BMJ Open

Effectiveness, cost-utility and implementation of a decision aid for patients with localised prostate cancer and their partners: study protocol of a stepped-wedge cluster randomised controlled trial

Hoda H M Al-Itejawi,[1] Cornelia F van Uden-Kraan,[2,3] Peter M van de Ven,[4] Veerle M H Coupé,[4] André N Vis,[1] Jakko A Nieuwenhuijzen,[1] Jeroen A van Moorselaar,[1] Irma M Verdonck-de Leeuw[2,3,5]

CrossMark

For numbered affiliations see end of article.

Correspondence to
Professor dr Irma M Verdonck-de Leeuw;
im.verdonck@vumc.nl

ABSTRACT

Introduction Patient decision aids (PDAs) have been developed to help patients make an informed choice for a treatment option. Despite proven benefits, structural implementation falls short of expectations. The present study aims to assess the effectiveness and cost-utility of the PDA among newly diagnosed patients with localised prostate cancer and their partners, alongside implementation of the PDA in routine care.

Methods/analysis A stepped-wedge cluster randomised trial will be conducted. The PDA will be sequentially implemented in 18 hospitals in the Netherlands, over a period of 24 months. Every 3 or 6 months, a new cluster of hospitals will switch from usual care to care including a PDA. The primary outcome measure is decisional conflict experienced by the patient. Secondary outcomes comprise the patient's quality of life, treatment preferences, role in the decision making, expectations of treatment, knowledge, need for supportive care and decision regret. Furthermore, societal cost-utility will be valued. Other outcome measures considered are the partner's treatment preferences, experienced participation to decision making, quality of life, communication between patient, partner and health care professional, and the effect of prostate cancer on the relationship, social contacts and their role as caregiver. Patients and partners receiving the PDA will also be asked about their satisfaction with the PDA. Baseline assessment takes place after the treatment choice and before the start of a treatment, with follow-up assessments at 3, 6 and 12 months following the end of treatment or the day after deciding on active surveillance. Outcome measures on implementation include the implementation rate (defined as the proportion of all eligible patients who will receive a PDA) and a questionnaire for health care professionals on determinants of implementing an innovation.

Ethics and dissemination This study will be conducted in accordance with local laws and regulations of the Medical Ethics Committee of VU University Medical Center, Amsterdam, The Netherlands. The results from

Strengths and limitations of this study

► With a stepped-wedge cluster randomised trial, we aim to evaluate the effectiveness and cost-utility in clinical care for patients with prostate cancer while simultaneously and sequentially implementing an intervention (the patient decision aid). The expectation is that this approach will lead to sustainable implementation of the patient decision aid.

► Because the majority of patients with prostate cancer (as well as partners themselves) have the opinion that their partner has played a major role in the treatment decision, we also involved the partners of patients with prostate cancer in this study.

► Disadvantage of the stepped-wedge cluster randomised trial is the extended study duration due to sequential intervention rollout and the complicated analysis due to the unidirectional crossover.

this stepped-wedge trial will be presented at scientific meetings and published in peer-reviewed journals.

Trial registration Nederlands Trial Register NTR TC5177, registration date: May 28th 2015.Pre-results.

BACKGROUND

Prostate cancer is the most common form of cancer in men over 55 years in the Netherlands. The vast majority of these men have a localised form of prostate cancer, meaning that the cancer is only present in the prostate gland and has not spread to another part of the body.[1] For the initial treatment of localised prostate cancer, there are multiple, medically equivalent curative treatment options (radical prostatectomy, external beam radiotherapy or brachytherapy) as well as the option not to

be treated immediately by following an active surveillance (AS) protocol. Each of these approaches has its own side effects, risks and possible consequences for the patient and his partner.[2–4] Currently, patients are informed about the treatment options, with often a well-intentioned preference by the healthcare professional (HCP).[5 6] As long as none of these treatment options has proven to be superior,[7] a patient should be able to make a decision based on his own preferences and values such as maintaining sexual function and urinary continence.[8]

Patient decision aids (PDAs) are tools, which can be used to help patients make specific and informed choices among options by providing information on the outcomes relevant to a person's health status.[9] Multiple studies showed that PDAs improve patients' knowledge, participation in decision making and support patients to reach choices that are more consistent with their informed values.[8 10–12]

Usually, PDAs are developed and consequently evaluated in randomised controlled trials investigating effectiveness. Despite proven benefits of PDAs, structural implementation falls short of expectations. Barriers for implementation were recently revealed in reviews[13 14]: HCPs do not trust the content of PDAs, they question if the information provided is evidence-based or they think that the PDA does not reflect 'local' data.[13] Time pressure, lack of applicability due to patient characteristics (eg, patients' literacy levels) and limitations due to clinical factors (eg, if a patient is not eligible for more than one option) were other barriers mentioned by HCPs.[14] To overcome these hurdles, we developed a PDA for patients with localised prostate cancer and prepared an overview of requirements for implementation using an iterative participatory approach, meaning that patients with prostate cancer and HCPs were involved in each step of the development process.[15–17] This approach resulted in a PDA that fits the needs of patients and HCPs with the aim to ensure adequate uptake in daily clinical practice. See the Methods section for more information on the PDA and its development process.

The present study aims to assess the effectiveness and cost-utility of the PDA among newly diagnosed patients with localised prostate cancer and their partners, alongside implementation of the PDA in routine care via a stepped-wedge clustered randomised controlled trial. To our knowledge, there are no stepped-wedge cluster randomised trials with PDAs for patients with prostate cancer that evaluate both the effectiveness, cost-utility and implementation of a PDA.

Based on the Cochrane study of Stacey *et al*,[8] we hypothesise that the PDA will improve knowledge on prostate cancer, satisfaction with the information provided and prepare patients for the treatment choice and can thus lead to a reduction in Decisional Conflict Scale (DCS). Moreover, we expect the PDA to make patients more aware of the choice and can thus lead to a change in the role patients want to have in the decision-making process (eg, be more active).[8] Additionally, we hypothesise that the PDA will also result in more realistic expectations of the treatment and to less regret afterwards.[18 19]

Because studies have shown that the majority of patients with prostate cancer (as well as partners themselves) have the opinion that their partner has played a major role in the treatment decision,[20 21] we will evaluate the effect of a PDA on partners as well.

METHODS/DESIGN
A prospective stepped-wedge cluster randomised controlled trial will be conducted to compare the PDA with usual care.[22] We followed the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) checklist[23 24] (see appendix A). A stepped-wedge cluster randomised controlled trial is a research design in which a new treatment is sequentially implemented in a set of clusters (see figure 1). A stepped-wedge design is applied to assure implementation of the PDA in all of the participating hospitals while still allowing for a comparison with usual care. The order in which the clusters start with the new intervention is randomised. Until the time of implementation of the new intervention, clusters serve as a control group. A flowchart of the trial is shown in figure 2.
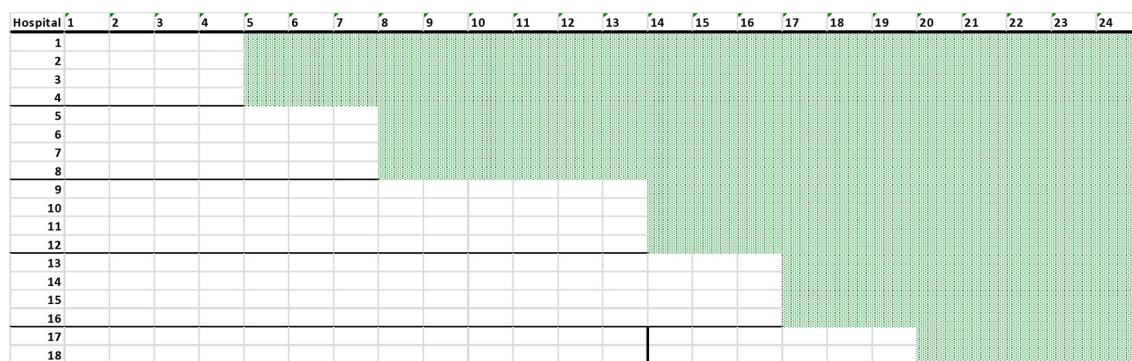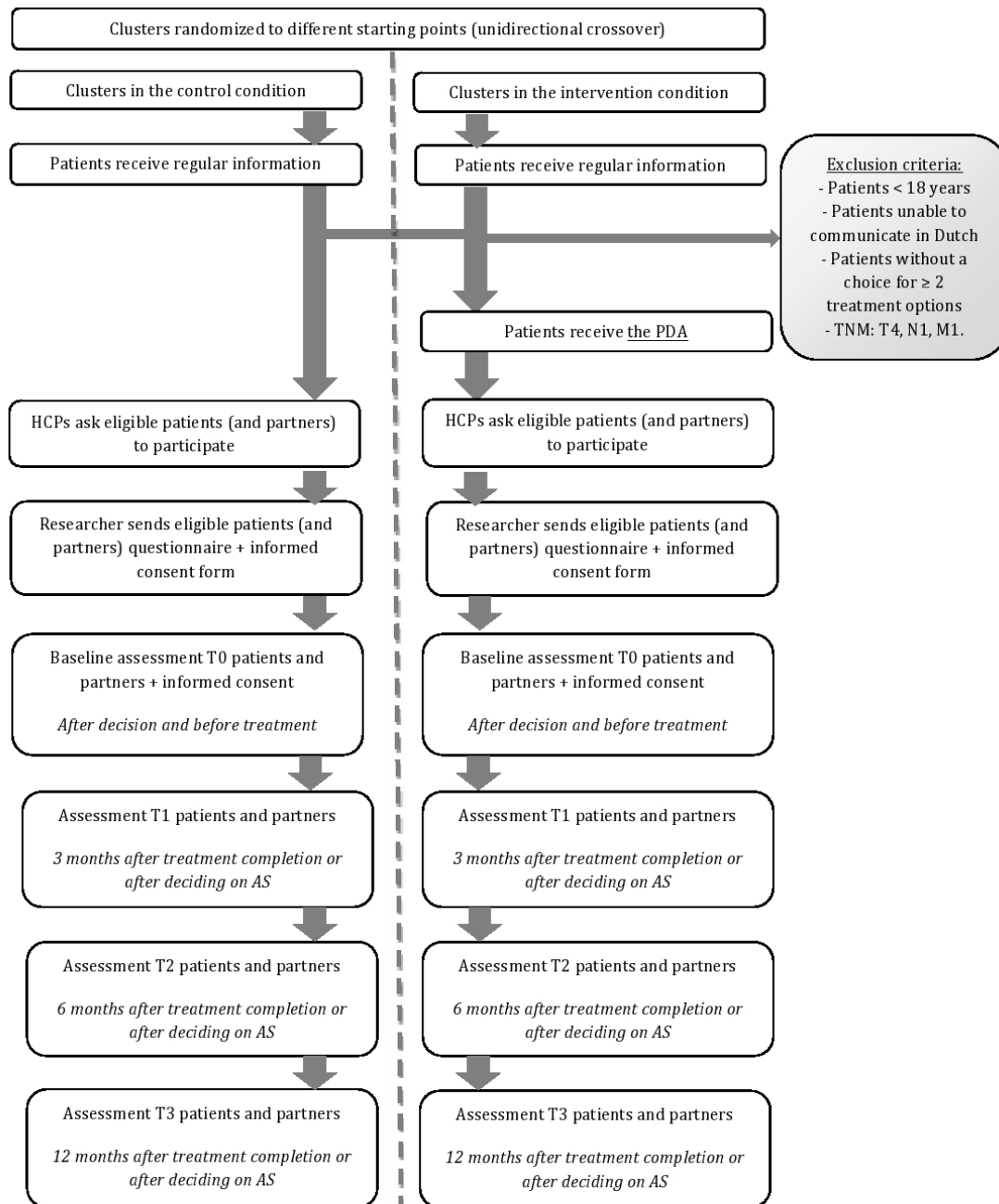

Figure 1 Time schedule of the stepped-wedge randomised controlled trial design. Hospital number 17 and 18 was an additional group of (non-randomised) hospitals, who started with the study on month 14. White blocks: Control conditions; Green dotted blocks: Interventaion condition.

*HCPs: Health care professionals, PDA: Patient decision aid, AS: active surveillance. The dotted line in middle: all clusters start with a control condition. The starting point of the use of the PDA is randomized between the participating clusters.

Figure 2 Flow chart of the stepped-wedge cluster randomised trial.

Study population
Newly diagnosed patients with prostate cancer and their partners from the participating centres between 2014 and 2016 (see figure 2) are asked to participate in the study.

Inclusion criteria
Newly diagnosed patients with localised prostate cancer (and their partners) who have to choose a curable treatment option (radical prostatectomy, external beam radiotherapy or brachytherapy) for prostate cancer and have

not undergone this treatment yet or have the option not to be treated immediately by following an AS protocol.

Exclusion criteria
Patients diagnosed with prostate cancer TNM classification: T4, N1, M1, patients younger than 18 years or patients not able to understand the Dutch language in speech and in writing.

The inclusion and exclusion criteria are limited in order to remain close to daily clinical practice.
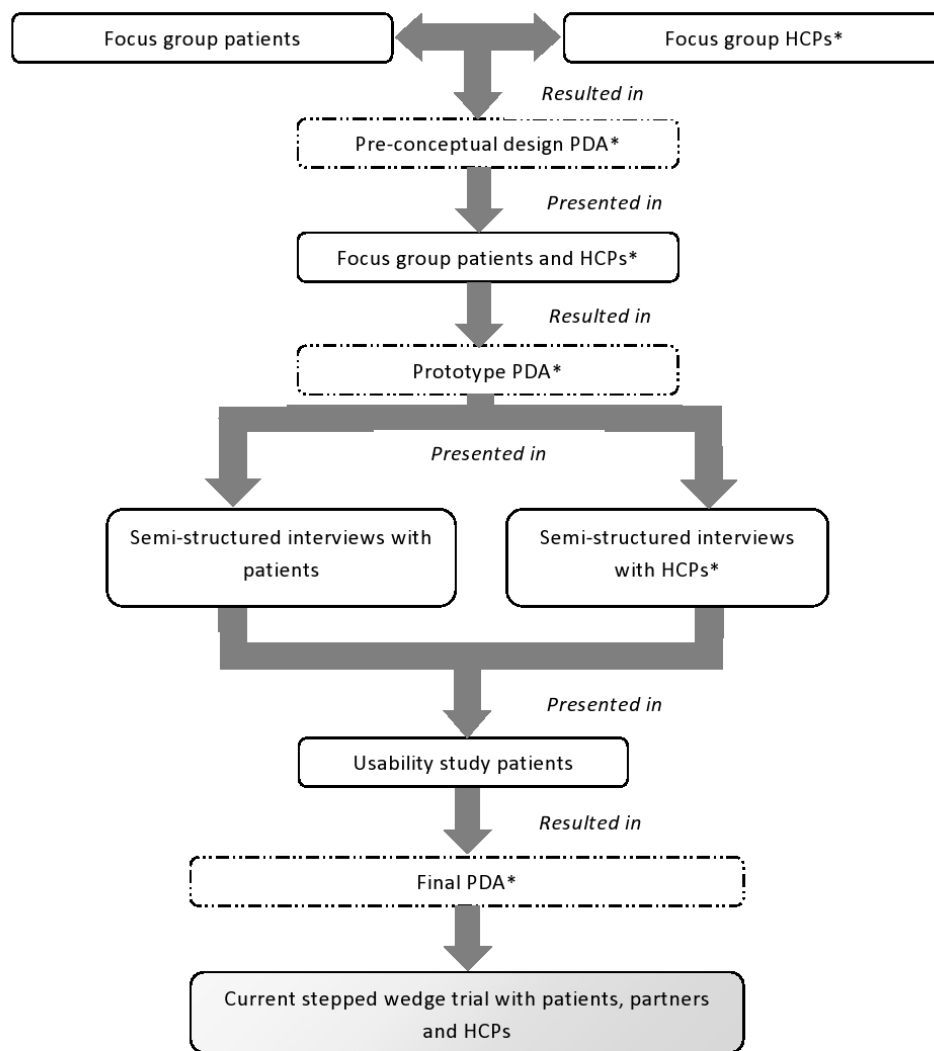
* HCPs: Health care professionals, PDA: Patient decision aid

Figure 3 Flow chart of the studies conducted in the participatory design approach.

Intervention description

At the time of development, there was no PDA available in Dutch covering all four treatment options, including AS. Therefore, we developed a web-based and booklet version of a PDA for patients with localised prostate cancer.[25] Figure 3 provides an overview of the followed steps in the development process. A qualitative assessment of needs among patients (n=12) recently treated for localised prostate cancer, their partners (n=4) and HCPs (n=10) by means of three focus group interviews was conducted (*step 1*).[25] HCPs considered medical information on treatments and side effects as most important to be included in the PDA. Patients also focused on non-medical considerations. Both patients and HCPs expected the PDA to support patients in making a treatment choice. Based on the results of the focus groups, a prototype of the PDA was developed. In *step 2*, the prototype was presented to patients with prostate cancer (n=14) and HCPs (six urologists, four radiation therapists and three oncology nurses) in semistructured

interviews. With these interviews, we also gained insight into requirements for implementing the PDA among HCPs.[25] According to HCPs incorporation of the PDA into clinical guidelines and using the guidelines as a basis for the PDA would promote implementation. Finally, in *step 3*, the usability of the PDA was tested in a usability study among newly diagnosed patients (n=5) with localised prostate cancer targeting system quality (ease-of-use), content quality (usefulness and relevance) and service quality (the process of care provided).[25–27] Usability tests showed that patients managed to 'navigate through' the PDA independently.[25]

However, some weaknesses were identified in the above-mentioned studies by HCPs and patients, for example, using jargon.[25] Based on these findings, the prototype of the PDA was finalised. An example of an adjustment was the addition of a glossary.

The PDA (see figure 4) includes all options for localised prostate cancer and is composed of the following parts:

- ► A general explanation with information about the content of the PDA. It also explains that patients have multiple (treatment) options and that the choice can be made in consultation with the HCP (see figure 4a).
- ► A section that describes all (treatment) options in short terms. The HCP can mark which (treatment) options are open for patients, if not all options are possible (see figure 4b).
- ► A component that answers the question: what are my arguments for and against different (treatment) options for my prostate cancer? All four (treatment) options are discussed separately. All the pros and cons are described and divided into three subcomponents: cure, treatment and quality of life (see figure 4c). All statements are presented in a clear manner from the patient's perspective ('As long as I am under active surveillance, I will not have any side effects'). The PDA does not include ranking of features of (treatment) options or a (treatment) advice but aids the patient to reach an informed treatment preference.
- ► A glossary of the terminology. Because of the difficulty of some terms, it was decided to include a glossary that defines all difficult terms in alphabetical order. To be comprehensible for patients low on health literacy, the content was adjusted to an intermediate preparatory vocational education level (see figure 4d).

STUDY DESIGN AND PROCEDURES

The PDA will be stepwise implemented in 18 hospitals (five groups of two or four hospitals) in the region of Amsterdam, The Netherlands, over a period of 24 months (2014–2016).

Every 3 or 6 months (starting in 2014), a subgroup of hospitals will switch from usual care to use of the PDA (see figure 1). In each hospital, there will be a period of 4–16 months of including newly diagnosed patients who receive usual care, followed by a period of at least 5 months and a maximum of 20 months in which the PDA is provided to newly diagnosed patients. The assignment of hospitals to groups switching at different times to use of the PDA is randomised by PMvdV. The only restriction on the randomisation is that both university hospitals will not be not assigned to the same group.

Participating centres know in advance when they will implement the PDA but will not receive the PDA before the start of the implementation. HCPs (urologists and oncology nurses) partaking in this study will be trained on how to introduce the PDA to eligible patients by means of a kick-off meeting organised in their hospital shortly before the start of the implementation of the PDA.

Patients (and their partners) receive a letter from their HCP with information on the study and an invitation to participate. Patients in the intervention condition will also receive the PDA. Depending on the local healthcare pathway for patients with localised prostate cancer, the PDA will be introduced by the HCP at diagnosis or during consultation following diagnosis. Next to the PDA, patients will receive all information (eg, brochures) that would also have been provided otherwise. Patients are offered the web-based version or the booklet version of the PDA (or both), depending on the preference of the patient. In case the patient is interested in participating, the researcher informs the patient on the study in more detail by telephone and invites the patient to participate in the study. In case the patient has a partner, the partner is also invited to participate. When the patient (and partner) agrees to participate (irrespective of the participation of a partner), the researcher sends the baseline questionnaire and an informed consent form (see figure 2).

Outcome measures

The primary outcome measure is decisional conflict (DCS) in patients (table 1). Secondary outcomes are quality of life, treatment preferences, role in the decision-making process, expectations of treatment, knowledge, communication between patient and partner, need for supportive care, decision regret and satisfaction with the PDA. Furthermore, cost-utility will be evaluated. Regarding the partners, their primary outcome measures are treatment preferences and the experienced participation and approach to decision making. Secondary outcome measures for partners include quality of life of partners, and the effect of prostate cancer on the relationship, communication between patient, partner and HCPs, social contacts and support and their role as caregiver and satisfaction with the intervention.

Participants can choose to complete the questionnaires online or by using a paper questionnaire. Non-respondents will be contacted by telephone within 2 weeks. If they do not respond to this reminder, they will be sent a reminder letter within 2 weeks.

The primary outcome (DCS), treatment preferences, preferred role in treatment decision, expectations of the treatment, knowledge and satisfaction with the intervention are collected at baseline (T0, directly after making the decision and before start of treatment). Other outcome measures are collected at baseline, after 3, 6 and 12 months follow-up. Follow-up starts on completion of treatment. Completion of treatment is defined as the last day after irradiation in case of brachytherapy or external beam radiation therapy or the day after the removal of the catheter in case of surgery, or the day after deciding on AS. An overview of the patient reported outcome measures is presented in table 1. The follow-up will end in June 2017.

Outcome measures on implementation include the implementation rate and a questionnaire for HCPs on determinants important for implementing an innovation based on the Measurement Instrument for Determinants of Innovations (MIDI) tool, which identifies barriers and facilitators at the level of the innovation (the PDA itself), the user (HCP) and the organisation (hospital).

Table 1 Study outcome measures

		Questionnaire at baseline (T0= directly after making a decision)	Questionnaires at follow-up (T1=3months, T2=6months, T3=12months after treatment)
Patients	Primary outcome	Decisional conflict scale	
	Secondary outcomes	Subjective and objective knowledge about prostate cancer (based on DQI knowledge, Karen Sepucha (Massachusetts General Hospital) and PCA 0915 of Carrie Levin)	
		Communication between patient and partner (study-specific questionnaire based on the study of Zeliadt)	
		Treatment preferences (study-specific questionnaire)	
		Experienced role in decision-making involvement (study-specific questionnaire based on the Deber-Kraetschmer Problem-Solving Decision-Making Scale)	
		Expectations of the treatment (SETS pretreatment)	Outcome of the treatment (SETS post-treatment)
		Quality of life (EORTC QLQ-C30 and PR25)	Quality of life (EORTC QLQ-C30 and PR25)
		The need for supportive care (SCNS SF-34 and prostate module)	The need for supportive care (SCNS SF-34 and prostate module)
			Decision regret (DRS)
	Cost-evaluation	Quality of life for the benefit of cost analysis (EQ-5D)	Quality of life for the benefit of cost analysis (EQ-5D)
		Direct medical and direct non-medical cost (TiC-P)	Direct medical and direct non-medical cost (TiC-P)
		Productivity costs (PRODISQ)	Productivity costs (PRODISQ)
Additional questions patients in the intervention group	Satisfaction with intervention	Use of the PDA (study-specific questionnaire)	
		Appreciation for the PDA (study-specific questionnaire)	
		Satisfaction with the use of the PDA (SCIP-B)	
		Preparation for decision making (Prep-DM)	
		Promoting and impeding factors using the PDA (study-specific questionnaire based on the study of Légaré)	
Partners	Secondary outcomes	Communication between patient, partner and HCPs (study-specific questionnaire based on the study of Zeliadt)	
		Treatment preferences (study-specific questionnaire)	
		Experienced role in decision-making involvement (study-specific questionnaire based on the Deber-Kraetschmer Problem-Solving Decision-Making Scale)	
		Social contacts and support (AES)	
		Quality of life of partners (SF-12)	Quality of life of partners (SF-12)
		Effect of prostate cancer on the relationship of patient and partner (study-specific questionnaire based on the study of Zeliadt)	Effect of prostate cancer on the relationship of patient and partner (study-specific questionnaire based on the study of Zeliadt)
		Role as caregiver (CSI)	Role as caregiver (CSI)

Continued

Table 1 Continued

	Questionnaire at baseline (T0= directly after making a decision)	Questionnaires at follow-up (T1=3months, T2=6months, T3=12months after treatment)
Additional questions **partners** in the intervention group	Satisfaction with intervention	Use of the PDA (study-specific questionnaire)
		Appreciation for the PDA (study-specific questionnaire)
		Promoting and impeding factors using the PDA (study-specific questionnaire based on the study of Légaré)
Moderating factors patients and partners		Study specific questionnaire including sociodemographic and clinical factors
		Threatening Medical Situations Inventory (TMSI) questionnaire
HCPs	Determinants important for implementing an innovation	Measurement instrument for determinants of innovation: Identifying barriers and facilitators at the level of the innovation (the PDA itself), the user (HCP) and the organisation (hospital), only measured 3months after using the PDA

AES, Active Engagement Scale; CSI, Caregiver Strain Index; DQI, Decision Quality Instrument; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of life questionnaire- Core questionnaire; EORTC QLQ-PR25, European Organisation for Research and Treatment of Cancer Quality of life questionnaire- Prostate cancer questionnaire; HCP, healthcare professional; PDA, Patient decision aids; Prep-DM, Preparation for Decision Making Scale; PRODISQ, PROductivity and DISease Questionnaire; SCIP-B, Satisfaction with Cancer Information Profile; SCNS, Supportive Care Needs Survey; SETS, Stanford Expectations of Treatment Scale; TiC-P, Trimbos and iMTA Questionnaire on Costs Associated with Psychiatric Illness.

Primary outcome measure patients
Decisional conflict
The DCS measures personal perceptions of uncertainty in choosing options, modifiable factors contributing to uncertainty such as feeling uninformed, unclear about personal values and unsupported in decision making and effective decision making such as feeling the choice is informed, values-based, likely to be implemented and expressing satisfaction with the choice. Items are given a score of 0=strongly agree, 1=agree, 2=neither agree nor disagree, 3=disagree and 4=strongly disagree. The 16 items are summed, divided by 16 and multiplied by 25. Scores range from 0 (no decisional conflict) to 100 (extremely high decisional conflict).[28]

Secondary outcome measures patients
Treatment preferences
With a study specific questionnaire, information regarding the preferred treatment option is obtained retrospectively. The four-item questionnaire contains questions about which of the four (treatment) options are open for the patient, which preference the patient had directly after diagnosis (retrospectively) and which preference patient has today. In addition, the degree of preference is asked.

Preferred roles in treatment decision making
For the degree of different roles in decision-making involvement, a study-specific questionnaire based on the Deber-Kraetschmer Problem-Solving Decision-Making Scale (four items) supplemented with study specific questions (two items), will be used to examine the role patients want to play in treatment decision making and the relation with the information received. In addition, the influence of the HCP and the partner on the choice made by the patient is added to this questionnaire (three additional items).[29]

Expectations of treatment
To assess the expectations for each of the possible treatments, the Stanford Expectations of Treatment Scale (SETS) is used. The six-item SETS is an instrument for measuring positive and negative treatment expectancies and contains two subscales: positive expectancy and negative expectancy. Positive expectancy is the average of items 1, 3 and 5. Negative expectancy is the average of items 2, 4 and 6. Questions 7–10 are not scored and just provide optional information.[30]

Knowledge about prostate cancer
Knowledge about prostate cancer is assessed by means of a study-specific subjective and objective questionnaire based on questionnaires on Decision Quality Instrument (DQI) knowledge and PCA 0915 and contains five objective items and four subjective items.[31 32]

Communication between patient and partner
Using a study-specific questionnaire based on the study of Zeliadt, patients and their partners will be asked about

their communication with each other about prostate cancer.[21]

The need for supportive care (including prostate specific part)

The Supportive Care Needs Survey (SCNS) SF-34 is an instrument for the assessment of the perceived needs for aftercare of people diagnosed with cancer. The questionnaire contains a total of 34 items, with the following five domains: psychological, health, physical and daily living, patient care and support and sexuality. The prostate-specific part is composed of eight questions and concern, inter alia, urinary incontinence, urinary symptoms and bowel problems.[33 34]

Decision regret

The Decision Regret Scale measures distress or remorse after a healthcare decision.[35] Respondents will be asked to reflect on their treatment decision, and then asked to indicate the extent to which they agree or disagree with the statements in the regret scale by indicating a number from 1=strongly agree to 5=strongly disagree that best indicates their level of agreement. Regret is measured at 3 months, 6 months and 12 months after the decision. A higher number indicates more regret. A score of 0 means no regret; a score of 100 means high regret.[35]

Quality of life

The 30-item European Organisation for Research and Treatment of Cancer Quality of life questionnaire- Core questionnaire (EORTC QLQ-C30) includes a global HRQOL scale (two items) and comprises five functional scales: physical functioning (five items), role functioning (two items), emotional functioning (four items), cognitive functioning (two items) and social functioning (two items). There are three symptom scales: nausea and vomiting (two items), fatigue (three items) and pain (two items) and six single items relating to dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties.[36]

The 25 items prostate-specific module of the European Organisation for Research and Treatment of Cancer Quality of life questionnaire- Prostate cancer questionnaire (EORTC QLQ-PR25) is a self-administered questionnaire that includes four subscales for assessment of urinary symptoms (nine items), bowel symptoms (four items), hormonal treatment-related symptoms (six items) and sexual activity and function (six items). Each of the items can be scored from 1 to 4 (1=not at all, 2=a little, 3=quite a bit and 4=very much). All items and scale scores of the EORTC QLQ-PR25 are linearly transformed to a 0–100 scale based on its scoring manual. Higher scores reflect either more symptoms (urinary, bowel and hormonal treatment-related symptoms) or higher levels of functioning (sexual activity and function).[37]

Satisfaction with the intervention

With a study-specific questionnaire, information on the experience of the use of the PDA is obtained, and the degree of appreciation for the PDA is asked.

Using the Satisfaction with Cancer Information Profile (SCIP-B) information regarding satisfaction is evaluated. The SCIP-B has previously been shown to be a valid and reliable measure responsive to changes in patient satisfaction over time. It can be used to guide the tailored provision of treatment information to patients. The SCIP-B is a 7-item Likert-type scale (very dissatisfied to very satisfied). A higher score means a higher satisfaction.[38]

The Preparation for Decision Making Scale (Prep-DM) assesses a patient's perception of how useful a PDA is in preparing the respondent to communicate with their HCP at a consultation visit and making a health decision. Items can be summed and scored (sum the 10 items and divide by 10). Scores can be converted to a 0–100 scale by: subtracting 1 from the summed score mentioned before and multiplying by 25. Higher scores indicate higher perceived level of preparation for decision making.[39]

Through a study-specific questionnaire based on the study of Légaré, we examined the reasons for using or not using the PDA.[40]

Costs

Direct medical and direct non-medical cost data are collected with the Trimbos and iMTA Questionnaire on Costs Associated with Psychiatric Illness (TiC-P) using the quality of life assessed with the EuroQol-5 domains (EQ-5D) for the benefit of cost analysis.[41] Indirect non-medical cost data related to production losses through work loss days and work cutback days will be sampled with the appropriate PROductivity and DISease Questionnaire (PRODISQ modules).[42] Indicators of return to work are: time to partial and to full return to work, meaning number of calendar days between end of treatment and first day at work and time to full return to work corrected for partial return to work. The costs leading up to treatment are measured with the baseline questionnaire (the previous 3 months).[41–45]

Primary outcome measures partners
Treatment preferences

With a study-specific questionnaire, information regarding the preferred (treatment) option is obtained retrospectively. The four-item questionnaire contains questions about which of the four treatment options are open for the patient, which preference the partner of the patient had directly after diagnosis (retrospectively) and which preference the partner of the patient has today. In addition, the degree of preference is asked.

Experienced participation and approach to decision making

For the degree of different roles in decision-making involvement, a study-specific questionnaire based on the Deber-Kraetschmer Problem-Solving Decision-Making Scale (four items) supplemented with study specific questions (two items) will beused to examine the role partners play in treatment deision making and the relation with the information received. In addition, the

influence of the HCP and their partner on the choice is added to this questionnaire (three items).[31]

Secondary outcome measures partners
Quality of life of partners

The SF-12 (Short Form Health Survey) contains 12 questions and consists of eight dimensions: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations by emotional problems and mental health. This instrument measures the quality of life, as it is experienced by the partners.

The SF-12 is a shortened version of the SF-36. Both positive and negative aspects of health are included. For each dimension, the scores are summed at the items and transformed to a scale from 0 to 100. A higher score means better health status.[46]

Effect of prostate cancer in the relationship

Using a study-specific questionnaire based on the study of Zeliadt, partners and patients will be asked what the impact of the diagnosis of prostate cancer in their relationship has been.[21]

Communication between patient and partner and interaction with HCPs

Using a study-specific questionnaire based on the study of Zeliadt, patients and their partners will be asked about their communication with each other about prostate cancer. Additionally, partners will be asked about their interaction with HCPs.[21]

Social contacts and support

For the degree of support provided for and dealing with the patient, we made use of the Active Engagement Scale (AES). The AES measures different styles of behaviour support. Five items form the active involvement scale, eight items measure protective buffering and six items measure protection. The questionnaire contains 16 items with a 5-point scale ranging from 1=never to 5=very often. The last three items are scored on a 5-point scale ranging from 1=no to 5=very strong.[47]

Role as caregiver

Using the Caregiver Strain Index (CSI) the role of the partner as caregiver is examined. The CSI is a questionnaire containing 13 items, which can be used to measure the degree of care. The following domains are examined: employment, financial, physical, social and time. Positive responses to seven or more points on the index point means a higher level of tension.[48]

Satisfaction with the intervention

The same items used in the questionnaire for patients as mentioned above, are examined in the questionnaire for partners.[42–44]

Moderating factors

A study-specific questionnaire comprises questions about sociodemographics (age, marital status, family situation,

education level). Clinical characteristics (ie, information on date of diagnosis of prostate cancer, treatment, Gleason score and PSA) of patients included in the study will be retrieved from the hospital information system.

The Monitoring and Blunting coping styles survey (The Threatening Medical Situations Inventory (TMSI) questionnaire) examines the information seeking style of people in certain threatening situations. There are two types of information-seeking styles that can occur: information seekers (monitoring strategy) and information avoiders (blunting strategy). In a threatening situation, both strategies can be used interchangeably.[49] We hypothesise that information seekers will have less decisional conflict than information avoiders.

The same moderating factors as mentioned above for patients are examined in the questionnaire for partners: sociodemographics (age, gender, marital status, family situation and education level) and monitoring and blunting coping styles.[49]

Implementation
Implementation rate

For the implementation rate of the PDA we will divide the number of patients who will receive the PDA by the number of eligible patients estimated from the Netherlands Comprehensive Cancer Organization Registry.[50] More specifically, the numerator is the number of patients who will receive the PDA. The denominator is the mean number of eligible patients with a localised form of prostate cancer (clinical stage T1c to T3b; T4, N1 and M1 are excluded) per hospital over the preceding 6 years, corrected for the period of inclusion (2 years).

Measurement Instrument for Determinants of Innovation

After using the PDA for 3 months, a questionnaire will be sent out to all participating HCPs. The implementation process and the actual use of the PDA are evaluated with this questionnaire measuring determinants of innovation (MIDI) among HCPs with regard to their experiences and the use of the PDA in the participating centres. This questionnaire is intended to identify the barriers and facilitators at the level of the innovation (use of the PDA), the user (HCP) and the organisation (hospital).[51]

Power calculation

The primary outcome measure in this study is the patient's score on the DCS. For the power calculation, we used results from the study of Stacey et al.[8] We assume an average score of 29.5 on the DCS in the usual care condition with a SD of 18.25. A decrease to an average DCS to 23.5 when using the PDA is considered clinically relevant, as was the result in the study of Stacey et al.[8] The SD is set at 12.5 for the intervention condition.[4] To achieve 80% power and using an independent sample t-test and a two-sided significance level of 5%, a standard randomised clinical trial will require 216 patients (108 in each arm). To account for clustering, the sample size was increased. Assuming an average cluster size of 24 patients

per hospital and an intraclass correlation of 0.05, a total of 465 patients are needed. As the stepped-wedge design will result in less power than a standard randomised clinical trial but more power when compared with a cluster randomised trial (with number of clusters and cluster size equal to the stepped wedge design), we chose to be conservative and aim for the sample size required for the cluster randomised trial.

Statistical analyses

The primary analysis (difference in mean DCS between usual care and intervention group) will be done using the mixed-model analysis. Intervention will be included in the model as a fixed factor. A random effect for hospital will be included in the model to account for between-hospital heterogeneity. In addition, time between inclusion of the patient and start of the study and the time between inclusion of the patient and implementation of the PDA in the hospital will be included in the model, if necessary, to correct for fluctuations over time (independent of treatment) and dependency of the intervention effect on time since implementation.

Dichotomous outcomes (such as yes/no questions about the decision) that are measured only one time during follow-up will be analysed using generalised estimating equations. An exchangeable correlation structure will be used (to model within-hospital correlation).

Repeatedly measured continuous outcomes (such as quality of life) will be analysed using mixed models in which in addition to a random effect for hospital also a random effect for patients (nested within hospitals) will be included in the model. The models will include an effect of time since inclusion and the interaction between time and intervention to test whether the course of the outcome over time differs between control and intervention condition.

Although this is a randomised study with measurements under control and intervention conditions in all participating centres, confounding may still occur because of the relatively small number of clusters that is randomised. Confounding will be checked and adjusted for in the analyses by including candidate confounders as fixed main effects in the models. Baseline characteristics of patients in intervention and control condition will be compared using independent t-tests and adjusted for when necessary.

We will record the percentage of drop-out and missing at each follow-up time point. If necessary, we will either use imputation techniques or sensitivity analyses to assess the impact of missing data on our conclusions.

Cost-utility analysis

The economic evaluation will be carried out using the applicable guidelines.[43 44] The societal perspective will be taken encompassing direct medical costs, direct non-medical costs and indirect costs. Units of resource use (doctor visits, treatment costs, hospital days, hours of work absenteeism and so on) will be multiplied by

their appropriate integral cost prices.[43 44] Production losses will be economically valued using the friction cost method.[44 52] With respect to the PDA, a bottom-up estimation of intervention costs and dissemination will be made. Costs and effects will be analysed simultaneously by calculating the incremental cost–effectiveness ratio (ICER) as the ratio between the difference in total costs and the difference in quality adjusted life years, as assessed with the EuroQol-5 domains (EQ-5D),[45] between the two trial arms. The difference in administered treatments between patients in the intervention and control arm is implicitly taken into account through the impact of treatment on health-related quality of life. A 95% CI of the ICER will be calculated using 5000 bootstrap replications. The bootstrap results will be projected on a cost-utility plane, and cost-utility acceptability curves will be plotted against different willingness-to-pay ceilings.[53] A sensitivity analysis will be conducted to study the effect of uncertainty in main cost drivers.

ETHICS AND DISSEMINATION

The Medical Ethics Committee of VU University Medical Center (Amsterdam, The Netherlands) has confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply to this stepped-wedge trial (reference number METC 2013–444). This study will be conducted in accordance with local laws and regulations of the Medical Ethics Committee of VU University Medical Center, Amsterdam, The Netherlands. Eligible patients will fully be informed about the study and asked to participate. The patients will receive a patient information letter and will be informed by telephone about the implications of participation. Patients will have sufficient opportunity to ask questions and to consider the implications of the study before deciding to participate. Before participation, patients will provide written informed consent, compliant with the local and ethical regulations. Patients will be allowed to withdraw from the study without giving a reason, at any time. The results arising from this stepped-wedge trial will be presented at scientific meetings and published in peer-reviewed journals. There is no intention to use professional writers and authorship will be based on the International Committee of Medical Journal Editors guidelines.

Author affiliations
[1]Department of Urology, VU University Medical Center, Amsterdam, The Netherlands
[2]Department of Clinical, Neuro- and developmental Psychology, Faculty of Behavioral and Movement Sciences, Amsterdam Public Health research institute, VU University, Amsterdam, The Netherlands
[3]Cancer Centre Amsterdam (CCA), VU University Medical Center, Amsterdam, The Netherlands
[4]Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands
[5]Department of Otolaryngology/Head and Neck Surgery, VU University Medical Center, Amsterdam, The Netherlands

INHOUDSOPGAVE

HOE WERKT DEZE KEUZEHULP?

Prostaatkanker kan op verschillende manieren behandeld worden. Veel voorkomende behandelingen zijn: oplettend volgen, opereren, inwendig bestralen en uitwendig bestralen. Daarnaast is soms een experimentele behandeling mogelijk.

Veel mannen met niet-uitgezaaide prostaatkanker kunnen zelf kiezen hoe ze behandeld willen worden. Uw behandelend arts kan u vertellen of dit ook voor u geldt en wat voor u de opties zijn waaruit u een keuze kunt maken.

Deze Keuzehulp helpt u bij het kiezen van een behandeling voor uw prostaatkanker. Hij vertelt u niet wat voor u de beste keuze is of wat u moet doen, maar biedt hulp bij het nemen van een beslissing door de volgende twee vragen te beantwoorden:

1 Hoe kan mijn prostaatkanker behandeld worden?

2 Wat zijn voor mij argumenten voor en tegen verschillende behandelingen van mijn prostaatkanker?

Omdat prostaatkanker over het algemeen langzaam groeit, heeft u de tijd om een keuze te maken. Het is gebruikelijk om tussen de 1 en 3 weken te nemen om tot een beslissing te komen.

Deze Keuzehulp is gemaakt op basis van de kennis en ervaring van mannen die prostaatkanker hebben (gehad), hun partners, zorgverleners en de richtlijn prostaatkanker 2013.

1 **Informatiekaart behandelingen** — 2
Wat zijn de verschillende behandelopties voor mijn prostaatkanker?

Argumentenkarten

2a **Argumentenkaart oplettend volgen** — 4
Wat zijn voor mij argumenten voor en tegen oplettend volgen van mijn prostaatkanker?

2b **Argumentenkaart opereren** — 6
Wat zijn voor mij argumenten voor en tegen opereren van mijn prostaatkanker?

2c **Argumentenkaart inwendig bestralen (brachytherapie)** — 8
Wat zijn voor mij argumenten voor en tegen inwendig bestralen van mijn prostaatkanker?

2d **Argumentenkaart uitwendig bestralen** — 10
Wat zijn voor mij argumenten voor en tegen uitwendig bestralen van mijn prostaatkanker?

Begrippenlijst — 12

Figure 4A Content of the PDA with a short description of it's use. PDA, Patient decision aids.
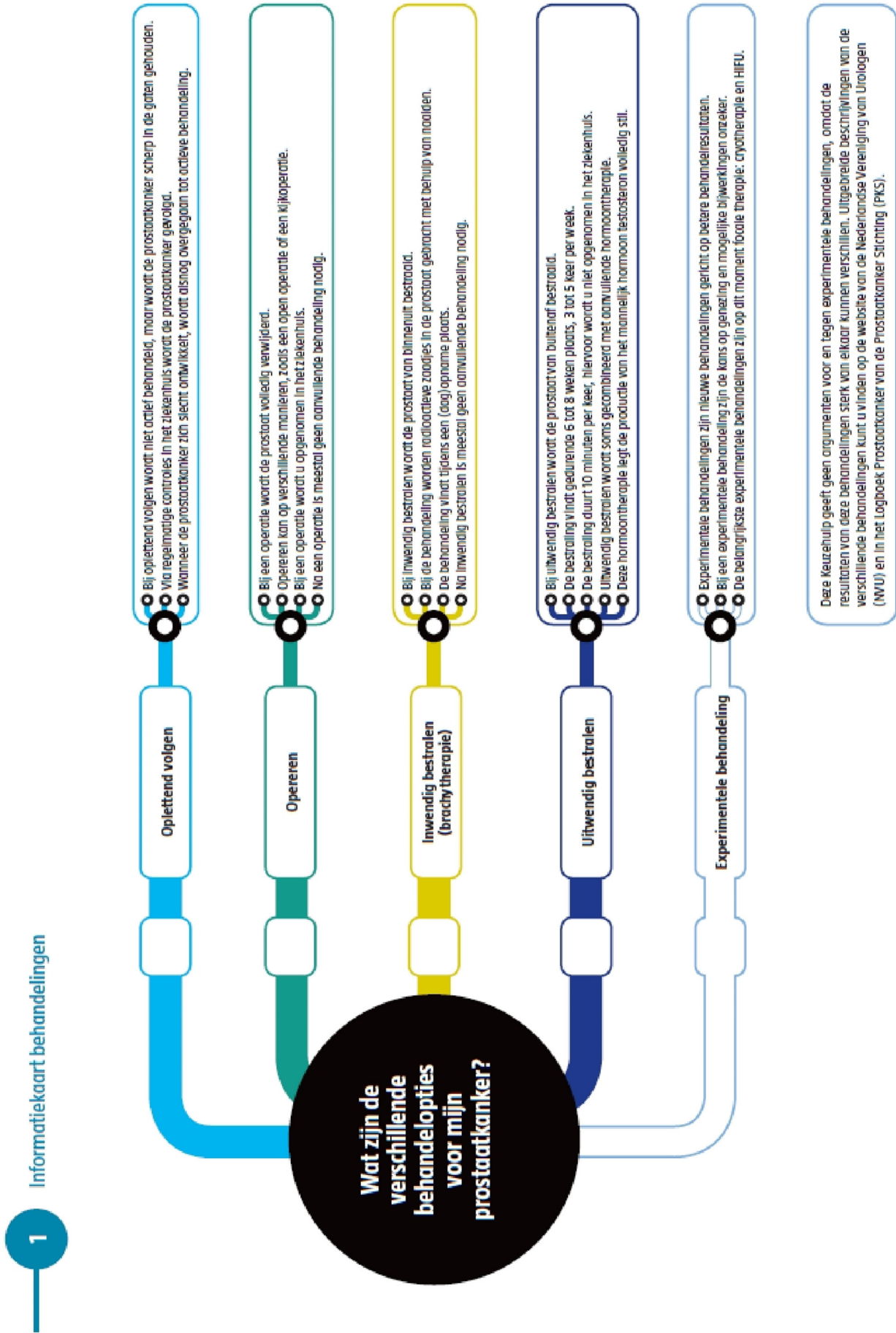
Informatiekaart behandelingen

1

Wat zijn de verschillende behandelopties voor mijn prostaatkanker?

Oplettend volgen

- Bij oplettend volgen wordt u niet actief behandeld, maar wordt de prostaatkanker scherp in de gaten gehouden.
- Via regelmatige controles in het ziekenhuis wordt de prostaatkanker gevolgd.
- Wanneer de prostaatkanker zich slecht ontwikkelt, wordt alsnog overgegaan tot actieve behandeling.

Opereren

- Bij een operatie wordt de prostaat volledig verwijderd.
- Opereren kan op verschillende manieren, zoals een open operatie of een kijkoperatie.
- Bij een operatie wordt u opgenomen in het ziekenhuis.
- Na een operatie is meestal geen aanvullende behandeling nodig.

Inwendig bestralen (brachytherapie)

- Bij inwendig bestralen wordt de prostaat van binnenuit bestraald.
- Bij de behandeling worden radioactieve zaadjes in de prostaat gebracht met behulp van naalden.
- De behandeling vindt tijdens een (dag)opname plaats.
- Na inwendig bestralen is meestal geen aanvullende behandeling nodig.

Uitwendig bestralen

- Bij uitwendig bestralen wordt de prostaat van buitenaf bestraald.
- De bestraling vindt gedurende 6 tot 8 weken plaats, 3 tot 5 keer per week.
- De bestraling duurt 10 minuten per keer, hiervoor wordt u niet opgenomen in het ziekenhuis.
- Uitwendig bestralen wordt soms gecombineerd met aanvullende hormoontherapie.
- Deze hormoontherapie legt de productie van het mannelijk hormoon testosteron volledig stil.

Experimentele behandeling

- Experimentele behandelingen zijn nieuwe behandelingen gericht op betere behandelresultaten.
- Bij een experimentele behandeling zijn de kans op genezing en mogelijke bijwerkingen onzeker.
- De belangrijkste experimentele behandelingen zijn op dit moment focale therapie: cryotherapie en HIFU.

Deze keuzehulp geeft geen argumenten voor en tegen experimentele behandelingen, omdat de resultaten van deze behandelingen sterk van elkaar kunnen verschillen. Uitgebreide beschrijvingen van de verschillende behandelingen kunt u vinden op de website van de Nederlandse Vereniging van Urologen (NVU) en in het Logboek Prostaatkanker van de Prostaatkanker Stichting (PKS).

Figure 4B   General explanation of all treatment options.

Argumentenkaart oplettend volgen

2 a

tegen

Genezing
Mijn prostaatkanker geneest niet
○ De prostaatkanker wordt niet uit mijn lichaam gehaald of bestraald en blijft aanwezig.

Behandeling
Ik moet regelmatig naar het ziekenhuis voor controle
○ Eens in de zoveel tijd worden prostaatbiopten en bloed afgenomen.

Kwaliteit van leven
Ik krijg te weinig zekerheid
○ Ik wil achteraf geen spijt krijgen omdat ik te laat ben om in te grijpen.
○ Ik heb behoefte aan zekerheid, terwijl oplettend volgen juist veel spanning en onzekerheid kan geven.

Wat zijn
voor mij argumenten
voor en tegen
OPLETTEND VOLGEN
van mijn
prostaatkanker?

voor

Genezing
Ik kan de ontwikkeling van mijn prostaatkanker in de gaten houden
○ Er is steeds meer bekend over de veiligheid van oplettend volgen.
○ De kans dat ik overlijd als gevolg van mijn prostaatkanker lijkt op basis van voorlopig onderzoek heel klein.

Behandeling
Ik word niet onnodig behandeld
○ Er wordt alleen overgegaan tot actieve behandeling als de prostaatkanker verergert.
○ Bij ongeveer 2 op de 3 mannen die oplettend worden gevolgd, is actief behandelen niet nodig in de eerste 5 jaar.

Kwaliteit van leven
Ik kan mijn leven blijven leiden zoals ik gewend ben
○ Mijn lichaam blijft intact en normaal functioneren.
○ Mijn concentratie, energie en tijd worden niet in beslag genomen door een behandeling.

Ik loop geen risico op bijwerkingen of klachten
○ Zolang ik oplettend gevolgd word, heb ik geen last van bijwerkingen.

Figure 4C Pros and cons of one treatment option.

BEGRIPPENLIJST

Actieve behandeling: een behandeling waarbij geopereerd, in- of uitwendig bestraald wordt.

Argumentenkaarten: kaarten waarin alle voor- en nadelen van de behandelingen worden uitgelegd.

Bestralingsafdeling: de afdeling waar de bestraling plaatsvindt.

Blaasontledigingsproblemen: problemen met plassen zoals een zwakke straal, moeilijk op gang komen met plassen en niet volledig kunnen uitplassen.

Cryotherapie: een behandeling waarbij de tumor wordt bevroren en gedood. De resultaten van deze behandeling zijn nog onzeker.

Dagopname: verblijf voor een behandeling of operatie korter dan één dag in het ziekenhuis.

Darmproblemen: diarree, bloedverlies uit de endeldarm of pijn bij de ontlasting.

Focale therapie: een behandeling van alleen de tumor, niet de gehele prostaat. De resultaten van deze behandeling zijn nog onzeker.

Goudstaafjes: een drietal metalen staafjes die via de anus in de prostaat wordt gelegd vóór de bestraling plaatsvindt, om de positie van de prostaat te herkennen als u bestraald wordt. Deze blijven permanent achter in de prostaat.

HIFU: een behandeling waarbij de tumor wordt verhit en gedood. De resultaten van deze behandeling zijn nog onzeker.

Hormoonbehandeling: een behandeling met tabletten of injecties die de groei van prostaatkankercellen remt.

Incontinent: geen beheersing meer over de blaas, waardoor urine niet kan worden opgehouden.

Informatiekaart: kaart waarin alle behandelingen voor prostaatkanker worden uitgelegd.

Ingreep: een operatie of behandeling waarvoor soms narcose nodig is.

Katheter: een plastic slangetje dat door de plasbuis naar de blaas loopt en de urine vanuit de blaas afvoert naar een opvangzak.

Kijkoperatie: een operatie waarbij met een kleine camera in de buik de organen goed te zien zijn en op deze manier wordt geopereerd.

Narcose: algehele verdoving waarbij u in slaap wordt gebracht tot de ingreep ten einde is.

Open operatie: een operatie waarbij een snee in de buik wordt gemaakt om de organen die geopereerd worden goed te kunnen zien.

Plasproblemen: klachten van moeite met de plas op te houden, vaker moeten plassen of een branderig gevoel bij het plassen.

Prostaatbiopten: met een naald worden meerdere stukjes weefsel uit de prostaat verwijderd via de endeldarm.

PSA-waarde: dit staat voor 'Prostaat Specifiek Antigeen'. Het is een stofje dat door de prostaat gemaakt wordt en normaal in het bloed aanwezig is. Bij prostaatkanker is de PSA-waarde verhoogd.

Retentie: ophouden van urine in de blaas door het niet goed kunnen legen van de blaas.

Ruggenprik: injectie in de onderrug, waarbij er geen pijn meer te voelen is in het onderlichaam tijdens de ingreep.

Testosteron: het mannelijke geslachtshormoon dat de zaadproductie en de ontwikkeling van mannelijke geslachtskenmerken stimuleert.

Zaadjes: kleine radioactieve metalen staafjes die in de prostaat worden gebracht en die daar permanent achterblijven in de prostaat.

Ziekenhuisopname: verblijf voor een behandeling of operatie langer dan één dag in het ziekenhuis.

Figure 4D General glossary.

REFERENCES

1. Mottet N, Bellmunt J, Briers E, et al. *Guidelines on Prostate Cancer*, 2015.
2. Gavin AT, Drummond FJ, Donnelly C, et al. Patient-reported 'ever had' and 'current' long-term physical symptoms after prostate cancer treatments. *BJU Int* 2015;116:397–406.
3. Gomella LG, Johannes J, Trabulsi EJ. Current prostate Cancer treatments: effect on quality of life. *Urology* 2009;73:S28–S35.
4. O'Shaughnessy PK, Ireland C, Pelentsov L, et al. Impaired sexual function and prostate cancer: a mixed method investigation into the experiences of men and their partners. *J Clin Nurs* 2013;22:3492–502.
5. Fowler FJ McNaughton Collins M Albertsen PC, et al. Comparison of recommendations by urologists and radiation oncologists for treatment of clinically localized prostate cancer. *J Urol* 2001;165:731–2.
6. Sommers BD, Beard CJ, D'Amico AV, et al. Predictors of patient preferences and treatment choices for localized prostate cancer. *Cancer* 2008;113:2058–67.
7. Wever EM, Heijnsdijk EA, Draisma G, et al. Treatment of local-regional prostate cancer detected by PSA screening: benefits and harms according to prognostic factors. *Br J Cancer* 2013;108:1971–7.
8. Stacey D, Légaré F, Col N, et al. Decision aids for people facing health treatment or screening decisions (Review). *Cochrane Collab* 2014;1.
9. O'Connor A, Bennett C, Stacey D, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Collab* 2009;3:116.
10. Davison BJ, Degner LF. Empowerment of men newly diagnosed with prostate cancer. *Cancer Nurs* 1997;20:187–96.
11. Auvinen A, Hakama M, Ala-Opas M, et al. A randomized trial of choice of treatment in prostate Cancer: the effect of intervention on the treatment chosen. *BJU Int* 2004;93:52–6.
12. van Tol-Geerdink JJ, Stalmeier PF, van Lin EN, et al. Do patients with localized prostate cancer treatment really want more aggressive treatment? *J Clin Oncol* 2006;24:4581–6.
13. Elwyn G, Scholl Dipl I, Caroline T, et al. The implementation of patient decision support interventions into routine clinical practice : a systematic review. *Cochrane Collab* 2013:1–34.
14. Légaré F, Ratté S, Gravel K, et al. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. *Patient Educ Couns* 2008;73:526–35.
15. O'Connor A, Elwyn G, Barratt A, et al. International Patient Decision Aid Standards (IPDAS) Collaboration Table 3. IPDAS Patient Decision Aid Checklist for Users. *Cochrane Libr* 2005.
16. van Gemert-Pijnen JE, Nijland N, van Limburg M, et al. A holistic framework to improve the uptake and impact of eHealth technologies. *J Med Internet Res* 2011;13:e111.
17. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. *Health Educ Behav* 1998;25:545–63.
18. van Tol-Geerdink JJ, Leer JW, Wijburg CJ, et al. Does a decision aid for prostate cancer affect different aspects of decisional regret, assessed with new regret scales? A randomized, controlled trial. *Health Expect* 2016;19:459–70.
19. Hacking B, Wallace L, Scott S, et al. Testing the feasibility, acceptability and effectiveness of a 'decision navigation' intervention for early stage prostate cancer patients in Scotland--a randomised controlled trial. *Psychooncology* 2013;22:1017–24.
20. Srirangam SJ, Pearson E, Grose C, et al. Partner's influence on patient preference for treatment in early prostate cancer. *BJU Int* 2003;92:365–9.
21. Zeliadt SB, Penson DF, Moinpour CM, et al. Provider and partner interactions in the treatment decision-making process for newly diagnosed localized prostate cancer. *BJU Int* 2011;108:851–857.
22. Hemming K, Haines TP, Chilton PJ, et al. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting. *BMJ* 2015;350:h391.
23. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200.
24. Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
25. Al-Itejawi HH, van Uden-Kraan CF, Vis AN, et al. Development of a patient decision aid for the treatment of localised prostate cancer: a participatory design approach. *J Clin Nurs* 2016;25:1131–44.
26. DeLone W, McLean E. The DeLone and McLean Model of Information Systems Success : A Ten-Year Update. *J Manag Inf Syst* 2003;19:9–30.
27. Kelders SM, Pots WT, Oskam MJ, et al. Development of a web-based intervention for the indicated prevention of depression. *BMC Med Inform Decis Mak* 2013;13:26.
28. O'Connor A. *User Manual – Decisional Conflict Scale*. : OHRI, 2010:1 : 1–16.
29. Deber RB, Kraetschmer N, Irvine J. What role do patients wish to play in treatment decision making? *Arch Intern Med* 1996;156:1414–20.
30. Younger J, Gandhi V, Hubbard E, et al. Development of the Stanford expectations of treatment Scale (SETS): a tool for measuring patient outcome expectancy in clinical trials. *Clin Trials* 2012;9:767–76.
31. Sepucha K. Prostate Cancer Decision Quality Instrument v.1.0. *Massachusetts Gen Hosp* 2013:1–4.
32. Fagerlin A, Sepucha KR, Couper MP, et al. Patients' knowledge about 9 common health conditions: the DECISIONS survey. *Med Decis Making* 2010;30:35–52.
33. Boyes A, Girgis A, Lecathelinais C. Brief assessment of adult cancer patients' perceived needs: development and validation of the 34-item Supportive Care Needs Survey (SCNS-SF34). *J Eval Clin Pract* 2009;15:602–6.
34. Steginga S, Occhipinti S, Dunn J, et al. The supportive care needs of men with prostate cancer. *Oncol Nurs Forum* 2001;10:66–75.
35. O'Connor A. User Manual - Decision Regret Scale. *OHRI* 2003;1:1–3.
36. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–76.

37. van Andel G, Bottomley A, Fosså SD, *et al*. An international field study of the EORTC QLQ-PR25: a questionnaire for assessing the health-related quality of life of patients with prostate cancer. *Eur J Cancer* 2008;44:2418–24.
38. Hankins MC, Llewellyn CD. Is the satisfaction with Cancer information Profile (SCIP) valid for tailoring information for patients with head and neck cancer? *BMC Cancer* 2008;8:164.
39. Bennett C, Graham ID, Kristjansson E, *et al*. Validation of a preparation for decision making scale. *Patient Educ Couns* 2010;78:130–3.
40. Légaré F, Ratté S, Gravel K, *et al*. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. *Patient Educ Couns* 2008;73:526–35.
41. Hakkaart-van Roijen L, Van Straten A, Donker M, *et al*. Handleiding Trimbos/iMTA questionnaire for Costs associated with Psychiatric illness (TiC-P). *Erasmus Univ Med Cent Rotterdam* 2007.
42. Koopmanschap MA. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res* 2005;5:23–8.
43. Oostenbrink JB, Koopmanschap MA, Rutten FF. Standardisation of costs: the Dutch Manual for costing in Economic evaluations. *Pharmacoeconomics* 2002;20:443–54.
44. Oostenbrink J, Bouwmans C, Koopmanschap M, *et al*. "Handleiding voor kostenonderzoek". *Inst voor Med Technol Assess* 2004;127.
45. Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37:53–72.
46. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–233.
47. Hagedoorn M, Kuijer RG, Buunk BP, *et al*. Marital satisfaction in patients with cancer: does support from intimate partners benefit those who need it the most? *Health Psychol* 2000;19:274–82.
48. Onega LL. The modified Caregiver Strain Index (MCSI). *Best Practices in NursingCare to Older Adults* 2013;43:1–2.
49. van Zuuren FJ, de Groot KI, Mulder NL, *et al*. Coping with medical threat: an evaluation of the Threatening Medical Situations Inventory (TMSI). *Pers Individ Dif* 1996;21:21–31.
50. Intergraal Kanker Centrum Nederland (IKNL): Netherlands Comprehensive Cancer organization Registry. https://www.iknl.nl/ (accessed 16 Jan 2015).
51. Fleuren M, Wiefferink K, Paulussen T. Determinants of innovation within health care organizations: literature review and Delphi study. *Int J Qual Health Care* 2004;16:107–23.
52. Brouwer WB, Koopmanschap MA, Rutten FF. Productivity losses without absence: measurement validation and empirical evidence. *Health Policy* 1999;48:13–27.
53. van Hout BA, Al MJ, Gordon GS, *et al*. Costs, effects and C/E-ratios alongside a clinical trial. *Health Econ* 1994;3:309–19.