treatment towards chronic disease management. In addition, the spectrum of treatment options for cancer increasingly demand for a personalised approach, in which the optimal treatment plan is fitted to cancer characteristics and to the individual preferences of the patient.

Personalised cancer care and shared decision making

Personalised care

Today, personalised care is an important focus in healthcare, advocated by policy makers, healthcare professionals and patients.[9] Personalised care is defined according to the National Health Service (NHS) in the United Kingdom as care were "people have choice and control over the way their care is planned and delivered".[10] It is based on "what matters' to them and their individual strengths and needs"[10] given their comorbidities and underlying diseases. The NHS states that personalised care will improve people's health and wellbeing, make care more efficient and reduce pressure on the current healthcare system.[10]

Personalised cancer care has several dimensions. First of all, the broadening spectrum of treatment options facilitates detailing of treatment to each individual type and stage of cancer. Individual treatment replaces the

standard one-size-fits-all approach. In addition, it is also adjusted to the medical and psychosocial profile of the patient taking into account comorbidity and lifestyle. Finally, personalised treatment is also fitted to the individual needs and preferences of the patient.

Patient empowerment and shared decision making are important in the development of personalised care. Patient empowerment is an individual as well as a community process, through which patients gain greater control over decisions and actions affecting their health.[11] In this process patients understand their role and are empowered by their health-care professional. They get the skills and knowledge needed to actively participate in their personal health care, in an environment that encourages patient participation.

Shared decision making

Shared decision making (SDM) is an important aspect of personalised cancer care.[12] SDM aims at the process "where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, in order to achieve informed preferences".[13] SDM between patients and healthcare professionals enables weighing the treatment options in the light of patient preferences and personal context. SDM is not only needed as a one-off intervention to enable choice of a tailored treatment, but it is a continuous process, which is required for each decision throughout the cancer continuum.

More patient involvement in decision making is demonstrated to improve compliance with treatment,[14] higher quality of life[15] and reduce healthcare costs[16]. In the palliative setting, studies suggest that SDM could improve emotional outcomes in palliative patients.[17]

But, presently, SDM is not yet optimally implemented in curative cancer care as is demonstrated by a study with audiotaped decision making consultations for preference-sensitive curative treatment decisions in patients with rectal cancer. The data of this study suggest that oncologists are not explicitly in discussing SDM with their patients.[18]

Continuity of care

In general, the cancer care trajectory consists of different phases: (prevention), diagnosis, choice of treatment, delivery of treatment, survivorship care (that entails follow-up care and palliative care) and end-of-life-care. In countries with gatekeeper systems, like in the Netherlands, there is a strict difference between primary care (e.g. general practitioner (GP)) and hospital care (i.e. secondary care and tertiary care).

In the traditional cancer care pathway the GP refers patients for diagnostic workup in the hospital, and in case of confirmation of the cancer diagnosis, delivery of treatment (including the treatment choice), follow-up and palliative care are provided in the hospital. Typically, treatment options are discussed in a multidisciplinary specialist team, following guideline recommendation. Hereafter, options are discussed by the treating physician with the patient. Treatment is delivered by a multidisciplinary team (including oncology nurses). When treatment is given with a curative intent, follow up care in the first 2-5 years is usually provided by care professionals in the hospital. Afterwards, patients are dismissed with sometimes the exception of an annual control visit. In case of a palliative setting, which may cover several years and is usually characterized by sequential tumour-targeted treatments, patients continue to be under the guidance and supervision of the multidisciplinary team in the hospital. When a terminal phase has been reached the care will usually be mainly provided by the general practitioner (GP).

The role of the GP at the start of the cancer journey is clear. The majority of the symptomatic patients visit their GP first, including patients with cancer types for which a screening program exists.[19] The key task of the GP is to identify those at increased risk for cancer and refer them for diagnostic work-up to the hospital.

The responsibilities of the GP during the curative and palliative treatment of cancer are less well defined.[20] The extent to which GPs are involved following a cancer diagnosis varies. In general, the GP is informed about the diagnosis by phone or by mail after the multidisciplinary team in the hospital has

reached consensus on the diagnosis and proposed treatment. While patients are being treated for cancer, the involvement of the GP varies. Information provision to the GP is not standard, and depends on the initiative of either the GP or the individual specialist.[8] Research shows that many GPs feel 'out of the loop' after referral, and experience a barrier to connect with the patient.[21–23] As a result the contact between the GP and the patient depends on the individual initiative of either the GP or the patient. Literature shows that cancer patients consult their GP during treatment more often as compared to healthy controls.[8, 24] Reasons for increased GP contact during treatment can be related to the physical or psychosocial consequences of cancer and its treatment, but also to the higher prevalence of co-morbidity.[8, 24] Currently, these GP contacts occur in response to patient's complaints, questions or worries, and are not built in a structured format during the cancer journey.

A survey of the Dutch patient organisation for cancer patients (NFK) showed that patients with cancer regard the GP as the trusted professional with whom they want to share concerns and from whom they expect advice regarding cancer, choice of treatment and its side effects . Patients want the GP to provide them with further information on the expected recovery, late treatment effects and on how to adjust to normal life after treatment.[25]

After primary treatment has been completed, patients have to restart their live, living with the consequences of cancer, its treatment, the fear of recurrence and the feeling of being left alone.[26]

Continuity of cancer care aims at coordination, information exchange and integrating care delivery during the whole cancer journey as much and often as possible.[27] Although generally considered as the individual 'care coordinator', and the trusted professional who safeguards continuity and integrated care for the patient,[20, 28] the GP is presently unable to fulfil this role in patients with cancer.[29, 30]

The changing role of the GP in cancer care

In general, the GP has a longstanding and personal relationship with the patients and their family, and is up to date with their medical and psychosocial background. Therefore, GPs are probably best positioned to help the patient to balance treatment options in the perspective of medical history and personal preferences.[31, 32]

Therefore for many years patients, governmental and professional organisations suggest a more prominent role of the GP during their cancer journey to facilitate personalised care and empowerment, to improve psychological and lifestyle support and to improve continuity of care.[7, 8, 33, 34]

With the increasing number and prolonged survival of cancer patients and, the need for personalised and continuity of care, the role of the GP in cancer care is rapidly changing. It does not only focus on traditional domains such as early diagnosis, palliative care and end-of-life care, but will also include care provision during and after treatment.

Interventions to improve GP involvement in cancer care

Even though an increased role of the GP and the primary care team is widely advocated, the most effective approach to involve primary care during cancer treatment remains unclear. So far, there are no effective interventions, and recommendations for GPs guidance during treatment are not embedded in professional guidelines. In 2012, a Cochrane review aimed to identify the evidence for effectiveness of interventions ensuring continuity of care in the follow-up of patients with cancer.[35] Three care models were identified to achieve this, i.e., case management, shared care and involving an interdisciplinary team. However, the review concluded that interventions were too divers and no effects on patients' health-related outcomes could be found. Structural involvement of the GP from diagnosis onwards was not addressed in these studies.

In 2013, the GRIP intervention was developed, aimed at improving personalised cancer care and continuity of care for cancer patients, by structural involvement of the primary care team after cancer diagnosis. The GRIP intervention includes two components: a Time Out consultation (TOC) with the GP after cancer was diagnosed, aimed at improving the SDM process, making more personalised treatment decisions and facilitating continuity of primary care. During the TOC, planned between diagnosis and treatment decision the GP discusses with the patient the diagnosis and prognosis of their cancer, reflects on psychosocial consequences, creates awareness that a choice of treatment exists and prepares the patient for the final treatment choice with the treating oncologist.[36] The second GRIP component is guidance during and after cancer treatment from primary care by a team consisting of the GP and a home care oncology nurse (HON). The guidance consists of a minimum of three contacts with the HON during and after treatment to monitor and support patients during and after treatment. The GRIP intervention was developed in close collaboration between the Dutch Federation of cancer patient organisations (NFK), the University Medical Centre Utrecht and regional primary care healthcare workers.

In this thesis we present the background, the design of the GRIP intervention and we discuss the results of the evaluation in a large regional, practice-based RCT.

Aim and outline of this thesis

The first aim of this thesis is to explore the current knowledge and the needs and experiences of cancer patients, regarding GP involvement after cancer is diagnosed.

In ***Chapter*** 2 we explore the patients' experiences and needs regarding GP involvement after a cancer diagnosis in patients treated with curative and palliative intend. In ***Chapter*** 3 we present a systematic overview of the current evidence from clinical trials on the effects of primary care interventions, which aimed to involve the GP shortly after cancer diagnosis, on patient reported outcomes and healthcare utilisation.

The second aim of this thesis is to investigate the effects of the GRIP intervention for cancer patients who are treated with curative intent on patient reported outcomes and healthcare use.

The protocol of the GRIP evaluation study is described in ***Chapter 4***. ***Chapter 5*** describes the effects of the efforts to implement the first part of the GRIP intervention; the TOC. In ***Chapter 6***, we report the effect of the complete GRIP intervention, so TOC and GP and HON involvement during and after cancer treatment on patient satisfaction and healthcare utilisation. Finally, ***Chapter 7*** discusses the main findings of this thesis and presents future perspectives.

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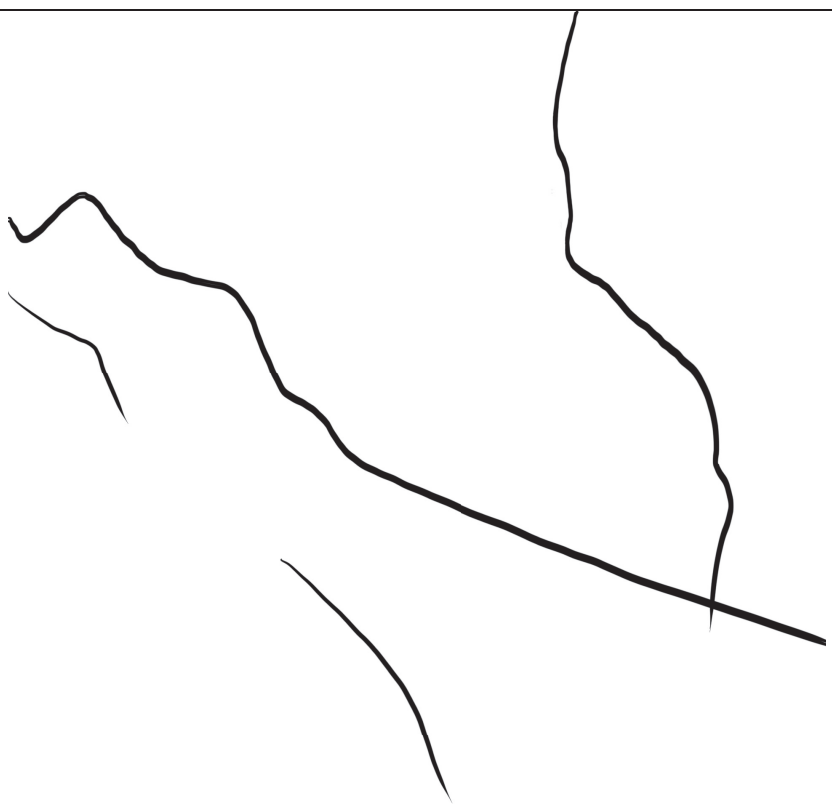

CHAPTER 2

GP involvement after a cancer diagnosis; patients' unmet need for decision support.

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Submitted

Abstract

Background

Shared decision making (SDM) is considered important to realise personalised cancer care. Increased general practitioner (GP) involvement after a diagnosis is advocated to improve SDM.

Aim

To explore if cancer patients are in need of GP involvement in cancer care in general and in SDM, and whether these needs are met.

Design and Setting

An online national survey distributed by the Dutch Federation of Cancer Patient Organisation (NFK) in May 2019.

Methods

The survey was sent to (former) cancer patients. Topics included GP involvement in cancer care in general and in SDM. Descriptive statistics and quotes were used.

Results

Among 4,763 (former) cancer patients, 59% (N=2,804) expressed a need for GP involvement in cancer care. Of these patients, 79% (N=2,193) experienced GP involvement. Regarding GP involvement in SDM, 82% of the patients (N=3,724) expressed that the GP should "listen to patient's worries and considerations", 69% (N=3,130) to "check patient's understanding of information", 66% (N=3,006) to "discuss patient's priorities in life and the consequences of treatment options for these priorities", and 67% (N=3,045) to "create awareness of the patient's role in the decision making". This happened in 47%, 17%, 15% and 10% of these patients, respectively.

Conclusion

The majority of (former) cancer patients expressed a need for active GP involvement in cancer care. Their needs for GP support in fundamental SDM steps remained largely unmet. Therefore, GPs should be made aware of these needs and enabled to support their patients in SDM.

How this fits in

Little is known about cancer patients' needs for GP involvement in cancer care and in shared decision making (SDM), and to what extent these needs are met. This study showed that the majority of (former) cancer patients has a need for GP involvement in cancer care and in SDM. However, the need for GP involvement in SDM remains largely unmet. Therefore, GPs should be made aware of these needs and enabled to support their patients to make personalised cancer treatment decisions.

Introduction

Cancer treatment decisions become more complex, due to the increasing number of treatment options. This enables a more personalised approach.[1] Incorporating personal preferences in treatment decisions requires shared decision making (SDM). SDM aims at establishing a treatment decision that optimally matches a patient's personal preferences and expectations.[2] An effective SDM process consists of four steps: 1) awareness of choice, 2) explanation of treatment options, 3) time for deliberation, and 4) making an informed decision.[2]

Unfortunately, in the present hospital oriented cancer care pathway, essential steps for successful SDM are usually insufficiently supported. First, patients are often unaware of their important role in choosing the 'best fitting' treatment.[3] Second, medical information, including treatment options, is often not understood by patients.[4] Third, time for deliberation is often limited, since the short in-hospital pathway between diagnosis and treatment choice generally does not facilitate reflection. This leaves little room to consider treatment options in the light of patient's personal preferences and expectations.[3,5,6]

General practitioners (GP) usually have longstanding relationships with their patients. Consequently, for many, the GP is the 'trusted healthcare professional', with longitudinal knowledge of their patients' medical and personal history.[1,7] Hence, the GP is considered to be in the ideal position to guide the patient through the different steps of the SDM process.[1,6] Patients and GPs support this extended role for the GP in cancer treatment decision-making, e.g., through determining patient's preferences, discussing treatment options and explaining medical information.[8-10]

Positive effects of increased GP involvement after a cancer diagnosis have been described previously. Wallner et al. showed that patient's experience of GP engagement, i.e., how informed the patient felt the GP was about the diagnosis, was associated with higher satisfaction of treatment decisions in cancer.[11] Wieldraaijer et al. showed that a consultation with the GP between diagnosis and start of treatment is beneficial for patient's feelings

of comfort and satisfaction.[12] We demonstrated earlier that a cancer related GP consultation before treatment decision may improve the SDM process of palliatively treated cancer patients according to patients, GPs and treating physicians.[13]

Despite this broadly shared call for more GP involvement in the process of making cancer treatment decisions, little is known about the patients' perspective. Therefore, we aimed to explore patients' needs for GP involvement after a cancer diagnosis in general, specifically in SDM after a cancer diagnosis and whether these needs are met.

Methods

Design

An online national survey was developed and distributed among (former) cancer patients in the Netherlands in May 2019 by the Dutch Federation of Cancer Patient Organisations (in Dutch: NFK).

Study population

NFK is an umbrella organisation of 19 cancer patient organisations. These cancer patient organisations together represent approximately 35,000 (former) cancer patients. The survey was distributed in several ways. First, the survey was dispersed to the affiliated cancer patient organisations, which represent adult cancer patients with a large variety in diagnoses. These cancer patient organisations were asked to distribute the survey among their members. This could either be directly to all members or indirectly through their newsletter. Second, a web link to the survey was distributed through social media accounts of NFK (Facebook, LinkedIn, Twitter and Instagram), via their website and via other relevant partner organisations (such as The Dutch Cancer Society and the website kanker.nl). Finally, a panel of (former) cancer patients, who were not a member of one of the cancer patient organisations, were sent an invitation to participate in the survey.

Online survey

The online survey was developed by NFK, in cooperation with experts in the fields of cancer, primary care and SDM, including patients, clinicians, researchers and policy makers. The survey consisted of two parts; one part focussing on the role of the GP and the other on the role of the specialised oncology nurse. For this study we only used data of the GP related questions.

The survey started with a selection question ensuring that the respondent has or had cancer and eight general questions about patient- and disease characteristics. Hereafter, ten questions addressing the patient's personal needs for GP involvement in cancer care were posed. These questions covered

the topics: 1) the need for GP involvement in cancer care at any time after diagnosis, 2) whether this need was met, 3) the need for GP involvement in SDM of cancer treatment, 4) whether this need was met, 5) the initiator of involvement of the GP in cancer care and 6) satisfaction with GP involvement in cancer care (see Supplementary document 1 for the survey).

The need for GP involvement in SDM of cancer treatment was assessed using the statement; "The GP should: (1) "Listen to my worries and considerations about the diagnosis, treatment and its consequences", (2) "Check if I understand the information about my diagnosis, treatment and its consequences", (3) "Discuss what I think is important in my life and the consequences of treatment options for these priorities" and (4) "Explain to me the importance of my own opinion when making a treatment decision." GP involvement in cancer care was defined as: "Any type of long or short contact with the GP about the diagnosis, treatment and/or its consequences. This could either be via telephone, an appointment at the GP's office or a home-visit."

The format of the questions was either closed (numeric, multiple choice) or open-ended. Needs, and whether these needs were met, was assessed with multiple choice questions and open-ended questions for clarification. Satisfaction with GP involvement in cancer care was scored on a 10-point number rating scale ranging from 1 (very unsatisfied) to 10 (very satisfied). The estimated time to complete the questionnaire was approximately 5-10 minutes. The data were collected with the online tool "Survey Monkey." Respondents participated anonymously in the survey. The survey was open for response for two weeks. Respondents could choose to answer only part of the questions. Only if the general questions and the question 'Did you have a need for contact with your GP about your cancer diagnosis, the treatment and/or its consequences?' was answered with 'yes', 'no' or 'don't know/n.a.', the survey was used in the analysis.

Analysis

Descriptive analyses of the closed questions were performed for the total population and for subgroups of the following characteristics: sex, age,

education, type of cancer, cancer stage and time since last treatment. Statistical testing was not performed, since with the current number of patients small often not (clinically) relevant differences would already be statistically significant. Categorical variables are presented as numbers and percentages. Continuous variables are presented, depending on whether or not normally distributed, with means and standard deviations (SD) or medians and interquartile ranges (IQR). All analyses were performed with IBM SPSS Statistics version 25. Relevant quotes from the open questions were used to illustrate the results.

Results

Patient characteristics

The survey was completed by 4,763 (former) cancer patients. The mean age of respondents was 62 years (SD±12), 56% was female and 48% of the respondents had a high education level (Table 1). The majority of the respondents was diagnosed with either breast cancer (26%), haematological cancers (18%) or colorectal cancer (16%). The median time since the last received cancer treatment was 2 years (IQR 1-6) and 46% reported to be cured.

Table 1. Baseline characteristics of respondents.

	Total N=4763	
	N	(%)
Female	2686	(56)
Age; mean (±SD)	62	(±12)
Education		
High	2276	(48)
Middle	1908	(40)
Low	464	(10)
Other	61	(1)
Missing	54	(1)
Diagnosis		
Breast cancer	1231	(26)
Haematological cancers	874	(18)
Colorectal cancer	787	(16)
Prostate cancer	569	(12)
Bladder cancer	270	(6)
Gynaecologic cancer	179	(4)
Lung cancer	153	(3)
Melanoma	125	(3)
Oesophageal cancer	105	(2)
Other	470	(10)
Years since last received cancer treatment; median (IQR)	2	(1-6)
Patients reported cancer stage		
Cured	2166	(46)
Will probably be cured	901	(19)
Will probably not be cured	1256	(26)
Don't know/n.a.	440	(9)

Abreviations N.a.; not applicable, SD; standard deviation, IQR; interquartile range.

GP involvement in general

Of all respondents, 59% (N=2,804) expressed a need for GP involvement in cancer care any time after diagnosis (Table 2). GP involvement in cancer care was experienced by 79% (N=2,193) of these respondents. A relatively high need for GP involvement was reported by women (women: 64%; men: 52%). An unmet need was also seen more often in women (need met in women: 77%; men: 82%). A relatively high need for GP involvement was reported by patients with lung, oesophageal and gynaecologic cancer (68-69%), versus other cancers (47-64%). A relatively small proportion of (former) patients with breast and gynaecologic cancer experienced GP involvement (74-76%), compared to other cancers (78-88%). Respondents who indicated "will probably not be cured" reported relatively high need of GP involvement (66%) compared to those who indicated to be "cured" (55%). The latter group reported a relatively high unmet need (need met in 75% vs. 85%). Quotes in Box 1 illustrate the (absence of) a need and unmet need for GP involvement in cancer care.

GP involvement in SDM

Table 3 shows the need for GP involvement in SDM of cancer treatment and whether this actually happened. Eighty-two percent (N=3,724) of the respondents expressed that their GP should listen to their worries and considerations about the diagnosis, treatment and its consequences. This actually happened in 47% (N=1,744) of these cases. The majority of the respondents expressed that the GP should: "check understanding of information" 69% (N=3,310), "discuss patient's priorities in life and the consequences of treatment options for these priorities" 66% (N=3,006), and "explain importance of patient's opinion in decision" 67% (N=3,045). This actually happened in respectively 17% (N=542), 15% (N=461) and 10% (N=294) of these cases.

In all subgroups, the need for GP involvement in the SDM process was high. However, this need remained largely unmet for vital SDM steps, especially in respondents older than 65, in those with low education, in those with breast, bladder, gynaecologic, haematological cancers, or colon cancer and

in the "cured" group of respondents. Quotes that illustrate the need for GP involvement in SDM are presented in Supplementary Box 1.

Table 2. Need for GP involvement in cancer care and whether this need is met. Presented for total and stratified per subgroup.

Need for GP involvement in cancer care any time after diagnosis					
		Need (yes)		**Need met? (yes)***	
	Total	Of total		Of need	
	N	N	%	N	%
All respondents	4763	2804	(59)	2193	(79)
Sexe					
Male	2077	1073	(52)	873	(82)
Female	2686	1731	(64)	1320	(77)
Age					
<65	2537	1577	(62)	1245	(80)
≥65	2226	1227	(55)	948	(78)
Education					
Low education	464	254	(55)	188	(75)
Middle education	1908	1134	(59)	849	(76)
High education	2276	1351	(59)	1105	(82)
Diagnosis					
Haematological cancers	874	478	(55)	380	(80)
Colorectal cancer	787	402	(51)	307	(78)
Bladder cancer	270	128	(47)	105	(83)
Gynaecologic cancer	179	121	(68)	91	(76)
Melanoma cancer	125	75	(60)	64	(85)
Breast cancer	1231	791	(64)	582	(74)
Prostate cancer	569	323	(57)	276	(86)
Lung cancer	153	105	(69)	83	(81)
Oesophageal cancer	105	72	(69)	63	(88)
Last treatment					
≤ 2years ago	2404	1462	(61)	1215	(84)
≥ 3 years ago	2359	1342	(57)	978	(74)
Patients reported cancer stage					
Cured	2166	1180	(55)	875	(75)
Will probably be cured	901	535	(59)	413	(78)
Will probably not be cured	1256	825	(66)	699	(85)

*Percentage 'Need met? (yes)' is calculated for those who responded to have a need for GP involvement and filled in the question 'Need met?'
Abbreviation: GP; general practitioner.

Initiator & satisfaction

Among those who reported that their GP was involved in cancer care, this was initiated by the patient in 52% (N=1650), by the GP in 31% (N=987), by significant others in 4% (N=116) and unknown in 13% (N=421). In case of GP involvement, satisfaction with GP involvement in cancer care was evaluated with a mean of 7.4 (±2.4). This involvement was rated higher if the GP was the initiator (8.0±2.0), instead of the patient (7.0±2.4). This is illustrated by the final quote in Supplementary Box 1.

Box 1. Illustrative quotes of respondents.

Topics	Quotes of respondents
Need for GP involvement in cancer care	"Because you are so busy with life-threatening things, you hardly understand your own feelings. My partner and I needed a lot of extra care from our GP." "Your GP is closer to you than a specialist and is often easier to reach." "It's always nice to talk to the GP, so she's up to date and can think along."
No need for GP involvement cancer care	"The contact, guidance and information I received from the hospital was enough." "I had many visits to the hospital. I had no need for more consultations."
Unmet need for GP involvement cancer care	"I never thought of contacting my general practitioner. In hindsight, it might have helped me." "I had a need, but he didn't even contact me after the diagnosis when he himself had referred me to the hospital when I felt a lump."
GP's SDM support	"I was facing the decision to take hormones for five years. The decision was with me, but I did not know what to do. That's when I went to my GP for a consultation." "I think the specific information should come from the treating physician. The GP can check if everything is clear and stress that the patient's opinion is important." "A GP is the right person to talk to you as patient about your expectations, possibilities, etc."
Initiator for GP involvement cancer care	"The doctor called me several times on his own initiative after the diagnosis and during treatment. That was nice and gave me the feeling that he was involved."

Table 3. Need for GP involvement in SDM of cancer treatment and whether this need is met. Presented for total and stratified per subgroup.

My GP should….		**Listen to my worries and considerations about the diagnosis, treatment and its consequences.**				**Check if I understand the information about my diagnosis, treatment and its consequences.**				**Discuss what I think is important in my life and the consequences of treatment options for these priorities.**				**Explain to me the importance of my own opinion when making a treatment decision.**			
		Need (yes)		Need met?(yes)*		Need (yes)		Need met? (yes)*		Need (yes)		Need met? (yes)*		Need (yes)		Need met? (yes)*	
	Total	Of total		Of need		Of total		Of need		Of total		Of need		Of total		Of need	
	N	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
All respondents	4526	3724	(82)	1744	(47)	3130	(69)	542	(17)	3006	(66)	461	(15)	3045	(67)	294	(10)
Male	1966	1561	(79)	755	(48)	1349	(69)	236	(18)	1274	(65)	217	(17)	1297	(66)	128	(10)
Female	2560	2163	(85)	989	(46)	1781	(70)	306	(17)	1732	(68)	244	(14)	1748	(68)	166	(10)
Aged <65	2434	2059	(85)	1008	(49)	1685	(69)	326	(19)	1639	(67)	257	(16)	1665	(68)	160	(10)
Aged ≥65	2092	1665	(80)	736	(44)	1445	(69)	216	(15)	1376	(65)	204	(15)	1380	(66)	134	(10)
Low education	422	326	(77)	127	(39)	308	(73)	51	(17)	296	(70)	33	(11)	296	(70)	32	(11)
Middle education	1810	1495	(83)	644	(43)	1305	(72)	221	(17)	1237	(68)	183	(15)	1239	(69)	119	(10)
High education	2185	1812	(83)	930	(51)	1439	(66)	260	(18)	1394	(64)	238	(17)	1435	(66)	138	(10)
Haematological cancers	832	680	(82)	311	(46)	530	(64)	90	(17)	512	(62)	75	(15)	507	(61)	38	(8)
Colorectal cancer	732	568	(78)	254	(45)	517	(71)	94	(18)	469	(64)	65	(14)	483	(66)	42	(9)
Bladder cancer	256	201	(79)	83	(41)	176	(69)	26	(15)	176	(69)	14	(8)	176	(69)	10	(6)
Gynaecologic cancer	170	141	(83)	66	(47)	119	(70)	16	(13)	119	(70)	17	(14)	127	(75)	11	(9)
Melanoma cancer	119	97	(82)	51	(53)	87	(73)	13	(15)	79	(66)	18	(23)	83	(70)	11	(13)
Breast cancer	1178	1002	(85)	442	(44)	818	(69)	143	(18)	801	(68)	104	(13)	804	(68)	76	(10)
Prostate cancer	543	447	(82)	229	(51)	384	(71)	70	(18)	358	(66)	67	(19)	377	(69)	52	(14)
Lung cancer	145	124	(86)	64	(52)	104	(72)	20	(19)	105	(72)	26	(25)	95	(66)	12	(13)
Oesophageal cancer	104	84	(81)	54	(64)	76	(73)	15	(20)	75	(72)	19	(25)	78	(75)	12	(15)

Table 3. Continued.

My GP should....		Listen to my worries and considerations about the diagnosis, treatment and its consequences.				Check if I understand the information about my diagnosis, treatment and its consequences.				Discuss what I think is important in my life and the consequences of treatment options for these priorities.				Explain to me the importance of my own opinion when making a treatment decision.			
		Need (yes)		Need met?(yes)*		Need (yes)		Need met? (yes)*		Need (yes)		Need met? (yes)*		Need (yes)		Need met? (yes)*	
	Total	Of total		Of need		Of total		Of need		Of total		Of need		Of total		Of need	
	N	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
All respondents	4526	3724	(82)	1744	(47)	3130	(69)	542	(17)	3006	(66)	461	(15)	3045	(67)	294	(10)
Last treatment ≤ 2years ago	2307	1897	(82)	995	(53)	1532	(66)	289	(19)	1510	(66)	289	(19)	1497	(65)	171	(11)
Last treatment ≥ 3 years ago	2219	1827	(82)	749	(41)	1598	(72)	253	(16)	1496	(67)	172	(12)	1548	(70)	123	(8)
Cured	2035	1658	(82)	711	(43)	1438	(71)	228	(16)	1340	(66)	147	(11)	1398	(69)	99	(7)
Will probably be cured	867	708	(82)	329	(47)	606	(70)	116	(19)	570	(66)	81	(14)	598	(69)	52	(9)
Will probably not be cured	1208	1017	(84)	553	(54)	806	(67)	142	(18)	818	(68)	200	(24)	776	(64)	115	(15)

Abbreviations: GP; general practitioner.
*Percentage 'Need met? (yes)' is calculated for those who responded to have a need for GP involvement and filled in the question 'Need met?'

Discussion

Summary

In the present study, we evaluated the needs of (former) patients for GP involvement in cancer care. More than half of the respondents reported that they wanted the GP to be involved in cancer care after the diagnosis. Presently, the need for GP involvement is met in over three-quarter of the cases. As for GP involvement in SDM of cancer treatment, the balance is different. Although more than 80% expressed a need for the GP to listen to worries and considerations, this was only met in almost half of these cases. In parallel, more than two-thirds of responding cancer patients indicated a need for GP involvement in several elemental SDM steps, such as explaining information, checking understanding and discussing priorities. This SDM support happened in a small minority of cases. Finally, the initiator of GP involvement was mostly the patient, whereas satisfaction with GP involvement in cancer care was higher if the GP was the initiator.

Strengths and limitations

Using a survey to assess the presence of needs in retrospect has several limitations. Recall bias may have occurred, since the median interval between last received treatment and participation was two years. Remembering needs, and whether these were met, may be hard after a relatively long and arduous period. Among those treated longer ago (≥3years) the reported needs were similar, but the unmet needs were slightly higher compared to those who were more recently treated (≤2years). This could either indicate that unmet needs are overestimated after a longer period of time, or that these needs are increasingly met. Also, the method used to recruit cancer patients may have caused selection of participants. The survey was distributed among a group of (former) cancer patients who are mostly affiliated to a cancer patient organisation. Consequently, our respondents may have been relatively committed, active and critical, thus may have different needs than the average cancer patient and have a stronger drive to meet those needs. This might have resulted in either an over- or underestimation of the presence of needs and the percentage of unmet needs. On one hand those who have a higher potential to meet their needs may be overrepresented. On the

other hand, as these participants might be more critical, their needs might be higher and less easy to meet.

The main strength of this study is the high number of (former) cancer patients who responded to this survey. The large population and the variety of cancer types support generalisability and enabled sub-group explorations.

Comparison with existing literature

To our knowledge, this is the first study among cancer patients that combines an exploration of the needs for GP involvement in cancer care and specifically in SDM, and to what extent these needs are met. Our findings are in line with the few studies that have addressed adjacent topics. It confirms the conclusion of Halkett et al., who reported that patients see a role for the GP in SDM support after a cancer diagnosis.[10] Lang et al. reported that 34.5% of the cancer patients discussed diagnostic and therapy related decisions with the GP.[9] Also, Klabunde et al. showed that 64.2% of the GPs reported to explore patient's preferences for treatment.[8] Both percentages are higher as compared to the 15% of the patients for whom this need was met in our study. This might be due to a different study population or due to differences in perception between GPs and patients. Additionally, our results imply that GPs mostly discuss worries and considerations, but are unaware of patients' needs to discuss the cancer treatment decision itself.

Furthermore, our results show that satisfaction with GP involvement is scored higher if the GP is the initiator of contact. This is supported by findings in a qualitative study by Brandenbarg et al. among curatively treated colorectal cancer patients who expressed dislike when the GP did not initiate contact after treatment.[14] Also, patients' preference for initiation of contact by the GP is expressed for other conversations, such as for advanced care planning.[15] In addition, previous studies show that patients are more satisfied if the GP is informed about the diagnosis[11] and if there is a contact moment with the GP (a "time out consultation") before start of treatment.[12] Our findings also support and explain the potential positive effect on SDM of actively involving the GP between diagnosis and therapy choice, which was recently reported for palliatively treated cancer patients.[13]

Conclusion and implications for practice

Although more GP involvement in cancer care is broadly supported by patients, GP involvement in SDM is presently insufficient. This calls for active and more adequate GP involvement after the cancer diagnosis, for instance through implementation of a "time out consultation" with the GP with SDM tools[16] to achieve better informed and more personalised therapy choices.[12,13,17]

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Appendix A. Survey.

1. This survey is meant for people ever diagnosed with cancer. Is this applicable to your situation?
   a. Yes, I have (had) cancer
   b. No

2. Wat is your sex?
   a. Male
   b. Female

3. What year you were born?

4. What is the highest education you achieved?
   a. No education achieved
   b. Primary school
   c. Primary professional education
   d. Secondary general education
   e. Secondary professional education
   f. Secondary general education
   g. Higher professional education
   h. Scientific education
   i. I'd rather not say
   j. Otherwise, namely

5. What type of cancer do/did you have? (if you had multiple diagnosis, fill in the most recent one) .....

6. In what year did you receive the most recent treatment? .....

7. Which situation is now applicable in your case?
   a. I'm cured
   b. I will (probably) cure
   c. I will (probably) not cure
   d. I don't know/not applicable

8. In how many hospitals were you treated?
    a. One hospital
    b. Two hospitals
    c. More than two

9. From which hospital did you receive the most care?

10. Did you have a need for contact with your GP about your cancer diagnosis, the treatment and/or its consequences?
    a. Yes
    b. No
    c. I don't know/n.a.
    d. Comment....

11. When did you have a need for contact with your GP about your cancer diagnosis, the treatment and/or its consequences? (Multiple answers possible)
    a. Shortly after diagnosis
    b. During treatment
    c. After treatment, during follow-up in hospital
    d. After finishing follow-up in hospital
    e. I don't know/n.a.

12. What was your reason for not having a need for contact with your GP about your cancer diagnosis, the treatment and/or its consequences?

13. Did you have contact with your GP about your cancer diagnosis, the treatment and/or the its consequences?
    a. Yes
    b. No
    c. I don't know/n.a.
    d. Comment....

14. When did you have contact with your GP about your cancer diagnosis, the treatment and/or its consequences? (Multiple answers possible)
    a. Shortly after diagnosis
    b. During treatment
    c. After treatment, during follow-up in hospital
    d. After finishing follow-up in hospital
    e. I don't know/n.a.

15. How many times (on average) did you have contact with your GP about your cancer diagnosis, the treatment and/or its consequences?
    a. 5 or less times
    b. 6-10 times
    c. 11 times or more
    d. I don't know/n.a.

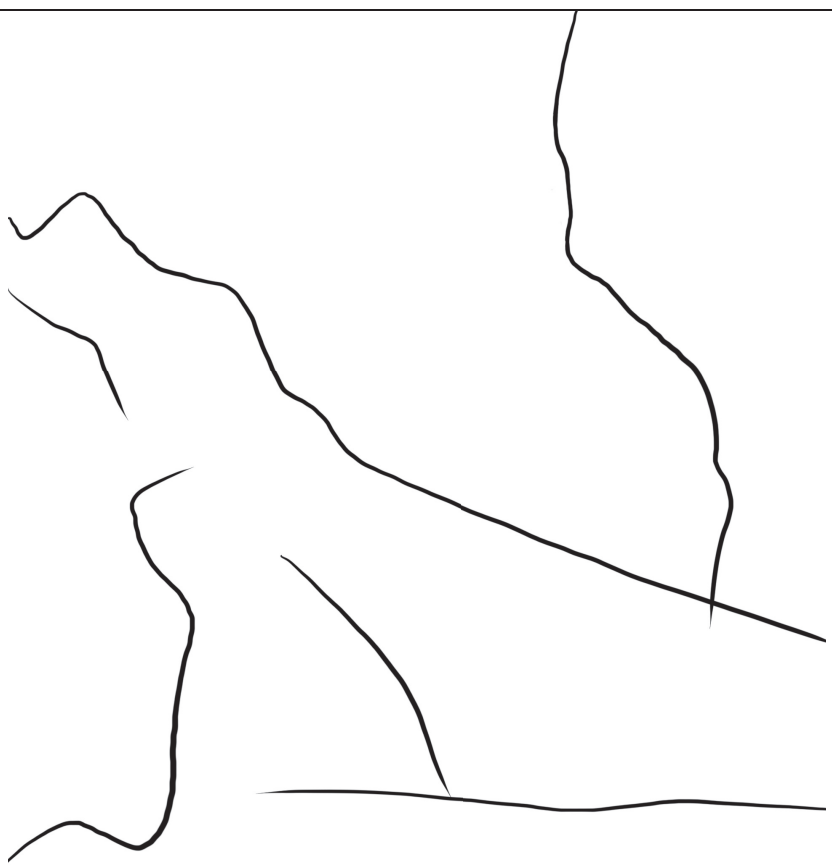
16. Who was the initiator of contact with your GP (most of the time) about your cancer diagnosis, the treatment and/or its consequences?
    a. Me
    b. My loved ones
    c. My GP
    d. I don't know/n.a.
    e. Other....

17. In which way did your GP support you with your cancer diagnosis, the treatment and/or its consequences? (Multiple answers possible)
    a. Listened to my worries and considerations about my diagnosis, treatment and its consequences.
    b. Asked if I understood the information about my diagnosis, treatment and its consequences.
    c. Discussed with me what I think is important in my life and the consequences of treatment options for these priorities.
    d. Explained to me the importance of my own opinion when making a treatment decision.
    e. Thought along with me about which hospital would be most suitable for me.
    f. Explained to me that no treatment is an option that I can choose.

g. Explained to me that I can change or stop the treatment in between.
h. Helped me with physical problems due to my diagnosis and treatment (e.g., fatigue or pain).
i. Helped me with psychological problems due to my diagnosis and treatment (e.g., anxiety, anger or sadness).
j. Helped me with cognitive problems due to my diagnosis and treatment (e.g., memory or concentration problems).
k. Helped me with social problems through my diagnosis and treatment (e.g., problems in relationships or with sexuality).
l. Discussed with me what my wishes and needs are in the last phase of life or around the end of life.
m. Had attention for my loved ones when dealing with my diagnosis and treatment.
n. I don't know/not applicable
o. Otherwise, namely

18. How (un)satisfied are you with the support or your GP with your cancer diagnosis, the treatment and/or its consequences?
    a. 1-10, no opinion
    b. Comment

19. Below you find statements about the role of your GP by make a treatment decision regarding your cancer diagnosis, the treatment and/or its consequences. Describe below if you agree or disagree with these statements.
    a. My GP should listen to my worries and considerations about the diagnosis, treatment and its consequences.
    b. My GP should check if I understand the information about my diagnosis, treatment and its consequences.
    c. My GP should discuss with me what I think is important in my life and the consequences of treatment options for these priorities.
    d. My GP should explain to me the importance of my own opinion when making a treatment decision.
    e. Comment...



CHAPTER 3

Involving the general practitioner during curative cancer treatment: a systematic review of health care interventions.

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Abstract

Objective

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

Study design

Systematic review

Participants

Patients with cancer treated with curative intent

Data sources

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

Results

Five RCTs and one CCT were included. Interventions and effects were heterogeneous across studies. Four studies implemented interventions focussing on information transfer to the GP and two RCTs implemented patient-tailored GP interventions. The studies have a low-medium risk of bias. Three studies show a low uptake of the intervention. A positive effect on patient satisfaction with care was found in three studies. Subgroup analysis suggests a reduction of healthcare use in elderly patients and reduction of

clinical anxiety in those with higher mental distress. No effects are reported on patients' quality of life (QoL).

Conclusion

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

PROSPERO registration number: CRD42018102253

Strengths and Limitations of this study

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

Background

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

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

improve patient outcomes and to ensure continuity in guidance from primary care.[3, 11] In the near future the GP might even be involved in treatments in primary care such as chemotherapy or hormone therapy. Currently however, involvement of primary care is generally restricted to supportive care during cancer treatment.

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

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

Methods

Data source and search

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

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

Study selection

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

Data extraction and management

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

Patient and public involvement

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

Quality assessment

Risk of bias for individual studies was scored by two authors (JB,IP) with the risk of bias criteria from the "Effective Practice and Organisation of Care Group (EPOC), which is a Cochrane review group.[13] In case outcomes of homogeneous study designs could be merged we rated the body of the evidence following the Grades of Recommendation, Assessment, Development and Evaluation approach (GRADE)[14] from the Cochrane collaboration. This systematic review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 checklist.[15]

Results

Study selection

As shown in Figure 1, 7,627 records were eligible for inclusion after removal of duplicates. Title and abstract screening yielded 97 articles. Of these, 90 were excluded after full-text screening. Main reasons for exclusion were (1) insufficient involvement of the GP, (2) GP involvement started after completion of primary cancer treatment, or (3) no RCT, CCT, controlled before and after study or interrupted time series design was used.

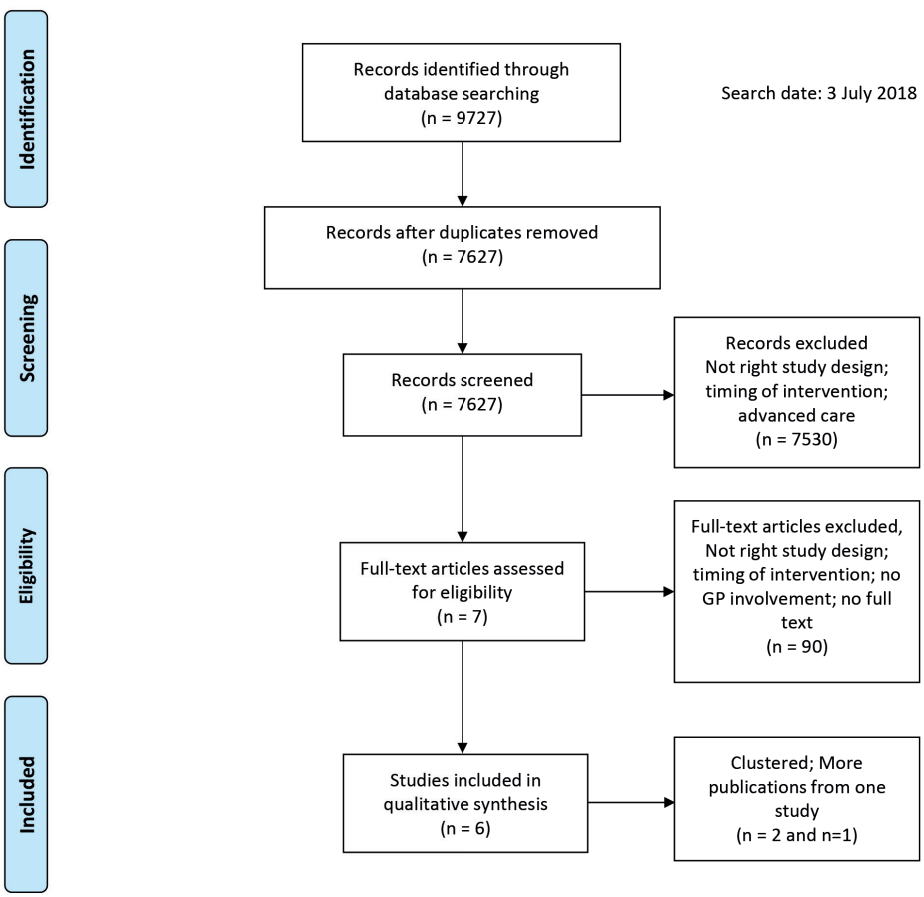

Figure 1. Flow diagram for selection of studies, based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[15]
Abbreviations: GP: General practitioner.

Three studies published multiple articles based on the same data.[16–23] As a result, five RCTs and one CCT were considered eligible for inclusion, which were described in 10 articles. No additional eligible studies were identified in the reference lists of selected studies. Figure 2, table 1, and 2 show a detailed account of the risk of bias, patient population, interventions, outcomes assessed and observed results for each study. Given the various research questions, interventions and heterogeneity of outcome measures, pooling of data, and GRADE assessment were not feasible.

Quality of studies

The EPOC risk of bias is presented in figure 2. Luker et al[24] and Nielsen/Kousgaard et al[16, 17] show a high risk of bias, resulting from high risk of selection and information bias. Drury et al[25] scored a medium risk of bias. And the studies of Johnson et al,[26] Johansson et al[23] and Bergholdt et al[18–21] show a low risk of bias. Regarding the RCT by Nielsen/Kousgaard et al[16, 17] several limitations should be kept in mind. The randomisation produced an imbalance, which influenced comparability of outcomes between study groups without corresponding correction in the analyses. Furthermore, it was not reported whether a baseline measurement was performed and the exact timing of the first measurement (table 2). Also, the percentage of missing data was 33% in the intervention and 26% in the control group.[16]

Study populations

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

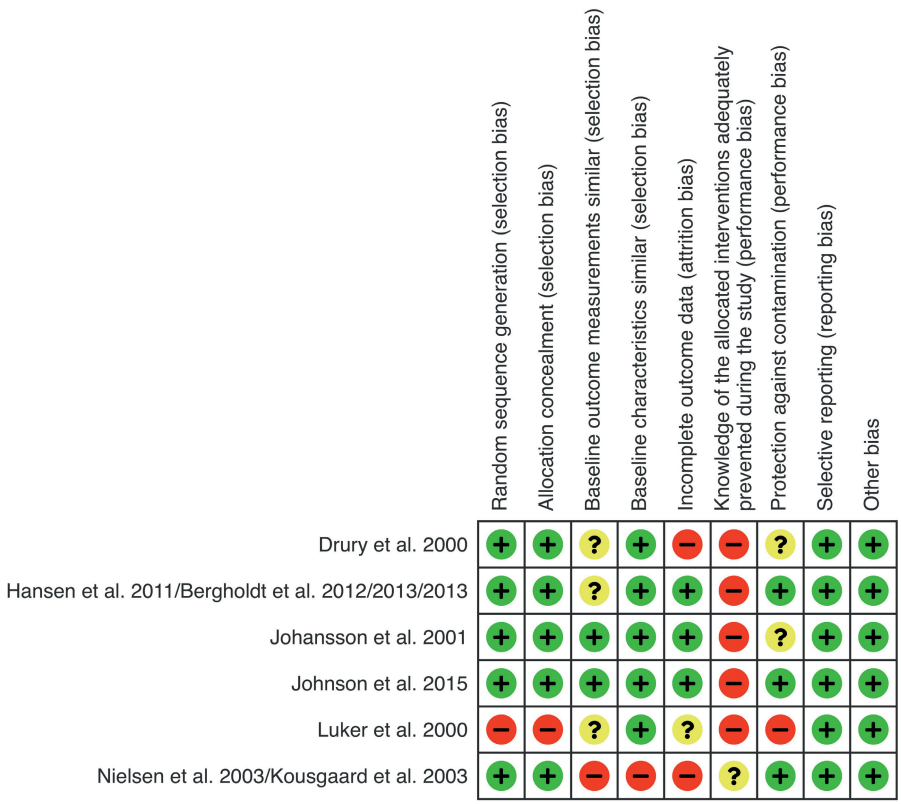

Figure 2. Risk of bias measured according to the EPOC criteria.

Usual care

In most studies, usual care was not described in detail. Only Luker et al[24] described the structured care that usual care patients received, which included home visits from a breast care nurse and written patient information on treatments. In general, the patient's GP received a discharge summary[16–18, 20, 21, 26] at the end of the treatment period[16, 17] or after each visit. [26] Other types of transferred information to the GP included an extract of the hospital record [16, 17] or communication by telephone.[26] Two studies did not describe what usual care entailed. [22, 23, 25]

Type of interventions

All participants received usual care, which was extended when the participant was appointed to the intervention. The interventions in the studies (table 1) were heterogeneous, but can be divided in mainly information transfer to the GP (n=4) [16, 17, 24–26] and tailored primary care interventions (n=2).[18–21, 23]

Interventions focusing on information transfer, provided additional, disease-specific educational and practical information concerning treatment and care directly to the GP or via the patient. Interventions were either directed at enhancing communication between GP and another party (ie, secondary care or patient), or directed at improving patient's attitude towards the healthcare system (ie, healthcare in general or intervention), physical or psychological complains. Three interventions provided patients with information, which was to be transferred to the GP. In one CCT,[24] informational cards were provided to the patients for use in primary care. Two other RCTs described an intervention with a Patient Held Record (PHR)[25, 26] aimed to facilitate intersectoral communication, to provide patients with an aide memoire and with the opportunity to stay actively involved in their treatment. One RCT supplied the GP with patient-specific discharge summaries by secondary care, aiming to enhance GP knowledge of chemotherapy treatment and expected adverse effects.[16, 17]

The tailored primary care interventions aimed to support patients in managing their disease and treatment.[18, 19, 21, 23] The interventions were to diverse to be merged and they are therefore described separately. In Johansson et al,[23] primary care was intensified by means of recruitment of a home care nurse, psychologist, dietician and training of the GP. The home care nurse initiated contact. The GP was regularly informed by the specialist and educated on management of patients with cancer. In the one RCT from Hansen et al and Bergholdt et al,[18–21] a rehabilitation team interviewed all patients on different aspects of rehabilitation. Afterwards the GP was informed on patient-specific rehabilitation needs and encouraged to proactively contact the patient to support the patient in his/her needs.

Study outcomes

The most often measured primary outcomes were healthcare utilization[16, 17, 23–25] and quality of life,[16–18, 25] as presented in table 2. Other outcomes consisted of patient and GP perceptions of care, symptoms, coping and empowerment. The following outcomes were not presented in the included articles: healthcare experience by informal caregivers and disease-specific outcomes (ie, progress, mortality). Outcomes are described in more detail below.

Intervention fidelity/compliance and healthcare use

Healthcare use is related to the uptake of the intervention. For example, if the intervention aims at more GP involvement, healthcare use is likely to increase. Although all interventions aimed at increased involvement of primary care, four interventions did not show a significant increase of GP consultations.[16, 19, 24, 25] Correspondingly, the uptake of interventions appeared to be low in the majority of the studies. This is illustrated by Bergholdt et al[19] which describes an 'active involvement' intervention, in which GP proactivity was comparable to GP proactivity in the control group (60% versus 52%, OR adjusted for sex and age 1.44 95%CI 0.80–2.36).[19] In two studies, information transfer to the GP by their patients was hardly used or remembered by the majority of the GPs.[24, 25]

Five studies, evaluated the effect of the intervention on hospital and/or primary care resource use. These studies showed no significant effect on secondary care healthcare use.[23–25] Only the subgroup of older patients (≥70 years of age) had a significantly lower use of secondary care[23] when primary care was actively involved. Even though GP consultations where part of the interventions, several studies reported no difference in the number of GP consultations in the intervention group compared with the control group.[16, 17, 24–26]

Patient perception

Positive effects on patients' satisfaction with care were indicated by three studies. Extended information by PHR or discharge summary improved patient perceived intersectoral cooperation.[16, 17] GP consultations were evaluated as useful. Also patients reported that 'the GP could help in the way a specialist could not'.[26] Regardless of the uptake of the intervention, one study showed an improved satisfaction with communication and participation with care.[25] The significantly higher levels of perceived GP support shortly after the intervention described in Nielsen et al[16] declined to non-significant levels at six months after start of intervention. The authors did not present a mean difference overtime. One study with a low uptake of intervention showed no significant effect on patients satisfaction.[21]

Quality of life and psychological outcomes

No study found a significant effect on quality of life.[16, 18, 25] Johnson et al,[26] showed a significant difference in change of depression scores (p0.04). In the intervention group, depression scores remained unchanged, whereas scores in the control group, deteriorated significantly. Also, using a PHR combined with routine visits to the GP led to a significantly higher reduction of the number of clinically anxiousness patients compared with usual care.[26]

GPs perceptions of care

Four out of five studies evaluating effects on GPs perceptions of care did not find relevant effects on GP's confidence in disease management and knowledge nor in the communication with the specialist.[17, 21, 24, 26] Studies in which information was carried by the patient (a PHR or informational cards) showed little impact on GP satisfaction with care mostly due to low uptake of intervention. Only Nielsen/Kousgaard et al[16, 17] found significant positive effects on GP perceived intersectoral cooperation and GP satisfaction with information.

3

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

Reference Country	Population n=number, Cancer origin, Stage	Timing of: Inclusion, Intervention, Follow-up
Drury et al. (2000)[25] UK	N = 650 60% ♀ 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.	*Inclusion* During any RT clinic visit Time after diagnosis not specified *Intervention* On enrolment *Follow-up* 3 months
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [18–21] Denmark	N = 955 72% ♀ MAM (43%), LUN, GI, other (19%), MEL Cancer stage unknown, no deceased	*Inclusion* Cancer diagnosis <3 months *Intervention* On enrolment *Follow-up* 14 months
Johansson et al. (2001)[23] Sweden	N = 463 57% ♀ MAM (47%), GI, PRO 22% with advanced disease.	*Inclusion* Newly diagnosed patients (<3 months after diagnosis) *Intervention* On enrolment *Follow-up* 3 months

	Nature of the intervention and comparison groups
	UC and intervention vs UC Patients received a PHR Initiative GP contact: Patient PHR: A4 size plastic wallet content: - Communication sheets for use by patient, family care givers and healthcare 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.
	Intervention vs UC Rehabilitation primary care programme Initiative GP contact: Healthcare worker Rehabilitation primary care programme 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 patients with cancer rehabilitation needs to GP. - RC encouraged GP to proactive contact patient to facilitate a rehabilitation process.
	Intervention vs UC Intensified primary care programme Initiative GP contact: Healthcare worker Individual Support intervention consisting of: - Intensified primary healthcare 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.

Table 1. Continued.

Reference Country	Population n=number, Cancer origin, Stage	Timing of: Inclusion, Intervention, Follow-up
Johnson et al. (2015)[26] Australia	N = 97 Stopped early (slow accrual); underpowered for the main analysis. 86% ♀ MAM (76%), HEM, GYN, GI Cancer stage 3.3% palliative	*Inclusion* During first course of CT *Intervention* First through last course of CT *Follow-up* 6 cycles of CT
Luker et al. (2000)[24] UK	N = 79 100% ♀ MAM (100%) Cancer stage 100% curative	*Inclusion* <4 weeks after diagnosis *Intervention* At start of treatment *Follow-up* 4 months

	Nature of the intervention and comparison groups
	UC and intervention vs UC (discharge summary) Shared Care programme + 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.
	UC and intervention vs UC Patients received information cards Initiative GP contact: Patient Information card content: - Rationale for patient specific treatment; Prognostic indicators, complications, side effects and referral indicators Patients received: - Informational cards to provide rapid access to treatment-specific information for members of the primary healthcare team - Encouragement to contact their primary healthcare team and show the Information cards

Table 1. Continued.

Reference Country	Population n=number, Cancer origin, Stage	Timing of: Inclusion, Intervention, Follow-up
Nielsen et al. (2003) [16] Kousgaard et al. (2003) [17] Denmark	N = 248 64% ♀ MAM(39%), GI, GER, GYN, H&N, LUN, others (16%), MEL Cancer stage 15% palliative	*Inclusion* Newly diagnosed patients *Intervention* From referral onwards; during treatment *Follow up* 6 months

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

	Nature of the intervention and comparison groups
	UC and intervention vs UC Shared care program Initiative GP contact: Patient Oncologists provided GP with a discharge summary with: - Specific disease, treatment and prognosis information - Expected physical, psychological, and social effects of treatment - Expected role of the GP - Contact information of all involved medical personnel Patients received: - Oral and written notification about the information provided to their GP - Encouragement to contact their GP when facing problems they assumed could be solved in this setting

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

Reference	Primary and secondary outcome measures (instrument used). Timing of measurement
Drury et al. (2000)[25]	*Primary* - Healthcare use (patient reported) - Patient satisfaction with communication and participation in care (SDQ) - Quality of life (EORTC QLQ-C30) *Secondary* - GP views on PHR (SDQ) *Measurements* Single measurement at 3 months
Bergholdt et al. (2012/ 2013/ 2013) Hansen et al. (2011) [18–21]	*Primary* Quality of life (EORTC QLQ-C30) *Secondary* - Psychological distress (POMS) - Symptoms (scale of the EORTC QLQ-C30) - Patient satisfaction with: their GP on five dimensions (Dan-PEP), support during the cancer course (one ad hoc question, likert scale, at 14 months) - GP proactivity measured on GP and patient level. (one ad hoc question, at 14 months) - GP's satisfaction with their contribution to the patient's rehabilitation course (two ad hoc questions, likert scale, at 14 months) *Measurements* At 6 and 14 months

Findings if applicable to study:
1. **Uptake of intervention**
2. **Healthcare use**
3. **Patient-related outcomes**
4. **GP-related outcomes**

Uptake of intervention
27.3% of 202 responding GPs had seen the PHR.

Healthcare use (intervention vs control)
Contact with care providers in 3 months follow-up;
- Visit GP 78% vs 85%.
- Visited secondary care clinics 95% vs 95%.

Patient-related outcomes (intervention vs control)
- Satisfaction communication and participation in care mean ±SD (scale 1-5): 3.83±0.59 vs 3.80±0.59, (95% CI 0.09 to 0.15).
- Confidence in facing future aspects of cancer: 62% vs 71%, p = 0.05.
- Quality of life mean global scores: 66.8±24.2 vs 65.3±23.7.

GP-related outcome (seen PHR vs not seen PHR)
- GP agrees that patients should have full access to their records 57% vs 57%.

Uptake of intervention
Proactivity 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.

Patient-related outcomes (intervention vs control)
- Quality of life; mean difference (95%CI);
  - at 6 months 1.25 (-2.4 to 4.9).
  - at 14 months -0.71 (-4.3 to 2.8).
- Psychological distress, mean difference (95%CI); -0.68 (-4.3 to 3.0).
- Patient participation on rehabilitation services, OR adj (95%CI); 1.0 (0.7 to 1.5).
- Patient satisfaction with:
  - GP on five dimensions, OR adj (95%CI) All NS; Doctor–patient relationship 0.94 (0.3 to-2.47), Medical care 1.2 (0.5 to 3.0), Information and support 1.6 (0.6 to 4.1), Organisation of care 1.3 (0.8-2.1), GP's accessibility 1.2 (0.6 to 2.3).
  - GP support during the cancer course, OR adj (95%CI); 1.14 (0.7 to 1.8).
- Proactivity GP and rehabilitation activity patient, OR adj (95%CI); 1.96 (1.2 to 3.3).

GP-related outcomes (intervention vs control)
- Overall satisfaction, OR adj (95% CI); 1.10 (0.47 to 2.56).

Table 2. Continued.

Reference	Primary and secondary outcome measures (instrument used). Timing of measurement
Johansson et al. (2001)[23]	*Primary* Healthcare use: - Hospital admissions and days of hospitalisation (with correction for weight loss and distress) (record reviewing) - Utilisation of outpatient care (record reviewing) *Measurements* Single measurement at 3 months

Findings if applicable to study:

1. **Uptake of intervention**
2. **Healthcare use**
3. **Patient-related outcomes**
4. **GP-related outcomes**

Uptake of intervention
Not reported.

Healthcare use (intervention vs control)
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 hospitalisation;
  - ≥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 vs12.9±11.5 (Student t-test p = 0.7257).
- Acute visits;
  - ≥70y: in 5% vs 15% of patients (χ^2 p = 0.034).
  - <70y: in 11% vs 10% of patients (χ^2 p = 0.80).

Table 2. Continued.

Reference	Primary and secondary outcome measures (instrument used). Timing of measurement
Johnson et al. (2015)[26]	*Primary* - Depression (HADS) - Anxiety (HADS) - Coping (Mini-MAC) - Empowerment (PES) *Secondary* - Healthcare use; hospital admission and emergency presentation (record viewing), number of GP visits (unknown) - Patient perception of care (SDQ) - GP perception of care (SDQ) *Measurements* - before treatment - midway through treatment - after treatment
Luker et al. (2000)[24]	*Primary* - Patient utilisation of the primary healthcare team (interview) - GP views after study (interview) *Measurements* - at baseline (preoperative) - 4 months after diagnosis

Findings if applicable to study:

1. **Uptake of intervention**
2. **Healthcare use**
3. **Patient-related outcomes**
4. **GP-related outcomes**

Uptake of intervention
Not reported.

Healthcare use (intervention vs control)
- Emergency department presentations: no significant between-group differences were observed.
- Average number of GP visits 2.79 vs 1.61, $p < 0.001$.

Patient-related outcomes (intervention vs control)
Patient perception of care;
- GP could help in ways specialist could not: 57% vs 19% ($\chi^2 = 11.5$; $p = 0.002$).
- Patient opinion concerning PHR/GP visit after CT course:
  - 81% considered PHR useful.
  - 35% considered visit inconvenient.

Depression; Geometric mean score (95%CI)
  - at baseline: 4.09 (3.31 to 4.86) vs 3.66 (2.92 to 4.40).
  - after treatment: 4.04 (3.25 to 4.83) vs 4.72 (3.72 to 5.72) p = 0.04 for comparison of groups over time.

Anxiety; Geometric mean score (95%CI)
  - at baseline: 8.05 (6.71 to 9.40) vs 7.91 (6.50 to 9.32).
  - after treatment: 5.49 (4.54 to 6.43) vs 5.24 (4.26 to 6.22) p = 0.80 for comparison of groups over time.

- Subgroup analysis for number of clinically anxious patients
  - at baseline: 14 patients with CA vs 11 patients with CA.
  - after treatment: 3 patients with CA vs 5 patients with CA.

Decline: intervention p=0.002; control p=0.014.
Coping; Geometric mean difference over time -0.7 vs 0.1 p=0.35.
Empowerment; Geometric mean difference over time 0.9 vs 0.9 p=0.47.

GP-related outcome (intervention vs control)
- GPs satisfied with communication: 82% vs 95%.
- GP confidence in managing:
  - side effects 85% vs 71% (p =0.45).
  - psychological issues 97% vs 81% (p= 0.04).

Uptake of intervention
8 of the 31 interviewed GPs recall seeing the Information Card.
Healthcare use (intervention vs control)
- Patient initiated contact;
  - with GP ≥1 contact in 71% vs 73%, p = 0.95.
  - district nurses no contact in 24% in both groups.

GP-related outcome (intervention)
- Recommending information card 7 of 8 GPs who recall intervention

Table 2. Continued.

Reference	Primary and secondary outcome measures (instrument used). Timing of measurement
Nielsen et al. (2003) [16] Kousgaard et al. (2003) [17]	*Primary* - Patient attitude towards the healthcare system: intersectoral cooperation and 'not feeling left in limbo' (SDQ) - Patient GP global assessment (one question) - Quality of life (EORTC QLQ-C30) - Performance status of function and self-care (ECOG) - Healthcare use: GP consultations (patient and GP reported SDQ) - GP assessment (SDQ) of: • Discharge information value • Own knowledge (patients confidence) • Own wishes to receive further information • Intersectoral cooperation *Measurements* Patient: - First measurement 'Soon after the introduction of the intervention.'(0 month) - 6 months GP assessment: timing unknown

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

Findings if applicable to study:

1. **Uptake of intervention**
2. **Healthcare use**
3. **Patient-related outcomes**
4. **GP-related outcomes**

Uptake of intervention
Not reported.

Patient-related outcomes (intervention vs control)
- At 6 months: attitude towards intersectoral cooperation; 59.22 vs 51.71, p = 0.055.
- At 6 months 'Not feeling left in limbo'; 65.49 vs 55.58, p=0.055.
- Patient GP global assessment;
  - at 0 months: 71.0 vs 58.68 (p = 0.04).
  - at 6 months: 68.9 vs 64.02 (p = 0.44).

Quality of life and performance status: nor relevant or significant differences described.

Healthcare use (intervention vs control)
- GPs reported regular contact; 75% vs 75%.
- Patient-reported GP consultation;
  - at 0 months: 67.8% vs 74.8% (p = 0.583).
  - at 6 months: 38.0% vs 31.5% (p = 0.046).

GP-related outcome (intervention vs control)
- Discharge information value GP on;
  - Psychosocial conditions 60% vs 26% (p <0.001).
  - Information their patient had received 84% vs 49%, (p <0.001).
- GP knowledge 94.8% vs 96.6% (NS).
- GP wish more information 21% vs 38% (p = 0.009).
- GP rate intersectoral cooperation 'satisfactory' 85% vs 73%, (p = 0.033).
- Intersectoral contacts: 25/100 vs 17/97 GPs had ≥1 contact, p = 0.23.

Discussion

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

Even though active involvement of the GP during cancer treatment might have positive effects, implementation appears to be difficult to realise. This is seen for all interventions, irrespective whether the GP contact is initiated by the patient or by the healthcare provider. This shows that finding a feasible intervention is challenging. Drury et al[25] suggested that a reason for the low uptake might be that GPs are not motivated to participate in the care of patients with curative disease as they do not feel closely involved in this stage.[25] This may explain why no studies were found where the GP was the initiator of involvement in care during cancer treatment. Low GP motivation is in contrast to what Dossett et al[27] show in their review on communication of specialist and GP during the cancer care continuum, they state that GPs desire involvement but think that specialist and patient prefer a specialist-based instead of shared-based cancer care.[27] Dossett et al[27] confirms a preference of a specialist-based model of care by specialists, which may result in a low motivation to activate the patient to see the GP.[27] Another reason for low uptake may be the difficulty to promote proactivity by GPs.[18, 19] Dossett et al[27] suggest that an adequate relationship and communication between the specialist and GP are important elements for the success of an intervention.[27] These findings suggest that, when designing an intervention, raising support of both primary and secondary healthcare workers is vital. The fact that healthcare systems have different challenges and needs (eg, communication between caregiver or distance to healthcare services), strengthens the need to tailor the potential solutions to local needs.

Specific subgroups may benefit more from involvement of primary care. A stronger decrease in anxiety was reported in patients with elevated levels of anxiety[26] and the GP involvement led to a reduction in secondary care use among older patients.[23] It has been suggested that different cancer diagnoses bring different psychological burdens and care needs,[28] but this could not be concluded from this review.

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

Current literature shows several important challenges for designing and studying interventions which effectively involve GPs in cancer care. First, finding a feasible intervention seems challenging. Second, when designing an intervention, raising support of primary and secondary healthcare workers seems vital.

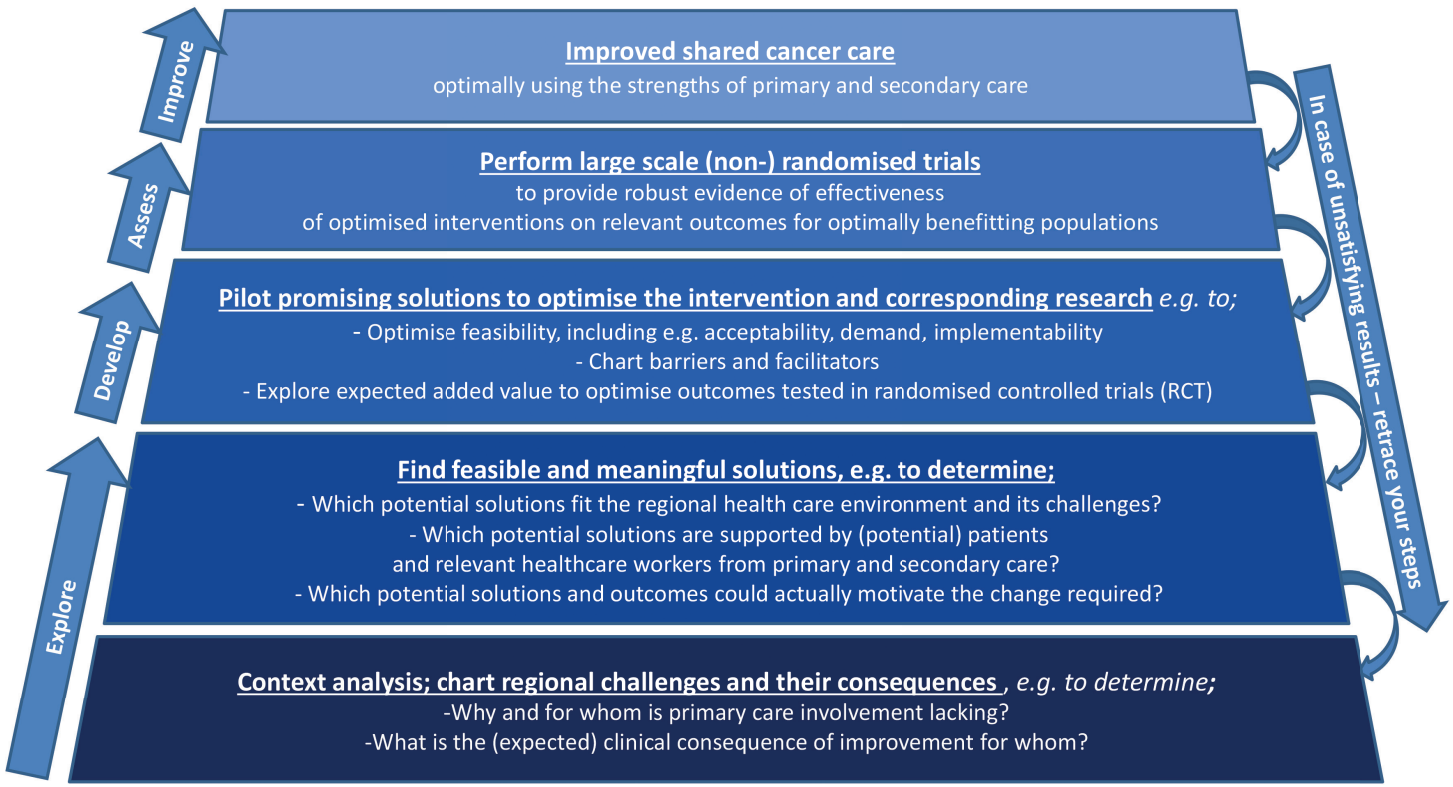

Figure 3. Framework for development of interventions aimed to effectively involve the GP in cancer care. In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care.

Third, challenges and solutions may be setting and population specific. For these reasons, exploratory research seems necessary to design feasible and effective interventions and meaningful studies. Fourth, large studies with a robust design are needed, which should focus on the effect of primary care involvement for various populations, including specifications for cancer types and vulnerable populations (eg, elderly and patients with physical or mental comorbidity).

Based on the findings in this review and guidelines for developing and evaluating complex interventions[29] and feasibility studies[30], we propose a framework, which describes consecutive steps that can guide the future development of effective interventions (figure 3). In this framework, each step is aimed to provide a foundation for the next step, thereby providing a stepwise approach to feasible and meaningful involvement of the GP in cancer care.

This framework should support us in finding definitive answers on the effects of GP involvement in the cancer care pathway in different healthcare settings, for a variety of populations. Interventions based on the framework should optimally facilitate primary care workers to appropriately implement their role in shared care, by making full use of their specific expertise by consideration of the patients' context and values, provided in a trusted environment.

Conclusion

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

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3

CHAPTER 4

Randomised controlled trial protocol (GRIP study): examining the effect of involvement of a general practitioner and home care oncology nurse after a cancer diagnosis on patient reported outcomes and healthcare utilization.

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Abstract

Background

Due to the ageing population and improving diagnostics and treatments, the number of cancer patients and cancer survivors is increasing. Policymakers, patients and professionals advocate a transfer of (part of) cancer care from the hospital environment to the primary care setting, as this could stimulate personalized and integrated care, increase cost-effectiveness and would better meet the patients' needs and expectations. The effects of structured active follow-up from primary care after cancer diagnosis have not been studied yet. Therefore the GRIP study aims to assess the effects of structured follow-up after a cancer diagnosis, by a primary care team including a general practitioner (GP) and a home care oncology nurse (HON), on satisfaction and healthcare utilization of patients treated with curative intent.

Methods

We will conduct a multicentre, two-arm randomised controlled trial in The Netherlands. We plan to include 150 patients who will be treated with curative intent for either breast, lung, colorectal, gynaecologic cancer, or melanoma. Further inclusion criteria are: age 18 years and older, able to answer questionnaires in Dutch, GP agrees to participate and the possibility to include the patient before the start of treatment. All patients receive care as usual. The intervention arm will receive additional structured follow-up consisting of a GP consultation before onset of treatment to empower the patient for shared decision making with the specialist and a minimum of three contacts with the HON during and after treatment. Primary outcomes are: patient satisfaction with care at the level of specialist, GP and nurse and healthcare utilization. Secondary outcomes include: quality of life, employment status, patient empowerment, shared decision making, mental health and satisfaction with given information. Repeated questionnaires, filled in by the participants, will be assessed within the 1-year study period.

Discussion

This randomised controlled trial will evaluate the effects of structured follow-up after a cancer diagnosis by a primary care team including a GP and HON, for patients undergoing treatment with curative intent. Results from the present study may provide the evidence needed to optimally rearrange responsibilities in cancer care delivery and consequently improve cancer care and patient related outcomes.

Trial registration: NTR5909.

Background

Due to the ageing population and improvements in diagnosis and treatment, the number of cancer patients and cancer survivors is increasing.[1, 2] The WHO estimates a worldwide increase in cancer incidence, from 14.1 million new patients in 2012 to more than 20 million in 2025.[3] In addition, survival is improving in the Netherlands, there will be an estimated increase of 57% in cancer survivors in 2020.[4]

In the near future, healthcare systems in several countries, such as The Netherlands, United Kingdom, Australia, USA and Canada, will face several challenges in fulfilling the needs and demands of this growing cancer patient population.[2, 5] In addition to the rising numbers of cancer patients, other changes concerning the cancer care path will challenge the healthcare system, such as the increased variety in treatment options,[2, 5] the increasing numbers of cancer patients with comorbidity resulting from aging[4, 6,7] of the population and the increased urge for patient involvement in decision making and self-management.[8, 9] Consequently, there is a need to create a personalised cancer care continuum for each patient, based on individual preferences, medical profile and best fitting treatment options.[6]

Traditionally, management of cancer is delivered by in-hospital specialists. In countries where the general practitioner (GP) is the gatekeeper in the care system, such as the Netherlands, the GP has a long-lasting personal relation with the patient, is up to date with the patients' medical history and preferences, and is considered as a trusted healthcare advisor by most patients.[10] These typical features of the GP provide opportunities for improving continuous and personalised care for the growing population of cancer patients. Therefore, patients, healthcare workers, governmental and professional organisations suggest a more prominent role of the GP in the guidance of patients during their cancer journey with a focus on empowerment, psychological and lifestyle support and follow-up care in the chronic disease stage. Even though a substantial role for primary care is advocated in the Netherlands and internationally, involvement of primary care in cancer care remains sporadic and unstructured.[4, 6, 7, 11]

At the same time, Dutch healthcare reports indicate that in 2020 the workload for GPs regarding care for patients with cancer will increase by about 66% within the Netherlands.[4] In order to divide this workload, policymakers suggest to involve the whole primary care spectrum, including GPs and primary care nurses.[4, 6] Beside keeping the workload acceptable, involving a primary care team may affect hospital care use.[12, 13] Also, increased GP involvement was associated with higher patient satisfaction with care and treatment decision.[14–17]

Scarce evidence suggests favourable effects of increased involvement of primary care in shared decision making and guidance during treatment, starting from diagnosis.[12–17] However, to our knowledge, the effectiveness of structured active follow-up by a primary care team starting from cancer diagnosis has not yet been published. Therefore, we designed the so called 'GRIP study'. In this paper, we describe the design and methods of the GRIP study.

Methods

Aim

The randomised GRIP study primarily aims to evaluate the effects of structured follow-up from primary care on patient satisfaction and healthcare utilisation for cancer patients treated with curative intent. In addition, we assess the effects on quality of life, mental health, patient empowerment, shared decision making and employment status.

Design

GRIP is a multi-centre, two-armed randomised controlled trial in the Netherlands.

Study population

We aim to include 150 newly diagnosed cancer patients who are to be treated with curative intent for one of the following types of cancer: breast cancer, colorectal cancer, all types of gynaecologic cancer, lung cancer, or melanoma. We primarily intended to include prostate cancer, but our study was incompatible with ongoing psycho-social research in this patient population in the participating hospitals.

Inclusion criteria

Patients are eligible for study participation, when they meet all of the following criteria:

- Newly diagnosed with one of the following types of cancer: breast cancer, colorectal cancer, all types of gynaecologic cancers, lung cancer or melanoma. Not being recurrent disease.
- Cancer therapy is initiated with curative intent (cancer staged I-III).
- Patient's general practitioner agrees to participate in the GRIP-study.
- Patient is 18 years or older.
- Patients can be included before start of the cancer treatment.
- Sufficient mastery of the Dutch language or translator available during study.

Exclusion criteria

A patient who meets any of the following criteria will be excluded from participation:

- Major psychiatric disease or personality disorders.
- Unable to fill in questionnaires.

Patients will be first screened for in- and exclusion criteria in the hospital by nurse (practitioners) or medical doctors and secondly by the researcher.

Recruitment and allocation

To ensure reaching the required sample size of 150 patients, we involved all three major hospitals (one academic and two-non-academic) located in the greater urban region of Utrecht, the Netherlands, in the study. In addition, researchers will visit all sites biweekly to motivate the sites for inclusion of patients. All four GP cooperative care organisations in the region, together representing 300 GPs, and two home care organisations employing primary care oncology nurses, participate in the study. The GP cooperative care organisations inform their member GPs about the GRIP study, and the GPs can decline to collaborate by opt-out.

Eligible patients will be recruited in the hospital by the treating physician or oncology nurse after the patient is informed of his/her cancer diagnosis. After verbal consent, the treating physician or oncology nurse informs the research team, who contacts the patient by phone the (working)day after diagnosis. Written informed consent is obtained from all participants by the researcher.

The researcher will randomise the participants to intervention or usual care by using an computer operated electronic randomisation module, which is designed and maintained by the independent data management department of the UMC Utrecht. For randomisation, gender, date of birth, study number and site of inclusion of the patient need to be filled in on the website. Minimisation is applied to ensure balance between groups in treating hospital and cancer type. Due to the nature of the intervention, patients and healthcare providers are not blinded.

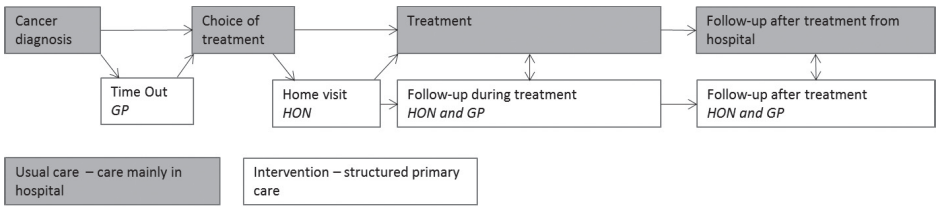

Figure 1. GRIP intervention in addition to usual cancer care.
Abbreviations: GP; General Practitioner, HON; Homecare Oncology Nurse.

Intervention

Patients in the intervention group are offered additional structured follow-up guidance from primary care, next to the usual secondary care, consisting of two components (Figure 1):

1) A "Time Out consultation" with the GP between the moment of diagnosis and the final decision on treatment in secondary care.
2) Follow-up care from primary care, delivered by a home care oncology nurse (HON) in cooperation with the GP during and after active treatment. Active treatment includes surgery, chemo- and radiotherapy.

All components of the intervention are developed in close cooperation with the Dutch patient organisation 'NFK (Dutch Federation of Cancer Patient Associations)' and the participating GP and home care organisations using existing healthcare services provided by regional organisations. Healthcare partners from the regional care network were chosen as preferred providers.

1) Time Out consultation

After informed consent and before the final treatment decision are made in the hospital, the patient will be invited for an appointment with his/her GP for a 'Time Out consultation' of 20 minutes. In preparation, the GP of a patient randomised to the intervention group is contacted by the researcher to be informed about the intervention procedure. The researcher shortly explains the content of the "Time Out consultation" to the GP, including the topics of

discussion with the patient as described below and an instruction to consult the HON after the Time Out consultation. In addition, the GP will be explained to not follow this structure when consulting cancer patients randomised to the control arm of the GRIP study in order to reduce contamination.

The Time Out consultation aims to facilitate continuity of primary care, to support the patient in a time of uncertainty, and to explore personal perspectives and preferences of the patients which may affect treatment choice to support shared decision making in secondary care.

During this consultation the GP addresses a number of issues preparing for active participation of the patient: reflection on the diagnosis and prognosis, psychosocial consequences, awareness that a choice of treatment exists and the recommendation to use the 'three questions' model in the consultation with the specialist on treatment decision.[18] These three questions are: What are my options? What are the possible benefits and harms of those options? How likely are the benefits and harms of each option to occur in the patients' specific information?[18] Incorporating the three questions model in decision making has been demonstrated to improve the quality of information about therapeutic options and facilitate patient involvement.

2) Follow-up care during and after active treatment

After the Time Out consultation and the final treatment decision in secondary care, the Homecare Oncology Nurse (HON) will be contacted by the GP to schedule a visit at the patients' home. During this visit the HON explains his/her role and makes a personal support plan together with the patient. In this plan, the patient's situation is mapped on four domains: living conditions, physical, psychosocial and existential domain. If one of the domains requires active support, the HON discusses the required actions with the patient and with the GP.

The number, type and duration of contact moments with the HON is patient driven, with a minimum number of two contacts during the primary treatment phase, including the first home visit, and two contacts within 3 months after active treatment has ended. The content of contacts is based

on the Dutch Distress Thermometer, which contains several items of the four domains on which patients are asked to rank their level of distress.[19] Throughout the cancer continuum the HON will report the status of the patient and the required actions to the GP, and if necessary the GP will be actively involved in the care provision. Secondary care will be actively approached by the HON, if supportive care, e.g., consultation of a psychologist, physiotherapist or dietician, is started based on HON's consultations or when treatment-specific questions arise.

Intervention training

All the participating HONs are registered nurses with a specialised training in oncology and have more than 2 years of clinical experience. In addition, the GRIP study team provides a 4-hour training regarding supportive care, recognizing alarm-symptoms and the details of the GRIP intervention in order to be able to comply optimally with the intervention procedures. This includes close collaboration with the GP, the minimal content and frequency of consultations and the registrations required for the GRIP study. Expectations of all actors are displayed in table 1.

Participating GPs receive basic information on the GRIP study by their GP cooperatives organisations at the start of the study. The GPs of patients who are randomised to the intervention group are notified by phone after the patient provides informed consent for participation. During this telephone contact, the researcher provides the necessary instruction to perform a Time Out consultation. In addition, information is given by e-mail and through a website which describes the steps GPs are expected to take. This website also provides the information required for optimal guidance from primary care and collaboration with HON and secondary care providers.

Table 1. Expected actions for all actors to enable involvement of a primary care team after diagnosis.

Patient	General Practitioner	HON
Between cancer diagnosis and treatment		
- Make appointment with GP for Time Out	- Prepare Time Out consultation	- Contacted by GP
	- Execute Time Out - Contact HON for follow up during treatment	
During and after treatment		
- Contacted and visited by HON	- Informed on progress by HON	- Plans and performs patient contacts (proposed minimum two during and two after treatment.)
- Contact with GP if required	- Patient guidance if required	- Informs GP
		- If required consults GP/ secondary care

Abreviations: GP; General practitioner, HON; Home care oncology nurse.

Control group

Patients in the control group receive care as usual during the cancer journey. Hence for this group of participants, follow up guidance after diagnosis takes place in secondary care and guidance from primary care is not structured. Details of usual care depend on disease, patients- and caretaker characteristics, patients' preferences and varying hospital protocols. In general, the phases of usual care can be described as: diagnosis, choice of treatment, delivery of treatment and follow-up care in hospital. Treatment options are discussed in a multidisciplinary team and generally follow national guidelines. Cancer care in the hospital is commonly delivered by a team consisting of a nurse (specialist) and a medical doctor specialised in oncology. In general, the GP is informed about the diagnosis by phone or by mail through Electronic Data Interchange after the multidisciplinary team reached consensus on the treatment.

Outcomes

The primary outcomes are patient satisfaction with care and healthcare utilisation. Secondary outcomes are health related quality of life, employment, patient empowerment (self-efficacy), shared decision making, mental health and satisfaction with information.

Primary outcome

To determine the primary outcome parameters the following validated questionnaires will be used: European Organisation for Research and Treatment of Cancer Satisfaction with care questionnaire (EORTC-IN-PATSAT32),[20] a Numeric Rating Scale (NRS) and the Medical Cost Questionnaire of the institute for Medical Technology Assessment (iMTA MCQ)[21]. EORTC-IN-PATSAT32 consists of 32 questions and measures patients' appraisal of hospital doctors and nurses, as well as aspects of care organisation and services.[20] The questionnaire will be adjusted to specify the satisfaction on specialists, GP and nurses. The NRS has a scale from 0 to 10 with the following question "How satisfied are you with the received care?". Herein 0 implies "not satisfied at all" and a 10 implies that the patient "could not have been more satisfied" with the received care. The iMTA MCQ contains 31 questions and measures healthcare utilization (specific to the Dutch situation).[21] The questionnaire will be adjusted to differentiate between the use of supportive care in primary or secondary care settings. Furthermore, questions evaluating medication use will be removed and questions evaluating the use of online websites and tools will be added. In addition, patients' health records will be used to assess healthcare consumption.

Secondary outcomes

The secondary outcomes are measured by eight questionnaires. Health related Quality of Life is assessed by the European Organisation Research and Treatment of Cancer-Quality of Life-C30 questionnaire (EORTC-QoL-C30), which incorporates functional scales (physical, role, emotional, cognitive and social functioning), one quality of life scale and symptom scales (including fatigue and pain).[22]

Employment is measured by the Productivity Cost Questionnaire of the institute for Medical Technology Assessment (iMTA PCQ), which contains 12 items.[23] Patient Empowerment will be measured based on two elements of empowerment, i.e. self-efficacy and Mastery. Self-efficacy is measured with the General Self-Efficacy Scale (GSE), a questionnaire with 10-hypothesises to assess optimistic self-beliefs to cope with a variety of difficult demands in life.[24] Mastery level will be measured with the Pearlin Mastery Scale, a 7-items questionnaire designed to measure self-concept and references the extent to which individuals perceive themselves in control of forces that significantly impact their lives. Shared Decision Making will be measured using two questionnaires.[25] The Shared Decision Making Questionnaire (SDM-Q-9) contains 9 items and assesses the effectiveness of interventions aimed at the implementation of SDM.[26] We added a question in order to evaluate the roll of the GP within this process, and the Perceived Efficacy in Patient-Physician Interactions (PEPPI), which contains 10 items.[27] Mental health is assessed by the RAND Mental Health Inventory (MHI-5), which contains 5 items and measures mental health.[28] Finally, satisfaction with information will be measured by the European Organisation for Research and Treatment of Cancer Assessment Satisfaction with information (EORTC-info 26), a 27-items cancer specific questionnaire which evaluates the information received by cancer patients.[29] In addition to the iMTA MCQ, several questions are added for the qualitative evaluation of online tools.

Data collection

Data will be collected at baseline (T0), after two weeks (T1) and every three months (T2, T3, T4), up to 12 months after the diagnosis (T5) (Figure 2). If primary treatment is already completed before T3 (e.g. for patients with a melanoma who only undergo surgery), patients receive the questionnaires from T3 directly and after 3 months the questionnaires of T5. The remaining questionnaires will be omitted. Questionnaires will be sent by email to the participant. When the participant does not fill in the questionnaires within one week, the electronic systems sends the participants one reminder. If this does not lead to completing the missing questionnaire, the researcher contacts the participant by phone for a final request to complete the questionnaire.

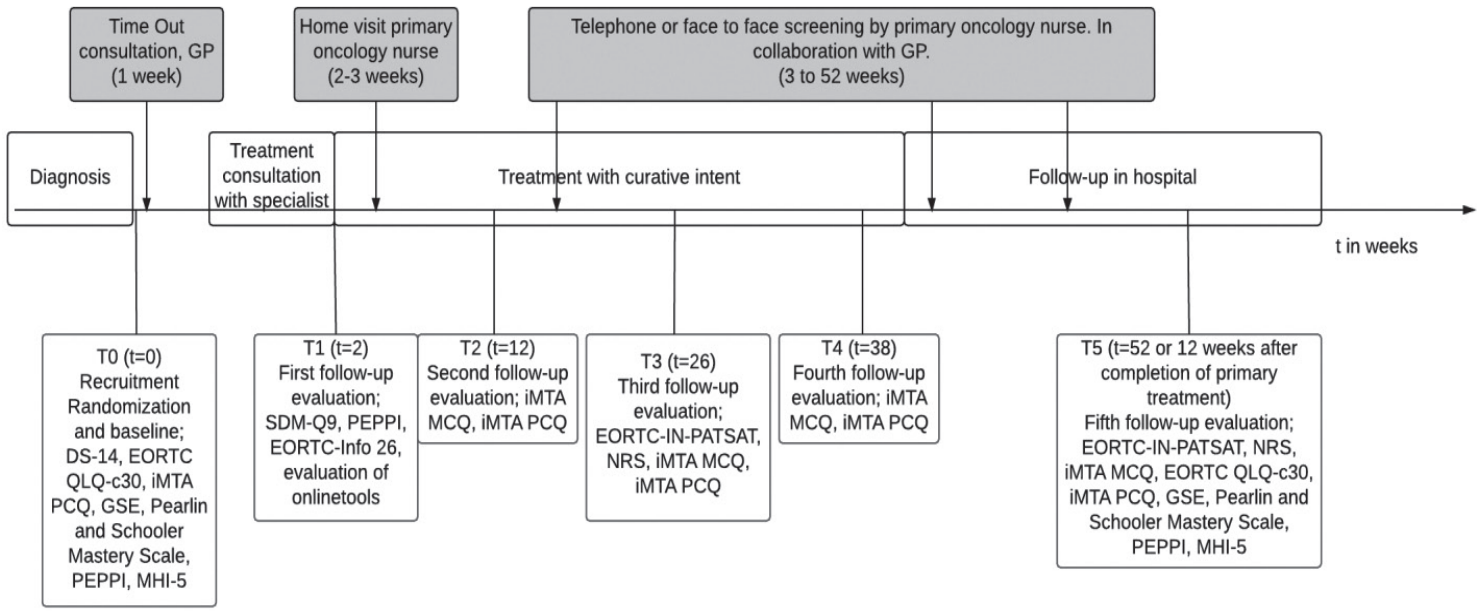

Figure 2. Questionnaire timeline in the cancer care pathway.
Abbreviations: GP; General Practitioner, EORTC QLQ-c30; European Organisation for Research and Treatment of Cancer Quality of life Questionnaire, GSE; General Self-Efficacy Scale, MHI-5; Mental Health Inventory, PEPPI; Perceived Efficacy in Patient-Physician Interactions, SDM-Q9; Shared Decision Making Questionnaire, iMTA PCQ; Productivity Cost Questionnaire of the institute for Medical Technology Assessment, DS-14; Assessment of negative affectivity, social inhibition, and Type D personality, EORTC-info 26; European Organisation for Research and Treatment of Cancer Assessment Satisfaction with information, iMTA MCQ; Medical Cost Questionnaire of the institute for Medical Technology Assessment, EORTC-IN-PATSAT; Satisfaction with care questionnaire, NRS; Numeric Rating Scale.

Adherence

The researcher will register whether the Time Out consultation took place and the HON will register the number of contacts with the patient and the content of the contact moment by using a checklist. Participants can discontinue the study on request.

Statistical analyses

All analysis will be performed following the intention-to-treat principle. Baseline characteristics will be shown by calculating means or medians for continuous variables and frequencies or percentages for categorical variables. Characteristics of patients who complete the study and patients who drop out, will be compared using T-tests for continuous variables and Pearson's Chi-square analyses for categorical variables.

Linear regression analyses will be used for continuous variables adjusted for baseline variables (if measured at baseline) and treating hospital and cancer type. Mixed linear regression modelling adjusted for baseline variables as fixed factors (if measured at baseline) and stratification factors (treating hospital and cancer type) will be used to compare outcomes on repeated follow-up measurements T3 and T5. In these longitudinal analyses, the statistic model accounts for missing data based on the observed data.[30] Differential intervention effects due to sex (men/women), age (≤65/>65 year), personality of type D (defined as 'scoring high on negative affectivity and social inhibition'[31]) (yes/no), type of cancer (breast/lung/colorectal/gynaecologic/melanoma), co-morbidity (none/1-2/>3) and baseline levels of the outcomes of interest will be explored by adding interaction terms to the regression model.

Sample size

We assumed a medium effect size (0.5) to be a clinically relevant difference in patients' satisfaction between the two study groups. Using a power of 0.8 and an alpha less than 0.05, at least 64 patients per study group are required. Accounting for an estimated dropout of 15%, 75 participants in each group are needed.

Discussion

The aim of the GRIP study is to assess the effects of structured follow-up from primary care after the diagnosis of cancer on satisfaction and healthcare utilization of patients treated with curative intent. To optimise personalised cancer care for a growing patient population and for effective implementation of structured follow-up from primary care, policymakers and professionals need more information on the effects of structured and continuous primary care involvement in the cancer continuum. The GRIP study will provide evidence on the effects on patient satisfaction and healthcare utilization and secondary outcomes. In this pragmatic study, patients with multiple cancer types will be included aiming at high generalizability of the results. It will be explored whether there are subgroups of patients for whom this structured primary care works best.

In this protocol some choices were made, that need clarification. First, we chose to assess the addition of structured follow-up from primary care by a GP and HON to care as usual instead of substitution of the supportive care provided in hospitals. This choice was made because we believe it is not feasible nor desirable to completely replace supportive care provided from secondary care by that from the primary care team. In addition, we aim to test the assumption that additional care from primary care will lead to a shift of the utilised care from the secondary to the primary care setting.

Second, patient satisfaction and healthcare utilisation are chosen as primary outcomes, since these factors are considered most relevant from the perspective of patient and society. Third, for the secondary outcome 'patient empowerment', so far, no uniform definition and no unique measurement tools exist. Therefore, we chose to use two validated questionnaires (GSE and Pearlin Mastery Scale) to estimate the effect of our intervention on patient empowerment. Although in previous intervention studies during cancer treatment comparable numbers of questionnaires were acceptable, the use of several questionnaires might induce loss to follow-up.

Last, we had to choose between random assignment at the patient or the caregiver level. We chose to randomise on patient level, using type of cancer

and hospital for weighed randomisation, to ensure optimal comparison of study arms. To minimize the chance of contamination, GPs are only personally informed about the study details after one of their patients is randomised to the intervention. Given the low incidence of cancer in general practice (about 3 new patients meeting our inclusion criteria annually in an average general practice), we accepted the low chance of contamination resulting from the situation were one GP will first have a patient who is randomised to the intervention arm, followed by a patient randomised to the control arm.

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CHAPTER 5

Effects of a Time Out Consultation with the GP on cancer treatment decision making; a randomised controlled trial.

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Submitted

Abstract

Objective

Improving shared decision making (SDM) enables more tailored cancer treatment decisions. We evaluated a Time Out Consultation (TOC) with the general practitioner (GP), between cancer diagnosis and treatment decision, which aims at supporting SDM and improving continuity of primary care. This study aims to evaluate the effects of a TOC.

Design

A randomised controlled trial.

Participants

Newly diagnosed patients with curable cancer (breast, lung, colorectal, gynaecologic, melanoma) from four Dutch hospitals.

Intervention

A TOC with the GP between cancer diagnosis and treatment decision.

Outcomes

Primary outcome is perceived SDM and secondary outcomes are information provision and self-efficacy.

Results

Of the 154 randomised patients (control n=77, intervention n=77), 75% were female. The mean age was 61 (SD±11.9) years. In the intervention group 80.5% (n=62) had a TOC, of which 82.3% (n=51) took place after treatment decision. Perceived SDM was lower in the intervention group (-8.9 (95% CI, 0.6-17.1)). Among those with a TOC before treatment decision (n=11), perceived SDM was comparable to the control group (66.5±27.2 vs 67.9±26.1).

Conclusion

Even though patients are motivated to have a TOC, implementing a TOC between diagnosis and treatment decision is challenging. Effects of a timely TOC could not be established. Non-timely TOC decreased perceived SDM. Planning of the TOC should be optimised, and future research should establish if an adequately timed TOC results in improved SDM in cancer patients.

Article summary

Strengths of this study:

- The present study contributes evidence from a pragmatic randomised controlled trial to the scarce knowledge on SDM interventions for curative cancer treatment involving the GP.
- Protocol adherence and contamination could be assessed since the researchers had full access to the free text and coded routine care data from the Electronic Medical Record of each general practitioner practice.

Limitations of this study:

- Patients and healthcare providers could not be blinded due to the nature of the intervention.
- The intervention is developed in close collaboration with the Dutch federation of cancer patient organisations and the participating general practitioners, but hospital care professionals had less input in the development of the intervention, which may have opposed effectiveness and hampered implementation.

Background

Cancer is the second leading cause of death globally. In 2018, over 17 million people worldwide were diagnosed with cancer, a number that is expected to reach 21 million patients by the year 2030.[1] As cancer mainly affects the elderly, the increase is to a large extent caused by aging.

Cancer treatment should be personalised. This means that, besides tailoring treatment choice to tumour characteristics, for every patient the treatment option should be chosen which best fits a patient's preferences and circumstances. This is increasingly complex because of several reasons. First, the spectrum of treatment modalities for cancer expanded in recent years. Second, 70% of cancer patients has at least one co-morbidity, which may interfere with cancer treatment.[2, 3] Furthermore, treatment decisions become more complex at higher age, due to co-morbidities, declining life expectancy and changing life perspectives and priorities. Consequently, personalised treatment decisions require a balanced decision-making process between patients and healthcare professionals, with thorough weighing of curative treatment options in the light of patient preferences and personal context.

Although many general practitioners (GPs) do participate in follow-up care after completion of cancer treatment, structural guidance and care by the GP starting from the moment of diagnosis onwards is uncommon.[4, 5] In view of their position this seems to be a missed opportunity. GPs are well equipped to support the patient during their cancer care pathway: they usually have a longstanding and personal relationship with their patients and work with an integral and personalised approach, including psychosocial support. In that regard, of all care-givers involved, GPs are probably best positioned to balance treatment options in the perspective of the patient's medical history and personal preferences.[6, 7] It is therefore that professional and patient organisations advocate a structured and expanded role for the GP in the cancer care pathway, starting from the moment cancer is diagnosed.[6]

Personalised cancer care requires active involvement of the patient in treatment decision by shared decision making (SDM). For successful SDM in complex decisions several steps are required; i.e., creating awareness of

choice, explanation of the treatment options, consideration of the treatment options provided and making an informed choice.[8] Research suggests that SDM improves knowledge and understanding of treatment options,[9–11] creates more realistic expectations[9] and better matches patient's preferences and subsequent treatment decisions.[9] Moreover, patients feel better informed,[12] are more determined on their personal values[12] and experience better communication with their practitioner.[9–11] Adequate SDM might also improve medication adherence,[11] mental health-related quality of life[13] and reduce healthcare costs[14]. Several large studies have demonstrated that patients want to be involved in decision making.[15–17] Additionally, a recent survey in the Netherlands among 4 700 patients treated for cancer showed that the majority of patients prefer their GP to be involved, as the GP can help to create awareness of choice and can prepare the patient for the treatment decision in hospital.[18]

So far, the effectiveness of GP involvement in SDM for cancer treatment decisions has not been evaluated. In the randomized controlled GRIP trial, we evaluate the effects of providing structural follow-up care from primary care during cancer treatment. This follow-up care starts with a Time Out Consultation (TOC) between patient and GP immediately after cancer diagnosis. Here we report the effects of a TOC after a cancer diagnosis for patients treated with curative intent, on patient-perceived SDM, information provision and perceived self-efficacy.

Methods

Design

The GRIP trial is a multicentre randomised controlled trial following the patient from cancer diagnosis until three months after completion of primary treatment with a maximum of one year follow-up. The study was conducted in four Dutch hospitals between April 2015 and May 2017 in the region of Utrecht, the Netherlands. In addition to the usual hospital care, patients randomized to the GRIP intervention group were offered structured follow-up guidance from primary care consisting of two components: (1) a time out consultation (TOC) with the GP and (2) structured follow-up during cancer treatment by a primary care oncology nurse and the GP. For full exploration and understanding of the effects of the first component (TOC), we report these effects in this paper separately. As follow-up care was delivered after and independently from the Time Out Consultation, we expect no interference.

The GRIP study protocol was published previously.[19] The study protocol was assessed by the Medical Ethical Committee of the University Medical Centre Utrecht and was considered non-eligible for full ethical review according to Dutch law (METC number 15-075/C).

Patient and Public involvement

The Dutch Federation of cancer patient organizations (NFK) was part of the GRIP project group. NFK contributed to the definition of research priorities and participated in the intervention and study design, including the choice of outcome measures (SDM). NFK also contributed to the writing of the manuscript.

Study population and setting

Patients were eligible for participation if they were aged 18 or older, newly diagnosed with either breast cancer, colorectal cancer, gynaecological cancer, lung cancer or melanoma, and scheduled for curative treatment. Patients were excluded in case of major psychiatric diseases, personality disorders,

inability to fill in questionnaires, if the patient's GP worked outside the study area or did not agree to participate or if the patient already started cancer treatment.

Recruitment and randomisation

After diagnosis, eligible patients were approached for participation by their treating physician or oncology nurse in the treating hospital. If patients consented, they were contacted by the researchers by phone the (working) day after diagnosis to verify eligibility and provide further study information. Upon confirmation of willingness to participate, patients were randomised. Equally allocated (1:1) randomisation was performed by using an online computerized randomization module provided by an independent data centre of the UMC Utrecht. Minimisation was applied to ensure balance between groups regarding treating hospital and cancer type. Due to the nature of the intervention, patients and healthcare providers could not be blinded for the intervention. All participants gave verbal and written consent for participation.

Usual care

All patients received cancer care as usual in the hospital, which is to a great extent protocolised. Protocols for curative treatment vary according to cancer type and patient and disease characteristics. In general, additional investigations are required such as determination of laboratory values and imaging, and multidisciplinary team discussions on treatment options. In one or more consultations with the medical specialist, the diagnosis is explained to the patient, information about cancer and treatment options is given and the final treatment decision is made.

Involvement of the GP following primary cancer diagnosis varies between hospitals, specialists and GPs. In general, the GP is informed about the diagnosis by phone or by mail through Electronic Data Interchange after the multidisciplinary team reaches consensus on the diagnosis and treatment. Thereafter, contact between the GP and the patient depends on the individual initiative of either the GP or the patient.

Intervention: the Time Out Consultation

In addition to usual care, patients in the intervention group were asked to schedule a TOC with their GP immediately after randomisation to prepare for the final treatment decision. The TOC was a 20-minute consultation with the GP. The aim of the TOC was to improve the SDM process and improve continuity of primary care. For the TOC, the GP was instructed to give psychosocial guidance, including discussing impact of diagnosis and consequences. Furthermore, the GP was instructed to check patient's understanding of information, create awareness that a choice of treatment exists and stimulate the use of the 'three questions' model during the specialist consultation on the final treatment decision. The three questions model is used to support patient involvement and information exchange when discussing therapeutic options.[20] The three questions are: What are my options? What are the possible benefits and harms of those options? How likely are the benefits and harms of each option to occur for me?[20]

The GPs of patients who were randomised to the intervention group were notified by phone by the researcher after the patient consented to participate. During this telephone contact, the researcher provided the necessary instructions to perform a TOC. In addition, information on the steps GPs were expected to take was provided by email and through a website.

Outcomes

To report the primary outcome (perceived level of SDM) and secondary outcomes (received information and perceived self-efficacy) patients filled in three validated questionnaires two weeks after inclusion (T1) online or, if preferred, on paper. Only perceived self-efficacy was measured at both baseline (T0) and T1. Non-responders were sent two automatic reminders by email after two and five days, and were contacted by phone by the researcher if non-response maintained.

Primary outcome

The perceived level of SDM was measured using the Shared Decision-Making Questionnaire (SDM-Q-9), which contains nine items with a six-point Likert

scale and focuses on the decision process in hospital.[21] A score was calculated, which ranged from 0-100. A higher score indicated higher perceived SDM. During the trial, we added a statement to specify the role of the GP in this process "My GP helped me make my choice of treatment", which was analysed separately.

Secondary outcomes

Received information was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Group information questionnaire (EORTC-info 26), a 27-item cancer specific questionnaire with a four-point Likert scale.[22] This questionnaire assessed the amount of information received on multiple cancer-related themes (diagnosis, medical tests, treatments, other services, places of care and self-help) and the satisfaction and usefulness of received information. With the items a score was calculated, which ranged from 0-100. A higher score indicates a better perceived information provision.

Self-efficacy is defined as "the individual's capacity to produce desired effects".[23] Perceived self-efficacy was measured using the Perceived self-Efficacy in Patient-Physician Interactions (PEPPI-5) questionnaire, which contains 10 items with a five-point Likert scale.[24] With these items a score was calculated which ranged from 5-25. A higher score indicates higher perceived self-efficacy.

Intervention adherence

Adherence to the protocol for the content and planning of the TOC was assessed using the free text in the Electronic Medical Record (EMR) data of GP contacts in the intervention group. EMR data are registered for each GP consultation as part of usual care. Performance of the content of the TOC according to protocol was confirmed if the free text noted referred to components of the TOC intervention. Timing of the TOC according to protocol was defined as a TOC between diagnosis and treatment decision. Dates from the primary care and hospital EMR were used. Consultations in the control

arm were evaluated for contamination. All GP consultations within two weeks were registered in both groups.

Data collection

Patient characteristics were collected online directly after inclusion (baseline). Data extraction at baseline, including the number of GP contacts (year prior to inclusion), was performed in the free text and coded routine care data from the EMR of each GP practice. GP characteristics at T0 and rurality were collected from public Dutch online databases for GP experience.[25, 26]

Comorbidities, date of diagnosis, cancer stage and treatment decision were extracted from the EMR in hospitals. The moment of treatment decision was defined as the moment the patient agreed with or chose the treatment.

Sample size

The sample size was based on the primary outcomes of the GRIP study, i.e., satisfaction with care at three months after the end of therapy (excl. hormone therapy), with a maximum of one year. We assumed a medium effect size (0.5) to be a relevant difference between the two study groups. Using a power of 0.8 and an alpha less than 0.05, at least 64 patients per study group were required. Accounting for an estimated dropout of 15%, 75 participants in each group were needed.[19]

Statistical analysis

The study population was described descriptively. Intervention effects compared to usual care were analysed following the intention-to-treat principle. Additionally, outcomes were described stratified for patients with a TOC before treatment decision (conform protocol), a TOC after treatment decision, and no TOC.

Paired sample T-test was used to calculate mean changes and 95% confidence intervals of self-efficacy from baseline to T1 within groups. ANOVA was used to calculate between-group differences (i.e., intervention versus control

group) at T1, adjusted for stratification factors (i.e., hospital and cancer type) and baseline measurements if present. Additional adjustment for comorbidity was done because of potentially relevant group differences at baseline.

All analyses were performed with IBM SPSS 25.0.0.2 and statistical significance was set at $p < 0.05$.

Results

Study population

In total 396 patients were approached for participation in the treating hospital (Figure 1). Sixty-five patients could not be included; 60 because they did not meet inclusion criteria and five because they could not be contacted. Of those invited to participate, 177 patients declined, with main reasons: "too much of a burden shortly after diagnosis" and "no extra guidance needed". Finally, 154 patients were randomised to either the intervention (n=77) or the usual care control group (n=77) (Table 1). The 154 patients were registered with 119 different GP's, from 79 different GP centres.

Patients in the intervention and control group were comparable with respect to baseline characteristics, except for the proportion of patients with co-morbidities, which was higher in the intervention group (67.5%) as compared to the control group (49.4%) (Table 1). The majority of patients had either breast (51%) or colorectal (25%) cancer. Most patients (75%) were female, and the mean age was 61 (SD ±11.9) years.

Most GPs of the study population worked in an urban setting (62%) and had a median work experience of 16 years (IQR 11-25.25).

Implementation of Time Out consultation

In the intervention group 80.5% (n=62) of the patients had a TOC (a GP consultation that included the elements of the TOC). However, only 17.7% (n=11) had the TOC scheduled according to protocol, i.e., between diagnosis and final treatment decision.

The median time from diagnosis to TOC was 7 days (IQR 6-12) for the 11 patients that had the TOC scheduled according to protocol and 16 days (IQR 11-23) if the TOC was planned after the treatment decision. The median time from diagnosis to treatment decision was 13 days (IQR 8-14) for those with a TOC before treatment decision, 5 days (IQR 1.0-7.0) for those with a TOC after the treatment decision and 5 days (IQR 0.5-9.8) for patients without a TOC. In the intervention group, 22% (n=17) of the patients received the diagnosis and treatment decision on the same day, and 51% (n=39) within 7 days.

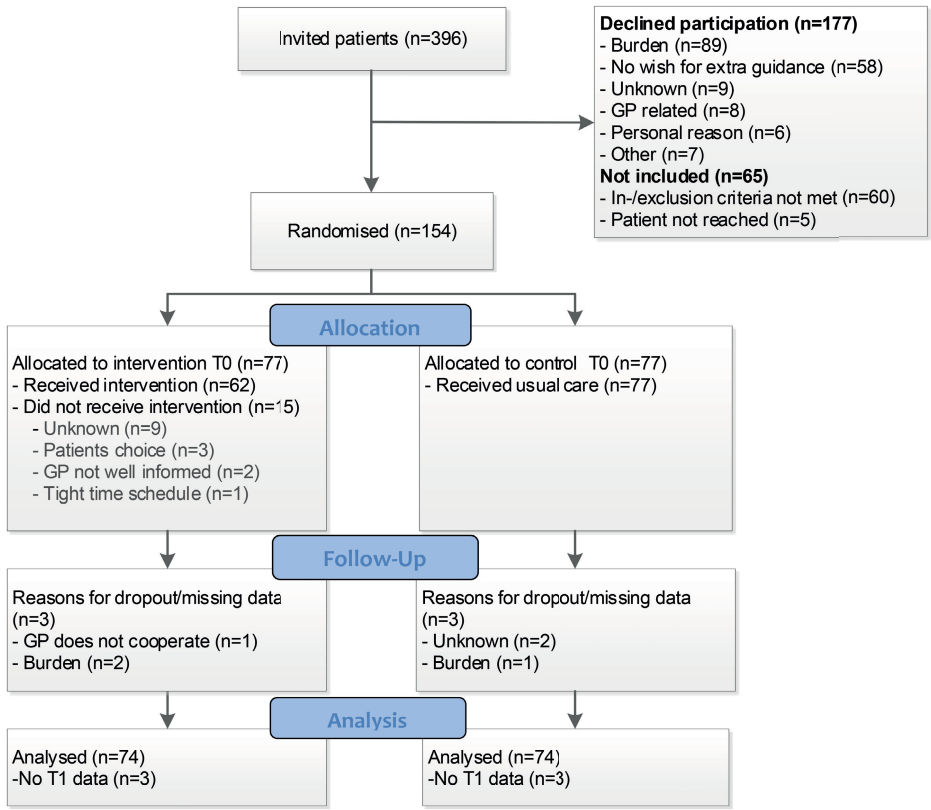

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the GRIP study after two weeks (T1).

GP consultations (including non-TOC) within two weeks after diagnosis took place for 53.2% (n=41) of the patients in the intervention group and 33.8% (n=26) of the control group. Potential contamination (i.e., a GP seeing an intervention patient first, followed by a patient from the control arm) occurred in two patients in the control arm.

Table 1. Baseline characteristics of the study participants, intervention patients divided into groups based on TOC timing.

	Intervention (N = 77)	TOC before treatment decision (N=11)	TOC after treatment decision (N=51)	No TOC (N=12)[1]	**Control (N = 77)**
Female N (%)	57 (74.0)	8 (72.7)	37 (72.5)	10 (83.3)	58 (75.3)
Age mean (±SD)	61.8 (11.4)	62.4 (8.7)	61.4 (11.0)	61.3 (15.6)	59.3 (12.2)
Cancer type N (%)					
Breast	38 (49.4)	6 (54.5)	24 (47.1)	8 (66.7)	40 (51.9)
Colorectal	20 (26.0)	4 (36.4)	14 (27.5)	2 (16.7)	18 (23.4)
Melanoma	13 (16.9)	-	9 (17.6)	2 (16.7)	11 (14.3)
Lung	3 (3.9)	-	3 (5.9)	-	2 (2.6)
Gynaecologic	3 (3.9)	1 (9.1)	1 (2.0)	-	6 (7.8)
Hospital setting N (%)					
Academic	22 (28.6)	6 (54.5)	13 (25.5)	2 (16.7)	24 (31.2)
Non academic	55 (71.4)	5 (45.5)	38 (74.5)	10 (83.3)	53 (68.8)
Cancer stage[2] N (%)					
0	2 (2.6)	-	2 (3.9)	-	2 (2.6)
I	34 (44.2)	4 (36.4)	21 (41.2)	7 (58.3)	34 (44.2)
II	22 (28.6)	2 (18.2)	15 (29.4)	4 (33.3)	27 (35.1)
III	18 (23.4)	5 (45.5)	12 (23.5)	1 (8.3)	14 (18.2)
IV	1 (1.3)	-	1 (2.0)	-	-
Education					
Low	32 (41.6)	5 (45.5)	20 (39.2)	5 (41.7)	25 (32.5)
Middle	13 (16.9)	1 (9.1)	10 (19.6)	2 (16.7)	18 (23.4)
High	32 (41.6)	5 (45.5)	21 (41.2)	5 (41.7)	34 (44.2)
Number of comorbidities (N %)					
None	25 (32.5)	5 (45.5)	15 (29.4)	5 (41.7)	39 (50.6)
≥1	52 (67.5)	6 (54.5)	36 (70.6)	7 (58.3)	38 (49.4)

Table 1. Continued.

	Intervention (N = 77)	TOC before treatment decision (N=11)	TOC after treatment decision (N=51)	No TOC (N=12)[1]	**Control (N = 77)**
Number of GP contacts (year prior inclusion) median (Q1-Q3)	7 (4.0-10.0)	7 (3.0-10.0)	6 (3.0-9.0)	8 (6.0-12.3)	6 (3.5-11.0)
Perceived self-efficacy (PEPPI-5) mean (±SD)	21.0 (±3.3)	21.3 (±2.4)	21.2(±3.0)	21.5 (±3.8)	21.5 (±3.0)
GP years of working experience median (Q1-Q3)	17 (12.0-25.5)	26 (10.0-34.0)	16 (12.0-22.0)	20 (12.3-27.5)	16 (10.5-24.5)
GP setting N (%)					
Urban[3]	51 (66.2)	7 (63.6)	36 (70.6)	6 (50)	45 (58.4)
Between rural - Urban[4]	14 (18.2)	1 (9.1)	9 (17.6)	3 (25)	15 (19.5)
Rural[5]	12 (15.6)	3 (27.3)	6 (11.8)	3 (25)	17 (22.1)

Abbreviations: SD; Standard deviation, Q1; Inter quartile range at 25%, Q3; Inter quartile rage at 75%. [1] Excluding lost to follow up n=3, [2] stage based on clinical TNM classifications, [3]1000 or more addresses per km^2, [4]1000-1500 addresses per km^2, [5]1000 or less addresses per km^2.

Perceived Shared Decision Making

Perceived SDM was significantly lower in the intervention group compared to usual care (between-group difference: 8.9 [95% CI, 0.6-17.1]) (Table 2). Additional adjustment for comorbidity yielded a comparable non-significant between-group difference (8.4 [95% CI, -0.0-16.8]). For the 11 intervention patients with a TOC planned according to protocol, perceived SDM was comparable to the control group 66.5 (±27.2) versus 67.9 (±26.1) respectively.

Received information

Levels of perceived information provision in the two study arms did not differ for all topics: "Disease", "Medical tests", "Treatment", "Other services", "Places of care", "Self-help", "Satisfaction with the amount of information", and "Helpfulness of information" (Table 2).

Self-efficacy

Self-efficacy in the intervention group improved significantly from baseline to T1, with a mean difference of 1.1 (95% CI, 0.4-1.8). For the control group this within mean difference was 0.5 (95% CI, -0.1-1.2). No significant between-group difference was found: 0.4 (95% CI, -0.4-1.1) (Table 2).

Table 2. Results of perceived shared decision making, provided information assessment and self-efficacy.

	Intervention (N=74)	TOC before treatment decision (N=11)	TOC after treatment decision (N=51)	No TOC (N=12)	**Control (N=74)**	**Estimated mean difference between study groups (95%CI)**
Perceived shared decision making						
T1 mean score (±SD)	59.2 (±27.9)	66.5 (±27.2)	55.7 (±28.7)	67.2 (±23.8)	67.9 (±26.1)	-8.9 (-17.1;-0.6) -8.4[1] (-16.8;0.0)
GP involved in treatment decision*	N=40	N=6	N=27	N=7	N=44	
T1 percentage agreement						
completely disagree	70.0%	50.0%	66.7%	100%	68.2%	
strongly disagree	12.5%	0.0%	18.5%	0.0%	6.8%	
somewhat disagree	0.0%	0.0%	0.0%	0.0%	4.5%	
somewhat agree	2.5%	0.0%	3.7%	0.0%	6.8%	
strongly agree	7.5%	16.7%	7.4%	0.0%	6.8%	
completely agree	7.5%	33.3%	3.7%	0.0%	6.8%	
Information assessment of patients						
T1 mean score (±SD)						
Disease	58.1 (±22.6)	57.6 (±24.3)	56.4 (±21.9)	66.0 (±24.2)	59.9 (±21.7)	-1.4 (-8.7;5.9)
Medical tests	73.4 (±24.0)	82.8 (±21.3)	71.7 (±24.7)	72.2 (±23.0)	75.5 (±22.2)	-2.2 (-9.8;5.5)
Treatments	41.9 (±21.0)	49.4 (±25.1)	38.1 (±17.7)	51.2 (±26.7)	45.1 (±20.5)	-3.1 (-9.9;3.7)
Other services	27.8 (±25.8)	26.5 (±20.7)	24.1 (±21.5)	44.4 (±39.5)	28.0 (±25.0)	-0.5 (-8.7;7.6)
Places of care	27.9 (±33.6)	18.2 (±22.9)	28.8 (±32.7)	33.3 (±44.9)	22.5 (±28.7)	4.2 (-6.0;14.5)
Self-help	40.1 (±35.7)	42.4 (±42.4)	38.6 (±32.9)	44.4 (±43.4)	43.7 (±32.6)	-4.3 (-15.5;6.9)
Satisfaction with information	75.2 (±23.4)	75.8 (±26.2)	74.5 (±23.7)	77.8 (±21.7)	75.2 (±23.4)	-0.5 (-8.2;7.2)
Helpfulness of information	79.3 (±21.9)	81.8 (±22.9)	77.8 (±22.8)	83.3 (±17.4)	76.6 (±21.9)	2.3 (-4.9;9.6)

Table 2. Continued.

	Intervention (N=74)	TOC before treatment decision (N=11)	TOC after treatment decision (N=51)	No TOC (N=12)	**Control (N=74)**	**Estimated mean difference between study groups (95%CI)**
Perceived Efficacy in patient-physician interactions						
T1 mean score (±SD)	22.3 (±2.4)	22.8 (±2.4)	22.1 (±2.5)	22.7 (±2.2)	22.1 (±2.9)	0.4[2](-0.4;1.1) 0.3[3] (-0.5;1.1)
Mean difference (±SD) T1-T0 within groups (95%CI)	1.1(0.4;1.8))	1.5 (-0.7;3.8)	1.0 (0.1;1.9)	1.2 (-1.0;3.4)	0.5 (-0.1;1.2)	

Abbreviations: TOC, Time Out Consult; T0, baseline measurement; T1, assessment after two week; CI, Confidence Interval; SD, standard deviation; * Question was added after the trial started; [1] added correction co-morbidities (None; ≥ 1 comorbidities); [2] added correction PEPPI at baseline; [3] added correction PEPPI at baseline and co-morbidities (None; ≥ 1 comorbidities).

Discussion

This study aimed to evaluate the effects of a TOC with a GP shortly after a cancer diagnosis for patients scheduled to be treated with curative intent, on perceived SDM, received information and perceived self-efficacy. Although the TOC was well accepted by patients (80.5% did make an appointment with the GP after diagnosis), only one fifth was adequately planned, i.e., before a treatment decision was made in the treating hospital. Therefore, we could not adequately evaluate if there is a benefit from the TOC on the SDM process. A GP consultation post treatment decision resulted in lower SDM.

It appeared to be challenging to plan a TOC preceding the treatment decision. This can be explained by the fact that current time interval between diagnosis and therapy decision is (too) short. For 22% of the patients, who were mainly patients with breast cancer or melanoma, the treatment decision was made on the day of the diagnosis. For half of all patients, a decision was made within seven days. The assumption that a short time to make a decision hampers TOC planning according to protocol is supported by the observation that the time between diagnosis to therapy decision was short (median 5 days) for those patients who had the TOC after treatment decision. Also, participating clinicians report that the current cancer care pathway is focused on rapid diagnostics[27] and early start of treatment. Delayed TOC planning in this study may also be partly related to the time required for patients to consider study participation. Finally, delayed TOC planning may also be related to the pragmatic design of our study: instead of the research team or the hospital scheduling the TOC for the patient, we decided to leave this responsibility to the patient, thus reflecting current daily care practice. In the short and stressful period between diagnosis and therapy choice, scheduling a TOC may not have been feasible for the majority of patients.

Our results show that perceived SDM was lower if a TOC was planned after treatment decision. The most likely explanation is that patients perceive SDM more negatively if they are informed and coached on the added value and possibility of SDM, after the possibility to actually apply SDM has already passed.

Compared to the literature, the number of patient-initiated GP contacts after diagnosis was high. In previous studies, which aimed to involve the GP in cancer care, the uptake of interventions was generally between 27% and 60%, as compared to more than 80% in our intervention group.[28–30] Even though we did not find a beneficial effect on the SDM process, the TOC may have an effect on the second aim of the TOC: continuity of primary care. On the short term, patients visited their GP more often in the intervention arm compared to the control arm. Results on continuity of primary care along the cancer care continuum will be published elsewhere.

This study has several strengths and limitations. The present study contributes evidence from a pragmatic, well powered randomised controlled trial to the scarce knowledge on SDM interventions for curative cancer treatment involving the GP. Another strength is the full access to the free text and coded routine care data from the EMR of each GP practice, therefore protocol adherence could be assessed. A limitation is that breast cancer patients are overrepresented, which might make the results less generalizable to the total cancer patient population.[31] Over-representation of breast cancer is often seen in cancer research,[32] probably due to the high incidence of breast cancer, and the fact that the breast cancer care path is usually highly structured, which facilitates recruitment. Also, our study focuses on cancer patients treated with curative intent and findings cannot be generalised to those treated with palliative intent, because the SDM process and the added value of the GP may well be different. This is supported by a recent non-controlled study, which suggested that patients and healthcare workers (GPs and treating physicians) experienced improvements in the SDM process after implementing a similar TOC, among palliatively treated cancer patients.[33] One reason for a potential difference in effect is that curatively treated patients might not always experience having a treatment choice.[34, 35] In addition, 66 (19.3%) of the eligible patients were not included in our study because they expressed "no wish for extra guidance" or "GP related" reasons. This selection resulted in a study population whose wish for additional contact with their GP may be relatively strong. Furthermore, patients and healthcare providers could not be blinded due to the nature of the intervention, which might have influenced the outcomes. Moreover, we were not able to assess which actor or actors delayed the planning of the TOC. In

addition, we cannot exclude that the GP provided contradicting information on the treatment decision. Last, during the development of the intervention, we involved the NFK and the participating general practitioners, but hospital care professionals had less input in the development of the intervention, which may have hampered implementation of the TOC.

The clinical implications of this study are not easy to define. Our study demonstrates that in the present cancer care continuum it is logistically difficult to adequately plan a TOC in primary care between diagnosis and treatment. This seems mainly due to the urgency to start treatment after a cancer diagnosis. Besides hampering TOC implementation, this perceived urgency may impede the potential to reflect on the optimal therapy choice by obstructing the deliberation process. This study also showed that the majority of patients was motivated to consult the GP in preparation for the final treatment decision with the specialist. Hence, to evaluate the effects of a TOC, the planning of the TOC needs to be optimised. To ensure that the TOC is effectively incorporated in the decision process, the hospital team should probably be involved in the TOC planning.

In conclusion, planning a TOC in primary care between diagnosis and treatment decision for cancer patients treated with curative intent was challenging due to the short time between diagnosis and treatment choice. Although patients' acceptance was high, the majority of TOCs in our study was planned after the treatment decision had already been made. Effects of a timely TOC could therefore not be established. Non-timely TOC decreased perceived SDM. Planning of the TOC should be optimised, and future research should explore if an adequately timed TOC results in improved SDM for cancer patients.

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CHAPTER 6

Structural involvement of the primary care team after a cancer diagnosis: the GRIP randomised controlled trial.

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Abstract

Purpose

The growing population of cancer patients treated with curative intent and the improved treatment possibilities call for more personalised and integrated cancer care. Primary care seems well positioned to support this. We assessed the effects of a primary care intervention, during and after curative cancer treatment, on patient satisfaction and healthcare utilisation.

Patients and methods

The GRIP study is a multicentre randomised controlled trial. Curatively treated cancer patients (breast, lung, colorectal, gynaecologic, melanoma) were included in four Dutch hospitals. All patients received usual care. In addition, patients randomised to the intervention group were offered follow-up guidance from primary care, which included two components: (1) a "Time Out consultation" (TOC) with the general practitioner (GP) after diagnosis and (2) subsequent structured follow-up during and after treatment by a home care oncology nurse (HON) in cooperation with the GP. Primary outcomes included patient satisfaction with care and healthcare utilisation. Secondary outcomes were quality of life, mental health, and patient self-efficacy. Data were collected using questionnaires at baseline (T0), after 2 weeks (T1), after 6 months or at completion of active treatment (T3) and 3 months after active treatment (T5). Healthcare utilisation was retrieved from routine care data registrations.

Results

We included 154 patients (control n=77, intervention n=77); who were mostly female (75%), mainly diagnosed with breast cancer (51%) or colorectal cancer (25%) and had a mean age of 61 (SD ±11.9) years. 81% of the intervention patients had a TOC and 68% had HON contact. Patient's overall satisfaction with care at T3 and T5 was high (a mean overall score of 8 out of 10) in both study groups. Three months after completion of active treatment (T5) GP satisfaction among patients who were in contact with their GP was significantly lower in the intervention group compared to the control group

on 3 out of 6 subscales, -14.2 (95% CI -27.0;-1.3) for GP quality, -15,9 (-29.1;-2.6) for GP availability and -15.2 (95% CI -29.1;-1.4) for information provision. Patients in the intervention group visited the GP practice and the emergency department more often compared to the control group (RR 1.3 (1.0;1.7) and RR 1.70 (1.0;2.8), respectively). Quality of life, mental health, and patient self-efficacy did not differ between groups.

Conclusion

In conclusion, the GRIP intervention, which aimed to involve the primary care team during and after cancer treatment, slightly increased the number of primary healthcare contacts. However, it did not improve patient satisfaction with care and it increased emergency department visits. As the high uptake of the intervention suggests that it addresses patients' needs, future research should focus on optimizing the design and implementation of the intervention.

Background

As cancer incidence is increasing[1] and prognosis is improving[2] more patients live longer with cancer and experience more late effects of treatment,[3] in the presence of co-existing chronic conditions.[4] Consequently, the nature of cancer treatment is shifting towards chronic disease management. This change requires more personalised and integrated care, based on individual preferences and medical profile.[5,6] In primary care based healthcare systems, general practitioners (GPs) may be best positioned to provide continuous, personalised and integrated care during the cancer care continuum.[4,5,7] GPs typically have a longstanding and personal relationship with their patients and are up to date with their patients' comorbidities. Additionally, they are well equipped to provide personalised disease management within the context of the patients' medical history and personal preferences.[7,8]

Traditionally, management of cancer is delivered by in-hospital specialists. Attempts to structurally involve primary care during cancer treatment have hardly been successful.[9] Even though patients increasingly want their GP to be involved in their cancer care,[10] the effects of more primary care involvement are unknown.

Aiming to involve primary care in cancer care on a more structural basis, we designed an intervention called 'GRIP', in close cooperation with medical professionals and patient organisations. The GRIP intervention consists of two steps: (1) a "Time Out consultation" (TOC) with the GP aimed to initiate primary care involvement during cancer treatment, and (2) structured follow-up during and after cancer treatment by a home care oncology nurse (HON) in cooperation with the GP.

Earlier we reported the effect of the TOC on perceived shared decision making (SDM) in cancer treatment.[11] We concluded that timely implementation of a TOC in the current cancer care pathway (i.e., between diagnosis and therapy choice) is challenging, mainly because of the tight time schedule between diagnosis and therapy decision. Here we report the effects of the full GRIP intervention in the year after cancer diagnosis on patient satisfaction, healthcare utilisation and patient related outcomes, for patients treated with curative intent.

Methods

Design

The GRIP study is a multicentre randomised controlled trial (RCT), of which the protocol paper has been published previously.[12]

The Medical Ethical Committee of the University Medical Centre Utrecht considered the study protocol non-eligible for full ethical review according to Dutch law.

Study population and setting

Patients were recruited in four hospitals in the centre of the Netherlands, between April 2015 and May 2017. Patients were considered eligible if aged 18 or older, newly diagnosed with either breast cancer, colorectal cancer, gynaecological cancer, lung cancer or melanoma, and scheduled for treatment with curative intent.

Patients were excluded if they were unable to fill in questionnaires, if they had a major psychiatric disease or personality disorder, if they already started cancer treatment or if the patient's GP worked outside the study area or did not agree to participate.

Recruitment and randomization

After being diagnosed, patients were recruited by the treating specialist or oncology nurse. After consent, the researcher contacted the patient by phone the following (working) day to evaluate eligibility and to provide detailed study information. After signing the informed consent form, patients were randomised 1:1 to the usual care or intervention group. Randomisation was performed using an online computerised randomisation module provided by an independent data centre of the UMC Utrecht. Minimisation was applied to ensure balance between the two groups regarding treating hospital and cancer type. Blinding was not possible due to the nature of the intervention.

Usual care

Usual care after a cancer diagnosis takes place in the hospital. It is to a great extent protocolised and differs depending on cancer type, hospital protocol, patient and caretaker characteristics and patients' preferences. Hospital based cancer care consists of different phases: diagnostic workup, choice of treatment, delivery of treatment and follow-up care. Treatment options are discussed in a multidisciplinary team and in general follow national guidelines. Cancer care in the hospital is usually delivered by medical doctors specialised in oncology and oncology nurses.

Primary care is not involved in cancer treatment on a structural basis. The GP receives information by phone or by mail after the multidisciplinary team in the hospital reached consensus on the treatment. Hereafter, some GPs may contact the patient proactively, but in most cases they take a more reactive role and participate during cancer treatment on patient's request. Supporting primary care services (e.g., psychologist, physiotherapist, dietician, social worker) are only involved if considered necessary. HONs are only incidentally involved during curative cancer treatment.

Intervention

In addition to usual care, patients in the intervention group were offered structured guidance from primary care, which consisted of two components.

Time Out Consultation (TOC)

Intervention patients were advised to make a TOC appointment with their GP. The TOC is a 20-minute consultation before the final treatment decision in the hospital. The TOC aims to initiate primary care involvement after diagnosis and prepare patients for SDM in the hospital. For this consultation, the GP was instructed to give psychosocial guidance, create awareness that a choice of treatment exists and to instruct the patient to use the three questions model (Shepherd et al. 2011) during the final discussion on the treatment options in the hospital.[13] These three questions are: What are my options? What are the possible benefits and harms of those options? How likely are

these benefits and harms to occur in my personal situation? Incorporating the three questions model in decision making has been demonstrated to improve the quality of information about therapeutic options and to stimulate patients' involvement in the treatment decision.[13]

Follow-up care from primary care

During the TOC, joint guidance by the GP and a HON was offered to the patient. If a patient accepted HON guidance, the HON was notified and contacted the patient to plan a visit at the patient's home. During this visit, the HON explained his/her role and made a personal support plan together with the patient. In this plan, the patient's situation was mapped on four domains: living conditions, physical domain, psychosocial domain and existential domain. If one of the domains required active support the HON discussed the required actions with the patient and if necessary with the GP.

The number, type, and duration of HON contacts was patient-driven, but it was recommended to have at least 3 contact moments, including one home visit during active treatment and two follow up contacts in the three months after completion of active treatment. To guide the content of all contact moments the Dutch Distress Thermometer[14] was used. This instrument includes items on five domains (i.e., practical, social, emotional, spiritual, physical), for which patients are asked to rank their level of distress.[14] The HON reported the condition of the patient and required actions to the GP. The hospital was also informed by the HON, in case supportive care was started based on the HON's consultations (e.g., consultation of a psychologist, physiotherapist or dietician) or when treatment-specific questions arose.

Intervention training

All the participating HONs were registered nurses with a specialised training in oncology and had more than 2 years of clinical experience. In addition, they received a 4-h training from the GRIP study team. Participating GPs received basic information on the GRIP study by their GP cooperative organisations at the start of the study. Also, the GPs of intervention patients received the

necessary instructions to perform a TOC and the expected steps to take by phone by email and through a website.

Outcomes

Primary outcomes were patient satisfaction with care and healthcare utilisation in the year after inclusion. Secondary outcomes were health related quality of life, mental health and patient empowerment.

Data collection

Patient reported outcomes and use of paramedical care were collected using questionnaires.

The timing of questionnaires depended on the duration of primary cancer treatment. If primary treatment lasted more than 9 months, questionnaires were provided at baseline (T0), after 2 weeks (T1), every 3 months (T2, T3, T4) and up to 12 months after inclusion (T5). If primary treatment was completed between 6 and 9 months after inclusion, T5 was provided 3 months after the end of primary treatment. In this case, the T4 questionnaire was omitted. If primary treatment was completed within 6 months after inclusion, T3 was planned at completion of treatment and T5 three months later. The remaining questionnaires were omitted. Consequently, every patient received at least the questionnaires from T0, T1, T3 and T5.

Questionnaires were filled in online or, if preferred by the patient, on paper. Non-responders received two reminders by e-mail after two and five days and were contacted by phone by the researcher if non-response persisted.

Healthcare utilisation was determined based on the Electronic Medical Records (EMR) registrations in primary care and hospital. These EMR data include free text and coded data describing daily care, i.e., consultation and referral descriptions, medication and diagnostic information.

From the primary care EMR, we also extracted GP consultation frequency in the year prior to inclusion. GP characteristics at T0 and rurality were

collected from public Dutch online databases for GP experience.[15, 16] From the hospital EMR, we extracted comorbidities, date of diagnosis, cancer stage, date of treatment decision and completion of active treatment. Date of treatment decision was defined as the moment the patient agreed with or chose the treatment. We defined the date of completion of active treatment (i.e., surgery, radiotherapy, chemotherapy) as the date of first follow-up contact with their treating physician.

Questionnaires

Patient satisfaction with care was measured at T3 and T5 with the European Organisation for Research and Treatment of Cancer Satisfaction with care questionnaire (EORTC-INPATSAT 32)[17] and with a Numeric Rating Scale (NRS). EORTC-INPATSAT 32 is a validated questionnaire and consists of 32 questions and measures patients' appraisal of hospital doctors and nurses, as well as aspects of care organisation and services.[17] We adjusted the EORTC-INPATSAT 32 to specify the satisfaction with specialists, GPs and nurses. Questions on GP and nurse satisfaction were left out if the patients did not receive this care.[12] The NRS, assessed at T3 and T5, is a self-developed question with a scale from 0 to 10 with the following question "How satisfied are you with the received care?". Herein, 0 implies "not satisfied at all" and 10 implies that the patient "could not have been more satisfied" with the received care.

Utilisation of paramedical care was assessed using the Medical Cost Questionnaire of the institute for Medical Technology Assessment (iMTA MCQ).[18] The iMTA MCQ includes 31 questions and measures healthcare utilisation of the past three months (specific to the Dutch situation).[18] The iMTA MCQ was filled in every three months after inclusion (T2, T3, T4, T5).

Health related Quality of Life was assessed at T0 and T5, using the European Organisation Research and Treatment of Cancer-Quality of Life-C30 questionnaire (EORTC-QoLC30). The EORC-QoLC30 is a validated questionnaire which incorporates functional scales, a quality of life scale and symptom scales.[19] In addition, we calculated the QLQ-C30 summary score.[20]

Mental health was assessed at T0 and T5 using the RAND Mental Health Inventory (MHI-5). It includes 5 items, resulting in a score between 0-100. Scores higher than 60 indicate the patient as psychologically healthy.[21]

Self-efficacy was measured with three validated questionnaires.[22–24] The General Self-Efficacy Scale (GSE) assessed the self-belief to cope with a variety of difficult demands in life at T0 and T5 using a questionnaire with 10 hypotheses.[22] A score was calculated, which ranged from 10-40. A higher score indicates higher self-efficacy.[22] Perceived Efficacy in Patient-Physician Interactions (PEPPI-5) was assessed at T0, T1 and T5. The PEPPI-5 includes 10 items resulting in a score from 5-25.[23] A higher score indicates higher perceived self-efficacy. Mastery level is an element of self-efficacy referring to "the extent to which an individual regards their life chances as being under their personal control rather than fatalistically ruled".[24] Mastery was measured with the Pearlin Mastery Scale at T0 and T5. It is a 7-item questionnaire designed to measure self-concept and the extent to which individuals perceive themselves in control of forces that significantly impact their lives.[24] From these items a score could be calculated ranging from 5-35, with higher scores indicate higher levels on mastery.[24]

Adherence to the GRIP intervention

Adherence to the TOC was assessed using free text and coded information in the GPs' EMR. The HON registered number and content of follow-up visits by using a personal plan and checklist. Data on collaboration between GP and HON was extracted from the EMR of the GP and based on data provided by the HON.

Statistical analysis

All analyses were performed following the intention to treat principle. Baseline characteristics were shown by calculating means or medians for continuous variables and frequencies or percentages for categorical variables. Characteristics of patients who completed the study and patients who dropped-out were compared using independent T-tests for continuous variables and Pearson's Chi-square used for categorical variables.

Linear mixed regression analyses were used for continuous outcome variables adjusted for baseline variables (if measured at baseline) and treating hospital and cancer type. In these longitudinal analyses, the statistic model accounts for missing data based on the observed data.[25] The questionnaires addressing satisfaction with the specialist, GP and nurse at T3 and T5, were only offered to the patients who had visited the corresponding healthcare workers. Besides, both the T3 and T5 assessments evaluated the period from inclusion to the assessment. So, the study population differs in size and the assessed period overlaps. Therefore, T3 and T5 were analysed separately using an ANOVA adjusted for treating hospital and cancer type (breast/lung/colorectal/gynaecologic/melanoma). The difference in healthcare utilisation for categorical data (i.e., paramedical care) was calculated with a Pearson Chi-Square or a Fisher exact test and for count data with a log-binomial regression. The majority of patients had no emergency department (ED) visits and/or emergency hospitalization. Therefore, we dichotomized the outcomes (i.e., no versus ≥1 ED visit). Healthcare utilisation outcomes were adjusted for treating hospital and cancer type. Additionally, because of group imbalances, we adjusted for co-morbidity (none/≥1) as sensitivity analysis.

Pre-specified subgroup analyses (co-morbidity (none/≥1), type of cancer (breast/colorectal/other), sex (male/female), age (≤65/> 65 year), baseline levels of the outcomes of interest)[12] were performed to investigate differential intervention effects on patient satisfaction by adding interaction terms to the regression model.

Sample size

A medium effect size (0.5) was assumed to be a clinically relevant difference in patients' satisfaction between the two study groups. Using a power of 0.8 and an alpha less than 0.05, at least 64 patients per study group were required. Accounting for an estimated dropout of 15%, 75 participants in each group were needed.

Results

In total, 396 patients were invited for participation by their treating physician or nurse in the hospital (Figure 1). Of these, 165 (42%) patients declined participation, mostly because of "too much of a burden shortly after diagnosis" (n=89) or "no extra support needed" (n=58). Sixty patients did not meet the eligibility criteria. Main reasons were: "patient already started therapy" (n=24), "GP worked outside the study area" (n= 18) and "patient received palliative treatment" (n=8). As a result, 154 patients were randomised to either the intervention (n=77) or the control group (n=77). These 154 patients were registered with 119 different GPs, from 79 different primary care practices.

Information about the timing of the completion of the T3 and T5 questionnaires is provided in the supplementary files (Appendix A).

The study population had a mean age of 61 (SD ±11.9) years. The majority was female (75%) and had either breast (51%) or colorectal (25%) cancer. At baseline, the two study groups were comparable, except for the presence of comorbidity, which was higher in the intervention group (68%) compared to the control group (49%) (Table 1). During the trial 18 (23%) patients did not complete the T5 questionnaires in the intervention group and 8 (10%) in the control group (Figure 1). Characteristics of the analysed patients and the patients who dropped out did not differ ($p>0.05$, Appendix A).

Compliance with the GRIP intervention

Of the 77 intervention patients 62 (81%) patients had a TOC.[11] However, only 18% (n=11) of these were scheduled according to the protocol, i.e., between diagnosis and treatment decision.[11]

Of the patients in the intervention group, 52 (68%) had at least one contact with the HON. Reasons for not having HON contact were: no wish for HON involvement for 13 patients (17% of patients in the intervention group) or no need for additional care providers for 5 patients (7%) (Figure 1). Of the patients who had HON contact, 62% (n=32) had three or more contact moments. The HON care was discontinued by 11 patients (18%) at their own request, after

an average of three contacts. These patients either had an appointment to call for continuation of care but never called or they "had already enough support" or "felt too well and no support was needed". HON contact was not continued after completion of active treatment by 24 patients (46%) who received HON guidance. Median number of contacts between the HON and GP was 2.0 (IQR 1;2). In the control group, no patient had a HON consultation.

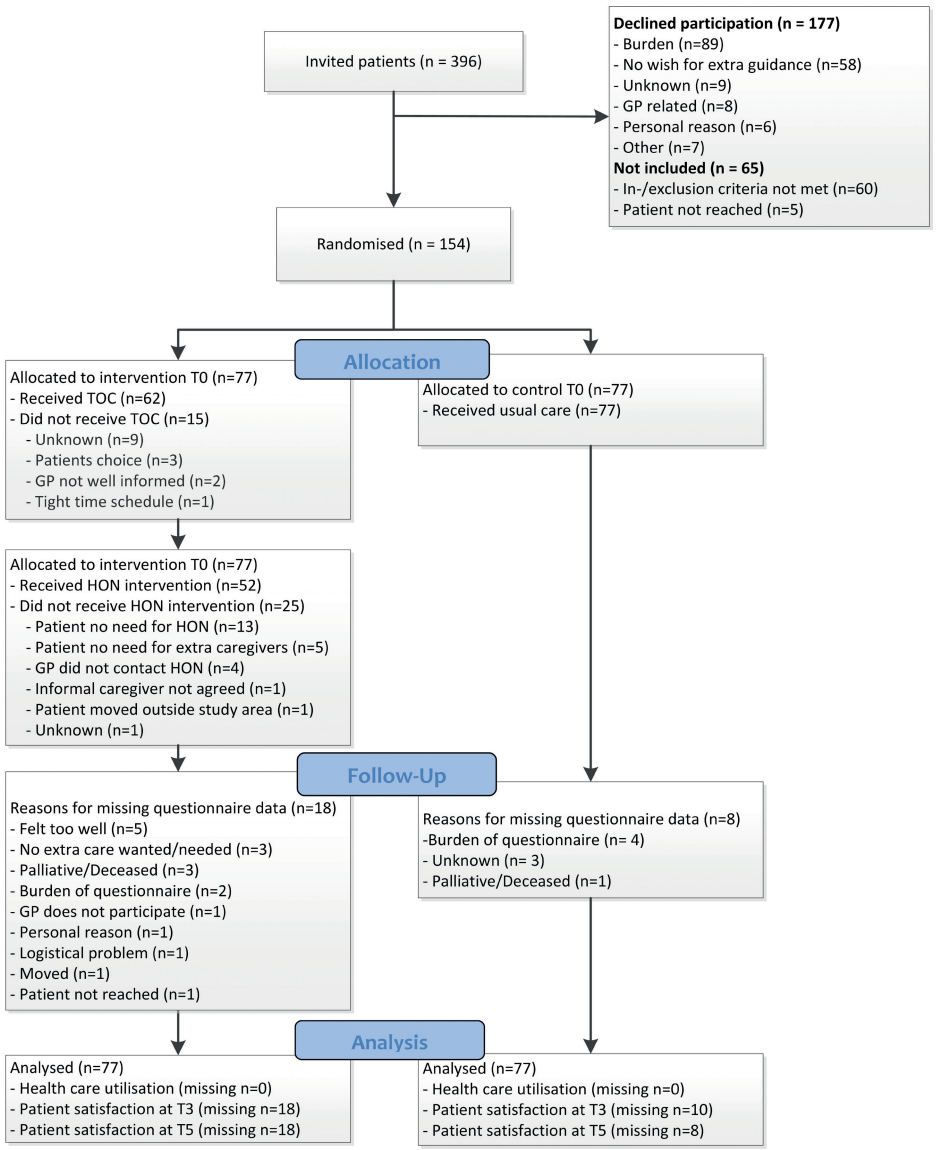

Figure 1. CONSORT, Consolidated Standards of Reporting Trials of the GRIP study.

Patient satisfaction

Satisfaction with overall cancer care

Patient satisfaction with overall cancer care on the NRS (0-10 scale) did not differ between groups (T5: intervention 8.0 (SD±1.3), control 8.0 (SD±1.3)) (Table 2).

Satisfaction with care delivered by GP

Between diagnosis and T3, 37 (48%) patients of the intervention group and 22 (29%) patients of the control group had received care from their GP. Among these patients, satisfaction with GP care at T3 did not differ between the intervention and control group (Table 4).

From diagnosis till three months after treatment (T0-T5), 38 (49%) patients in the intervention group and 31 (40%) in the control group had received care from their GP. At T5, among these patients, patient satisfaction scores were significantly lower in the intervention group as compared to the control group on three subscales, i.e., Quality: between-group difference -14,2 (95% CI -27,0;-1,3), Availability: -15,9 (95% CI -29,1;-2,6) and Information provision -15.2 (95% CI -29.1;-1.4). Technical skills -9.9 (95% CI -21.6;1.7) scored non-significantly lower (Table 4). On the questionnaire scale, the mean satisfaction scores at T5 correspond with a "Reasonably - Very Good" (score 40/100 to 80/100) in the intervention group compared to "Good - Very Good" (score 60/100 to 80/100) in the control group.

Satisfaction with care delivered by nurse

At T3, 33 (43%) patients of the intervention group and 30 (39%) patients of the control group had received care from a nurse. Among these patients, no difference was found in satisfaction with nursing care between the intervention and control group. At T5, 30 (39%) patients of the intervention group and 24 (31%) of the control group had received care from a nurse. Patient satisfaction concerning Experience/Knowledge, Availability, Attention and Willingness were, not significantly, higher in the intervention group compared to the control group (Table 5).

Table 1. Characteristics of all study participants at baseline and missing study participants at T5.

	Intervention N = 77	Intervention missing T5 N = 18 (23%)	**Control N = 77**	Control missing T5 N =8 (10%)
Female n (%)	57 (74.0)	13 (72.2)	58 (75.3)	6 (75.0)
Age mean (±SD)	61.8 (11.4)	64 (9.5)	59.3 (12.2)	62 (11.9)
Cancer type N (%)				
Breast	38 (49.4)	8 (44.4)	40 (51.9)	4 (50.0)
Colorectal	20 (26.0)	6 (33.3)	18 (23.4)	1 (12.5)
Melanoma	13 (16.9)	2 (11.1)	11 (14.3)	1 (12.5)
Gynaecologic	3 (3.9)	2 (11.1)	2 (2.6)	2 (25.0)
Lung	3 (3.9)	-	6 (7.8)	-
Hospital setting N (%)				
Academic	22 (28.6)	7 (38.9)	24 (31.2)	2 (25)
Non academic	55 (71.4)	11 (61.1)	53 (68.8)	6 (75)
Cancer stage[1]				
0	2 (2.6)	-	2 (2.6)	-
I	34 (44.2)	6 (33.3)	34 (44.2)	5 (62.5)
II	22 (28.6)	5 (27.8)	27 (35.1)	3 (37.5)
III	18 (23.4)	6 (33.3)	14 (18.2)	-
IV	1 (1.3)	1 (5.6)	-	-
Education				
Low	32 (41.6)	9 (50)	25 (32.5)	1 (12.5)
Middle	13 (16.9)	1 (5.6)	18 (23.4)	4 (50.0)
High	32 (41.6)	8 (44.4)	34 (44.2)	3 (37.5)
Number of comorbidities N (%)				
None	25 (32.5)	4 (22.2)	39 (50.6)	2 (25.0)
>1	52 (67.5)	14 (77.8)	38 (49.4)	6 (75.0)
Number of GP practice contacts (year prior inclusion) median (IQR)	7 (4.0;10.0)	7 (6.0;11.5)	6 (3.5;11.0)	9 (3.5;12.0)
GP years of working experience median (IQR)	17 (12.0;25.5)	17 (11.8;21.0)	16 (10.5;24.5)	18 (13.0;26.0)
GP setting N (%)				
Urban[2]	51 (66.2)	10 (55.6)	45 (58.4)	6 (75.0)
Between rural and urban[3]	14 (18.2)	3 (16.7)	15 (19.5)	2 (25.0)
Rural[4]	12 (15.6)	5 (27.8)	17 (22.1)	-

[1]Stage based on TNM classifications, [2] 1000 or more addresses per km^2, [3] 1000-1500 addresses per km^2, [4] 1000 or less addresses per km^2).
Abbreviations: SD; Standard deviation, IQR; Inter quartile range.

Subgroup analyses suggest a non-significant, but potentially relevant higher satisfaction with overall care in patients with colorectal cancer in the intervention group compared to the control group (mean difference 9.9 (95% CI-3.8;23.6), Appendix C). Intervention patients with colorectal cancer were less satisfied with the GP as compared to the control group. Also, patients with ≥ 1 comorbidities, patients 65 years or younger and female patients scored lower on several GP satisfaction subscales (Appendix C). In contrast, nurse satisfaction score was lower among patients with colorectal cancer and breast cancer compared to the other cancer types (gynaecologic cancer, lung cancer or melanoma), in patients without comorbidities, in patients above the 65 years and female patients.

Healthcare utilisation

The intervention group had a significantly higher "risk" of having contact with the GP practice (RR: 1.3 (95% CI 1.0;1.7) p=0.03) and ED visits (RR: 1.7 (95% CI 1.0;2.8) p=0.04) compared to the control group (Table 6). After adjustment for co-morbidity, RRs were 1.3 (95% CI 0.994;1.603) p=0.056 for contact with GP practice and 1,9 (95% CI 1.01;3.45) p=0.045 for ED visits. No other significant differences in use of hospital or paramedical care were found between the study groups (Table 6 & 7). In the year after inclusion, the intervention group had a median number of 7 (IQR 4.5;12.0) GP contacts and the control group had 6 (IQR 4.0;9.5) GP contacts (Table 6). The median number of contact moments in hospital the year after inclusion was 49 (IQR 27.5;88.5) in the intervention group and 50 (IQR 24.5;78.5) in the control group.

Secondary outcomes

No significant between-group differences were found for quality of life and the subscales. Between-group differences were -1.2 (95% CI -7.6;5.3) for Global Quality of life and -0.4 (95% CI -5.4;4.6) on the Summary scale (Table 8). Also, mental health was not different between groups (-0.6 (95% CI -6.0; 4.9) (Table 9).

Self-efficacy was also not significantly different between the study groups. At T5, the between-group differences were 0.3 (95% CI -1.0;1.5) for General Self-Efficacy, -0.6 (95% CI -1.4;0.3) for Perceived Efficacy in Patient-Physician Interactions and -0.0 (95% CI -1.6;1.6) for Mastery level (Table 9).

Table 2. Patient satisfaction with overall care.

OVERALL		**T3 measurement Mean (SD)**		**T5 measurement Mean (SD)**	**Between group[1] Mean diff. (95% CI)**	
Information exchange					T3	T5
Intervention	n=59	54.7 (21.5)	n=59	54.2 (20.3)	-0.4 (-8.5;7.7)	1.4 (-6.7;9.4)
Control	n=67	55.2 (22.8)	n=69	53.3 (24.6)	Ref.	Ref.
Overall assessment						
Intervention	n=59	65.3 (21.3)	n=59	66.1 (20.6)	1.9 (-5.8;9.7)	3.6 (-3.7;10.9)
Control	n=67	63.8 (21.4)	n=69	63.0 (21.3)	Ref.	Ref.
NRS (higher scores indicate better performance) 0-10 scale						
Intervention	n=59	8.1 (1.3)	n=59	8.0 (1.3)	-0.1 (-0.5;0.4)	0.0 (-0.4;0.4)
Control	n=67	8.2 (1.1)	n=67	8.0 (1.3)	Ref.	Ref.

[1] Adjusted for stratification factors.
Abbreviation: NRS; Number Rating Scale, Ref.; reference group.

Table 3. Patient satisfaction with care scored on various themes – Specialist assessment.

MEDICAL SPECIALIST		**T3 measurement Mean (SD)**		**T5 measurement Mean (SD)**	**Between group[1] Mean diff. (95% CI)**	
Interpersonal skills – Spec.					T3	T5
Intervention	n=59	69.9 (23.9)	n=59	66.9 (23.9)	3.0 (-5.1;11.0)	4.8 (-2.8;12.5)
Control	n=67	68.4 (22.6)	n=69	62.8 (20.1)	Ref.	Ref.
Qualities - Spec.					T3	T5
Intervention	n=59	79.2 (22.3)	n=59	76.3 (22.9)	6.2 (-1.8;14.1)	3.9 (-3.9;11.6)
Control	n=68	73.9 (23.0)	n=69	73.6 (21.8)	Ref.	Ref.
Availability - Spec.					T3	T5
Intervention	n=59	73.3 (21.2)	n=59	69.9 (20.6)	3.3 (-4.4;11.1)	3.3 (-4.5;11.1)
Control	n=67	70.1 (22.7)	n=69	67.4 (23.6)	Ref.	Ref.
Relationship - Spec.					T3	T5
Intervention	n=59	70.3 (22.5)	n=59	71.2 (22.7)	5.7 (-2.6;14.0)	2.4 (-5.7;10.5)
Control	n=68	65.4 (25.2)	n=69	69.2 (22.7)	Ref.	Ref.
Tech. skills - Spec.					T3	T5
Intervention	n=59	75.7 (19.0)	n=59	72.6 (20.1)	4.2 (-2.4;10.8)	3.8 (-2.9;10.5)
Control	n=68	72.9 (20.3)	n=69	69.6 (18.4)	Ref.	Ref.
Info. Provision - Spec.					T3	T5
Intervention	n=59	70.3 (23.8)	n=59	68.4 (21.6)	2.3 (-6.1;10.6)	3.7 (-3.6;11.0)
Control	n=67	68.8 (22.7)	n=69	65.1 (20.2)	Ref.	Ref.

[1] Adjusted for stratification factors.
Abbreviation: diff.; difference, Ref.; reference group, Spec; Specialist.

Table 4. Patient satisfaction with care scored on various themes - General practitioner assessment.

GENERAL PRACTITIONER		**T3 measurement Mean (SD)**		**T5 measurement Mean (SD)**	**Between group[1] Mean diff. (95% CI)**	
Interpersonal skills - GP					T3	T5
Intervention	n=37	73.6 (24.3)	n=38	63.2 (26.6)	2.6 (-11.5;16.6)	-9.6 (-22.6;3.3)
Control	n=22	69.3 (26.9)	n=31	70.7 (25.7)	Ref.	Ref.
Qualities - GP					T3	T5
Intervention	n=37	78.4 (22.1)	n=38	67.8 (25.9)	6.3 (-7.7;20.3)	-14.2 (-27.0;-1.3)
Control	n=22	69.3 (29.8)	n=31	79.8 (24.5)	Ref	Ref.
Availability - GP					T3	T5
Intervention	n=37	75.7 (24.6)	n=38	62.5 (26.5)	5.6 (-9.0;20.2)	-15.9 (-29.1;-2.6)
Control	n=22	67.0 (29.3)	n=31	75.0 (25.8)	Ref	Ref.
Relationship - GP					T3	T5
Intervention	n=37	77.0 (22.3)	n=38	70.4 (25.2)	8.2 (-5.7;22.1)	-6.2(-19.2;6.8)
Control	n=22	67.0 (30.3)	n=31	74.2 (27.0)	Ref	Ref.
Tech. skills - GP					T3	T5
Intervention	n=37	66.9 (20.6)	n=38	55.3 (21.9)	6.9 (-6,2;20.0)	-11.4 (-23.2;0.4)
Control	n=22	59.5 (27.1)	n=30	64.2 (24.1)	Ref	Ref.
Info. Provision - GP					T3	T5
Intervention	n=37	60.4 (23.8)	n=37	48.9 (24.9)	4.0 (-11.9;20.0)	-15.2 (-29.1;-1.4)
Control	n=22	55.7 (31.2)	n=29	60.6 (28.4)	Ref.	Ref.

[1] Adjusted for stratification factors.
Abbreviation: diff.; difference, GP; General practitioner, Ref.; reference group.

Table 5. Patient satisfaction with care scored on various themes[1] – Nursing care assessment

NURSE		**T3 measurement Mean (SD)**		**T5 measurement Mean (SD)**	**Between group[2] Mean diff. (95% CI)**	
Interpersonal skills - Nurse					T3	T5
Intervention	n=33	72.7 (19.8)	n=30	75.3 (20.9)	-0.3 (-11.5;10.8)	7.1 (-3.4;17.6)
Control	n=30	73.6 (24.5)	n=21	68.3 (21.3)	Ref.	Ref.
Experience/Knowl. - Nurse					T3	T5
Intervention	n=33	68.2 (20.0)	n=30	73.3 (20.7)	1.0 (-10.3;12.3)	10.8 (-0.3;21.9)
Control	n=30	67.5 (24.7)	n=24	63.5 (22.1)	Ref.	Ref.
Availability -Nurse					T3	T5
Intervention	n=33	74.2 (20.2)	n=30	72.5 (23.1)	1.6 (-10.1;13.3)	7.7 (-3.7;19.0)
Control	n=30	73.3 (26.2)	n=22	65.9 (19.7)	Ref.	Ref.
Relationship-Nurse					T3	T5
Intervention	n=33	68.2 (20.0)	n=30	70.8 (22.8)	1.2 (-10.7;13.1)	1.2 (-9.6;12.1)
Control	n=30	67.5 (26.4)	n=24	70.8 (20.4)	Ref.	Ref.
Attention - Nurse					T3	T5
Intervention	n=33	68.9 (20.8)	n=30	75.8 (22.2)	0.2 (-11.9;12.4)	9.6 (-0.3;19.4)
Control	n=30	69.2 (26.8)	n=24	67.7 (20.2)	Ref.	Ref.
Willingness- Nurse					T3	T5
Intervention	n=33	71.2 (21.8)	n=30	75.8 (23.2)	1.4 (-10.7;13.5)	7.5 (-3.5;18.5)
Control	n=30	70.8 (25.5)	n=24	69.8 (20.8)	Ref.	Ref.

[1] Three themes not shown: Information disease, Information diagnostics and Information treatment. [2] Adjusted for stratification factors. Abbreviation; diff.; difference, Knowl; Knowledge, Ref.; reference group

Table 6. Healthcare utilisation in primary care and hospital one year after inclusion.

	Intervention N=77 Median (IQR)	**Control N=77 Median (IQR)**	**Negative binomial regression RR (95% CI)**
Healthcare utilisation primary care			
Contacts with GP practice (incl. out of office hours)	9 (5.0;16.0)	8 (5.0;13.5)	1.3 (1.0;1.7)#
Contacts with GP (incl. out of office hours)	7 (5.0;12.0)	6 (4.0;9.5)	1.3 (1.0;1.6)
Contacts with GP (excl. out of office hours)	7 (4.5;12.0)	6 (4.0;9.5)	1.2 (1.0;1.5)
Healthcare utilisation hospital care			
Total contacts (incl. by phone + consultations + ED + hospitalizations+ diagnostics)	49 (27.5;88.5)	50 (24.5;78.5)	1.2 (1.0;1 .4)
Contacts by phone	6 (3.0;14.5)	7 (3.0;13.0)	1.2 (0.9;1.5)
Consultations	20 (11.5;31.0)	20 (13.0;30.0)	1.0 (0.9;1.2)
	n (%)	n (%)	RR[1] (95% CI).
Patients visiting the emergency department	29 (37.7)	17 (22.1)	1.7 (1.0;2.8)*
Patients with emergency hospitalizations	13 (16.9)	9 (11.7)	1.5 (0.7;3.2)

#p value = 0.03 *p value = 0.04. [1] Adjusted for stratification factors.
Abbreviations: GP; General practitioner, yr; year, RR; relative risk, int.; intervention, cont.; control.

Table 7. Use of paramedical care in the three months before T5.

T5	**Intervention n=59 N (%)**	**Control n=69 N (%)**	**p-value**
Physiotherapy total	29 (49.2)	35 (50.7)	0.86
in primary care	22 (75.9)	29 (82.9)	
in hospital	1 (3.4)	2 (5.7)	
both	6 (20.7)	4 (11.4)	
Ergo therapy	1 (1.7)	2 (2.9)	1.00
in hospital	1 (100)	2 (100)	
Acupuncture/homeopathy	3 (5.1)	3 (4.3)	1.00
in primary care	3 (100)	3 (100)	
Psychologist	10 (16.9)	10 (14.5)	0.70
in primary care	6 (60.0)	7 (70.0)	
in hospital	2 (20.0)	1 (10.0)	
both	2 (20.0)	2 (20.0)	
Dietician	2 (3.4)	3 (4.3)	1.00
in primary care	1 (50.0)	2 (66.7)	
in hospital	1 (50.0)	1 (33.3)	
Speech therapist	-	-	-

Table 8. Quality of life at T5.

	Intervention (N = 59) Mean (SD)	Control (N = 69) Mean (SD)	Between group[1] Mean diff. (95% CI)
Function scales			
Physical Function	78.8 (22.1)	81.5 (18.4)	-0.5 (-6.0;4.9)
Role Function	70.6 (31.0)	75.4 (28.4)	-4.6 (-14.7;5.5)
Emotional Function	80.4 (22.6)	79.8 (23.5)	-1.7 (-9.4;6.1)
Cognitive Function	79.4 (23.8)	77.3 (24.9)	3.2 (-4.7;11.2)
Social Function	79.7 (25.0)	78.7 (28.9)	-1.2 (-10.6;8.1)
Symptom scales			
Fatigue	31.3 (27.2)	32.9 (27.4)	-2.0 (-10.8;6.9)
Nausea/vomiting	2.8 (9.9)	2.9 (8.1)	-0.2 (-3.4;3.0)
Pain	23.7 (30.5)	20.5 (24.4)	2.1 (-7.0;11.3)
Single items			
Dyspnoea	13.6 (24.9)	12.1 (24.9)	2.2 (-4.1;8.5)
Insomnia	30.5 (34.1)	28.0 (31.1)	2.2 (-8.0;12.4)
Appetite loss	4.0 (12.5)	8.2 (20.9)	-4.4 (-10.1;1.3)
Constipation	10.2 (25.0)	5.8 (16.1)	2.7 (-4.5;9.8)
Diarrhoea	5.7 (19.7)	7.7 (19.9)	-1.6 (-8.7;5.5)
Financial difficulties	7.9 (17.9)	11.6 (24.1)	-4.1 (-11.7;3.6)
Global scales			
Global Quality of life	71.9 (19.1)	72.6 (20.5)	-1.2 (-7.6;5.3)
Summary functioning scale	82.1 (17.0)	82.7 (15.5)	-0.4 (-5.4;4.6)

[1] Adjusted for stratification factors and baseline.

Table 9. T5 Secondary outcomes – Mental health and Self-efficacy.

	Intervention N= 59 mean (SD)	Control N=69 mean (SD)	Mean difference[1] (95% CI)
MHI-5 (>60 score indicate mentally healthy) 0-100 scale.	75.1 (15.7)	73.6 (17.2)	-0.6 (-6.0; 4.9)
Pearlin-Schooler Mastery scale (higher scores indicate better performance) 5-35 scale.	25.0 (4.9)	24.8 (4.2)	-0.0 (-1.6;1.6)
GSE (higher scores indicate better performance) 10-40 scale.	32.3 (4.1)	31.3 (4.2)	0.3 (-1.0;1.5)
PEPPI (higher scores indicate better performance) 5-25 scale.	20.7 (3.3)	21.4 (3.0)	-0.6 (-1.4;0.3)

[1] Adjusted for stratification factors and baseline.

Discussion

All cancer patients in our study reported high satisfaction with care, independent whether they received specialist care alone or additional care from a GP and home care oncology nurse. Although the GRIP intervention was designed to improve primary care involvement, the ability to measure its effectiveness was limited because it was often not implemented as intended: 82% of the TOCs were not planned before the treatment decision and 46% of patients receiving HON care did not continue after the end of their treatment. In our trial, structured involvement of primary care during cancer treatment did not result in increased patient satisfaction, nor did it improve quality of life, mental health or self-efficacy. Additional guidance from primary care resulted in slightly more ED visits.

Patients seem well motivated to actively involve their primary care team, since the intervention uptake was relatively high; 81% of patients in the intervention group scheduled a TOC and 68% had HON consultations. Other studies investigating primary care involvement reported a lower uptake, varying from 27% to 60%.[26–28] The high uptake of primary care involvement

is in line with earlier reports of the Dutch Cancer patients organisation,[10] which demonstrated a strong wish for more GP involvement.

Unfortunately, high uptake was followed by suboptimal implementation to the intended intervention and, in its current form, it did not result in improved satisfaction. Therefore, adjustment of the design and/or implementation of the intervention is required. Several findings provide clues for improving the intervention, including its integration in the daily workflow. First, the majority of the TOCs were scheduled after the treatment decision was already made, which makes active participation in the treatment decision impossible. The time between diagnosis and therapy choice was too short to enable active TOC planning by the patient. Hence, to enable adequate timing of TOCs, its planning should preferably be embedded in the hospital care pathway. Second, almost half of the patients did not want the suggested contacts with the HON after treatment completion (46%). Obviously, the design and content of the HON intervention did not match the needs of almost half of the patients. Possibly, the patients expected their GP to be personally involved, and not to delegate it to the primary care nurse. This needs further exploration.

In contrast to our hypothesis, patients in the intervention group were less satisfied with their GP and slightly more with their nurse. This may be explained by several reasons. First, the intervention itself may have raised expectations about GP involvement in the intervention group, that were not met in practice. Patients receiving the intervention were notified that they would receive extra care from the primary care team: both their GP and a HON. They might have expected more contact with their GP, but met the HON instead. The significantly lower scores on "GP-Availability" in the intervention group support this hypothesis. Another possible explanation may be found in the GP involvement in the control group, as a result of an independent proactive approach by the GP. More proactive GP contacts might have led to higher patient satisfaction in the control group. Finally, the lack of difference in satisfaction with care may be the result of a ceiling effect, which is supported by the high overall satisfaction scores in both study groups. In the Netherlands, patients usually have a nurse as case manager in the hospital, which might contribute to the high satisfaction.

Other studies evaluating primary care interventions after cancer diagnosis in the curative patient population indicate either positive effects on patient satisfaction[25,27,28] or no effects[31] and showed less ED visits in the older population.[32] These studies examined various interventions, which involved information provision using patient health records[25,27,28] or intensified primary care with the focus on GP[28] or on a primary care team.[32] The variety of interventions, different healthcare systems, or the use of self-developed questionnaires to measure patient satisfaction[25,27–29] might explain the more positive outcome as compared to our study.

The higher number of ED visits among intervention patients was in contrast with our expectations. Reasons for ED consultations were mostly oncology-related and seemed unavoidable, for example ED visits because of fever during chemotherapy. Although the ED records did not provide clues for the increased ED use, it may be related to the fact that GPs referred cancer patients at a lower threshold because of study participation. Another explanation might be that patients in the intervention group have more co-morbidities. However, adjustment only slightly affected the estimates.

This study has both strengths and limitations. A strength is the pragmatic approach and the implementation of the study in daily practice. Consequently, this pragmatic RCT adds to the scarce evidence on the real-life effects of involving a primary care team during and after curative cancer treatment, in a daily practice setting. Also, outcome measurements were aligned to individual patient's cancer treatments, thereby enabling different cancer types to be included.

Present study results might not be generalizable to all cancer patients who are to be treated with curative intent, since our study population might be a selection of patients who were positive towards primary care. Also, our intervention may have been prematurely implemented, as supported by the relatively high uptake but incorrect scheduling (TOC) and relatively high number of discontinued HON contacts. Future studies might benefit from following strategies to develop and evaluate a complex intervention as presented in the framework of the Medical Research Council[33] more strictly. This approach would require more elaborate pilot evaluations to optimize

the individual elements of the intervention and to optimize the definition and assessments of outcomes.

Another limitation was that patients and healthcare providers could not be blinded, due to the nature of the intervention. This may have affected outcomes, e.g., by the previously mentioned consequences of raising expectations among patients. Furthermore, several patients stopped study participation and we found a higher drop-out in the intervention group compared to the control group, which might have caused selection bias. However, patients' characteristics of drop-outs did not differ.

Conclusion

The GRIP intervention, which aimed to structure involvement of primary care during and after cancer treatment with curative intent, was well accepted but sub-optimally implemented and adhered to. It slightly increased primary healthcare contacts, did not improve patient satisfaction with care and slightly increased use of the ED. As the high uptake of the intervention suggests that it addresses patients' needs, future research should focus on optimizing the design and implementation of primary care involvement. This future effort may benefit from an integrated and collaborative approach with patients and healthcare professionals.

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Appendix A.

Table A. Overview of patient characteristics at baseline and at T5 the analysed and missing population.

	Intervention N = 77	Intervention Analysis T5 N=59 (77%)	Intervention Missing T5 N=18 (23%)	**Control N = 77**	Control Analysis T5 N= 69 (90%)	Control Missing T5 N=8 (10%)
Female N (%)	57 (74.0)	44 (74.6)	13 (72.2)	58 (75.3)	52 (75.4)	6 (75.0)
Age mean (±SD)	61.8 (11.4)	61 (11.9)	64 (9.5)	59.3 (12.2)	59 (12.3)	62 (11.9)
Cancer type N (%)						
Breast	38 (49.4)	30 (50.8)	8 (44.4)	40 (51.9)	36 (52.2)	4 (50.0)
Colorectal	20 (26.0)	14 (23.7)	6 (33.3)	18 (23.4)	17 (24.6)	1 (12.5)
Melanoma	13 (16.9)	11 (18.6)	2 (11.1)	11 (14.3)	10 (14.5)	1 (12.5)
Gynaecologic	3 (3.9)	1 (1.7)	2 (11.1)	2 (2.6)	4 (5.8)	2 (25.0)
Lung	3 (3.9)	3 (5.1)	-	6 (7.8)	2 (2.9)	-
Hospital setting N (%)						
Academic	22 (28.6)	15 (25.4)	7 (38.9)	24 (31.2)	22 (31.9)	2 (25)
Non academic	55 (71.4)	44 (74.6)	11 (61.1)	53 (68.8)	47 (68.1)	6 (75)
Cancer stage[1]						
0	2 (2.6)	2 (3.4)	-	2 (2.6)	2(2.9)	-
I	34 (44.2)	28 (47.5)	6 (33.3)	34 (44.2)	29 (42.0)	5 (62.5)
II	22 (28.6)	17 (28.8)	5 (27.8)	27 (35.1)	24 (34.8)	3 (37.5)
III	18 (23.4)	12 (20.3)	6 (33.3)	14 (18.2)	14 (20.3)	-
IV	1 (1.3)	-	1 (5.6)	-	-	-
Education						
Low	32 (41.6)	23 (39.0)	9 (50)	25 (32.5)	24 (34.8)	1 (12.5)
Middle	13 (16.9)	12 (20.3)	1 (5.6)	18 (23.4)	14 (20.3)	4 (50.0)
High	32 (41.6)	24 (40.7)	8 (44.4)	34 (44.2)	31 (44.9)	3 (37.5)

Table A. Continued.

	Intervention N = 77	Intervention Analysis T5 N=59 (77%)	Intervention Missing T5 N=18 (23%)	**Control N = 77**	Control Analysis T5 N= 69 (90%)	Control Missing T5 N=8 (10%)
Number of comorbidities N (%)						
None	25 (32.5)	21 (35.6)	4 (22.2)	39 (50.6)	37 (53.6)	2 (25.0)
>1	52 (67.5)	38 (64.4)	14 (77.8)	38 (49.4)	32 (46.4)	6 (75.0)
Number of GP practice contacts (yr. prior inclusion) median (IQR)	7 (4.0;10.0)	6 (3.0;10.0)	7 (6.0;11.5)	6 (3.5;11.0)	6 (3.5;11.0)	9 (3.5;12.0)
GP yrs of working experience median (IQR)	17 (12.0;25.5)	17 (12.0;28.0)	17 (11.8;21.0)	16 (10.5;24.5)	16 (10.0;24.5)	18 (13.0;26.0)
GP setting N (%)						
Urban[2]						
Between rural and	51 (66.2)	41 (69.5)	10 (55.6)	45 (58.4)	39 (56.5)	6 (75.0)
urban[3]	14 (18.2)	11 (18.6)	3 (16.7)	15 (19.5)	13 (18.8)	2 (25.0)
Rural[4]	12 (15.6)	7 (11.9)	5 (27.8)	17 (22.1)	17 (24.6)	-

Baseline characteristics between the drop-out and analysed group at T5 did not differ.
[1]Stage based on TNM classifications, [2] 31000 or more addresses per km^2, [3]1000-1500 addresses per km^2, [4]1000 or less addresses per km^2)
Abbreviations: SD; Standard deviation, IQR; Inter quartile range, yr; year.

Appendix B.

Timing of questionnaires during- and after cancer treatment

Patients received the T3 questionnaire when they completed active treatment or 6 months after inclusion. Patients received the T5 questionnaire 3 months after primary treatment or 12 months after inclusion. In both study groups the majority of patients (69%) completed primary treatment at T3 (n=41/59 in the intervention group and n= 46/67 in the control group). At T5 one patient still received primary treatment (control). The median number of days between completion of active treatment and T5 was 94 (IQ 90;100) for the intervention group and 93 (IQR 90;102.5) for the control group. The timing of questionnaires in the varying cancer treatment schedules is shown in figure 2. In the intervention group, the median time between T0 and T3 was 134 days (IQR 72-183) and from T0 to T5: 209 days (IQR 150-332). For the control group, the T3 median duration was 155 days (IQR 71-186) and T0 to T5 was 219 days (IQR 147-309).

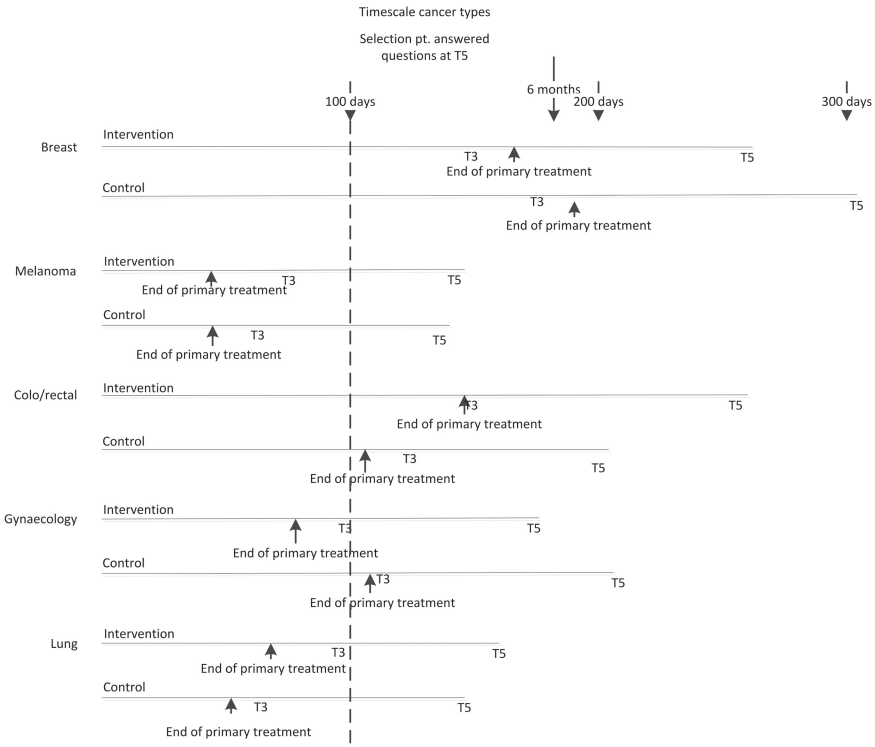


Figure B. Study time frame of patients filled out T5 – per cancer type. Mean number of days between inclusion and assessed questionnaires: T3 and T5.

Appendix C. Subgroup analysis – Patient Satisfaction with care.

Table C1. Subgroup effects on overall patient satisfaction with care.

Overall Satisfaction	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	59/67	1.9 (-5.8;9.7)		59/69	3.6 (-3.7;10.9)	
Sexe						
Male	15/17	-0.2 (-15.7;15.2)		15/17	-2.9 (-15.9;10.2)	
Female	44/50	2.2 (-7.2;11.5)	0.78	44/52	4.8 (-4.2;13.9)	0.52
Type of cancer						
Breast	28/34	1.7 (-8.8;12.2)		30/36	4.3 (-6.6;15.3)	
Colorectal	16/16	10.9 (-5.5;27.4)		14/17	9.9 (-3.8;23.6)	
Other	15/17	-8.2 (-25.5;9.1)	0.28	15/16	-7.7 (-23.1;7.6)	0.33
Age						
≤65	37/46	5.4 (-5.1;15.9)		36/47	5.7 (-3.8;15.2)	
>65	22/21	-0.8 (-10.9;9.3)	0.52	23/22	4.3 (-7.4;16.0)	0.77
Comorbidity						
None	21/35	-1.0 (-13.4;11.4)		21/37	0.7 (-11.8;13.1)	
≥1	38/32	5.9 (-4.5;16.2)	0.50	38/32	5.7 (-3.7;15.2)	0.40

Abbreviation: int; intervention group, cont; control group.

Table C2. Subgroup effects on patient satisfaction with general practitioner's interpersonal skills scale.

Interpersonal skills - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	2.0 (-12.2;16.2)		38/31	-8.6 (-21.2;4.0)	
Sexe						
Male	8/8	11.3 (-10.0;32.7)		8/12	-0.4 (-22.5; 23.2)	
Female	29/14	1.7 (-19.8;23.3)	0.67	30/19	-7.5 (-25.7;10.7)	0.77
Type of cancer						
Breast	17/13	-1.7 (-23.7; 20.3)		20/14	-4.8 (-27.0;17.4)	
Colorectal	11/5	0.4 (-20.4;21.1)		9/11	-22.3 (-43.2;2.5)	
Other	9/4	13.4 (-21.7;48.5)	0.95	9/6	-8.7 (-29.9;12.6)	0.49
Age						
≤65	25/12	3.5 (-15.6;22.5)		24/19	-6.8 (-22.6;9.0)	
>65	12/10	7.6 (-11.8;26.9)	0.35	14/12	-7.8 (-29.0;13.5)	0.83
Comorbidity						
None	16/11	16.0 (-17.5;49.5)		13/15	3.2 (-23.1;29.6)	
≥1	21/11	-2.6 (-19.1;13.9)	0.43	25/16	-13.6 (-29.6;2.4)	0.22

Abbreviation: GP; general practitioner, int; intervention group, cont; control group.

Table C3. Subgroup effects on patient satisfaction with general practitioner's quality.

Qualities - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	6.0 (-7.8;19.8)		38/31	-13.8 (-26.2;-1.3)	
Sexe						
Male	8/8	10.8 (-11.8;33.5)		8/12	-7.6 (-35.0;19.8)	
Female	29/14	7.3 (-13.0;27.7)	0.87	30/19	-11.3 (-28.4;5.7)	0.98
Type of cancer						
Breast	17/13	4.7 (-17.8;27.3)		20/14	-7.2 (-26.9;12.5)	
Colorectal	11/5	0.1 (-22.0;22.3)		9/11	-23.7 (-49.0;1.5)	
Other	9/4	18.8 (-6.6;44.1)	0.85	9/6	-20.5 (-47.8;6.9)	0.46
Age						
≤65	25/12	4.5 (-15.0;23.9)		24/19	-16.5 (-32.8;-0.3)	
>65	12/10	15.4 (0.7;30.1)	0.13	14/12	-5.1 (-26.1;15.8)	0.45
Comorbidity						
None	16/11	18.2 (-14.9;51.3)		13/15	-8.2 (-33.1;16.6)	
≥1	21/11	2.6 (-13.3;18.5)	0.49	25/16	-15.8 (-32.9;1.2)	0.60

Abbreviation: GP; general practitioner, int; intervention group, cont; control group.

Table C4. Subgroup effects on patient satisfaction with general practitioner's availability.

Availability - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	5.0 (-9.7;19.8)		38/31	-14.3 (-27.4;-1.3)	
Sexe						
Male	8/8	13.5 (-9.8;36.8)		8/12	5.4 (-18.0;28.9)	
Female	29/14	4.6 (-17.8;26.9)	0.67	30/19	-16.5 (-34.4;1.4)	0.24
Type of cancer						
Breast	17/13	2.3 (-22.0;26.5)		20/14	-14.1 (-35.9;7.70	
Colorectal	11/5	0.1 (-22.0;22.3)		9/11	-16.9 (-42.7;8.8)	
Other	9/4	21.7 (-8.7;52.2)	0.79	9/6	-15.6 (-39.7;8.5)	0.90
Age						
≤65	25/12	4.0 (-16.9;24.8)		24/19	-12.2 (-29.4;4.9)	
>65	12/10	13.3 (-7.4;33.9)	0.24	14/12	-16.2 (-37.3;5.0)	0.81
Comorbidity						
None	16/11	17.2 (-16.2;50.7)		13/15	-4.9 (-28.6;18.8)	
≥1	21/11	1.4 (-17.0;19.9)	0.53	26/16	-16.6 (-34.6;1.5)	0.45

Abbreviation: GP; general practitioner, int; intervention group, cont; control group.

Table C5. Subgroup effects on patient satisfaction with their general practitioner relationship.

Relationship - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	7.1 (-6.9;21.1)		38/31	-5.3 (-18.2;7.5)	
Sexe						
Male	8/8	15.5 (-11.3;42.2)		8/12	-5.4 (34.1;23.2)	
Female	29/14	10.9 (-9.6;31.3)	0.92	30/19	-1.5 (-19.2;16.1)	0.69
Type of cancer						
Breast	17/13	9.2 (-12.8;31.1)		20/14	1.5 (-20.1;23.2)	
Colorectal	11/5	3.1 (-21.3; 27.4)		9/11	-14.8 (-41.1;11.4)	
Other	9/4	14.9 (-14.7;44.6)	0.99	9/6	-16.9 (-33.9;0.1)	0.54
Age						
≤65	25/12	11.3 (-8.0;30.5)		24/19	-6.9 (-23.7;10.0)	
>65	12/10	13.1 (-5.6;31.8)	0.37	14/12	3.7 (-14.6;22.0)	0.60
Comorbidity	16/11	15.3 (-16.5;47.1)	0.90	13/15	-1.7 (-27.7;24.2)	0.94
None	21/11	6.2 (-11.6;24.1)		25/16	-4.5 (-22.4;13.3)	
≥1						

Abbreviation: GP; general practitioner int; intervention group, cont; control group.

Table C6. Subgroup effects on patient satisfaction with the general practitioner's technical skills.

Tech. skills - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	5.9 (-7.4;19.2)		38/30	-9.9 (-21.6;1.7)	
Sexe						
Male	8/8	11.3 (-10.0;32.5)		8/11	1.6 (-19.7;22.9)	
Female	29/14	7.4 (-12.9;27.8)	0.96	30/19	-11.4 (-27.9;5.1)	0.48
Type of cancer						
Breast	17/13	5.8 (-16.6;28.2)		20/14	-10.3 (-30.5;10.0)	
Colorectal	11/5	0.2 (-20.2;20.5)		9/10	-17.2 (36.9;2.4)	
Other	9/4	16.5 (-7.1;40.0)	0.90	9/6	-9.1 (-32.1;13.9)	0.68
Age						
≤65	25/12	9.4 (-10.0;28.9)		24/18	-8.3 (-23.8;7.3)	
>65	12/10	7.9 (-10.0;25.9)	0.68	14/12	-9.6 (-27.2;7.9)	0.79
Comorbidity						
None	16/11	13.9 (-14.7;42.5)		13/15	-5.5 (-27.7;16.6)	
≥1	21/11	2.5 (-15.0;20.1)	0.48	25/15	-12.0 (-27.7;3.8)	0.52

Abbreviation: GP; general practitioner, int; intervention group, cont; control group.

Table C7. Subgroup effects on patient satisfaction with information provision from their general practitioner.

Info. provision - GP	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	37/22	3.8 (-11.8;19.4)		37/29	-13.2 (-26.9;0.5)	
Sexe						
Male	8/8	6.9 (-21.5;35.3)		8/11	-1.4 (-19.2;22.0)	
Female	29/14	6.8 (-16.4;30.0)	0.87	29/18	-13.1 (-33.4;7.2)	0.53
Type of cancer						
Breast	17/13	3.2 (-23.4;29.7)		19/13	-16.0 (-41.4;9.4)	
Colorectal	11/5	-3.9 (-30.9;23.2)		9/10	-18.8 (-40.8;3.3)	
Other	9/4	10.7 (-14.5;23.9)	0.89	9/6	-9.7 (-33.5;14.0)	0.69
Age						
≤65	25/12	8.8 (-13.9;31.4)		24/18	-11.7 (-30.5;7.1)	
>65	12/10	4.9 (-17.5;27.3)	0.76	13/11	-8.3 (-25.7;9.0)	0.88
Comorbidity						
None	16/11	5.6 (-28.9;40.0)		13/15	-9.1 (-36.1;17.9)	
≥1	21/11	-1.4 (-20.8;18.1)	0.59	24/14	-14.1 (-33.6;5.5)	0.82

Abbreviation: GP; general practitioner, int; intervention group, cont; control group.

Table C8. Subgroup effects on patient satisfaction with nurse's interpersonal skills.

Interpersonal skills - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	-0.3 (-11.5;10.8)	0.95	30/21	7.1 (-3.4;17.6)	0.18
Sexe						
Male	7/7	-2.0 (-29.6;25.6)		7/6	11.2 (-14.3;36.7)	
Female	26/23	2.9 (-10.3;16.0)	0.88	23/15	6.5 (-5.6;18.6)	0.19
Type of cancer						
Breast	17/18	-3.4 (-17.4;10.6)		18/12	-0.1 (-13.7;13.6)	
Colorectal	11/6	9.3 (-18.3;37.0)		8/7	13.4 (-8.0;34.9)	
Other	5/6	-10.5 (-31.8;10.7)	0.98	4/2	28.6 (16.0;41.1)	0.037
Age						
≤65	21/20	3.2 (-11.9;18.2)		20/13	11.6 (-1.0;24.1)	
>65	12/10	-6.8 (-22.8;9.2)	0.88	10/8	-5.5 (-20.5;9.4)	0.44
Comorbidity						
None	12/18	-4.3 (-22.3;13.6)		11/11	1.4 (-18.1;20.8)	
≥1	21/12	1.3 (-16.3;18.8)	0.77	19/10	12.2 (-3.5;27.8)	0.15

Abbreviation: int; intervention group, cont; control group.

Table C9. Subgroup effects on patient satisfaction with nurse's knowledge and experience.

Knowledge & Experience - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	1.0 (-10.3;12.3)	0.86	30/24	10.8 (-0.3;21.9)	0.06
Sexe						
Male	7/7	10.3 (-16.4;37.0)		7/6	14.8 (-10.4;40.0)	
Female	26/23	1.2 (-12.1;14.6)	0.42	23/18	10.4 (-2.4;23.2)	0.08
Type of cancer						
Breast	17/18	-3.6 (-18.1;11.0)		18/14	6.0 (-8.7;20.7)	
Colorectal	11/6	13.7 (-12.3;39.6)		8/7	7.5 (-16.4;31.3)	
Other	5/6	-11.7 (-38.5;15.0)	0.81	4/3	41.7 (20.0;63.3)	0.008
Age						
≤65	21/20	3.1 (-13.4;19.6)		20/16	13.3 (-0.7;27.3)	
>65	12/10	-1.7 (-16.5;13.1)	0.91	10/8	2.1 (-15.5;19.7)	0.12
Comorbidity						
None	12/18	1.2 (-19.7;22.0)		11/14	1.1 (-17.3;19.6)	
≥1	21/12	-2.9 (-18.9;13.0)	0.73	19/10	13.8 (-2.8;30.4)	0.06

Abbreviation: int; intervention group, cont; control group.

Table C10. Subgroup effects on patient satisfaction with nurse's availability.

Availability - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	1.6 (-10.1;13.3)	0.79	30/22	7.7 (-3.7;19.0)	0.18
Sexe						
Male	7/7	0.0 (-26.3;26.3)		7/6	14.8 (-13.9;43.6)	
Female	26/23	4.4 (-9.7;18.4)	0.82	23/16	6.3 (-6.1; 18.8)	0.15
Type of cancer						
Breast	17/18	1.3 (-14.2;16.7)		18/13		
Colorectal	11/6	10.0 (-16.7;36.6)		8/7		
Other	5/6	-16.3 (-44.0;11.3)	0.98	4/2	[1]	0.08
Age						
≤65	21/20	3.3 (-13.1;19.8)		20/14	13.2 (-1.5;27.9)	
>65	12/10	1.0 (-14.6;16.6)	0.72	10/8	-6.9 (-21.5;7.8)	0.45
Comorbidity						
None	12/18	-3.8 (-24.6;16.9)		11/12	1.0 (-20.5;22.6)	
≥1	21/12	0.7 (-16.4;17.8)	0.65	19/10	15.0 (-0.7;30.8)	0.14

[1]Data not shown, since the residual variance is zero. Abbreviation: int; intervention group, cont; control group.

Table C11. Subgroup effects on patient satisfaction with the relationship with the nurse.

Relation - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	1.2 (-10.7;13.1)	0.84	30/24	1.2 (-9.6;12.1)	0.82
Sexe						
Male	7/7	4.4 (-23.6;32.4)		7/6	14.8 (-10.4;40.0)	
Female	26/23	3.9 (-10.2;18.1)	0.71	23/18	-2.7 (-14.9;9.6)	0.39
Type of cancer						
Breast	17/18	-1.1 (-16.9;14.7)		18/14		
Colorectal	11/6	11.7 (-14.9;38.3)		8/7		
Other	5/6	-17.3 (-42.2;7.5)	0.91	4/3	[1]	0.15
Age						
≤65	21/20	1.8 (-15.8;19.5)		20/16	7.5 (-5.5;20.4)	
>65	12/10	-0.6 (-16.4;15.1)	0.83	10/8	-14.8 (-33.6;4.0)	0.60
Comorbidity						
None	12/18	-1.6 (-21.6;18.3)		11/14	-2.2 (-22.5;18.0)	
≥1	21/12	1.1 (-17.8;19.9)	0.75	19/10	2.0 (-14.2;18.3)	0.72

[1]Data not shown, since the residual variance is zero. Abbreviation: int; intervention group, cont; control group.

Table C12. Subgroup effects on patient satisfaction with nurse's attention.

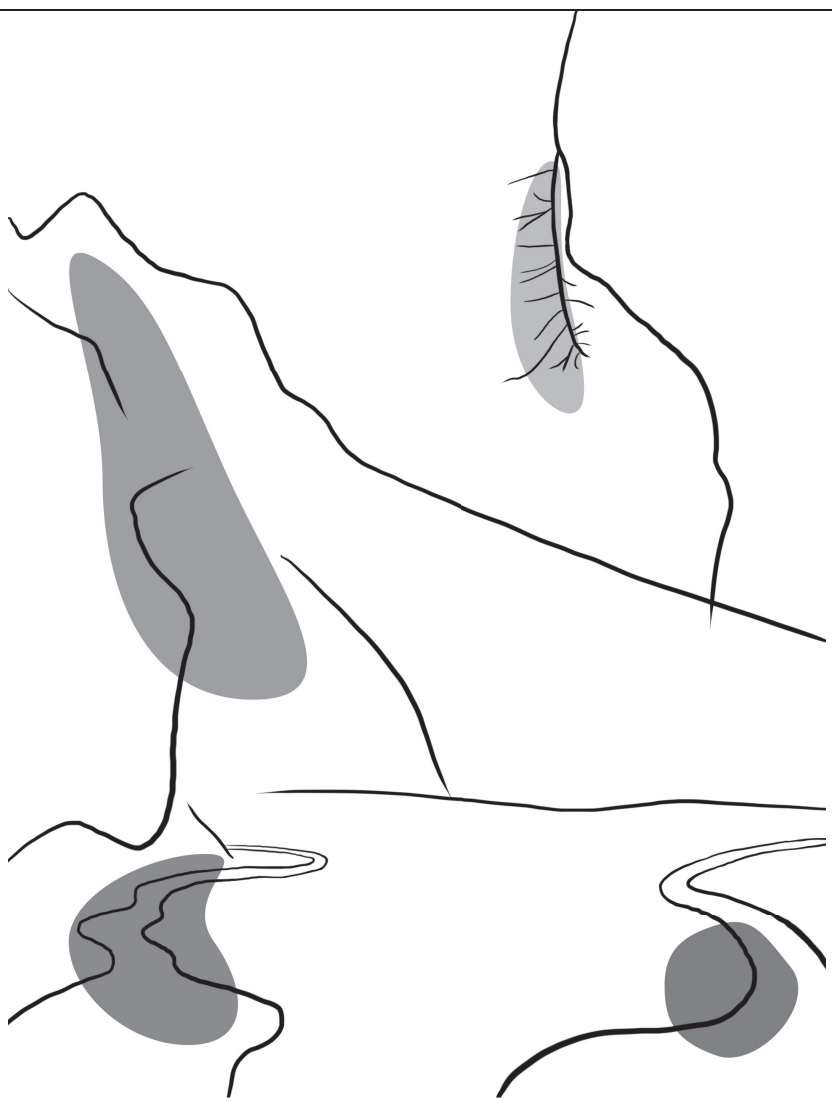
Attention - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	0.2 (-11.9;12.4)	0.97	30/24	9.6 (-0.3;19.4)	0.06
Sexe						
Male	7/7	8.8 (-19.7;37.3)		7/6	7.8 (-18.6;34.2)	
Female	26/23	0.3 (-14.3;14.9)	0.72	23/18	10.9 (0.08;21.7)	0.15
Type of cancer						
Breast	17/18	-3.9 (-19.4;11.7)		18/14	5.4 (-7.2;18.1)	
Colorectal	11/6	18.2 (-7.2;43.6)		8/7	7.5 (-14.4;29.4)	
Other	5/6	-21.9 (-49.3;5.4)	0.92	4/3	33.3 (11.7;55.0)	0.012
Age						
≤65	21/20	-1.2 (-18.6;16.3)		20/16	11.5 (0.79;22.2)	
>65	12/10	-2.3 (-18.8;14.2)	0.95	10/8	1.2 (-14.8;17.2)	0.10
Comorbidity						
None	12/18	-1.3 (-21.6;18.9)		11/14	7.0 (-7.1;21.1)	
≥1	21/12	-0.4 (-19.2;18.5)	0.71	19/10	13.6 (-3.8;31.0)	0.04

Abbreviation: int; intervention group, cont; control group.

Table C13. Subgroup effects on patient satisfaction with nurse's willingness to help.

Willingness - Nurse	N int./ N cont.	**T3 estimated mean difference int. vs cont. (95% CI)**	**p value**	N int./ N cont.	**T5 estimated mean difference int. vs cont. (95% CI)**	**p value**
Total effects	33/30	1.4 (-10.7;13.5)	0.82	30/24	7.5 (-3.5;18.5)	0.18
Sexe						
Male	7/7	8.8 (-27.4;45.1)		7/6	7.0 (-23.2;37.3)	
Female	26/23	2.0 (-11.7;15.8)	0.64	23/18	8.4 (-3.7;20.5)	0.29
Type of cancer						
Breast	17/18	-4.4 (-18.3;9.4)		18/14	4.0 (-10.4;18.4)	
Colorectal	11/6	18.2 (-11.1;47.4)		8/7	7.1 (-17.9;32.1)	
Other	5/6	-13.3 (-46.8;20.2)	0.79	4/3	25.0 (-16.9;66.9)	0.08
Age						
≤65	21/20	3.3 (-13.9;20.5)		20/16	10.0 (-3.1;23.0)	
>65	12/10	-3.1 (-19.8;13.5)	0.87	10/8	-0.9 (-15.4;13.5)	0.31
Comorbidity						
None	12/18	0.8 (-19.3;20.9)		11/14	2.2 (-15.7;20.1)	
≥1	21/12	2.7 (-15.8;21.3)	0.66	19/10	17.4 (-0.3;35.0)	0.08

Abbreviation: int; intervention group, cont; control group.



CHAPTER 7

General Discussion

Ietje Perfors

Aim of this thesis

This thesis focussed on structural involvement of the general practitioner (GP) in the cancer care pathway. On this topic, we assessed the patients' needs (Chapter 2), gathered the available evidence from interventions aiming to achieve this (Chapter 3), and presented the design of the GRIP intervention (Chapter 4). GRIP aimed to improve primary care involvement from diagnosis onwards and included two components: First, patients were offered a Time Out consultation (TOC) with the GP, aimed to support shared decision making (SDM) on cancer treatment. Second, patients were offered structured guidance during and after treatment by the GP and a homecare oncology nurse. The effectiveness of the GRIP intervention was assessed in a large randomised controlled trial (RCT) in the region of Utrecht among cancer patients treated with a curative intent, involving all hospitals, GPs and homecare organisations (Chapters 5 and 6).

In this final chapter, the main results are summarized. We also reflect on the methodological and organisational challenges we encountered. Finally, we describe lessons learned and suggest a roadmap to enlarge the role of primary care in the cancer care path.

Main findings

In a large survey among Dutch cancer patients, the call for more GP involvement shortly after cancer diagnosis was confirmed. The results also revealed that patients presently feel that their need for SDM support by the GP is inadequately met (Chapter 2). Our systematic review of (randomised) controlled trials on interventions to improve GP involvement in patients with cancer treated with a curative intent demonstrated that various types of interventions were reported, but most had low uptake and their results were heterogeneous. However, a shared observation was that patients generally reported more satisfaction with care when they received an intervention in which the GP was involved (Chapter 3).

The evaluation of the GRIP intervention facilitated detailed conclusions for each of the two components. The concept of a TOC with the GP was well accepted, given the fact that 4 out of 5 patients scheduled a TOC. Adequate timing of a TOC, however, proved challenging in the current healthcare system. The majority of patients (82%) in the GRIP trial had their TOC with the GP after the treatment decision in the hospital was already made.

This poor timing probably also explains the finding that patients in the intervention arm experienced reduced involvement in the treatment decision making process

The second part of the GRIP intervention, structured guidance during treatment by the GP and the homecare oncology nurse, was also well accepted, given the fact that almost 70% of the participants had at least 1 contact with the nurse. But again, implementation proved suboptimal, as almost half of the patients (46%) discontinued the schedule of follow-up visits by the homecare oncology nurse after treatment completion. The poor implementation of the two components affected the overall results of the GRIP program in the evaluation. After one year the intervention group had only a slightly increased number of contacts with the GP practice, and an increased use of the emergency department. We also found that, although satisfaction with overall care was comparable between the two groups (both high), patients in the intervention group were less satisfied with their GP. This may be explained by the fact that the increased GP involvement did not to meet their expectations (chapter 6).

We conclude that, although increased involvement of the GP and homecare oncology nurse clearly did address the needs of the cancer patient, implementation of the TOC and scheduled homecare oncology nurse follow-up visits in primary care needs to be improved in order to reach the intended ambition. This requires a less tight time-schedule in the cancer care path where patients, following the primary diagnosis, are supported by a consultation with their GP to make a well-balanced decision. The suboptimal adherence to the intended homecare oncology nurse consultations during treatment needs further evaluation.

Lessons learned

Disappointingly, the GRIP program did not show favourable outcomes in the RCT. Several lessons were learned that may help to improve future interventions aiming at enlarging the involvement of the GP in cancer care.

The concept of a TOC between the cancer diagnosis and treatment choice, although broadly supported, does not seem to fit in the cancer care pathway as it is presently organised. One of the key factors is a lack of time between diagnosis and therapy choice. This is related to two factors. For most ***patients*** the cancer diagnosis is regarded as an imminent threat of life expectancy, and immediate removal of the cancer is perceived as mandatory. Waiting times for treatment are associated with even more psychological burden. To limit this burden, oncologists have put in every effort to limit the time between diagnosis and start of treatment[1] and ***hospital***s have organised 'short track routes' for treatment planning after cancer diagnosis, including frequent multidisciplinary team discussions and fast treatment schedules. These efforts leave limited time for deliberation with the patient about the preferred treatment choice, even in hospital practice. In addition, it is even more challenging to get the GP involved in supporting the patient in the decision making process. There seems wide recognition by patients and professionals for the added value of the GP in empowering the patient for SDM[2, 3] given the longitudinal relation with the patient and the importance of individual context and personal preferences. In the current cancer care pathway, integration of a TOC before treatment choice is only possible if primary and secondary care actively match appointment schedules, and if oncologists timely transfer information to the GP. In addition, all professionals should communicate to the patient that SDM is of key importance, thereby jointly communicating that the GP is best positioned to support the patient in decision making and that the extra time required for the GP visit will not affect life expectancy.

As for the primary care guidance during and after treatment, the suboptimal adherence to the scheduled homecare oncology nurse consultations was most likely related to a suboptimal fit between the content of the GRIP follow-up

care and the patients' expectations. It seems that the intervention may have raised expectations about GP involvement in the intervention group, that were not met during the trial. Our intervention registrations indicate that, while we presented the follow-up care as a joint effort of the primary care team, the homecare oncology nurse, and not the GP became the main provider of follow-up care in daily practice. This mismatch between expectations and reality, namely being seen by the GP instead of the homecare oncology nurse, may have resulted in disappointment, and negatively influenced the perception by the patients of the GP's role. We did not assess patients' expectations, but literature shows that met expectations positively influence satisfaction measurements.[4] This suboptimal role distribution between GP and homecare oncology nurse was probably due to the fact that the setting for their cooperation was new. GP's and home care nurses are used to working together in elderly care, in home care and in palliative care, and also in these fields has taken time to reach agreement about professional roles and responsibilities, and define the optimal model of collaboration. Generally, the process of interdisciplinary task delegation and differentiation in healthcare is complex and implementation is time consuming. It needs to be matched with the patients' expectations, and at an organisational level, it needs to be facilitated by adequate financial reimbursement, information exchange, staffing and training. We would strongly advise all these aspects to be further developed, in order to optimize the collaboration between GP and home care nurse in the follow-up care of cancer patients outside the hospital.

Evaluation of complex healthcare interventions; design and methodological challenges

Interventions intended to improve primary care involvement, such as the GRIP intervention, are complex interventions. Complex interventions are generally multifaceted and include several interacting components.[5] This requires conscious design and adequate evaluation methodology. The MRC Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health, provides guidance for the design and evaluation of complex interventions (Figure 1).[6]

Following the steps of the MRC Framework, we now critically evaluate the process of the GRIP intervention, aiming to provide guidance or improved intervention models targeting GP involvement in cancer care in the near future.

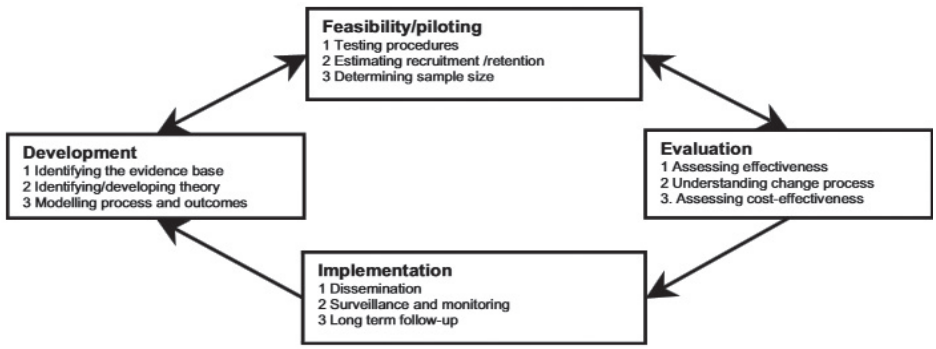


Figure 1. Key elements of the development and evaluation process. Source: The MRC Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health (depicted from MRC[6])

1. Development

In retrospect, earlier identification of the available evidence from the literature could have improved the "Development process" (figure 1) of the GRIP intervention. Choices in the design of the GRIP trial were based on several recent publications, e.g. Wagner et al., but not on systematic review of the literature.[7] If the systematic review on primary care interventions in cancer care was performed upfront, it could have informed the GRIP developing team that f.i. the outcome 'quality of life' is usually difficult to improve; that in general a low uptake of complex interventions is to be expected and that special attention for vulnerable populations is warranted, given the fact that effectiveness in these subgroups is often higher.

In addition, according to the MRC Framework it is important to "develop a theoretical understanding of the likely process by using existing evidence", for example supplemented by interviews with stakeholders. We mainly consulted stakeholders, formal organisational reports and had informal conversations with the GPs, homecare oncology nurses, specialists and patient advocates, to comment on our present theoretical framework. We

involved the stakeholders in the early stage of development of the GRIP trial, in order to adjust the implementation of the intervention to the local setting. For example, from the original theoretical framework we aimed at an intervention that substituted most of the psychosocial care provided by the hospital. However, the participating hospitals preferred not to adjust their usual care. As a result, the focus of the intervention changed and the GRIP program became additional care instead of substituted care.

Regarding the development process of the GRIP intervention, the compliance by patients shows that the TOC and the involvement of a homecare oncology nurse do address a need, but their organisation and content was not sufficiently built on understanding of the underlying problem. Effective communication between primary care and hospital care and joint planning is vital to enable a true transmural shared care approach.

2. Feasibility

A feasibility study was not conducted. Instead, we tried to promote acceptance by adjusting the intervention to the local needs and to fit in within the local healthcare pathways. Yet, conducting a pilot or feasibility study would have provided the research team with valuable information, such as the limitation of the timeframe in which the TOC should be performed, and might have resulted in adjustments of the GRIP intervention. A pilot study could have protected us from too optimistic estimates of subject recruitment and we might have noticed earlier that the TOC could not be properly implemented in the present care system. A recent pilot project has shown that if a secondary care worker (e.g. secretary or nurse) is made responsible for scheduling a GP consultation between diagnosis and therapy choice, the chances of a timely TOC dramatically improve (unpublished results).

3. Evaluation

When evaluating a complex intervention, the MRC framework suggests a study design with randomisation, as this is the most robust method of preventing selection bias. In accordance with this recommendation

we designed the GRIP evaluation in a RCT design. This brought several methodological challenges.

The RCT showed a higher drop-out in the intervention group (23%) compared to the control group (10%), which may have caused selection bias. Reasons for drop-out in the intervention group were 'felt to well' (n=5) and 'no extra care needed' (n=3). This may have left selected patients in the intervention group with lower baseline functioning, resulting in worse outcome in the intervention group. However, we did not find differences in quality of life between the two study groups.

The GRIP trial focuses on the patient experiences and uses a wide range of subjective outcomes measures. The use of PROMs in this study may have affected the results. Patients were not blinded, which could have influenced the outcomes, especially the subjective ones. We hypothesized that the intervention may have raised expectations about GP involvement in the intervention group, that were not met in practice since the homecare oncology nurse was usually the primary care professional involved. This may have caused disappointment among patients in the intervention arm, resulting in an extra negative evaluation. We did not assess these expectations, but literature shows they have an influence on satisfaction measurements.[8, 9] Chow et al. 2009 even suggest a paradox between patient satisfaction and quality of care, in which patient satisfaction might also decrease if quality of care increases, due to the higher expectations.[10] In future evaluations optimal blinding, e.g. by using a cluster randomized or stepped wedge design, and the measurement of expectations should be aimed for, especially when assessing satisfaction as an outcome. Some constructs that might be affected by the intervention are difficult to measure. The hypothesis behind GRIP was that the intervention would result in more patient centred care and in more continuity of care. Both of these constructs proved difficult to measure.[11, 12]

Even though RCTs are reputed for providing the most robust effect evaluation alternative designs could be considered. To prevent contamination of the control group we discussed a cluster randomized trial.

However, we chose to randomise on patient level to ensure optimal comparison of study arms. Therefore, we used a conventional RCT design. We found little contamination in the GRIP trial.

Recently, action research is suggested in case the intervention under study is not yet optimal.[13] In action research, interventions are iteratively improved during the course of research, by continuous adaptations to local settings. In case a format is found that seems to include all the basic elements for success, a rigid but robust RCT design could be the next step.

The MRC framework also recommends to assess cost-effectiveness. As we did not find positive effects when considering the primary outcomes, the cost-effectiveness analysis was omitted. For future interventions, we think that cost-effectiveness analyses are important since they provide vital arguments to (not) adopt policy changes. For such analyses, we advise a combination of questionnaires and healthcare registry extractions, to complement each other for the assessment of healthcare use.

We used the iMTA-PCQ questionnaire for productivity costs and medical records for healthcare use, and found that these sources of information complement each other.

4. Implementation

Although the results do not allow large scale implementation of the GRIP intervention, some important lessons can be learned for future implementation of TOC and primary care involvement in clinical practice.

If future implementation of primary care involvement in cancer care is aimed for, broad support should be created to change the healthcare pathway where necessary and to strive for a more integrated and collaborative approach between healthcare professionals. The MRC framework states that "Successful implementation depends on changing behaviour – often of a wide range of people. This requires a scientific understanding of the behaviour that needs to change, the factors maintaining current behaviour and barriers and facilitators to change".[6] In the GRIP RCT we aimed for integrated cancer care

but we could only realise an additional care intervention, since adjustments in the cancer care pathway in the hospital were not broadly supported and difficult to realise.

Facilitation of contextual factors by healthcare management and policy makers such as dedicated time, staff and financial reimbursement is vital for successful implementation.[14] Within the Dutch healthcare system there was financial reimbursement present to support implementation of the GRIP trial. At first instance, a lack of time was foreseen for GP's, but this was overcome by involving the homecare oncology nurse. However, this might have resulted in dissatisfaction of patients.

In conclusion, although we did follow the MRC framework when designing and evaluating the GRIP intervention, we did not complete all the necessary steps to the required level of detail. In retrospect, better planning of the intervention (i.e., better coordination between all stakeholders involved), outcomes, and especially a pilot study might have prevented some of the implementation problems that we encountered.

Primary care involvement in cancer care; future developments and recommendations

Primary care involvement in future cancer care remains of growing importance. Worldwide, the number of patients that have or had cancer continues to rise, a growth which is not expected to decline in future years. At the same time, scientific breakthroughs result in gradually expanding opportunities in diagnostics, treatments and in ways of supportive and palliative care. Cancer patients are therefore exposed to an increasing number of options, sometimes requiring difficult choices to be made in determining their personal cancer care path. As the general practitioner, of all healthcare providers, usually is the most 'nearby' healthcare professional, who is most familiar with comorbidities and the psychosocial and cultural issues of their patients, structural involvement of the GP in the cancer care path could help cancer patients to make well-balanced choices.

Therefore, the GP is foreseen to play a larger role for patients, both during and after (curative) cancer treatment.

Since cancer increasingly has a chronic instead of an acute nature, and since 70% of cancer patients suffer from other co-morbidities such as cardiovascular, lung, or metabolic diseases, in the future cancer care may be best delivered in the home environment, and from the hospital only when needed. Combined with the increased potential to deliver cancer treatment care at the patients' home, a substantial part of the present cancer care pathway may even be transferred to primary care. If so, a transmural shared cancer care model with continuous GP involvement is adamant.

Based on the experiences from the GRIP study, we have the following recommendations to facilitate these developments in future:

- Collaborative effort is needed between the oncologist and the GP and their teams to ensure that the GP's intervention is compatible to the care provided in hospital. Treating physicians and GP's have to develop joint commitment to change the current care path, and support the implementation of this change in their daily practice.
- The collaboration between the GP and the home care oncology nurses in the GRIP intervention was not yet matured. The task differentiation and delegation in cancer care needs to be further developed, both interprofessionally as well as between general practice and hospital care. Alternative approaches could be to organise a shared practice between primary care and hospital oncology nurse in primary care, or transmural care paths with oncologist consultation sessions in general practice.
- Future interventions should be piloted first before a large scale evaluation is developed and assessed.

Primary care involvement in cancer care is a developing field. This provides a lot of new opportunities for new cancer care models, new interprofessional and multidisciplinary collaborations and better patient participation. Even though the potential and need for primary care involvement seems obvious, we showed that the design, evaluation and implementation of new

interventions in the cancer care continuum is challenging. This thesis, and the GRIP study that lies at its foundation, has exposed many barriers and opportunities, and provided 'lessons learned'. This knowledge, can now be used as a starting point for continuous development of interventions to support primary care involvement in cancer care.

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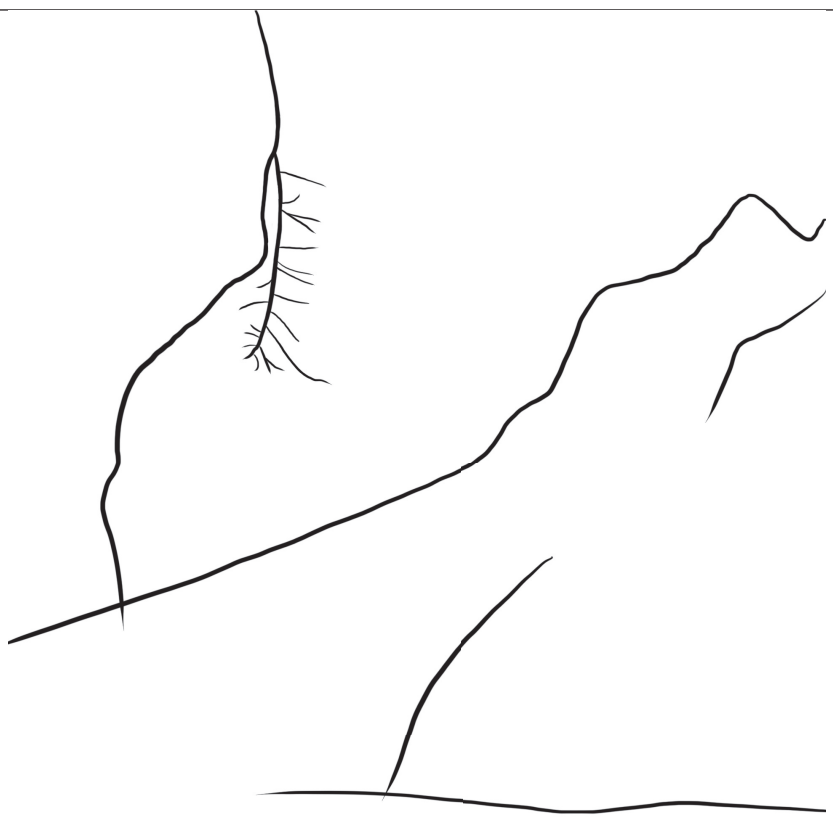

APPENDICES

Summary

As cancer incidence is increasing and prognosis is improving, more patients live longer with cancer and experience more late effects of treatment, in the presence of co-existing chronic conditions. Consequently, the nature of cancer treatment is shifting towards chronic disease management. This shift requires more personalised and integrated care, based on individual preferences and medical profile. In primary care based healthcare systems, general practitioners (GPs) may be best positioned to provide continuous, personalised and integrated care during the cancer care continuum. GPs typically have a longstanding and personal relationship with their patients and are up to date with their patients' comorbidities. Additionally, they are well equipped to provide personalised disease management within the context of the patients' medical history and personal preferences. Therefore, patients, healthcare professionals and policy makers suggest a more prominent role of the GP in the guidance of patients during their cancer pathway with a focus on empowerment, psychological and lifestyle support and follow-up care in the chronic disease stage. Even though a substantial role for primary care is advocated in the Netherlands and internationally, involvement of primary care in cancer care remains sporadic and unstructured. Attempts to structurally involve primary care during cancer treatment have hardly been successful.

This dissertation has two aims. The first aim of this thesis is to explore the needs and experiences of cancer patients, regarding GP involvement after cancer is diagnosed. The second aim is to investigate the effects of the GRIP intervention on patient outcomes and healthcare use for patients treated with curative intent. The GRIP intervention consists of structured care provided after diagnosis of cancer by a primary care team, including the GP and a homecare oncology nurse (HON). The aim of the GRIP intervention is to provide structured primary care and facilitate personalised continuous primary care to patients with cancer.

Current needs and experiences of cancer patients regarding GP involvement after diagnosis.

First, we explored the patients' experiences and needs regarding GP involvement after a cancer diagnosis for patients treated with curative and palliative intent (Chapter 2). In a large survey among Dutch cancer patients distributed by the Dutch Federation of cancer patient organizations (NFK), patients' call for more GP involvement shortly after cancer diagnosis was confirmed. Among 4,763 (former) cancer patients, 59% (N=2,804) expressed a need for GP involvement in cancer care, Of these patients, 79% experienced GP involvement. Regarding GP involvement in shared decision making (SDM), 82% of the patients (N=3,724) expressed that the GP should "listen to patient's worries and considerations", 69% (N=3,130) to "check patient's understanding of information", 66% (N=3,006) to "discuss patient's priorities in life and the consequences of treatment options for these priorities", and 67% (N=3,045) to "create awareness of the patient's role in the decision making". This GP involvement occurred in 47%, 17%, 15% and 10% of these patients, respectively. Patients' needs for GP support in fundamental SDM steps remained largely unmet. Therefore, GPs should be made aware of these needs and enabled to support their patients in SDM.

Current interventions to gain more GP involvement

To explore the current knowledge of the effects of primary care interventions aimed to involve the GP shortly after cancer diagnosis we conducted a systematic review of clinical trials (Chapter 3). The small number of clinical trials we found examined various types of interventions. The studies reported a low uptake of intervention and heterogeneous results. However, results suggest a positive effect of GP involvement on patient satisfaction with care, but not on quality of life. Additional effects for vulnerable subgroups were found. More robust evidence for tailored interventions is needed to enable efficient and effective involvement of the GP during curative cancer treatment.

The GRIP intervention

In close collaboration with NFK, the University Medical Centre Utrecht and regional primary care healthcare workers we developed the GRIP intervention with structural involvement of the primary care team after cancer diagnosis. The study protocol of the GRIP trial is presented in ***chapter 4***. The GRIP trial is a multicentre, two-arm randomised controlled trial in the region of Utrecht, The Netherlands. Newly diagnosed patients with curable cancer (breast, lung, colorectal, gynaecologic, melanoma) from four Dutch hospitals were included. All patients received care as usual. The intervention arm received additional structured follow-up consisting of two parts: 1) a Time Out consultation (TOC) with the GP before onset of treatment to empower the patient for SDM with their specialist, and 2) support during and after cancer treatment provided by the HON in close cooperation with the GP. Repeated questionnaires, filled in by the participants, were assessed within the 1-year study period. These questionnaires were assessed at inclusion (T0), after 2 weeks (T1), after 6 months or at completion of active treatment (T3) and 3 months after active treatment (T5). Data of healthcare utilisation was retrieved from routine care data registrations in primary care and hospitals.

First, we evaluated the first part of the GRIP intervention (Chapter 5), the TOC. As described above, patients in the intervention arm were offered to schedule a TOC with their GP immediately after they were diagnosed with cancer and prior to their treatment decision. Two weeks after inclusion, we evaluated the experienced SDM, information provision and self-efficacy. Our results showed that most patients were motivated to plan a TOC, since 80.5% (n=62) of the patients in the intervention group had a TOC. Yet, planning of a TOC seems challenging as 82.3% (n=51) of the TOCs took place after treatment decision. Perceived SDM was lower in the intervention group (0-100 scale, higher values equal higher experienced SDM: mean difference of -8.9 (95% CI, 0.6-17.1)) compared to the control group. Among those with a TOC before treatment decision (n=11), perceived SDM was comparable to the control group (66.5 SD ±27.2 vs 67.9 SD ±26.1). Since these groups were too small, effects of a timely TOC could not be established. Planning of the TOC should be optimised, and future research should establish if an adequately timed TOC results in improved SDM for cancer patients.

In chapter 6, the second part of the GRIP intervention is evaluated. We assessed the effects of guidance by an HON in collaboration with the GP, during and after cancer treatment, on the primary outcomes of patient satisfaction and healthcare use. Secondary outcomes were quality of life, mental health and self-efficacy. We found that 68% of the intervention patients had at least one HON contact, which showed that the initial acceptance was good. However, the implementation of HON contacts was suboptimal as almost half of the patients (46%) did not complete the recommended contacts with HON after treatment. Overall patient satisfaction with care in both study groups on T3 and T5 was high (an average score of 8 on the scale 0-10). Three months after completion of oncological treatment (T5), satisfaction with the GP was significantly lower in the intervention group compared to the control group measured on 3 out of the 6 subscales (on a 0-100 scale, with higher satisfaction at higher values). We found mean differences between the intervention and control group of -14.2 (95% CI -27.0;-1.3) for the quality of the GP, -15.9 (-29.1;-2.6) for the availability of the GP and -15.2 (95% CI -29.1;-1.4) for the provision of information. This may be the result of sub-optimal expectation management, caused by the newly introduced care path where the division of roles between GP and HON was not yet matured. Patients in the intervention group visited GP practices and emergency care more often than the control group (RR 1.3 (95% CI 1.0;1.7) and RR 1.70 (95% CI 1.0;2.8) respectively). The other outcomes did not show differences between the intervention and the control group. In conclusion, the GRIP intervention, which aimed to better involve a primary care team during and after cancer treatment, slightly increased the number of contacts in primary care. Yet, timely planning of the TOC proved to be challenging and patient satisfaction with care did not improve. The emergency department was also visited more often. The high degree of acceptance of both components of the intervention (TOC and HON) suggests that such an intervention meets the needs of the patient. The sub-optimal implementation and effects indicate that the intervention needs to be further improved. Future research should further optimise and evaluate the structure and implementation of the intervention.

In conclusion, patients express a need for GP support after their cancer diagnosis. Particularly for SDM, GP support is now experienced infrequently.

Evidence for effective interventions aimed at GP involvement is limited and the GRIP intervention does not yet offer a conclusive solution.

It seems that the TOC with the GP between diagnosis and choice of therapy meets the needs of the cancer patient. Yet, the integration of TOC in daily care pathways and the collaboration between GP and HON needs to be improved. For improvement of both the intervention and research, we advise to follow the steps of the MRC model for evaluation of complex interventions. This model highlights elements such as development, feasibility, evaluation and implementation. If development of a structured primary care intervention in cancer is strived for, it is recommended to critically examine the conditions for successful embedding a TOC in the oncological pathway, before it can be effectively integrated.

Furthermore, the desired role of the GP and HON after the diagnosis of cancer should be further examined, in order to better provide support from the primary care team. After development, pilot studies should also be executed to test and optimise the "feasibility" of the intervention.

Based on this dissertation, we have some recommendations to facilitate the future development of primary care involvement:

- Consider adequate structured cancer care not as a primary care goal, but as a shared goal for personalised cancer care. This means that effective GP involvement after diagnosis should be developed and implemented together with both primary care teams and hospital teams.
- The task differentiation and delegation in cancer care needs to be further developed, both interprofessionally as well as between general practice and hospital care. For example, the collaboration between the GP and the home care oncology nurses in the GRIP intervention was not yet matured.
- Complex interventions such as shared cancer care, in which the primary care is given a structural role, will have to be subject to continuous evaluation. We recommend that a new approach is always evaluated in a pilot study before a large-scale study is performed.

Nederlandse Samenvatting

In de oncologische zorg vinden veranderingen plaats. Door de vergrijzing van de maatschappij en de hogere incidentie van kanker onder ouderen, stijgt het aantal patiënten dat met kanker gediagnosticeerd wordt. Daarnaast zorgt eerdere opsporing en betere behandeling ervoor dat deze mensen langer leven ten opzichte van voorheen. De behandeling en begeleiding van de korte - en lange termijn effecten zijn in deze nieuwe patiënten, die met kanker als 'chronische ziekte' moeten leven, extra uitdagend vanwege de hoge prevalentie van comorbiditeiten. Hiernaast is het aantal behandel mogelijkheden de laatste jaren toegenomen en complexer geworden, waardoor een gepersonaliseerde benadering mogelijk en nodig is. Doel hierbij is om zowel patiënt- en tumor karakteristieken als persoonlijke voorkeuren en wensen mee te nemen in het behandel plan. Gedeelde besluitvorming, oftewel 'shared decision making' (SDM), lijkt de aangewezen manier om de kanker specifieke voorkeuren voor behandeling optimaal in balans te brengen met de persoonlijke prioriteiten en voorkeuren van de patiënt. Hiermee is SDM de manier om tot meer gepersonaliseerde keuzes voor therapie te komen.

In zorg systemen waar de huisarts een poortwachtersrol heeft, zoals in Nederland, heeft een huisarts vaak een langdurige en persoonlijke zorgrelatie met de patiënt en zijn/haar gezinsleden. Hierdoor lijkt de huisarts in een ideale positie om patiënten met kanker te begeleiden in het maken van een gepersonaliseerde behandelkeuze en om hiernaast continuïteit van zorg te creëren tijdens en na de behandeling. Zowel beleidsmakers, patiënten als huisartsen promoten meer betrokkenheid van de huisarts in het oncologische traject van zowel de curatief als de palliatieve te behandelen patiënt.

Echter, wetenschappelijk bewijs voor de optimale opbouw en de effecten van gestructureerde begeleiding van patiënten met kanker door de huisarts, zijn nauwelijks beschikbaar.

Daarom heeft dit proefschrift twee doelen.

Het eerste doel is om in kaart te brengen wat de huidige behoeften en ervaringen zijn van patiënten met kanker, betreffende de inmenging van huisartsen in de zorg na de diagnose kanker. Het tweede doel is om de effecten van gestructureerde huisartsbegeleiding na de diagnose kanker, zoals vormgegeven in de zogenoemde GRIP interventie, te onderzoeken voor patiënten die curatief worden behandeld. De GRIP interventie bestaat uit gestructureerde zorg door een eerstelijnsteam, met als doel om gepersonaliseerde zorg en continuïteit van zorg te bieden aan patiënten met kanker.

Behoeften en ervaringen van patiënten met kanker, met betrekking tot huisarts betrokkenheid.

Allereerst is het belangrijk om te onderzoeken wat patiënten belangrijk vinden en nodig hebben van hun huisarts direct na de diagnose kanker (Hoofdstuk 2). Middels een nationale online enquête, gedistribueerd door de Nederlandse Federatie voor Kankerpatiëntenorganisaties (NFK), zijn de ervaringen en behoeften van patiënten nagegaan, betreffende de betrekking van hun huisarts in de oncologische zorg in het algemeen en specifiek bij de gezamenlijke besluitvorming rondom de behandeling. Aan deze enquête deden zowel curatief als palliatief behandelde patiënten mee. Meer dan de helft 59% (n=2,804) van de (behandelde) patiënten met kanker gaf aan dat ze graag de huisarts betrokken zien in de oncologische zorg. Van deze groep patiënten, gaf 79% aan dat zij daadwerkelijk huisarts betrokkenheid hadden ervaren. Hiernaast wensten patiënten verschillende belangrijke onderwerpen voor SDM te bespreken; 82% (n=3,724) van de patiënten gaf aan behoefte te hebben dat de huisarts "luistert naar zorgen en overwegingen over diagnose, behandeling en gevolgen daarvan", 69% (n=3,130) gaf aan dat de huisarts "moet vragen of de informatie over diagnose, behandeling en de gevolgen daarvan begrepen worden", 66% (n=3,006) dat de huisarts "moet uitleggen dat hun mening belangrijk is bij het maken van een keuze voor een behandeling" en 67% (n=3,045) gaf aan dat hun huisarts "moet bespreken wat belangrijk wordt gevonden in het leven en welke gevolgen de behandeling van kanker daarop kan hebben". Ondanks behoefte, was de ervaring van de

patiënten dat deze ondersteuning vaak ontbrak. Zij ervoeren bespreking van deze onderwerpen in respectievelijk 47%, 17%, 15% en 10% van de gevallen. Er is mogelijk meer bewustzijn nodig onder huisartsen dat patiënten deze behoeften hebben, om zo hun patiënten te kunnen ondersteunen bij SDM.

Bestaande interventies om huisarts betrokkenheid te vergroten

Om inzicht te krijgen in de bestaande interventies en bewezen effecten van eerstelijnsinterventies die meer huisarts betrokkenheid na de diagnose kanker beogen te stimuleren, hebben we een literatuurstudie gedaan (Hoofdstuk 3). De gevonden interventies die bedoeld zijn om de huisarts actief te betrekken bij de curatieve behandeling van kanker zijn schaars en divers. De gevonden onderzoeken suggereren dat de betrokkenheid van de huisarts een positief effect heeft op de patiënt tevredenheid, maar geen effect lijkt te hebben op de kwaliteit van het leven. Enkele onderzoeken vonden meer effect in kwetsbare subgroepen. Er blijkt meer onderzoek en bewijs nodig te zijn in welke vorm de huisarts efficiënt en effectief betrokken kan worden bij de curatieve behandeling van kanker.

De GRIP interventie

In nauwe samenwerking met de Nederlandse Federatie van Kankerpatiëntenorganisaties (NFK), het Universitair Medisch Centrum Utrecht en regionale eerstelijnsgezondheidswerkers ontwikkelden we een gestructureerd zorgpad door een eerstelijnszorgteam na een kankerdiagnose. Dit zorgpad oftewel de GRIP-interventie hebben we ge-evalueert in een gerandomiseerde gecontroleerde studie (RCT), de GRIP-studie, in de regio Utrecht in Nederland. Het protocol van deze studie is beschreven in ***hoofdstuk 4***. Nieuwe patiënten die in opzet curatief behandeld werden voor verschillende soorten kanker (borstkanker, longkanker, colorectale kanker, gynaecologische kanker of melanoom) uit vier Nederlandse ziekenhuizen namen deel aan de GRIP-studie. We analyseerde o.a. de effecten op patiënttevredenheid en zorggebruik. Binnen de GRIP-studie kregen alle patiënten gebruikelijke zorg. Indien gerandomiseerd naar de interventie arm kreeg de patiënt gestructureerde zorg aangeboden die bestond uit twee componenten. De eerste component was een Time Out consult (TOC), dat is

een gesprek met de huisarts tussen de diagnose en definitieve therapiekeuze, waarbij de patiënt ondersteund kan worden bij gezamenlijke besluitvorming met de specialist. De tweede component bestaat uit begeleiding van een eerstelijnsoncologie verpleegkundige (EOV) in samenwerking met de huisarts. De uitkomsten werden binnen 1 jaar na inclusie gemeten aan de hand van door patiënten ingevulde vragenlijsten. Deze vragenlijsten werden afgenomen ten tijden van inclusie (T0), na 2 weken (T1), na 6 maanden of bij voltooiing van de actieve behandeling (T3) en 3 maanden na actieve behandeling (T5). Data over zorggebruik kwamen uit de routine registraties in de eerste lijn en het ziekenhuis.

Eerst evalueerden we het eerste deel van de GRIP-interventie (Hoofdstuk 5), de TOC. Zoals hierboven beschreven werd aan de patiënten in de interventie-arm aangeboden om een TOC te plannen met hun huisarts direct na hun diagnose kanker en voorafgaand aan therapiekeuze. We evalueerde twee weken na inclusie de ervaren SDM, informatievoorziening en zelfredzaamheid. Het lijkt erop dat patiënten, indien hen een TOC aangeboden wordt, gemotiveerd zijn om deze te accepteren, aangezien 80,5% (n=62) van de patiënten in de interventiegroep een TOC had. Echter, het tijdig plannen van een TOC blijkt een uitdaging, namelijk 82,3% (n=51) van de geplande TOC's vond plaats ná de behandelkeuze. We vonden dat de ervaren SDM lager was in de interventiegroep ((schaal 0-100, hogere waarde betekend meer ervaren SDM): het gemiddelde verschil -8,9 (95% CI, 0,6-17,1)) ten opzichte van de controle groep. Bij degenen met een TOC vóór de behandelkeuze (n=11) was de ervaren SDM vergelijkbaar met de controlegroep (66,5 SD ±27,2 versus 67,9 SD ±26,1), omdat deze aantallen te klein zijn konden de effecten van een juist geplande TOC niet worden vastgesteld. Om de effecten van een tijdig geplande TOC wel te kunnen evalueren zou de inbedding van de TOC in het oncologisch zorgpad geoptimaliseerd moeten worden waarna vervolg onderzoek moet uitwijzen of een juist geplande TOC leidt tot betere SDM bij patiënten met kanker.

In ***hoofdstuk 6*** wordt het tweede deel van de GRIP interventie geëvalueerd, waarbij we de effecten van de begeleiding, tijdens en na de behandeling voor kanker, door een EOV in samenwerking met de huisarts op de primaire uitkomsten patiënt tevredenheid en het zorggebruik beoordelen. Secundaire uitkomsten waren kwaliteit van leven, geestelijke gezondheid

en de zelfredzaamheid van de patiënt. We vonden dat 68% van de interventiepatiënten ten minste één EOV-contact had, waaruit bleek dat de eerste acceptatie goed was. Echter, de implementatie van EOV contacten was suboptimaal; er werd aanbevolen om na het einde van de behandeling ook een contactmomenten met de EOV te hebben, maar bijna de helft van de patiënten (46%) voltooide de geadviseerde contacten met de EOV niet. De algemene patiënttevredenheid in beide studiegroepen met de zorg op T3 en T5 was hoog (een gemiddelde score van 8 op de schaal 0-10). Drie maanden na afronding van de oncologische behandeling (T5) was de tevredenheid met de huisarts significant lager in de interventiegroep in vergelijking met de controlegroep gemeten op 3 van de 6 subgroepen (schaal 0-100 hogere tevredenheid bij hogere waardes), gemiddelde verschil tussen interventie- en controle groep van -14,2 (95% CI -27,0;-1,3) voor de kwaliteit van de huisarts, -15,9 (-29,1;-2,6) voor de beschikbaarheid bij de huisarts en -15,2 (95% CI -29,1;-1,4) voor de informatievoorziening. Dit is mogelijk het gevolg van suboptimale verwachting management, ontstaan door het nieuw ingevoerde zorgpad waarbij de rolverdeling tussen huisarts en EOV niet uitgekristalliseerd was. Patiënten in de interventiegroep bezochten de huisartsenpraktijk en de spoedeisend hulp vaker dan de controlegroep (respectievelijk RR 1.3 (95% CI 1.0;1.7) en RR 1.70 (95% CI 1.0;2.8)). Op de andere uitkomsten vonden we geen verschil tussen beide studie groepen. Concluderend kan worden gesteld dat de GRIP-interventie, die tot doel had een eerstelijnsteam tijdens en na de behandeling van kanker beter te betrekken, het aantal contacten in de eerstelijnsgezondheidszorg licht heeft doen toenemen. Tijdige planning van de TOC bleek echter uitdagend en de tevredenheid van de patiënten met de zorg verbeterde niet. Ook werd de spoedeisende hulp vaker bezocht. De hoge mate van acceptatie van beide onderdelen van de interventie (TOC en EOV) suggereert dat een dergelijke interventie tegemoetkomt aan behoeften van de patiënt. De suboptimale uitvoering en effecten wijzen uit dat de interventie verder verbeterd moet worden. Toekomstig onderzoek moet de opbouw en de uitvoering van de interventie verder optimaliseren en evalueren.

Concluderend, patiënten hebben behoefte aan betrekking van de huisarts na de diagnose kanker. Met name op gebied van ondersteuning bij besluitvorming wordt deze steun nu weinig ervaren. Bewijs voor effectieve

interventies gericht op huisartsbetrekking is erg beperkt en de GRIP-interventie biedt nog geen sluitende oplossing.

Het lijkt er op dat de het Time Out consult bij de huisarts tussen diagnose en therapiekeuze in behoeften van de kankerpatiënt voorzien. Echter, de integratie van het TOC in dagelijkse zorgpad en de invulling van de samenwerking tussen huisarts- en EOV, moeten worden verbeterd. Voor verdere verbetering van zowel de interventie als het onderzoek ernaar adviseren wij om de stappen van het MRC-model voor evaluatie van complexe interventies te volgen. Hierbij worden elementen als ontwikkeling, haalbaarheid, evaluatie en nadenken over implementatie extra belicht. Voor verdere ontwikkeling van een gestructureerde eerstelijns interventie bij kanker, verdient het aanbeveling om vooral kritisch te kijken naar de mogelijkheden voor inbedding van een TOC in het oncologische traject, zodat het effectief geïntegreerd kan worden. Ook dient er aandacht te zijn voor de gewenste rol van de huisarts en EOV na de diagnose kanker, zodat begeleiding door het eerstelijns team beter kan worden ingevuld. Na ontwikkeling moet ook niet nagelaten worden om middels pilot studies de "feasibility" van de interventie te testen en te optimaliseren.

Op basis van dit proefschrift hebben we enkele aanbevelingen om de toekomstige ontwikkeling van eerstelijnsbetrokkenheid te faciliteren:

- Beschouw passende gestructureerde kankerzorg niet als eerstelijns doel, maar als doel voor lijn-overstijgende, gepersonaliseerde kankerzorg. Dit betekent dat effectieve betrekking van de huisarts na de diagnose kanker samen met eerstelijns- en ziekenhuis teams moet worden ontwikkeld en uitgevoerd.
- De taakdifferentiatie en -delegatie in de oncologische zorg moet verder worden ontwikkeld. Bijvoorbeeld de samenwerking tussen de huisarts en de EOV in de GRIP-interventie is nog niet uitgekristalliseerd.
- Complexe interventies zoals gedeelde kankerzorg, waarbij de eerstelijn een structureel een rol krijgt, zal continue aan evaluatie onderhevig moeten zijn, waarbij we aanbevelen om een nieuwe aanpak altijd in een pilot studie te evalueren, voordat een grootschalig onderzoek wordt uitgevoerd.

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Curriculum vitae

Ietje Perfors was born on the 10th of August 1987 in Zeist, the Netherlands. During breakfast her father performed single-blind tests to evaluate which was best. After graduation from De Breul in Zeist, she moved to Utrecht in 2007 to start her studies in Medicine at Utrecht University. During her medical studies she completed senor internships in Urology (UMC Utrecht) and Internal Medicine (Garoua Baptist Hospital, Cameroon) and did her research internship about the bulbourethral artery under supervision of prof. dr. Laetitia de Kort and prof. dr. R.L.A.W. Bleys. After obtaining her medical degree, she started in 2014 working on this thesis as a PhD candidate at the Julius Center for Health Sciences and Primary Care of the University Medical Center Utrecht. She worked under supervision of prof. dr. N.J. de Wit, prof. dr. E. van der Wall, prof. dr. A.M. May and dr. C.W. Helsper. She continued the research project as an AIOTHO, combining her work as a general practice trainee with her PhD project. After one-and-a-half years of research, she did her first year as a general practice trainee in Utrecht. Subsequently, she continued her research, alternated with her second year of general practice vocational training and completed her postgraduate Master in Clinical Epidemiology at Utrecht University. As of September 2020, Ietje will continue her training to become a general practitioner.

Improving primary care involvement in cancer care

Ietje Perfors