TREATMENT DECISION MAKING IN PATIENTS WITH PROSTATIC DISORDERS

R.E.D. LAMERS

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Romy Lamers

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ISBN:	978-94-6375-569-6
Coverdesign:	Lieke Derde, www.liekederde.nl
Layout and design:	Marilou Maes, persoonlijkproefschrift.nl.
Printing:	Ridderprint BV | www.ridderprint.nl

Dit proefschrift werd (mede) mogelijk gemaakt met financiële steun van stichting Delectus, IPSEN PHARMACEUTICA B.V., ASTELLAS PHARMA B.V., ChipSoft en Elisabeth-Tweesteden Ziekenhuis

Treatment decision making in patients with prostatic disorders

Besluitvorming bij de behandeling van patiënten met prostaataandoeningen
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de

Universiteit Utrecht

op gezag van de

rector magnificus, prof.dr. H.R.B.M. Kummeling,

ingevolge het besluit van het college voor promoties

in het openbaar te verdedigen op

donderdag 21 november 2019 des middags te 2.30 uur

door

Rosalia Eleonora Desideria Lamers

geboren op 2 februari 1988

te Dordrecht

Promotoren:

Prof. dr. J.L.H.R. Bosch
Prof. dr. L.V. van de Poll-Franse

Copromotoren:

Dr. P.J.M. Kil
Dr. M. de Vries

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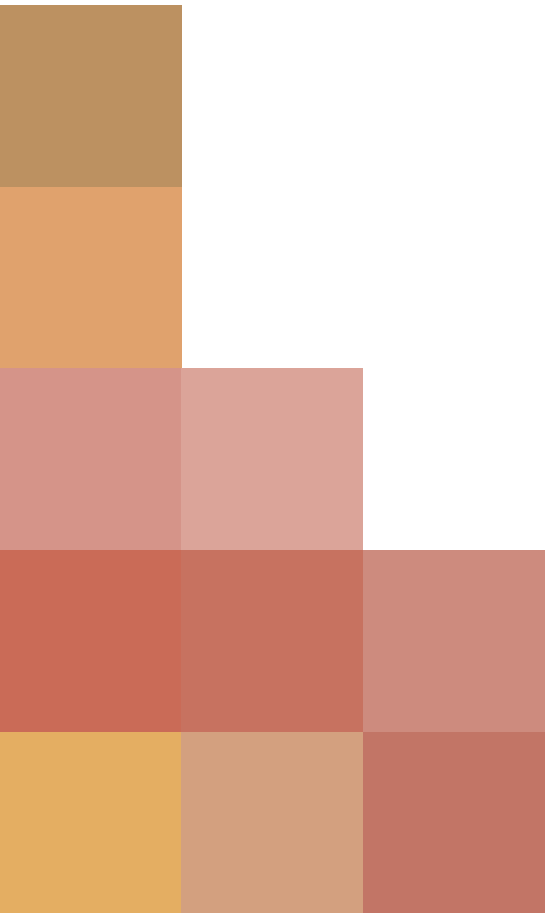


Chapter 1

General introduction

General introduction

Any of the diseases or abnormalities that afflict the prostate are called prostatic disorders. Most prostatic disorders are benign like benign prostatic enlargement (BPE) due to benign prostatic hyperplasia (BPH). However, the incidence of malignancies is rising (1). For patients with BPH and patients with prostate cancer, age of onset is comparable (1, 2). After diagnosis, patients should be supported and involved by their clinician to choose the best treatment according to the patients' values and preferences (3). To choose the best treatment for each patient, treatment decision making involves trade-offs between side effects and efficacy, for both prostate cancer (PC) and BPH.

Decision aids (DAs) may help the patient in the decision making process (2). However, for prostate cancer and benign prostatic hyperplasia it is still unclear how the use of decision aids affects treatment choice and shared decision making.

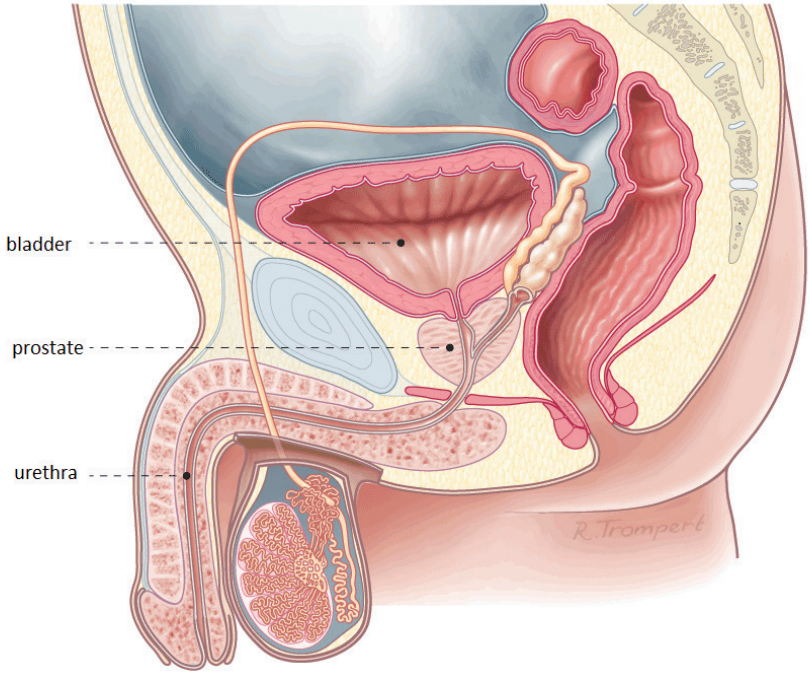
Objectives of this thesis were: 1. to study the level of information satisfaction after prostate cancer diagnosis and 2. to describe how the use of a decision aids affects the shared decision making process with regard to treatment choice, values clarification and satisfaction with information provision for patients diagnosed with both PC and BPH.

The prostate

The small gland, with its truncated cone shape, just below the bladder and only present in men, is called the prostate (Figure 1). It secretes prostatic fluid which keeps the spermatozoa alive during their journey outside the body and inside the vagina. In young men, the prostate has the size of a walnut, but as men age the prostate increases in size. As figure 1 shows, the urethra runs through the prostate and may be constricted by prostatic enlargement which can then cause urinary symptoms.

The prostate also secretes prostate specific antigen (PSA), an enzyme which can be measured by blood tests. Increased levels of PSA may be a result of a benign prostatic enlargement, an infection or prostate cancer.

Figure 1. Position of the prostate



Prostate cancer

Prostate cancer (PC) is the most common malignancy in European men (excluding skin cancer) with the highest incidence in the Northern and Western Europe (1). Ten-year overall survival percentages of all stages have increased from approximately 73% to 83% in the last decades, possibly as a result of improved treatment techniques and earlier diagnosis (4-7). Because PC typically affects elderly men more often it is a much bigger health issue in developed countries than in developing countries (8). In the Netherlands, more than 10.000 patients are diagnosed with PC each year. Due to earlier detection and an ageing population the incidence is growing (6, 9, 10). As the number of PC diagnoses and bad news conversations will increase it is most important patients are supported by their clinician with regard to information provision and treatment decision making.

Prostate cancer Classification

PC is classified into low-, intermediate and high risk PC (localized or locally advanced) based on PSA levels, Gleason patterns and tumour extension (Table 2) (1, 10). The

Tumour Node Metastasis (TNM) classification and risk group stratification are used to group patients with similar clinical outcomes and similar risk of biochemical recurrence after treatment, Table 1 (10). In this thesis, the focus will be on low- and intermediate risk localized PC since multiple treatment options with comparable survival outcomes are available for these patients (1).

Table 1: Tumour Node Metastasis (TNM) classification of prostate cancer

T – Primary Tumour	
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Clinically unapparent tumour not palpable or visible by imaging
T1a	Tumour incidental histological finding in 5% or less of tissue resected
T1b	Tumour incidental histological finding in more than 5% of tissue resected
T1c	Tumour identified by needle biopsy (e.g. because of elevated PSA level)
T2	Tumour within the prostate [1]
T2a	Tumour involves one half of one lobe or less
T2b	Tumour involves more than half of one lobe, but not both lobes
T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule[2]
T3a	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter,rectum, levator muscles, and/or pelvic wall.
N - Regional Lymph Nodes[3]	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis[4]
M - Distant Metastasis[5]	
Mx	**Distant metastatis cannot be assessed**
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

1. *Tumour found in one or both lobes by needle bbiopsy, but not palpable or visible by imaging, is classified as T1c*
2. *Invasion into the prostatic apex, or into (but not beyond) the prostate capsule, is not classified as pT3, but as pT2*
3. *The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries*
4. *Laterality does not affect the N-classification*
5. *When more than one site of metastasis is present, the most advances category should be used*

Table 2: European Association of Urology (EAU) risk groups for biochemical recurrence of localized and locally advanced prostate cancer

Low-risk	Intermediate-risk	High-risk	
	Definition		
PSA < 10 ng/mL	PSA 10–20 ng/mL	PSA > 20 ng/mL	any PSA
and Gleason < 7	or Gleason 7	or Gleason >7	any Gleason
and cT1-2a	or cT2b	or cT2c	cT3–4 or cN+
Localised	Localised	Localised	Locally advanced

PSA=prostate specific antigen

Prostate cancer treatment and side effects

Patients diagnosed with low- or intermediate risk localized PC are often eligible for multiple treatment options with comparable oncological outcomes. The most common curative treatment options are radical prostatectomy (RP), external beam radiation therapy (EBRT) and brachytherapy (BT). However, curative treatment is not always necessary. In fact for many low-risk patients active surveillance (AS) can be considered to avoid or defer curative treatment, this accounts for approximately 30% of the newly diagnosed patients (1). Given the lack of evidence for the superiority of any one of the possible treatment options, current guidelines offer multiple treatment options (1, 10). Unfortunately, all these treatment options are accompanied by their own risks and side effects which may influence health related quality of life (HRQoL) negatively (16-20). For instance, AS has been associated with distress and anxiety, RP with erectile dysfunction (approximately 50-90%) and urinary incontinence (approximately 5-65%), EBRT with bowel problems (approximately 5-57%) and erectile dysfunction (approximately 38-73%) and BT with erectile dysfunction (approximately 40-64%) and obstructive/irritative urinary complaints (approximately 50-80%) (1, 16, 18-23). In order to make the best treatment decision it is therefore important to inform PC patients about the risks and benefits of each treatment option and clarify patients' preferences.

Information provision

Proper information provision helps patients to understand their illness, prepares them for treatment, promotes recovery and assists patients to cope with the disease (11, 12). Moreover, providing information that is congruent with patients' needs, is a well-known determinant for information satisfaction and may also affect Health related quality of life (HRQoL) positively (11).

Patients diagnosed with prostate cancer may experience barriers to obtain information from clinicians. Most frequent barriers are ‘worrying about asking too many questions’ and ‘worrying about having enough time (24). Furthermore they are uncertain about the quality of information printed or found on the internet and patients are uncertain if the information is applicable for their personal situation (24). Subsequently patients want urologists to provide them with information.

Unfortunately, many PC patients are dissatisfied about the information they received or have unmet information needs after being diagnosed (13, 14). Even worse: in some European countries around a third of the PC patients did not receive any information about their condition at diagnosis (14). These are very disconcerting facts when taking into account that approximately 80% of the PC patients want to know all possible information, both good and bad news (12, 15). Because PC treatment options differ in their benefit-risk profiles it is highly important that patients are well informed about the accompanying risk profiles in order to make a well-considered and deliberate treatment choice. Moreover, accurate information provision is necessary to enable shared decision making (SDM) after PC diagnosis.

Shared decision making for prostate cancer

Improvement can be achieved in PC information provision and patient involvement in the treatment decision making process. Since no strong treatment recommendations are provided in current guidelines, PC treatment decision making is highly preference-sensitive and requires shared decision making (SDM). SDM is defined as ‘an approach 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, to achieve informed preferences’ (25). Applying SDM in clinical practice results in knowledge gain, more confidence in decisions and more patient involvement. But despite this evidence clinicians are frequently sceptical about applying SDM while they think that patients do not want to be involved, lack the capacity/ability to be involved, might make ‘wrong’ decisions or clinicians worry that SDM is not practical considering time pressure (25). Consequently, treatment choices for PC are often based on a urologist’ advice as this is rated as an important factor influencing treatment decision by patients (26-29). This is an unwanted situation because multiple studies show that urologists and patients differ in their preferences and trade-offs, indicating that urologist alone cannot properly decide what is the best treatment option for patients when multiple options are available (30-32).

Taking into account that approximately 70-80% of the patients want to be involved in decision making, the first step for clinicians is to explain that there is no superior

treatment choice, that a decision needs to be made and (if eligible) active surveillance is an appropriate option as well. The next step is to discuss the accompanying risks and benefits of all possible treatment options and relevant evidence-based information. Then, the patient's expectations, values, idea's and concerns should be elicited and a form of partnership must be built between the patient and clinician. To prevent that the patient's responsibility becomes a personal burden, the clinician needs to explain that the process preferably is a shared one. In other words, the clinician should encourage the SDM process. After information provision the patient's preferred role (active/passive/collaborative) needs to be explored because patients who initially may be reluctant towards participation in decision making often change their mind after the options have been laid out (25, 33). In short, SDM is applied in order to choose the best treatment option, adjusted to the patients' individual preferences and values. Decision aids (DAs) are instruments which can be used to support SDM in clinical practice (3, 34).

Decision aids

Decision aids (DAs) are decision support tools varying from paper pamphlets, booklets to web-based instruments. All designed to assist the patient and clinician in SDM by explaining the decision to be made, providing evidence-based information about treatment options and their associated outcomes compared to their alternatives and sometimes by eliciting values (3). DAs are used for a variety of medical trade-offs, for example for PSA screening decisions, bariatric surgery, prostate cancer treatment, prenatal screening and ischaemic heart disease treatment (3). Patients using a DA feel more knowledgeable, better informed, have more accurate risk perceptions and may play a more active role in decision making compared to patients not using a DA (3).

To elicit preferences values clarification exercises (VCEs) are frequently used methods. Several types of VCEs exist in order to make clear that a trade-off should be considered. The use of VCEs in decision aids may facilitate the comparison of options and elicit personal values and preferences (35, 36).

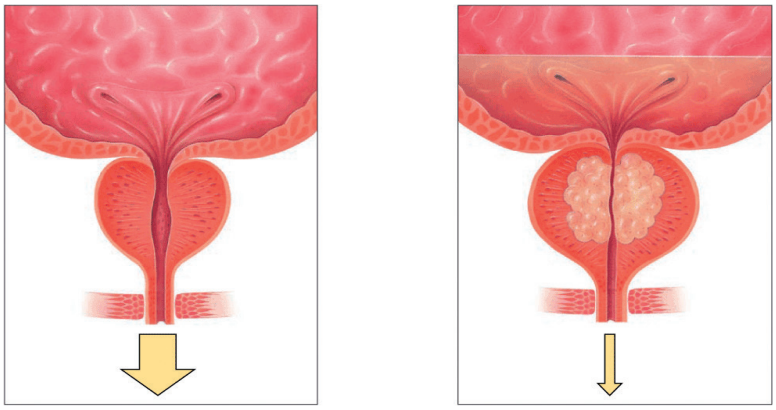
In this thesis, decision aids for the treatment of low- and intermediate risk prostate cancer and lower urinary tract symptoms are studied.

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a benign histologic condition which can cause bladder outlet obstruction (BOO) resulting in lower urinary tract symptoms (LUTS), see figure 2. LUTS is one of the most common complaints in the ageing men with a

prevalence ranging from 50% to 75% in men over the age of 50 years (37). Clinical manifestations of BPH often are a combination of diverse symptoms like weak urinary stream, interrupted stream, hesitancy, leaking/dribbling, increased frequency of urination, urgency and nocturia. In practice, LUTS is divided into 3 categories: storage, voiding and post-micturition symptoms, often caused by BOO due to BPH (from here indicated as LUTS/BPH) (2, 38).

Figure 2.



Prostate without BOO, normal urinary flow

Prostate with BOO, obstructed urinary flow

In contrast to prostate cancer, LUTS/BPH is a benign condition. However, LUTS/BPH can lead to bothersome severe complaints. Complications include acute urine retention, urinary tract infections, hydronephrosis and even renal failure (39). Furthermore, literature shows that LUTS/BPH can negatively impact quality of life (QoL) (2, 40, 41). Treatment is focused on symptom improvement and the increase of QoL, as well as the prevention of the risks and complications (2).

To quantify and objectify symptoms EAU guidelines recommend symptom score questionnaires for the initial assessment of male LUTS (38, 42) . The International Prostate Symptom Score (IPSS) is a widely used and validated eight-item questionnaire covering 7 symptoms (frequency, nocturia, weak urinary stream, hesitancy, intermittency, incomplete emptying, urgency) and QoL (43). IPSS Scores can be divided in *mildly* (1-7 points), *moderately* (8-19 points) and *severely* (20-35 points) symptomatic (38). QoL is scored separately with a range from 0-6 points.

LUTS/BPH treatment

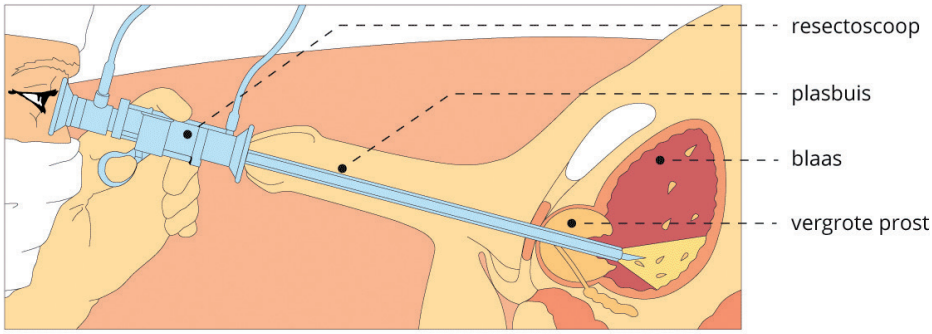
Treatment options for LUTS/BPH include watchful waiting (lifestyle advises/monitoring), medication and surgery (different approaches).

Watchful waiting comprises lifestyle advises such as the reduction of fluid intake at specific times (e.g. in the evening or when going out in public) or avoiding intake of caffeine or alcohol (which may have a diuretic effect). Other advises are distracting techniques like penile squeeze, breathing exercises, perineal pressure and mental tricks to help control storage symptoms (38).

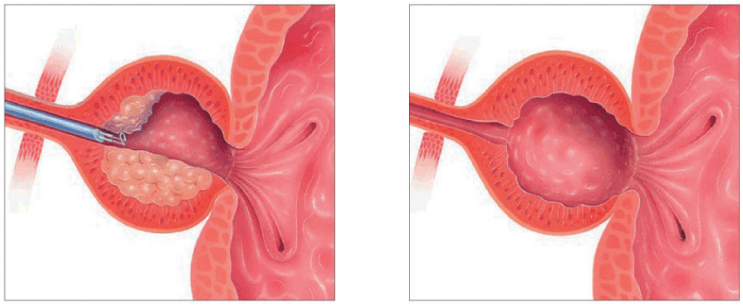
There are different types of medication. Frequently used pharmacological treatments for voiding symptoms are α1-blockers and/or 5-alfa reductase inhibitors. For storage symptoms, muscarinic receptor antagonists or beta-3 agonists are often prescribed drugs to reduce symptoms. Sometimes a combination of medication is used to improve urinary complaints (38). Like all pharmacological treatments, every type of medication has his own specific accompanying side effects.

When medication does not lead to a sufficient decrease in symptoms, surgery can be helpful. Various types of surgical treatments have been developed to reduce symptoms; however, transurethral resection of the prostate (TURP) is the gold standard treatment for LUTS caused by BOO/BPH, see Figure 3 (38). Most often encountered side effects are retrograde ejaculation (65%), bladder neck contracture (4.7%) urinary tract infections (4.1%) , urethral stricture (3.8%), urinary incontinence (2.2%), post-surgical bleeding requiring transfusion (2%) and incontinence (38). Next to the TURP, open prostatectomy, laser vaporisation, laser enucleation, prostatic urethral lift, transurethral microwave therapy and transurethral needle ablation are possible surgical treatment options with their own specific benefit and harm profiles (38).

Figure 3. Transurethral resection of the prostate (TURP)



Uroloog verwijdert via een resectoscoop het vergrote prostaatweefsel



TURP procedure

result after TURP

Shared decision making for LUTS/BPH

Indications for the various treatment options are not sharply demarcated in European guidelines and require shared decision making (2, 38). In the absence of well-defined guidelines there are strong differences between doctors' interpretations and treatment variation.

Furthermore, the doctors' opinion appears to play an important role in the management of LUTS/BPH, but studies showed that doctors expectations about treatment can differ from patients expectations (44). Thereby, the information patients have about BPH may not be accurate, leading to a false impression about the disease and its treatment. Obviously, trade-offs must be made between expected benefits, side effects, risks and burden of treatments, and disease burden. A potential route to provide sufficient information about LUTS/BPH, clarify patient preferences, and reduce unwanted treatment variation is by shared decision making (SDM) using decision aids (45-47) .

Despite the high prevalence rate of LUTS/BPH, attention for the development and evaluation of DAs is far less than for other (oncological) conditions. Most available LUTS/BPH DAs contain outdated LUTS/BPH content, did not involve patients and/or urologists or did not clarify patient preferences (45-47). Thereby, no structured LUTS/BPH DA development has been described before.

Outline of this thesis

This thesis critically evaluates the current level of satisfaction with information provision among prostate cancer survivors. Furthermore, we attempt to improve and evaluate the shared decision making process for the treatment of patients with low- and intermediate risk prostate cancer and LUTS/BPH by using preference sensitive decision aids.

Part 1

Accurate information provision is needed to enable SDM after PC diagnosis. In **Chapter 2** we investigate the level of perceived information satisfaction approximately four years after PC diagnosis. Furthermore, we describe correlations between perceived satisfaction with information provision and QoL and illness perception, to give insight in possible confounders.

After the development of a web-based DA for the treatment of low- and intermediate risk prostate cancer we closely investigate the effect of this DA on treatment decision making in **Chapter 3**. Using data extracted from the DA, an accurate study of the shifts in treatment preferences before and after DA use is possible. This chapter shows analyses of values clarification exercises and the values patients think are important in choosing for certain PC treatments.

A cluster randomized controlled trial is performed in 18 hospitals in the Netherlands to study the effect of the DA on treatment differences, decisional regret and information satisfaction between patients receiving the DA and patients receiving care as usual. We hypothesise that more patients would choose for AS after DA use compared to when receiving care as usual. **Chapter 4** describes the DA effect on treatment differences between the two groups. To more closely investigate trends in the treatment decision making process after DA use, we assess “received treatment” between the two groups, focussing on patients eligible or not eligible for AS.

The next chapter studies patient reported outcomes regarding decisional regret and information satisfaction one year after PC diagnosis. Higher levels of information

satisfaction and less regret are expected in patients using the DA compared to patients in the control group. **Chapter 5** presents 12-months follow-up results regarding decisional regret, treatment satisfaction and information satisfaction. Anxiety and depressive symptoms are determined to find correlations between anxiety/depression and patient reported outcomes.

Part 2

For patients with LUTS/BPH, we aim to improve and standardize information provision and involve patients in decision-making (45-47). By involving urologists and patients in development we try to facilitate implementation since clinicians may find that offering DAs will not fit in their workflow, are concerned that patients are not able to process the DA information or because they report a lack of confidence regarding DA content (48). Our objective is to structurally develop an interactive web-based DA for the treatment of LUTS/BPH which fits clinical practice. **Chapter 6** shows a structured, 4 stage DA development for the treatment of LUTS/BPH.

Subsequently, **Chapter 7** illustrates the results of patients using the DA regarding treatment preferences before and after DA use, values clarification exercises and patients' and healthcare satisfaction with the DA. This chapter discusses whether the DA supports the SDM process in LUTS/BPH treatment decision making for both patients and physicians.

Chapter 8 discusses the main results of the studies presented in this thesis with special emphasis on the implications for daily practice and future research.

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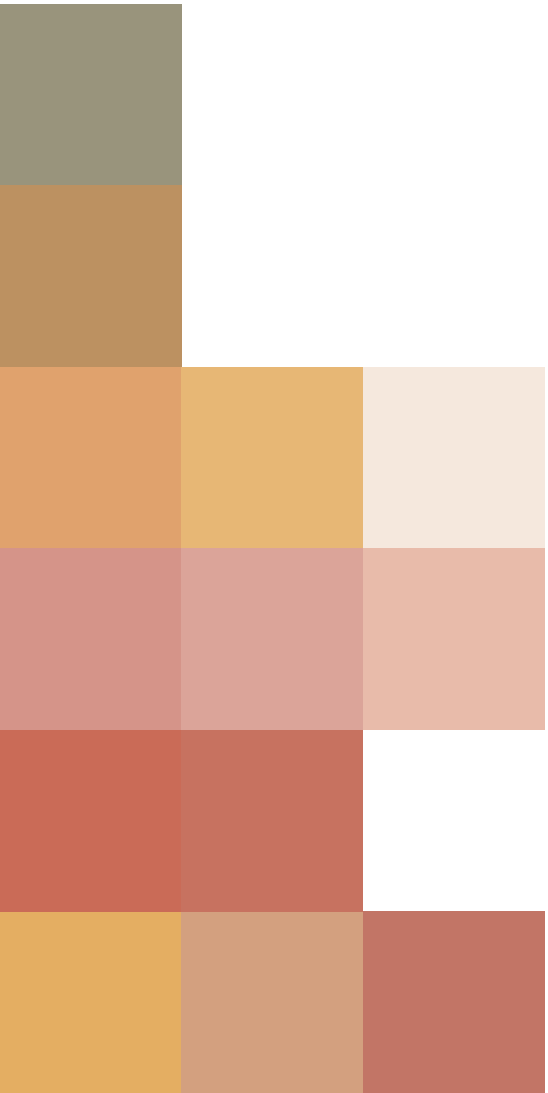
Part 1



Chapter 2

Patients are dissatisfied with information provision: perceived information provision and quality of life in prostate cancer patients

R.E.D. Lamers, M. Cuypers, O. Husson, M. de Vries, P.J.M. Kil, J.L.H.R Bosch, L.V. van de Poll-Franse

Psycho Oncology
2016;25(6):633-40

Abstract

Objective To determine the satisfaction with information received by prostate cancer survivors and associations with health-related quality of life (HRQoL) and illness perception.

Methods A cross-sectional study was performed among 999 patients diagnosed between 2006 and 2009. All patients received a questionnaire on HRQoL (EORTC QLQ-C30), illness perception (B-IPQ) and satisfaction with information provision (EORTC QLQ-INFO-25). Multivariate regression analyses were performed to assess the association between satisfaction with information provision and HRQoL as well as illness perception.

Results Response rate was 70% (N = 697), 34% (N = 222) indicated to be dissatisfied with the information received. Multivariate linear regression analyses showed a significant positive association between satisfaction with information provision and global health (P= <0.001), emotional functioning (P = 0.004), social functioning (P = 0.027), physical functioning (P = 0.002) and role functioning (P = 0.001). Satisfaction was negatively associated with illness perception subscales on consequences (P = 0.020), timeline (P= 0.031), personal control (P = 0.013), treatment control (P < 0.001), illness concern (P< 0.001), coherence (P = 0.001) and emotional representation (P = 0.004). Hence, more satisfied patients reported fewer consequences of disease, illness concern and emotional representation, but higher personal and treatment control and coherence.

Conclusions A third of all prostate cancer survivors reported to be dissatisfied with the information received and scored worse on HRQoL and illness perception. A prospective randomized study is needed to study the effect of an intervention that improves information provision on HRQoL and illness perception outcomes.

Background

After introduction of PSA testing, prostate cancer (PC) has become a disease with an increased number of long- term survivors related to stage shift and generally favourable outcomes (1,2). Proper information provision after diagnosis helps patients understand their illness, prepares them for treatment, promotes recovery and assists them to cope with the disease (3,4). Unfortunately, many prostate cancer patients have unmet information needs or are dissatisfied with information provision after being diagnosed with PC (5,6). Worse, in some European countries around a third of prostate cancer patients do not receive information about their condition at diagnosis (5,6). This is an unwanted situation, considering the fact that over 80% of the patients indicate that they want to know all possible information, both good and bad news (4,7).

Previous studies have described the importance of information provision considering the association with illness perception and health-related quality of life (HRQoL) (3,8). In Dutch patients diagnosed with lymphoma, multiple myeloma, endometrial or colorectal cancer it has been described that satisfaction with the information received is associated with better illness perception and higher overall HRQoL (3,9,10). However, despite the growing number of PC survivors the association between information provision and illness perception and HRQoL in prostate cancer survivors is indistinct (11). Hence, better insight in this relation is needed to investigate if improvement of satisfaction with information provision may possibly improve illness perception and HRQoL in the near future.

This study aims to assess satisfaction with information received and the relationship with illness perception and HRQoL in PC patients. We hypothesized that dissatisfied prostate cancer patients would indicate worse scores on illness perception and HRQoL scales.

Methods

Setting and participants

In 2011, a cross-sectional study was performed among 999 patients, diagnosed with prostate cancer between 2006 and 2009, as registered in the Eindhoven Cancer Registry (ECR) of the Comprehensive Cancer Centre the Netherlands (CCCN). The ECR is part of the nationwide Netherlands Cancer Registry and collects data of all new cancer patients in the southern part of the Netherlands. This geographic area covers 2.4 million inhabitants (12). The ECR registry comprises 10 general public hospitals and 2 public radiotherapy departments. Patients in 10 hospitals were selected using the ECR.

We made a random selection of approximately 150 patients for each hospital. Seven hospitals were willing to participate, leaving 1053 patients eligible for study participation. In 54 cases the address was unverifiable; as a result 999 participants were approached for participation. A total of 697 patients responded to the invitation and 302 patients did not respond (70% response rate). Similar PROFILES studies reported response rates between 69% and 86% (9,13).

Data collection

All prostate cancer patients (tumour stage T1–T4) were eligible for participation. Participation implied that a patient filled in a web-based or, on request, a paper-based questionnaire. Patients were asked for participation through their (ex-)urologist by a letter explaining the study and questionnaire. After obtaining informed consent the questionnaire form was returned to the CCCN. Patients also consented to link to their clinical disease history as registered in the ECR. When the questionnaire was not received after informed consent the patients were reminded within 2 months by sending a new information letter. Medical characteristics had been prospectively collected between 2006 and 2009 within the ECR.

In 2011 data were collected within the PROFILES (Patient Reported Outcomes Following Initial treatment and Long Term Evaluation of Survivorship) registry. PROFILES is a registry for the study of the physical and psychosocial impact of cancer and its treatment from a dynamic, growing population-based cohort of both short- and long-term cancer survivors. It contains a large web-based component and is linked directly to clinical data from the ECR. Detailed information on the PRO- FILES registry has been described earlier (14). The study was approved by the Medical Ethics Committee of the Maxima Medical Centre Eindhoven.

Disease and patient characteristics

We collected socio-demographic data (i.e. marital status, employment status and level of education) using questionnaires. The ECR data was used to obtain clinical characteristics and further patient information, for example date of birth, treatment characteristics, date of diagnosis, Gleason score and Tumour-Node-Metastasis (TNM) stage at diagnosis (15). To assess co-morbidity we used the Self-administered Co-morbidity Questionnaire (SCQ) whereby patients were asked to identify the presence of co-morbidities in the previous 12 months (16).

Questionnaires

Information provision

For the evaluation of perceived level of and satisfaction with information provision the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-INFO-25) questionnaire was used. This is a 25-item questionnaire to evaluate the provided information received by cancer patients (17). The response format is a 4-point Likert scale ('not at all'–'a little'–'quite a bit'–'very much'), except four items that have a dichotomous yes/no response. For the current analyses the 4-point Likert scale of the 'satisfaction with information provision' item was dichotomized in dissatisfied ('not at all'–'a little') and satisfied ('quite a bit'–'very much') to ease clinical interpretation. The questionnaire is divided in four subscales: information about the disease, medical tests, treatment, other services and eight additional single items (among others: satisfaction with the amount of received information and helpfulness of the information disclosed). All scales (except for satisfaction with information provision) were linearly converted to a 0–100 scale where higher scores implicate higher level of information received or higher information wishes (18). Previous studies reported good internal consistency for all scales ($\alpha > 0.7$) as for test–retest reliability (intraclass correlations > 0.70) (18). Internal consistency based on the current data was good ($\alpha = 0.74–0.89$).

Health-related quality of life

We used the EORTC QLQ-Core 30 (EORTC QLQ-C30) and prostate module (EORTC QLQ-PR25) to assess HRQoL in prostate cancer survivors (19,20). The EORTC QLQ-C30 questionnaire includes 30 items, divided in several scales: five functional scales (physical, role, emotional, social and cognitive functioning), three symptom scales (fatigue, pain and nausea/vomiting) and several single items considering global health and quality of life, financial impacts and symptoms. Side effects of cancer treatment, bowel- and urinary symptoms, sexual activity and sexual functioning were assessed using the 25-item EORTC QLQ-PR25. The answer format of both scales is a 4-point Likert scale ('not at all'–'a little'– 'quite a bit'–'very much'). In line with the prescribed scoring instructions of the EORTC all scales were linearly converted to a 0–100 scale. Higher scores are unfavourable for the symptom items whereas for the functional items higher scores indicate favourable outcomes. For urinary symptoms and sexual function scales internal consistency is good ($\alpha = 0.70–0.86$) (21). The use of these questionnaires to assess the HRQoL in prostate cancer patients is internationally validated and well accepted in Europe as well in the Netherlands (22–25). Internal consistency based on the current data was good for ORTC QLQ-C30 ($\alpha = 0.65–0.92$).

Illness perception

Illness perception was evaluated using the Brief Illness Perception Questionnaire (B-IPQ), a nine item scale which assesses cognitive and emotional representations of the illness (26). The questionnaire is divided in cognitive and emotional domains concerning consequences (How much does your illness affect your life?), timeline (How long do you think your illness will continue?), personal control (How much control do you feel you have over your illness?), treatment control (How much do you feel your treatment can help your illness?), identity (How much do you experience symptoms from your illness?), concern (How concerned are you about your illness?), emotional representation (How much does your illness affect you emotionally?) coherence (How well do you understand your illness?).

The response format is a single item scale approach to assess perceptions on a linear 1–10 point scale (9). A good test–re-test reliability and concurrent validity is described (26). Higher scores indicate a more threatening view of patients' illness, except for personal control, treatment control and coherence where higher scores indicate a more positive view of their illness. Therefore these reversed answer scales on personal control, treatment control and coherence are converted. Based on the current data internal consistency was good ($\alpha = 0.71$).

Statistical analyses

We conducted a one-way ANOVA to estimate differences in age between responders, non-responders and patients with unverifiable addresses. Chi-square test was used to examine group differences for discrete variables. Means on different subscales were compared between satisfied and dissatisfied patients using independent samples T-tests. The association between the dichotomized outcome satisfaction with information and HRQoL was assessed using a multiple linear regression analysis. We adjusted for age at the time of questionnaire, T-stage, partnership, co-morbidity, time since diagnosis and education. Covariates were determined a priori as has been done in similar previous studies and as earlier has been described as a solid method (10,27).

For further analyses of the EORTC QLQ-PR25 we excluded bowel function and side effects of hormonal treatment subscales because of poor internal consistency in these subscales ($\alpha < 0.7$) (21). Bivariate correlation analyses (Pearson's) were performed to investigate correlations between prostate cancer specific symptoms and global health. Clinically relevant differences were determined with 'Norman's rule of thumb'. This implicates that a difference of approximately half a standard deviation (SD) indicates a clinically relevant threshold of discrimination for changes (28).

All analyses were performed using SPSS version 19.0 (Statistical Package for Social Sciences, Chicago, IL, USA). A P-value < 0.05 was considered statistically significant.

Results

Patient and tumour characteristics

Six hundred and ninety seven patients completed and returned the questionnaire which resulted in a response rate of 70%. Patients with unverifiable addresses were younger compared with non-respondents (mean 73, 76, respectively, P < 0.001). There were no group differences in tumour stage (P = 0.198) between respondents, non-respondents and patients with unverifiable addresses. Baseline demographics and clinical characteristics are represented in Table 1.

Perceived information provision

Of the PC patients, 34% (N = 222) indicated to be dissatisfied with information provision. Mean age did not significantly differ between patients satisfied with information provision and dissatisfied patients (P = 0.107, Table 1). Over a quarter (27%, N = 177) of the patients indicated that they had wanted to receive more information about PC whereas 4% (N = 25) wanted to have received less information about their PC. The information actually received was found to be helpful by 72% (N = 469). Satisfaction with information provision was 66% for radical prostatectomy, 78% for brachytherapy, 63% for EBRTx, 66% for EBRTx + hormones, 66% for expectant management and 63% for hormonal treatment (Table 1). No significant differences in satisfaction between initial treatment options were found (P = 0.243, Table 1).

Multivariate linear regression analyses, adjusted for covariates, showed a statistically significant positive association of the EORTC INFO-25 subscale ‘information about disease’ with global health (Beta 0.161, P < 0.001), and emotional functioning (Beta 0.087, P = 0.034).

Health-related quality of life

In total 688 patients completed the EORTC QLQ-C30. Mean global health score for all prostate cancer survivors was 77.8 (SD 18.1). Dissatisfied patients scored significantly lower (P ≤ 0.001) compared with satisfied survivors on global health (mean 74 vs. 80), physical functioning (mean 80 vs. 85), role functioning (mean 76 vs. 84), emotional functioning (mean 84 vs. 89) and social functioning scale (mean 86 vs. 91). Only for

cognitive functioning (mean 83 vs. 85, respectively) this was not statistically significant (P = 0.163), see Figure 1. Mean scores on symptom scales fatigue (23 vs.19, P = 0.02) and pain (19 vs. 14, P = 0.029) were statistically significantly higher for dissatisfied patients; nausea/vomiting (3 vs. 2, P = 0.4) was not different. Multivariate linear regression analysis, including confounding variables, showed a statistically significant positive association between satisfaction with information provision and global health (P = <0.001), emotional functioning (P = 0.004), social functioning (P = 0.027), physical functioning (P = 0.002) and role functioning (P = 0.001) (Table 2).

Table 1. Baseline demographics and clinical characteristics of respondents *N* = 697[a]

Demographic characteristics				
	Total	**Dissatisfied patients**	**Satisfied patients**	**P-value**
Age at time of survey in years, mean (SD)	71.3 (7.2)	71.8 (7.3)	70.8 (7.1)	0.107
Years since diagnosis, mean (SD)	4.0 (1.2)	4.0 (1.1)	4.0 (1.2)	0.679
	Total *N* (% column)	Dissatisfied patients *N* (% row)	Satisfied patients *N* (% row)	*P*-value
Education*				
Low	105 (16)	42 (40)	63 (60)	
Medium	386 (59)	141 (37)	245 (63)	
High	161 (25)	36 (22)	125 (78)	
				0.002
Current occupation				
Employed	87 (14)	26 (30)	61 (70)	
Not employed	546 (86)	181 (33)	365 (67)	
				0.539
Partnership				
Partner	554 (85)	181 (33)	372 (67)	
No partner	100 (15)	39 (39)	61 (61)	
				0.218
Clinical characteristics	Total	Dissatisfied patients	Satisfied patients	*P*-value
	N (% column)	*N* (% row)	*N* (% row)	
Clinical stage				
T1	306 (47)	94 (31)	212 (69)	
T2	226 (35)	81 (36)	145 (64)	
T3	107 (16)	40 (37)	67 (63)	
T4	13 (2)	2 (15)	11 (85)	

Table 1. (Continued)

Demographic characteristics				
	Total	**Dissatisfied patients**	**Satisfied patients**	**P-value**
				0.222
Gleason score				
2–6	347 (54)	112 (32)	235 (68)	
7	193 (30)	67 (35)	125 (65)	
8–10	103 (16)	37 (36)	66 (64)	
				0.730
Initial treatment**				
Prostatectomy	174 (26)	60 (34)	114 (66)	
Brachytherapy	87 (13)	19 (22)	68 (78)	
EBRT***	52 (8)	19 (37)	33 (63)	
EBRT + hormones	106 (16)	36 (34)	70 (66)	
Managed expectantly	121 (18)	41 (34)	80 (66)	
Hormonal treatment	75 (11)	28 (37)	47 (63)	
Other combinations/ treatments	44 (7)	19 (43)	25 (57)	
				0.243
Co-morbidity (self report)				
none	155 (24)	56 (36)	99 (64)	
1	208 (33)	50 (24)	158 (76)	
≥2	275 (43)	105 (38)	170 (62)	
				0.003

[a]Because of missing values number do not always add up to count 697.
*Education: low (no or primary school), medium (lower general secondary education or vocational training) and high (pre-university education, high vocational training and university).
**Treatment received in the first 6 months after diagnosis.
***External Beam Radiotherapy

Prostate cancer specific quality of life

The EORTC QLQ-PR25 was completed by 639 patients (urinary function N = 639, incontinence N = 208, sexual activity N = 641 and sexual functioning N = 312). Higher scores indicate better functioning or increased symptoms. Dissatisfied patients had lower mean scores on sexual activity and sexual functioning (24 vs. 25, P = 0.531 and 50 vs. 56, P = 0.028, respectively). Furthermore, dissatisfied patients reported statistically significantly higher mean scores on urinary symptoms and incontinence (23 vs. 17, P < 0.001 and 24 vs. 12 (clinically relevant difference), P = 0.004, respectively). We also found statistically significant correlations between global health scores and sexual activity (r =

0.15, P < 0.001), sexual functioning (r = 0.23, P < 0.001), urinary symptoms (r = 0.24, P < 0.001) and incontinence (r = 0.22, P < 0.002). Higher global health scores were reported in patients with higher sexual activity and sexual functioning. Negative correlations were found between global health and prostate cancer treatment symptoms indicating lower global health scores when urinary symptoms and incontinence increase. Data not shown.

Table 2: Multivariate linear regression analysis evaluating the association of dissatisfaction/satisfaction with information provision with HRQoL functioning scales.

	Global Health N = 573 Beta	**Cognitive Functioning N = 569 Beta**	**Emotional Functioning N = 564 Beta**	**Social Functioning N = 571 Beta**	**Physical Functioning N = 560 Beta**	**Role Functioning N = 560 Beta**
Satisfaction						
Satisfied vs. dissatisfied	.143**	.046	.116**	.092*	.123**	.14**
Partner						
Yes vs. No	.024	.062	.026	-.009	-.020	-.033
Co morbidity						
1vs. 0	-.060	-.077	-.016	.026	-.082	-.029
>1vs. 0	-.307**	-.280**	-.319**	-.202**	-.353**	-.303**
T-stage						
T2 vs. T1	-.036	-.011	.000	-.081	-.033	-.003
T3 vs. T1	-.056	-.032	-.110*	-.102*	-.079	-.032
T4 vs. T1	-.120*	-.065	-.041	-.114**	-.152**	-.109**
Education						
Medium vs.low	-.016	-.003	.017	.094	.020	-.041
High vs. low	-.007	-.025	.060	.116	.083	.020
Age at time of questionnaire	.005	-.024	.099*	.076	-.199**	-.035
Years since diagnosis	.025	-.044	-.063	-.086	-.041	-0.37

* *P*< 0.05
** *P* < 0.01

Illness perception

In total 677 patients completed the B-IPQ questionnaire. Dissatisfied patients scored significantly higher on all illness perception subscales in comparison with satisfied patients: consequences (mean 4.4 vs. 3.4, P < 0.001), timeline (mean 6.4 vs. 5.6, P = 0.008), personal control (6.2 vs. 5.4, P = 0.005), treatment control (mean 4.4 vs. 3.1, P < 0.001), identity (3.9 vs. 3.5, P = 0.039), illness concern (4.6 vs. 3.4 P = 0.001), coherence (4.4 vs. 3.3 P < 0.001) and emotional representation (mean 3.8 vs. 3.15 P = 0.001, respectively). In multivariate regression analyses, satisfaction was negatively associated with subscales on consequences (P = 0.020), timeline (P = 0.031), personal

control (P = 0.013), treatment control (P < 0.001), illness concern (P < 0.001), coherence (P = 0.001) and emo- tional representation (P = 0.004), indicating better illness perception in satisfied patients (Table 3).

Post-hoc analyses

The above mentioned results describe the relationship between prostate specific symptoms, global health and satisfaction with information provision. With regard to possible confounders we therefore performed additional analyses to eliminate the effect of prostate cancer specific symptoms on HRQoL and satisfaction with information provision. Multiple linear regression analyses including the previous described confounding variables with the additional covariates 'urinary symptoms' and 'incontinence' still showed a statistically significant positive association between satisfaction with information provision and global health (Beta 0.112, P = 0.008 and 0.187, (P = 0.018)). For the additional covariate sexual functioning Beta was 0.061 (P = 0.315) (data not shown).

Table 3: Multivariate linear regression analysis evaluating the association of satisfaction with information provision with illness perception (B-IPQ) subscales

	Conse-quences N = 571 Beta	Timeline N = 557 Beta	Personal control N = 555 Beta	Treatment control N = 558 Beta	Identity N = 565 Beta	Illness concern N = 572 Beta	Cohe-rence N = 562 Beta	Emotional Representation N = 568 Beta
Satisfaction								
Satisfied vs. dissatisfied	-.149**	-.093*	-.110*	-.207**	-.081	-.192**	-.150**	-.120**
Partner								
Yes vs. no	.061	.080	.047	.023	.041	.053	-.082	.058
Comorbidity								
1 vs. 0	.075	-.030	-.030	-.109*	.054	-.031	-.071	.008
>1vs. 0	.209	-.072	-.010	-.057	.148**	.163**	-.014	.190**
T-stage								
T2 vs. T1	.117**	.081	.136**	-.025	.048	.064	.020	.057
T3 vs. T1	.261**	.127	.014	.007	.129**	.215**	-.032	.209**
T4 vs. T1	.131**	.086*	.029	.002	.072	.093*	.017	.048
Education								
Medium vs. low	-.111	-.001	-.004	-.010	.013	-.021	.052	-.077
High vs. low	-.035	.103	.067	.058	.022	-.023	-.015	-.112
Age at time of question-naire	-.145**	.126**	.013	.044	-.100*	-.058	.077	-.182**
Years since diagnosis	-.016	-.041	.032	-.009	.060	-.052	-.006	-.007

* *P* < 0.05; ** *P* < 0.01;

Answer scales on "personal control", treatment control" and "coherence" are converted due to reversed answer scales.

Discussion

The present study shows that more than a third of all prostate cancer patients is dissatisfied with the received information provision. Patients who were dissatisfied with information provision reported clinically relevantly lower scores on all subscales of provided information provision compared to satisfied patients. Similar results were earlier described in patients with lymphoma, multiple myeloma, endometrial cancer, colorectal cancer and thyroid cancer (9,29). Furthermore, over a quarter of the respondents indicated they had wanted to receive more information. These are undesirable results taking into account that information provision plays an important role in understanding the illness, preparing for treatment and treatment choice and coping with the disease (3,4). When comparing satisfaction with information provision between different treatment groups we found no statistically significant differences.

In our study we revealed that patients dissatisfied with information provision scored statistically significantly lower on HRQoL subscales global health, emotional functioning, social functioning, physical functioning and role functioning. Concerning the information provision sub- scales we found a significant association between the EORTC INFO-25 subscale 'information about disease' and global health indicating higher global health scores in patients who received a larger amount of information about disease. This is in line with our previously described results that patients dissatisfied with information provision scored significantly lower on the HRQoL subscale global health. Similar effect sizes between these scales are found in lymphoma patients; however the direction of these associations (positive/negative) was different which may be a result of a different malignancy, longer time since diagnosis and/or lower age in the lymphoma study (10). Husson and colleagues investigated the relationship between satisfaction with information provision and illness perception among patients with lymphoma, multiple myeloma, endometrial and colorectal cancer. They found significant associations between satisfaction and better ill- ness perception in all subscales, except for personal control (9). In our current analyses we found statistically significant correlations between all subscales except for identity. Apparently the effect of satisfaction with received information provision is, just like in other malignancies, highly associated with illness perception in prostate cancer patients.

The negative impact of prostate cancer and treatment- related symptoms as urinary symptoms, bowel symptoms and sexual dysfunction on HRQoL is well described (23,30,31). In our study, we found a significant but weak correlation between global health and sexual activity, sexual functioning, urinary symptoms and incontinence ($r = 0.22$, $P < 0.002$), confirming the earlier described findings.

Also in accordance with our hypothesis we showed that patients dissatisfied with information provision scored significantly lower on sexual activity and sexual functioning and higher on urinary symptoms and incontinence com- pared to satisfied patients. However, this study does not provide information on the direction or origin of these associations. We hypothesize that more symptoms will lead to dissatisfaction in retrospect and lower HRQoL scores (and vice versa). Therefore we performed post-hoc analyses to adjust for the association between prostate cancer specific symptoms and HRQoL. Addition of the covariate 'sexual functioning' eliminated the statistical significance of this association. However, after addition of the covariates 'urinary symptoms' and 'incontinence', a positive significant association between satisfaction with information provision and global health remained.

These results may imply that there is a possible relation- ship of the perceived information provision on HRQoL so that improving information provision may lead to higher HRQoL scores, regardless accompanying symptoms. The observed association between perceived information provision and HRQoL suggests that improving information provision may lead to higher HRQoL scores. However, as our findings are based on a cross-sectional data collection with retrospective questions, strong conclusions about causal associations between information provision, HRQoL and illness perception cannot be drawn.

Another limitation is that patients with unverifiable ad- dresses were younger compared with non-respondents which could led to selection bias in our study population. Furthermore, the mean time since diagnosis was 4 years which could influence results because of disturbed recall. It is for example possible that non-respondents are more negative, depressed or have overall lower HRQoL com- pared to respondents. As well for dissatisfied patients compared to the satisfied patients. On the other hand, the satisfied patients can be more optimistic, or have a better overall HRQoL compared to dissatisfied patients. Or patients with higher HRQoL scores indicate better received information provision when asked retrospectively and vice versa. These HRQoL issues will be addressed in a prospective RCT (The Dutch National Trial Register NTR4554), where satisfaction with information provision and HRQoL is measured directly after actual information provision (but before treatment) and 6 and 12 months after treatment. We will also investigate whether or not the use of a decision aid will improve satisfaction with information provision. This can then answer the question if higher satisfaction with information provision will improve HRQoL. Strengths of our population-based study are the high response rate of 70%, large sample size and the use of widely validated questionnaires.

In conclusion, after they had been treated, one in three of all prostate cancer survivors reported to be dissatisfied with the information received from the moment of diagnosis and these men scored worse on HRQoL outcomes and illness perceptions. A prospective randomized study is needed to study the effect of an intervention that improves information provision at diagnosis on HRQoL outcomes.

Acknowledgements

The authors would like to thank all respondents for participation in the study. Second we would like to thank the PROFILES registry and ECR for using their data.

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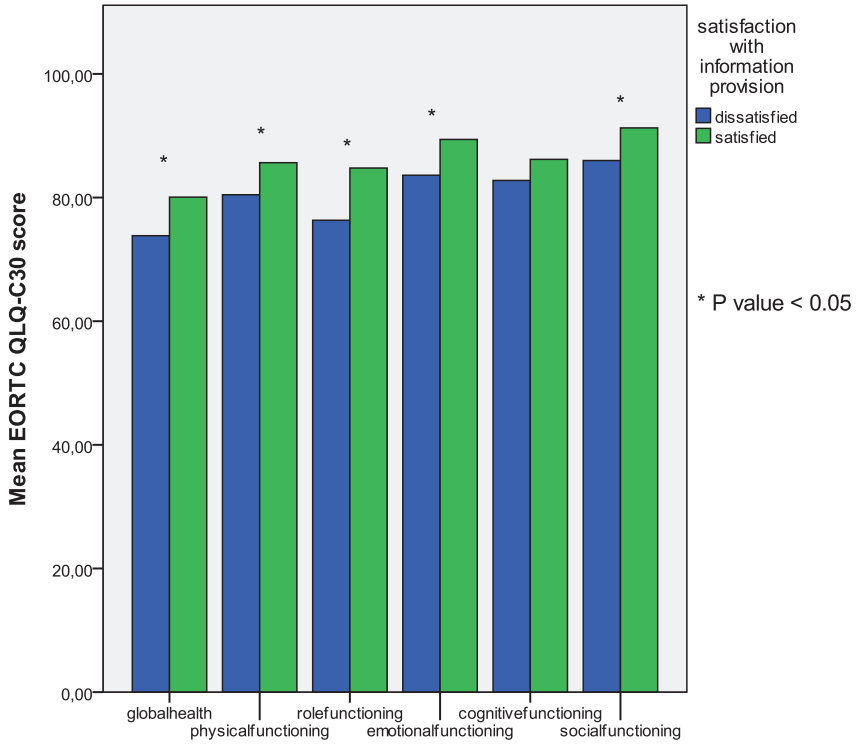
Figure 1: HRQoL and satisfaction with information provision. Mean EORTC QLQ-C30 scores (range 0-100) on different HRQoL subscales in satisfied and dissatisfied patients (univariate).



Chapter 3

How do patients choose between active surveillance, radical prostatectomy, and radiotherapy? The effect of a preference-sensitive decision aid on treatment decision making for localized prostate cancer

R.E.D. Lamers, M. Cuypers, M. de Vries, L.V. van de Poll-Franse, J.L.H.R. Bosch, P.J.M. Kil

Urologic Oncology
2017 Feb;35(2):37

Abstract

Purpose To determine the effect of a decision aid (DA) on treatment preferences and to investigate which patient preferences are important for final treatment preferences. We also determined if the patient's treatment decision was influenced by the urologist's treatment preference.

Patients and methods Between August 2014 and July 2015, newly diagnosed patients with low-/intermediate-risk prostate cancer were offered to use a web-based DA after diagnosis. Treatment preferences and patient's values were extracted from the DA. Urologists' treatment preferences were indicated at the time of inclusion.

Results We included 181 patients, of whom 21% preferred active surveillance, 33% radical prostatectomy, 10% brachytherapy, 3% external beam radiotherapy, and 34% did not indicate a specific preferred treatment option after DA use (missing N 6). Among 67%, treatment preference before DA use did not change after DA use.

In men who chose active surveillance after DA use, 97% (37/38) preferred to postpone unnecessary treatment. For radical prostatectomy, 91% (52/57) of the patients valued tumour removal, and for brachytherapy, 88% (15/17) valued incontinence worse than bowel complaints.

For 64% (missing N 21) of the patients, urologists indicated one specific preferred treatment option as most suitable for the patient concerned.

Agreement between final treatment decision and urologist's preference was lower (κ 0.68) than between final treatment decision and preferred treatment after DA use (κ 0.82).

Conclusion Most patients with prostate cancer chose the treatment in accordance with the post-DA preference and to a lesser extent the urologists preference; implications of this are prospectively investigated in an ongoing study.

Introduction

Patients diagnosed as having localized prostate cancer (PC) are often eligible for multiple treatment options with comparable oncology outcomes. Therefore, patients' values and preferences play an important role in treatment decision making (1,2). Although treatment options include active surveillance (AS), radical prostatectomy (RP), external beam radiotherapy (EBRT), and brachytherapy (BT), cur- rent guidelines do not indicate the best oncological treatment option (3). Unfortunately, treatment-related adverse effects and complications occur frequently and may influence the quality of life negatively (4–8). AS is mainly associated with anxiety and distress, RP with erectile dysfunction and urinary incontinence, EBRT with bowel problems and erectile dysfunction, and BT with erectile dysfunction and irritative/obstructive urinary complaints (4,6–10). Thus, the various PC treatment options differ in their benefit-risk profiles; therefore, treatment decision making is sensitive to patients' values and preferences (11). It is, therefore, important that patients are well informed about the possibilities of complications to make a value-based treatment decision. A recently published review article showed that patients who prefer AS over active treatment valued the avoidance of complications of surgery, and patients who chose for active treatment over AS reported pressure from urologists and family (12). In addition to this, specific treatment choices were more often related to intrinsic characteristics (e.g., duration of therapy and invasiveness) of treatment alternatives than to the probabilities of treatment-related adverse effects (12,13). The most common reasons for choosing RP were removal of the tumour; for EBRT, it was "evidence for the treatment"; and for BT, it was short duration of the treatment (13).

Despite the importance of patient preference clarification in the decision-making process, treatment choices are often based on a urologist's advice, rated as the most important factor influencing treatment decision (12,14–16). This is a disconcerting fact as studies have shown that patients and urologists differ in their preferences and trade-offs (1,11,17). Additionally, treatment recommendations of urologists may be biased, as urologists and radiation oncologists have been shown to often recommend the therapy that they themselves deliver (18).

Decision aids (DAs) are instruments to improve shared decision making, stimulate patients to take a more active role in decision making, and improve accurate risk perceptions and knowledge regarding treatment options (19). We developed a web-based DA containing evidence-based information about AS, RP, EBRT, and BT, including benefits and risks, success rates, and complication rates according to the current guidelines and literature (3,20). Values clarification exercises (VCEs) are used to clarify patients' preferences and support patient involvement in decision making.

In this study, we investigated the initial PC treatment preference after diagnosis (before DA use and initial treatment preference) and how this treatment preference may change owing to the use of a DA (final treatment preference). In addition, we determined which patient preferences are important in the determination of patients final treatment choice. Finally, we determined to what extent a patient's treatment decision was influenced by the urologist's treatment preference.

Patients and methods

Between August 2014 and July 2015, newly diagnosed patients with low- or intermediate-risk PC (T1–T2N0M0) were recruited in 9 nonacademic Dutch hospitals (21). Patients were eligible for inclusion if they were offered ≥2 treatment options according to their urologist and had access to a PC, laptop, or tablet with an internet connection. Exclusion criteria were cognitive impairment or being too ill at the time of the study and insufficient comprehension of the Dutch language to complete questionnaires and understand the DA.

After diagnosis, urologists requested informed consent and offered the web-based DA by handing out a "DA recipe" containing the DA URL, possible treatment options, prostate-specific antigen (PSA) level (<10 µg/l or 10–20 µg/l), and Gleason score. At the same time, urologists indicated their preferred treatment option for the patient concerned on a separate form; this information was not communicated to patients. If patients did not return their informed consent form, they still had the opportunity to use the DA. DA users without informed consent could not be identified. Once informed consent was given, patients also received questionnaires, and subsequently, the questionnaire data were linked to the patients' DA data. This study took place within an ongoing 2-armed pragmatic cluster randomized controlled trial that assessed the effect of a web-based DA on the decision-making process and patient-reported outcomes. In the trial, one arm received usual care after PC diagnosis, and the other arm received usual care and a web-based DA to support treatment decision making. The current analyses only included the intervention arm. The complete study protocol as well as the information about timing, location, and administration of the decision aid has been described before in more detail (22).

Patients' demographics and medical characteristics

Information regarding treatment preferences pre-DA and post-DA use and patients' preferences/values (VCEs) was entered directly into the DA by the patients. All statements used in the VCEs were developed by a team of urologists, psychologists,

and engineers based on previous experience and observation of conversations where treatment decisions were discussed. The statements were evaluated during usability testing among patients, urologists, and nurses (N=10). After informed consent, additional data were obtained on sociodemographics, patient characteristics, and final treatment decisions from online (or paper on request) questionnaires that were sent after DA use and treatment decision making but before treatment was received (22). Urologists' treatment preferences and medical characteristics (possible treatment options, PSA levels, and Gleason scores) were provided by the recruiting urologist at time of inclusion on a paper form.

Decision aid

Patients were offered the use of a web-based DA after PC diagnosis (www.prostaat.keuzehulp.nl). The DA provides a stepwise guidance through the decision process, depending on the possible treatment options for a particular patient. The first step provides general information about PC and treatment options (benefits and risks, success rates, and complication rates according to the current guidelines and literature) (3,20). The second step offers the consideration between AS and curative treatment (surgery or radiotherapy). VCEs are presented in this step to elicit a patient's preference based on 3 main differences between AS and curative treatment: deferring treatment, possible overtreatment, and adverse effects. Each statement is related to 1 of the 2 treatment alternatives offered in this step. On a slider scale, patients could indicate for each set of statements the strength of their preference toward one of the alternatives (e.g., "If treatment might be unnecessary, I would rather wait." vs. "I prefer treatment, even if it might be unnecessary."). For patients who indicated to prefer active treatment in the previous step, the next step supports the consideration between surgery and radiotherapy (BT and EBRT). Again, information provision was followed by VCEs. The VCEs in this step emphasized the main differences between surgery and radiation therapy (both BT and EBRT) regarding treatment procedure, adverse effects, secondary treatment, and fear for surgery. In the next part of the DA, patients were asked to indicate their final treatment preference. A summary then provided an overview of all VCEs and patients' final treatment preference. To facilitate discussion with the urologist, this summary could be printed or accessed online during the next consultation (22).

Statistical analyses

We used Pearson chi-square test to analyse differences in PSA levels (<10 µg/l or 10–20 µg/l) between the various treatment options and hospitals. One-way analysis of variance (ANOVA) was conducted to analyse differences in mean age for the various final

treatment decisions and hospitals. The concordance between treatment preferences and final treatment decision was measured using kappa (κ). We considered a $P < 0.05$ to be statistically significant. All analyses were performed using SPSS version 19.0 (Statistical Package for Social Sciences, Chicago, IL, USA).

Results

A total of 209 patients were invited for participation, 87% (181) used the DA after PC diagnosis, 64% (134) returned their informed consent forms, and 52% (109) returned a questionnaire. From 175 DA users, pre-DA and post-DA treatment preferences were obtained. From 160 DA users, data on urologists' preferences at time of diagnosis were available (Figure 1). Mean age was 65 years (SD = 6). No differences in mean age were found between received treatment options (P=0.103) and hospitals (P=0.758). We found fewer PSA levels between 10 µg/ l and 20 µg/l in the AS group (P=0.022). No differences in PSA levels were found between hospitals (P=0.518). Offered treatment options included AS among 41% (75/181), RP among 88% (159/181), BT among 74% (133/181), and EBRT among 69% (125/181). Patient characteristics are shown in Table 1. Numbers were too low to analyse differences in final treatment options between hospitals. Baseline comparison between non- responders (patients who did not return a questionnaire) and responders (patients who did return a questionnaire) showed no differences in age in years (P=0.100), Gleason score (Gleason 6 vs. Gleason 7, P=0.177), and PSA level (<10 µg/l vs. 10–20 µg/l, P=0.866).

Initial and final treatment preferences

Of the 181 patients who used the DA, 175 patients (missing N=6) indicated whether or not they had an initial (pre-DA use) treatment preference. Of those patients, 74% (129/175) indicated one specific initial treatment preference after PC diagnosis but before DA use. Indicated options were AS among 22%, RP among 30%, BT among 15%, EBRT among 7%, and no initial preference among 26%. After DA use, the final preferred treatment options were AS among 21%, RP among 33%, BT among 10%, EBRT among 3%, and 34% did not indicate a specific preferred treatment option after DA use. Of the patients who had indicated an initial preference, 67% (87/129) stayed with their initial treatment preference and 33% (42/129) changed their treatment preference after DA use. Of the 42 patients who had changed their preference after DA use, 36 did not indicate a specific final treatment preference or were undecided after DA use. Half of the patients who did not indicate an initial treatment preference were able to indicate a final treatment preference after DA use (Table 2).

Figure 1: Flowchart

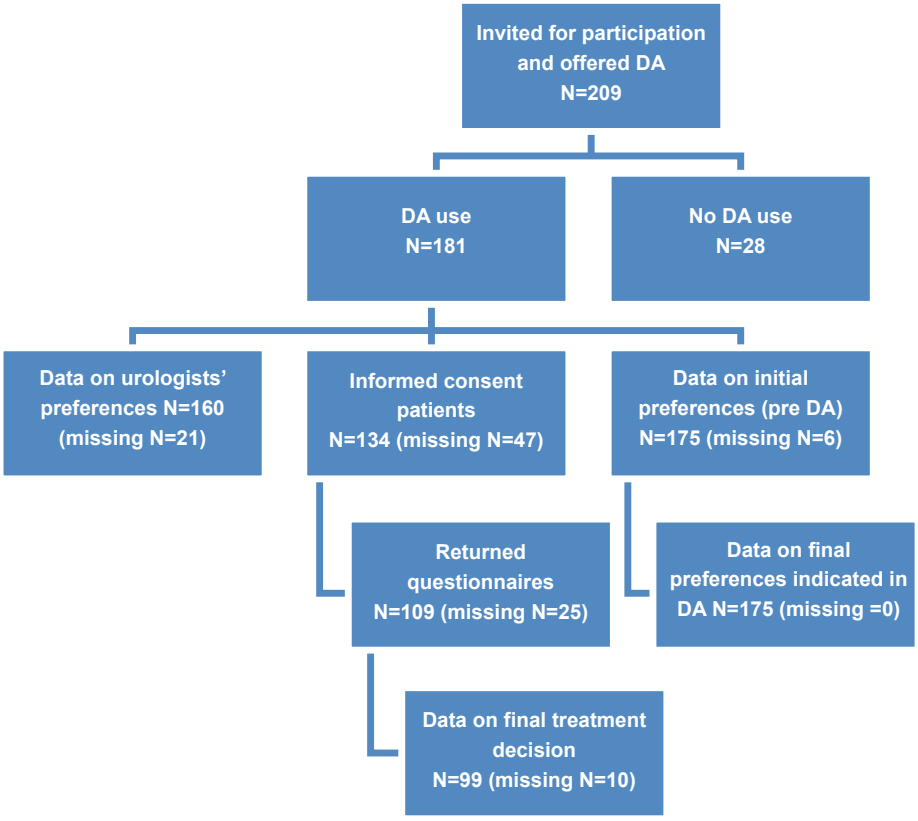


Table 1: Patient characteristics

CHARACTERISTICS		
Mean age, years (SD, N=109))		65 (6.0)
		N (%)
DA users		181 (100)
Returned Questionnaires		109 (100)
PSA level ug/l (entered in DA)		
	<10	135 (75)
	10-20	44 (24)
	Missing	2 (1)
	Total	181 (100)
Gleason score (entered in DA)		
	6	60 (33)
	7	113 (63)
	Missing	8 (4)
	Total	181 (100)
Education*		
	Low	4 (3)
	Medium	44 (41)
	High	58 (53)
	Other	2 (2)
	Missing	1 (1)
	Total	109 (100)
Accrual in hospital		
	A	7 (4)
	B	1 (1)
	C	23 (13)
	D	21 (12)
	E	10 (5)
	F	10 (5)
	G	53 (29)
	H	34 (19)
	I	22 (12)
	Total	181 (100)

*Low (no or primary school), medium (lower general secondary education or vocational training), High (preuniversity education, high vocational training, university)

Table 2: Initial and final treatment preferences

N	Final preference = AS (%row)	Final preference = RP (%row)	Final preference = BT (%row)	Final preference = EBRT (%row)	NO Final preference indicated/ undecided (%row)	Total
Initial treatment preference = AS	28 (74)	2 (5)	0 (0)	1 (3)	7 (18)	38 (100)
Initial preference = RP	1 (2)	43 (83)	0 (0)	0 (0)	8 (15)	52 (100)
Initial preference = BT	0 (0)	1 (4)	12 (46)	0 (0)	13 (50)	26 (100)
Initial preference = EBRT	0 (0)	0 (0)	1 (8)	4 (31)	8 (61)	13 (100)
I don't have an initial preference	8 (17)	11 (24)	4 (9)	0 (0)	23 (50)	46 (100)
Total*	37 (21)	57 (32)	17 (10)	5 (3)	59 (34)	175 (100)

* Missing: N=6

Themes of patient preferences and final preferred treatment option

Of the men who indicated a preference for AS after DA use, 97% (37/38) preferred to postpone or avoid unnecessary treatment, and 87% (33/38) were confident enough that they would be treated on time if needed. For RP, 91% (52/57) valued tumour removal and 90% (51/57) were comforted by the thought that additional radiation would be possible (Table 3). Of the BT patients, 88% (15/17) valued incontinence worse over bowel complaints. For EBRT, numbers were too low to draw conclusions (Table 3). Vice-versa, after transposing Table 3, we found that most men who responded positively to VCEs preferred the final treatment congruent with that particular VCE (Table 4)

Patients who indicated that they were comforted by the thought that additional radiation would be possible after RP were younger than those who indicated to accept that surgery is difficult after radiation (age in years 68 vs 64, respectively, P=0.015).

Table 3: Themes of patient preferences

	Final preference = AS N (%column)	Final preference = RP N(%column)	Final preference = BT N (%column)
Values Clarification Excercises (VCEs) themes			
Decision moment: AS versus active treatment			
Deferring treatment*			
'I am confident enough that I will be treated on time, if necessary'	33 (87)	1(12.5)	0 (0)
vs			
'I do not want to postpone treatment because I do not want to be too late'	1 (3)	6 (75)	7 (88)
Equally important	4 (10)	1 (12.5)	1 (12)
Unnecessary treatment*			
'If treatment might be unnecessary, I would rather wait	37 (97)	3 (30)	2 (25)
vs.			
'I prefer treatment, even if it might be unnecessary'	0 (0)	6 (60)	6 (75)
Equally important	1 (3)	1 (10)	0 (0)
Treatment side effects*			
'I find possible treatment side effects like erectile and urinary dysfunctions difficult to accept'	25 (66)	3 (30)	3 (38)
vs.			
'I find the possible treatment side effects acceptable'	6 (16)	6 (60)	4 (50)
Equally important	7 (18)	1 (10)	1 (12)
Decision moment: RP versus radiotherapy			
Tumour removal**			
'I find it important that all cancer cells are removed from my body'	na	52 (91)	2 (12)
vs.			
'I find it important that the cancer cells die and not grow further'	na	1 (2)	11(65)
Equally important	na	4 (7)	4 (23)
Differences in side effects**			
'I find bowel problems worse than incontinence'	na	25 (44)	0 (0)
vs.			
'I find incontinence worse than bowel problems'	na	7 (12)	15 (88)
Equally important	na	25 (44)	2 (12)
Secondary treatment**			
I am comforted by the thought that I can have additional radiation if surgery is unsuccessful'	na	51 (90)	5 (29)
vs.			
'I accept that surgery is difficult after radiation'	na	1 (2)	9 (53)
Equally important	na	5 (88)	3 (18)
RP anxiety**			
'I am not anxious about surgery'	na	44 (77)	9 (53)
vs			
'I am anxious about surgery'	na	7 (12)	4 (23.5)
Equally important	na	6 (11)	4 (23.5)
Total	38 (100)	57 (100)	17 (100)

* only presented to patients suitable for AS
** only presented to patients who preferred active treatment
na= not applicable

Table 4: Distribution of treatment preferences by VCEs

	Values Clarification Excercises (VCEs) themes			
	Decision moment: AS versus active treatment			
	Deferring treatment*			
	'I am confident enough that I will be treated on time, if necessary'	*'I do not want to postpone treatment because I do not want to be too late'*	Equally important	
Final preference = AS	33	1	4	38
Final preference = RP	1	7	2	10
Final preference = BT	0	7	1	8
	Unnecessary treatment*			
	If treatment might be unnecessary, I would rather wait '	*'I prefer treatment, even if it might be unnecessary'*	Equally important	
Final preference = AS	33	1	4	38
Final preference = RP	3	6	1	10
Final preference = BT	2	6	0	8
	Treatment side effects*			
	'I find possible treatment side effects like erectile and urinary dysfunctions difficult to accept'	*'I find the possible treatment side effects acceptable'*	Equally important	
Final preference = AS	25	6	7	38
Final preference = RP	3	6	1	10
Final preference = BT	3	4	1	8
	Decision moment: RP versus radiotherapy			
	Tumour removal**			
	'I find it important that all cancer cells are removed from my body'	*'I find it important that the cancer cells die and not grow further'*	Equally important	
Final preference = AS	na	na	na	na
Final preference = RP	52	1	4	57
Final preference = BT	2	11	4	17
	Differences in side effects**			
	'I find bowel problems worse than incontinence'	*'I find incontinence worse than bowel problems'*	Equally important	
Final preference = AS	na	na	na	na
Final preference = RP	25	7	25	57
Final preference = BT	0	15	2	17
	Secondary treatment**			
	'I am comforted by the thought that I can have additional radiation if surgery is unsuccessful'	*'I accept that surgery is difficult after radiation'*	Equally important	
Final preference = AS	na	na	na	na
Final preference = RP	51	1	5	57
Final preference = BT	5	9	3	17
	RP anxiety**			
	I am not anxious about surgery'	*'I am anxious about surgery'*	Equally important	
Final preference = AS	na	na	na	na
Final preference = RP	44	7	6	57
Final preference = BT	9	4	4	17

* only presented to patients suitable for AS
** only presented to patients who preferred active treatment
na= not applicable

Urologists' treatment preference and patient preferences

We asked urologists "What do you consider the most suitable treatment option for this patient?" on paper forms at the time of inclusion. In 64% (102/160, missing N 21) of the cases, urologists indicated one specific preferred treatment option as most suitable for the patient concerned. If urologists indicated more than 1 treatment option, this was labelled as "No specific preference indicated by urologist." The most frequently indicated preferred treatment options by urologists were AS (39%) and RP (35%). From 155 patients, we obtained data on both patients' and urologists' initial treatment preferences (Table 5). In 62% (61/98) of the cases, the initial treatment preference was in correspondence with the urologists' treatment preference (κ=0.72).

Table 5: Urologists' treatment preferences

N	Initial preference = AS (%row)	Initial preference = RP (%row)	Initial preference = BT (%row)	Initial preference = EBRT (%row)	I don't have an initial preference (%row)	Total N
Urologist's preference = AS	26 (70)	5 (13.5)	1(3)	0 (0)	5 (13.5)	37 (100)
Urologist's preference =RP	0 (0)	19 (53%)	1 (3)	1 (3)	15 (41)	36 (100)
Urologist's preference = BT	1 (5)	3 (15)	12 (60)	0 (0)	4 (20)	20 (100)
Urologist's preference = EBRT	0 (0)	1 (20)	0 (0)	4 (80)	0 (0)	5 (100)
No specific preference indicated by urologist	7 (12)	17 (29)	11 (19)	6 (10)	17 (30)	57 (100)
Total N*	34 (22)	45 (29)	25 (16)	11 (7)	41 (26)	155 (100)

*Missing N=26

Final treatment decision

Questionnaires after decision making clarified which treatment was finally chosen (final treatment decision). We received 109 questionnaires from DA users, and 99 patients indicated their final treatment decision. These data showed that most patients finally chose the treatment which they preferred post-DA use (κ=0.82, excellent agreement). Comparing the urologists preference with the final treatment decision, we found a moderate to good agreement (κ=0.68).

Of the patients who did not indicate a final treatment preference after DA use and indicated a final treatment decision in the questionnaire (N=20), most chose the treatment their urologist preferred (κ=0.66).

Discussion

In this study, we analyzed the development of treatment preferences throughout the decision-making process using a DA. Analyses included the response to VCEs and correlation between patients' and clinicians' preferences. We found that most patients who chose RP did so because they valued tumor removal and they were comforted by the thought that additional radiation would still be possible. Patients who were comforted by the thought that additional radiation would be possible after RP were younger than those who indicated to accept that surgery is difficult after radiation. Not surprisingly, this shows that younger patients are more concerned about long-term consequences than older patients are.

AS patients indicated that they wanted to postpone unnecessary treatment and were confident enough that if needed they would be treated on time. Patients who chose BT after DA use valued incontinence worse than bowel complaints. Values indicated as important for choosing RP and AS are in line with other studies. In the current DA, we used VCEs to distinguish between surgery and radiotherapy (both BT and EBRT). Therefore, we have no specific information about treatment-related values considered important for specifically choosing BT or EBRT (e.g., duration of therapy and radio nuclear activity), as was shown in other studies (12,13). For BT, we used other themes of patient preferences, which makes comparison with findings from the literature more difficult. This study has shown that patients' responses to our VCEs are congruent with the final treatment preference, indicating that the VCEs used in the DA can properly support decision making for a treatment that is compatible with each patient's preferences and values.

After DA use, RP and AS preference percentages did not alter; however, EBRT preference percentages changed from 7% to 3% after DA use. Reasons for this decrease in EBRT preference may be regional patient preferences or potentially imbalanced information provision at the disadvantage of EBRT. However, radiation oncologists were involved in the DA content development and endorsed the current content. Another reason for the decrease in EBRT preference may be explained by the fact that not all patients are offered to visit a radiation oncologist. This often depends on the presence of a multidisciplinary outpatient clinic (patients then see both an urologist and a radiation oncologist) or local practice. Of 4 of newly diagnosed patients with PC, 3 already had a

specific initial treatment preference before DA usage, usually RP or AS. We found that 2 of 3 of these patients did not change their preference after DA use. For these patients, use of this DA may lower decisional conflict because patients might be more convinced of their initially preferred treatment option, which would be in line with current literature that describes that DAs lower decisional conflict (19). Results concerning decisional conflict would follow from an ongoing study (22). However, a third of the DA users did not indicate a specific final treatment preference after DA use. Additionally, we investigated this group and found that most of them eventually chose for the treatment their urologist preferred. This is not surprising, as this is known as one of the most important issues in the decision-making process (12,14–16). Further investigation of this group is interesting to evaluate whether or not this group is satisfied with the DA or became more confused in the decision-making process. It is possible that this DA is not the most optimal decision support tool for this group, and alternative decision support would be more suitable.

In 64% of the cases, urologists indicated one specific treatment preference, and in 62%, the initial patients' treatment preference was in line with the urologist's preference. It is possible that urologists already revealed (unintentionally or intentionally) their treatment preference at the time of diagnosis, which may have influenced initial patients' treatment preferences. Another hypothesis is that urologist have made a good estimate of the best treatment option for each individual. Qualitative research of the conversations at the time of diagnosis should be performed to investigate these hypotheses.

We additionally investigated the final treatment decisions and discovered that most patients decided to choose their preferred treatment option after DA use (κ=0.82). Correlation between final treatment decision and urologist's preference was lower (=0.68). This implies that urologists' treatment preferences did not affect patients' treatment decisions as much as observed from the literature, probably because the DA overrules the urologist's preference after indicating a final treatment preference (12,14–16).

However, it is possible that urologists have most influence at diagnosis, at the start of the decision-making process.

Using VCEs, we objectively measured patients' preference themes as they were recorded in the DA without the interference of a researcher of urologist as has been described in other studies (24). This made our results more reliable; moreover, these were not influenced by clinicians. More strengths of this study are the high response rate (87% DA use), identification of the initial (pre) and final (post) treatment preferences by indicating these items directly in the DA, the inclusion of all treatment options (including AS), and

the treatment preference of the recruiting urologist. This also differentiates our study from other studies, which studied only differences in treatment preferences/ received treatment, but none investigated the urologists preferences, initial (pre-DA) preferences, patients' values clarification (VCEs), final (post-DA) preferences, and final treatment decisions in a single study (12,15,23). We, therefore, were able to prospectively follow the full decision-making process and the changes made during this process, including the urologists' preference.

Some limitations should be addressed. First, we could not obtain questionnaires from all DA users, because we did not obtain informed consent forms from 47 patients. A reason for this gap in numbers is that we offered the DA to all eligible patients, according to the inclusion criteria set for this study. Many patients used the DA, and after decision making, they did not return their questionnaires. This is not surprising, because patients then had obtained the benefits (DA use), and a questionnaire sent weeks later would only be an extra burden without the prospect of more benefits. Therefore, we did not succeed in obtaining complete information about patient's characteristics and final treatment decisions. We do not know if this group was as consistent in their final treatment decision as the patients who did complete their questionnaires. Also, it remains unclear if the patients who did not indicate a final preference after DA use (1 in 3) were actually undecided or just did not indicate a final preference (missing data). Therefore, we are unable to indicate whether or not more patients were truly undecided after DA use. Furthermore, not all patients were invited to visit a radiation oncologist, as this depends on local practices. Unfortunately, no information is available on radiation oncology counseling or on general practitioner counseling. Therefore, we are not informed on a possible influence on final decision making by the counseling of these health providers. Finally, we found significantly fewer PSA levels between 10 µg/l and 20 µg/l in the AS group, but this can be explained by the fact that most AS protocols only include PSA levels <10 (25,26).

In conclusion, we measured important values and preferences for choosing AS, RP, or BT, and we showed that most patients chose the treatment they themselves preferred after DA use (κ =0.82). Finally, the influence of the DA was shown to be higher than the urologist's preference; implications of this are being prospectively investigated in an ongoing study.

The authors suggest to incorporate DA use in clinical practice to stimulate PC shared decision making and to facilitate elicitation of patients' values and preferences.

Acknowledgments

We would like to thank R. Thé and K. Karssen from Zorgkeuzelab for their contribution to the decision aid development.

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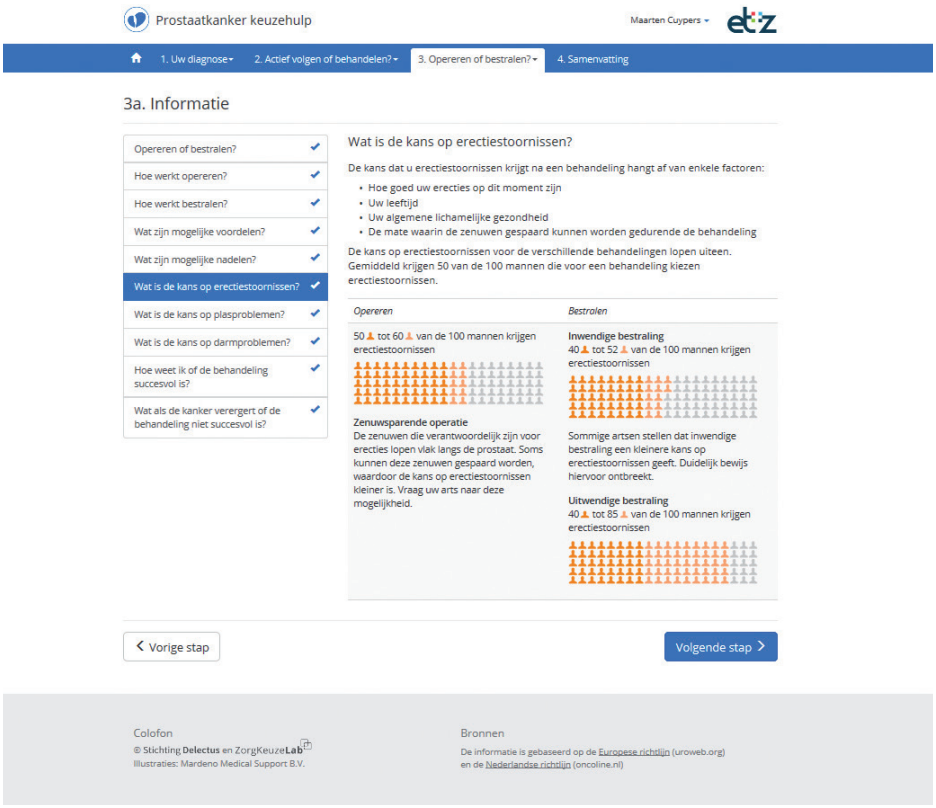
Appendix A: Decision aid



4. Samenvatting

Dit is de samenvatting van uw afwegingen en voorkeur. U kunt deze printen en bespreken met uw dokter.

Print samenvatting

Help ons verbeteren

Hoe tevreden bent u over het gebruik van deze keuzehulp?

- ○ Zeer tevreden
- ○ Tevreden
- ○ Neutraal
- ○ Ontevreden
- ○ Zeer ontevreden

Wat vindt u goed en wat kan er beter?

Geef uw feedback door

Samenvatting om te bespreken met mijn dokter

Wat is mijn diagnose? wijzig

PSA	Lager dan 10
Gleason	Lager dan 7
Mijn opties	Actief volgen, opereren, inwendig bestralen, uitwendig bestralen
Hoe wil ik kiezen?	Niet ingevuld

Heeft actief volgen of behandelen mijn voorkeur? wijzig

Informatie	8 / 8 veelgestelde vragen over actief volgen en behandelen gelezen

Actief volgen		Behandelen
Actief volgen geeft mij genoeg zekerheid dat ik, indien nodig op tijd behandeld word		Ik wil niet wachten met behandelen omdat ik niet te laat wil zijn
Als behandelen mogelijk overbodig is, wil ik liever wachten		Mijn voorkeur gaat uit naar behandelen, ook al is het misschien niet nodig
Ik vind de mogelijke bijwerkingen zoals erectiestoornissen en urineverlies, moeilijk te accepteren		Ik vind de mogelijke bijwerkingen van behandelen acceptabel
Actief volgen		Behandelen

Toelichting	Niet ingevuld

Heeft opereren of bestralen mijn voorkeur? wijzig

Informatie	10 / 10 veelgestelde vragen over opereren en bestralen gelezen

Opereren		Bestralen
Ik vind het belangrijk dat alle kankercellen uit mijn lichaam worden verwijderd		Ik vind het belangrijk dat de kankercellen afsterven en niet verder groeien
Darmproblemen vind ik erger dan incontinentie		Incontinentie vind ik erger dan darmproblemen
Het stelt mij gerust als ik na operatie eventueel nog bestraald kan worden		Ik accepteer dat een operatie na bestraling lastiger is
Ik ben niet angstig voor een operatie		Ik heb angst voor een operatie
Opereren		Bestralen

Toelichting	Niet ingevuld
Mijn verwachting	Niet ingevuld

Chapter 4

Differences in treatment choices between prostate cancer patients using a decision aid and patients receiving care as usual: results from a randomized controlled trial

R.E.D. Lamers, M. Cuypers, M. de Vries, L.V. van de Poll-Franse, J.L.H.R. Bosch, P.J.M. Kil

Submitted

Abstract

Background Patients frequently use decision aids (DAs) when deciding about treatment for low and intermediate risk prostate cancer (PC). However, the effect of DA-use on treatment decisions concerning active surveillance (AS), radical prostatectomy (RP), external beam radiotherapy (EBRT), and brachytherapy (BT) is unclear.

Objective To determine whether or not DA-use influences treatment decisions in patients with low and intermediate risk prostate cancer.

Design, Setting, and Participants In a two-armed pragmatic, cluster randomized controlled trial (CRCT), patients were randomized at hospital level to either DA-use (DA group) or no DA-use (control group). Between August 2014 and July 2016, newly diagnosed patients with low or intermediate risk PC were recruited in 18 hospitals in the Netherlands. Informed consent was given by 382 patients (DA group N=273, control group N=109). Questionnaire response rate was 88% (N=336).

Intervention DA-users had access to a web-based DA that provided general PC information, PC treatment information, and values clarification exercises to elicit personal preferences towards the treatment options. Control-group patients received care as usual. Patients completed questionnaires directly after making their treatment decision.

Outcome Measurements and Statistical Analysis Primary outcomes (differences in treatment choice) were analysed using multilevel logistic regressions. Differences in eligible treatment options between groups were compared using Pearson Chi-square tests.

Results and Limitations AS was an option for 38%, RP for 98%, EBRT for 88%, and BT for 79% of patients. DA-users received AS significantly more often than control-group patients (29% vs 16%, p=0.01), whereas the latter more often chose BT (29% vs 18 %, p<0.01). No differences were found between groups regarding RP and EBRT. The main limitation was unbalanced patient enrolment, resulting in lower control-group patient numbers. However, patient and disease characteristics were evenly distributed between groups.

Conclusions DA-using PC patients chose the AS treatment option more often than non-DA-using patients did.

Patient summary We studied differences in treatment choices among patients with low or intermediate risk prostate cancer using a decision aid (DA) compared to patients not using a decision aid during the decision-making process. We found that DA-users significantly more often chose AS and less often BT compared to the control group.

Take home message Currently, DAs are being used more often in the prostate cancer treatment decision-making process. This may lead to different treatment decisions, in particular in favour of AS.

Introduction

Prostate cancer (PC) is the most frequent malignancy in European men, and incidence rates are rising (1). The treatment for low and intermediate risk PC often comprises multiple options with comparable oncology outcomes (active surveillance (AS), radical prostatectomy (RP), external beam radiotherapy (EBRT), and brachytherapy (BT)) (2). However, each treatment option entails specific risks and complications that may negatively impact quality of life. Given the variety of benefit and harm profiles and the lack of strong treatment recommendations in current guidelines, localized PC treatment decision making is highly preference-sensitive and requires adequate shared decision making to find the “best” treatment option for each individual (2, 3).

Decision aids (DAs) support the decision-making process. Previous research has shown that DA-users have more accurate risk perceptions and make better-informed and value-based choices than non-DA-users (4-6). Furthermore, there is evidence that DA-use may affect treatment decisions in favour of less invasive and conservative therapies (4, 6). Previous published work attempted to review the literature on the effect of a DA specifically on PC treatment; however, the included studies were at high risk of bias or did not compare all relevant treatment options (7-14). Consequently, clear results were not shown concerning treatment differences when a DA was used in PC decision making. Given these uncertainties, we investigated the effect of a preference-sensitive web-based DA on treatment choice in comparison with usual care (15).

We developed a Dutch-language web-based DA for treatment-eligible patients with low and intermediate risk PC. To investigate differences in treatment choice with and without DA-use, we conducted a cluster randomized controlled trial (CRCT) (15). As the literature shows more conservative therapies consequent to DA-use, we hypothesized that use of this DA would result in more AS in the DA group.

Patients and Methods

Between August 2014 and July 2016, newly diagnosed patients with low or intermediate risk PC (EAU/ESTRO criteria) were recruited in 18 hospitals in the Netherlands (16). Patients were eligible for inclusion if, according to their urologist, they could be offered ≥ 2 treatment options (AS, RP, EBRT, and/or BT) and had internet access. Exclusion criteria were cognitive impairment, insufficient understanding of the Dutch language, or being too ill at the time of the study (15).

Methods

In a two-armed pragmatic CRCT, clustering was performed at hospital level, meaning that all included patients from a participating hospital were in the same study group. Participating hospitals could therefore provide the same type of care to all of their patients, making a CRCT less prone to contamination bias resulting from shared decision making (15, 17). The hospitals were pre-randomized to either 'usual care' (control group) or 'usual care + DA' (DA group) by a statistician not involved in the study and blind to the identity of the hospitals, using SPSS version 24.0 (Statistical Package for Social Sciences, Chicago, IL, USA) (18).

Patients were included by their urologist immediately after prostate cancer diagnosis. Urologists (who themselves completed a separate informed consent form) requested informed consent by providing a paper informed consent form in both groups. At this point, the urologist indicated the offered eligible treatment options. After a prostate cancer diagnosis, but before a treatment decision had been made, patients in the intervention group received access to an online DA. Patients in the control group received decisional counselling as usual in the relevant hospital. Patients in both groups were requested to complete online questionnaires (or paper on request) after deciding on a treatment but before treatment was started (15, 19). The full study protocol has already been extensively described (15).

Decision Aid

The DA offers stepwise guidance through the decision process, depending on the possible treatment options (*in Dutch*: www.prostaat.keuzehulp.nl). First, general information about PC and treatment options is provided (benefits and risks, success rates, and complication rates according to the current guidelines and literature) (2). Next, the DA offers the choice between active surveillance (if eligible) and active treatment (surgery or radiotherapy).

Values clarification exercises (VCEs)/statements are presented in this step to elicit a patient's preference. Patients can indicate for each set of statements the strength of their preference towards one of the alternatives (e.g. '*If treatment might be unnecessary, I would rather wait'* vs '*I prefer treatment, even if it might be unnecessary'*). The last step is the choice between surgery and radiotherapy (EBRT and BT) and includes VCEs to elicit preferences in relation to surgery and radiotherapy. Appendix A shows a screenshot of the DA with VCEs concerning the decision trade-off 'surgery versus radiotherapy'. The development and content of the DA has already been described (20).

Outcome measures

The primary outcome measure for this study was received treatment. For participants whose treatment could not be verified in their medical records, we analysed treatments as reported in the questionnaires. Offered eligible treatment options were obtained from the informed consent forms completed by the urologists.

Standard sociodemographic and clinical information was obtained from the patients' informed consent forms (date of birth, date of diagnosis) and questionnaires (PSA level, Gleason score, marital status, occupation, and education).

Statistical analyses

For continuous data, we presented descriptive statistics as means with standard deviations. We reported frequencies and percentages for categorical data. Between group differences were examined using independent samples T-tests for continuous variables and Chi-square analyses for categorical variables. Fisher's Exact Test was used when expected count in cells was less than 5.

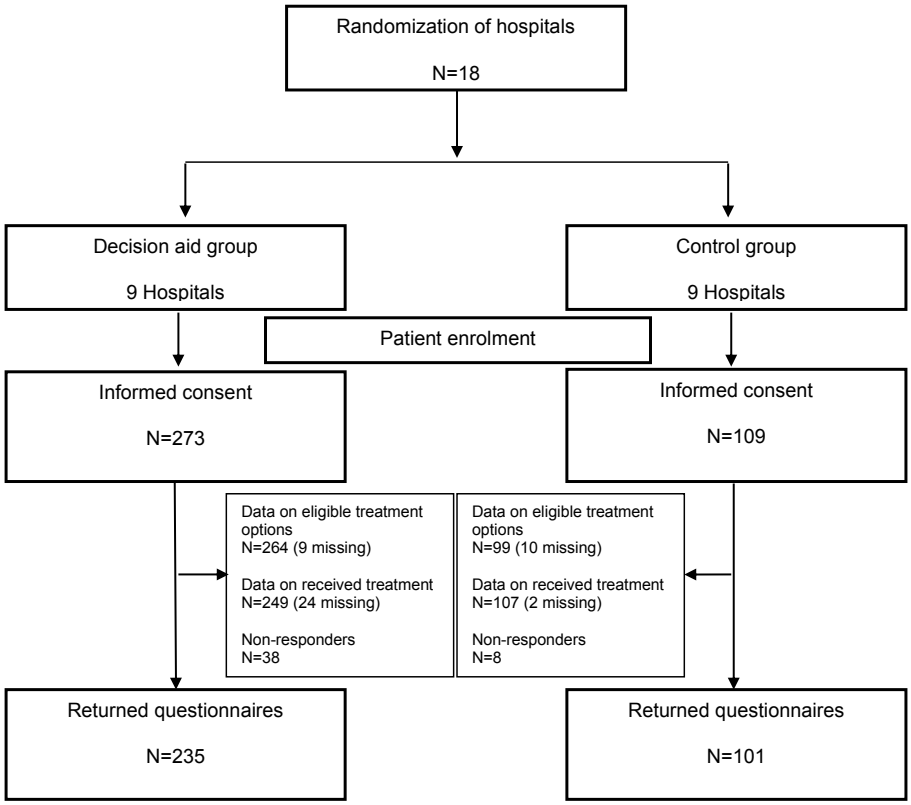
Because of the multilevel structure of our data and the hospital-level randomization, we performed multilevel logistic regressions to assess treatment differences between groups. Marital status, level of education, PSA level (dichotomized to ≤10 µg/l and 10.1-20 µg/l), and Gleason score (6 or 7) were used in our model as fixed effects at the person level. Treatment was randomized at hospital level and added as fixed effect in the relevant analysis; odds ratios (OR) and 95% confidence intervals were reported.

All statistical analyses were conducted using SPSS version 24 (Statistical Package for Social Sciences, Chicago, IL, USA). A p-value <0.05 was considered statistically significant.

Results

Informed consent was given by 382 patients (DA group N=273, control group N=109). Information regarding eligible treatment options was available for 264 (97%) DA-group patients and for 99 (91%) control-group patients. Received treatment could be verified for 249 DA patients (91%, missing N=24) and for 107 control patients (98%, missing N=2). In total, 336 patients completed the questionnaire (questionnaire response rate 88%), see Figure 1.

Figure 1. Enrolment numbers and flowchart



Non-responders were younger than responders (mean=65.3 vs mean=62.9, p=0.01). There was no difference in number of offered treatment options between responders and non-responders (p=0.45). For non-responders, no information was available concerning PSA levels and Gleason scores (data not shown).

Offered/eligible treatment options

Patients were offered ≥ 2 treatment options after PC diagnosis. For 23%, two eligible treatment options were offered, for 49% three options were offered, and for 28% all four treatment options were offered (Table 1).

Eligible treatment options were available for 363 patients who gave informed consent (this figure includes questionnaire responders and non-responders). The majority (98% for both groups) were offered RP (Table 2). AS was offered to 39% in the DA group and to 36% in the control group ($p=0.72$), EBRT to 88% and 90% ($p=0.70$), respectively, and BT to 81% and 73% ($p=0.19$), respectively. We found no differences in offered treatment options between the groups.

Received treatment

Received treatment analysis was performed only for patients who were eligible for that particular treatment. DA-group patients more often chose AS compared to patients in the control group (N=71 (29%) vs N=17 (16%), respectively, OR=3.7, 95% CI=1.33-10.50, $p=0.01$; Table 3). Patients in the control group received BT more often than DA-users (N= 31 (29%) vs N=44 (18%), respectively, OR=0.22, 95% CI=0.10-0.47, $p<0.001$). We found no differences between groups in proportions of patients receiving RP and EBRT.

Post-hoc analysis

Of the patients who were eligible for AS, 71/102 patients pursued AS in the DA group and 17/36 patients pursued AS in the control group (70% vs 47%, $p=0.01$, respectively), as shown in Table 4. This implies that some patients were eligible for AS but still received active treatment: 26 (25%, missing N=5) DA-group patients and 19 (53%) control-group patients chose this option (data extracted from Table 4).

In the DA group, 17/26 patients pursued RP although AS was an eligible treatment option; in the control group, this was the case for 11/19 patients (65% vs 58%, $p=0.96$, respectively). BT was chosen more often in the control group than in the DA group when active treatment was preferred over AS (7/19 (37%) vs 7/26 (27%) $p=0.34$, respectively), (data extracted from Table 4).

Finally, DA patients who were not eligible for AS more often chose RP than control patients (53% vs 35%, $p=0.01$, respectively; Table 4).

Table 1. Baseline demographics and clinical characteristics of responders[a] N=336

Characteristics		DA group N= (%)	Control group N= (%)	Total N= (%)	*p*
Age at informed consent in years, mean (SD)		64.9 (6.0)	66.3 (5.7)	65.3 (5.9)	.06
Marital status	Married/living together	208 (89%)	87 (87%)	295 (88%)	0.54
	Other	27 (11%)	13 (13%)	41 (12%)	
Education					
	Low	76 (33%)	36 (36%)	112 (34%)	0.40
	Medium	54 (23%)	28 (28%)	82 (25%)	
	High	101 (44%)	36 (36%)	137 (41%)	
Gleason Score					
	6	156 (61%)	46 (70%)	202 (63%)	0.25
	7	97 (39%)	2 (30%)	117 (37%)	
PSA level					
	≤10.0 µg/l,	207 (81%)	73 (79%)	280 (80%)	0.65
	10.1-20.0 µg/l	49 (19%)	20 (21%)	69 (20%)	
Number of eligible treatments					
	2	49 (21%)	25 (28%)	74 (23%)	0.51
	3	115 (50%)	42 (46%)	157 (49%)	
	4	65 (29%)	24 (26%)	89 (28%)	
Hospital					
	1	11 (5%)			
	2	1 (1%)			
	3	46 (19%)			
	4	28 (12%)			
	5	13 (6%)			
	6	17 (7%)			
	7	64 (27%)			
	8	35 (15%)			
	9	20 (8%)			
	10		6 (6%)		
	11		18 (18%)		
	12		9 (9%)		
	13		9 (9%)		
	14		23 (23%)		
	15		8 (8%)		
	16		20 (20%)		
	17		8 (8%)		
	18		0 (0%)		

[a] Because of missing values, numbers do not always add up to 336. SD=standard deviation

Table 2. Offered/eligible treatment options

	DA group N=264 (%column)	Control group N=99 (%column)	Total[a] N=363 (%column)	*p*
Offered/eligible treatment options				
AS	102 (39)	36 (36)	138 (38)	0.72
RP	259 (98)	96 (97)	355 (98)	0.45
EBRT	232 (88)	89 (90)	321 (88)	0.70
BT	214 (81)	66 (73)	288 (79)	0.19

[a] Percentages add to more than 100% because patients were offered multiple treatment options. AS=active surveillance, RP=radical prostatectomy, EBRT=external beam radiotherapy, BT=brachytherapy

Table 3. Received treatment

	DA group N (%column)	Control group N (%column)	Total N (%column)	Exp (β)/OR (95% CI)[a]	*p*[a]
Received treatment					
AS	71 (29)	17 (16)	88 (25)	3.7 (1.33-10.50)	*0.01*
RP	103 (41)	32 (30)	135 (38)	2.2 (0.96-4.96)	*0.06*
EBRT	20 (8)	15 (14)	35 (10)	0.67 (0.24-1.9)	*0.46*
BT	44 (18)	31 (29)	75 (21)	0.22 (0.10-0.47)	*<0.001*
Missing/unknown	11 (4)	12 (11)	23 (6)		
Total	249 (100)	107 (100)	356 (100)		

[a] Multilevel regression analyses, marital status, level of education, PSA level (dichotomized to ≤10 µg/l and 10.1-20 µg/l), and Gleason score (6 or 7) were used as fixed effects at the person level. Analyses include only patients who were eligible for the selected treatment.
OR=Odds Ratio, CI: 95% confidence interval for Exp (β)/Odds Ratio. AS=active surveillance, RP=radical prostatectomy, EBRT=external beam radiotherapy, BT=brachytherapy

Table 4. Received treatment by AS eligibility

	DA group N (%column)	Control group N (%column)	Total N (%column)	*p*
Eligible for AS				
Received treatment AS	71 (70)	17 (47)	88 (64)	0.01
Received treatment RP	17 (16)	11 (31)	28 (20)	0.09
Received treatment EBRT	2 (2)	1 (3)	3 (2)	1.00
Received treatment BT	7 (7)	7 (19)	14 (10)	0.05
Missing/unknown	5 (5)	0 (0)	5 (4)	
Total	102 (100)	36 (100)	138 (100)	
Not eligible for AS				
Received treatment AS	4 (3)	1 (2)	5 (2)	1.00
Received treatment RP	86 (53)	22 (35)	108 (48)	0.01
Received treatment EBRT	19 (12)	14 (22)	33 (15)	0.06
Received treatment BT	40 (24)	24 (38)	64 (28)	0.07
Missing/unknown	13 (8)	2 (3)	15 (7)	
Total	162 (100)	63 (100)	225 (100)	

AS=active surveillance, RP=radical prostatectomy, EBRT=external beam radiotherapy, BT=brachytherapy

Discussion

In this study, we determined differences in treatment choice between patients diagnosed with low and intermediate risk PC using a DA versus not using a DA. Our findings confirm our hypothesis that DA-use affects treatment choice: patients who used a DA more often chose AS compared to the control group. Also, we found that BT was chosen more often in the control group.

Our study is, to our knowledge, the first to show that more patients choose AS after DA-use compared to a control group that does not use a DA. Our results are in line with other studies showing that DA-use results in more conservative than invasive treatment options (4, 6).

However, in studies in which a specific prostate cancer treatment was determined after DA-use in comparison to usual care, no strong differences in treatment choice were found (7, 9, 13, 14). In systematic reviews, AS was often not well defined, or even watchful waiting was included, and therefore the combination of these two deferred treatment options may be an explanation for the differences in findings (13). In addition, some studies did not include deferred treatment as an option and therefore differences in AS proportions could not be assessed (21). Most studies involved a variety of decision support tools such as videos, printouts, CD-ROMs, and websites, making them difficult to compare [17-22]. Our results may implicate that our DA provides sufficient information about AS and therefore DA patients are more confident to pursue AS. In our study, we found no statistically significant difference for RP between groups; as mentioned, this conforms with the current literature (7, 9, 13, 14).

Another main finding in the current study is that non-DA-use patients pursued BT more often in comparison to DA-use patients. A comparable Dutch study showed more BT after DA-use in comparison to usual care; however, that study did not include AS (12). Because we determined patients in our population who were not eligible for AS, we were able to compare our results with the relevant study. However, in our analysis, we did not find any differences in BT between groups if patients were not eligible for AS (p=0.07, Table 4, post-hoc analyses).

Furthermore, we determined which treatment options were offered to patients after diagnosis, thereby providing insight into clinical practice. Thirty-eight per cent of patients were eligible for AS; this proportion is in line with other Dutch studies (22). Nonetheless, in the present study, 25% of all patients pursued BT. In an American study, the percentage of patients pursuing BT was nearly 10% (among patient of the same age at diagnosis

and diagnosed with low and intermediate risk PC) (23). Therefore, differences in clinical practice for low and intermediate PC between countries make it complicated to generalize the current results.

Finally, we studied patients' received treatment options with regard to AS eligibility. Our results show more AS in DA-users; this made us think about the differences in received treatment when patients were not eligible for AS. Surprisingly, in post-hoc analyses, we found that, if patients were not eligible for AS, more patients in the DA group received surgery compared to the control group (53% vs 35%, p=0.01, respectively). So, if patients are eligible for AS, then DA-users choose AS more often than non-users do. However, if AS is not an option, DA-users choose the most invasive option more often than control-group patients do. Possibly, DA-use may enable patients to choose between extremes. Another explanation may be the bias of counselling by a urologist only, which may lead to more RP instead of radiotherapy.

Another finding worth mentioning is that a substantial number of patients suitable for AS preferred active treatment over AS. It is surprising that patients choose (invasive) surgery with risk- and complication rates when AS is an eligible option. Fagerlin et al. previously described this tendency towards active treatment: few people can imagine standing by and doing nothing after a cancer diagnosis, regardless of the risks (24). Possibly, the patients who prefer active treatment over AS are more neurotic/anxious, as neuroticism is associated with PC-specific anxiety (25). Consequently, these patients' characteristics should be investigated during PC counselling and information provision should be optimized.

The main limitation of our study is the imbalanced patient enrolment between groups leading to low control group numbers. A reason for the lower patient enrolment in the control group might be that control-group physicians were not as motivated as DA-group physicians to include patients as they felt they had nothing to offer to the patient. However, patient and tumour characteristics as well as treatment offered were not different between treatment arms, so the lower patient recruitment in the control arm led only to a power reduction and not to a selection bias. Another limitation is the variety in inclusion rates across hospitals (in both groups) varying from 0% to 64%. Unfortunately, hospital visits and meetings did not lead to more inclusions for the relevant 'poor inclusion' hospitals, resulting in a substantial variety in inclusion numbers. The major strength of this study is the inclusion of all four treatment options, including AS, in the analyses. Another strength is the cluster randomized design, which reduces the risk of contamination of usual care with components of the DA, making comparison between groups more solid.

The advantage of this design was the relatively natural fit of the DA in clinical practice and patients were not aware of randomization.

Conclusions

DA-use during treatment decision making for low and intermediate risk prostate cancer may affect treatment decisions. Compared with the control group, our results show more AS and less BT in the DA group. No differences in RP and EBRT proportions were found between groups.

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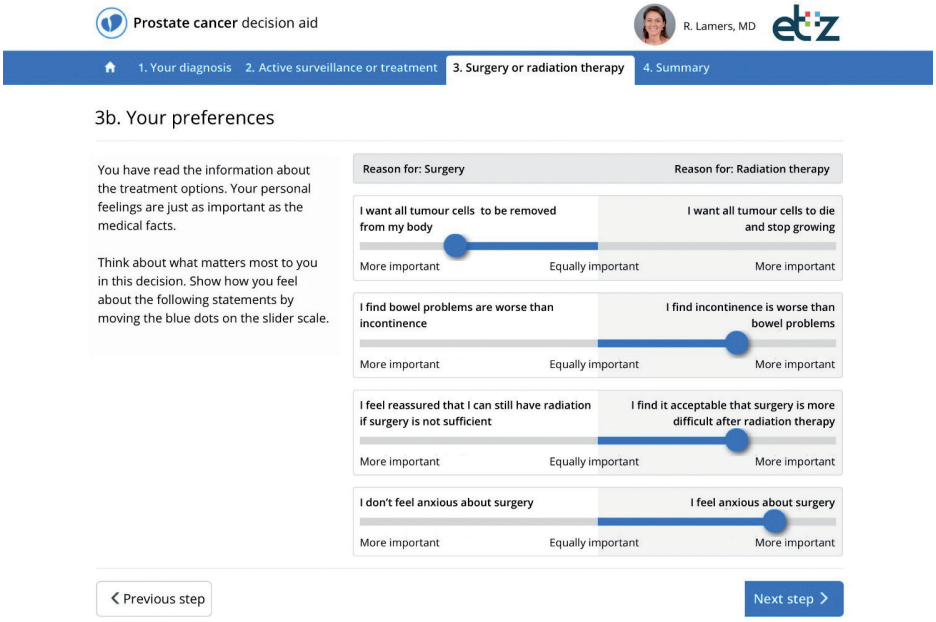
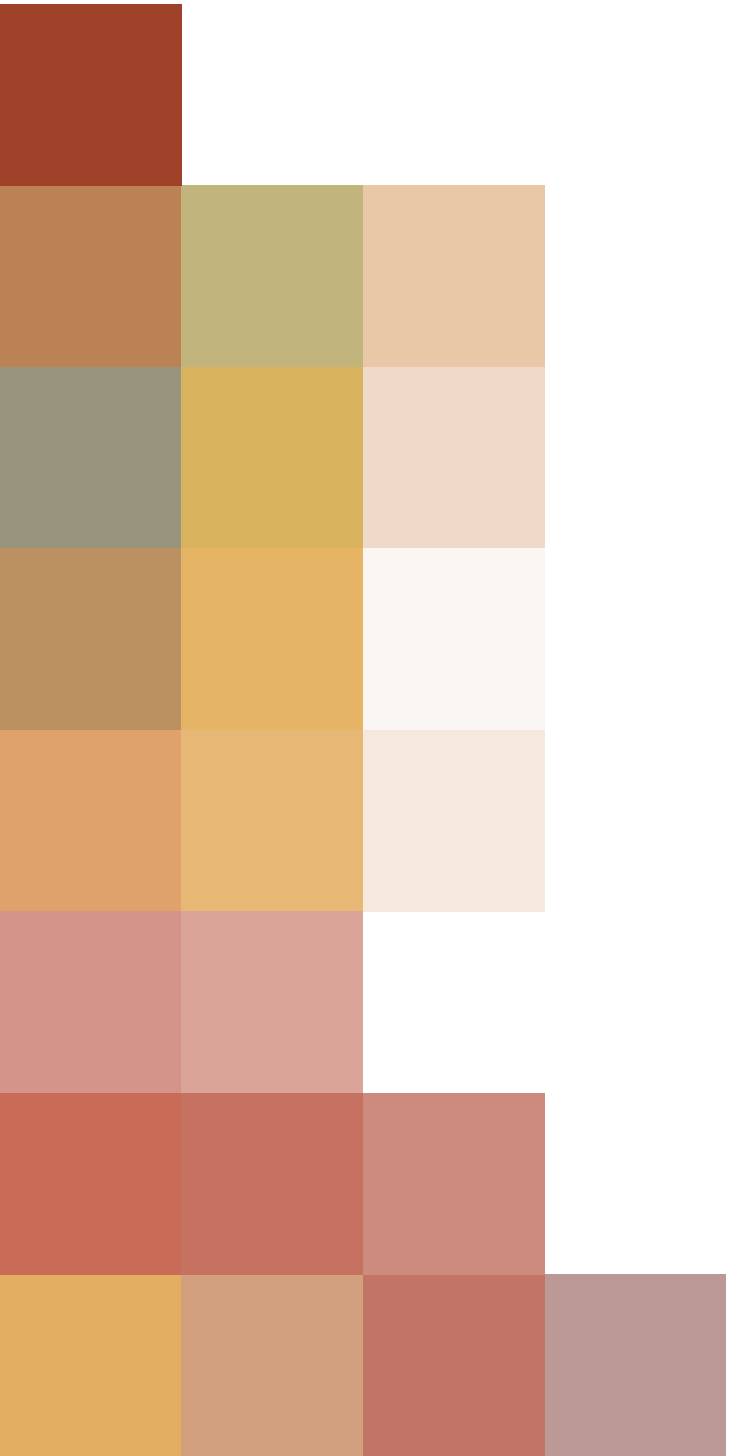
Appendix A


Prostate cancer decision aid
R. Lamers, MD
1. Your diagnosis
2. Active surveillance or treatment
3. Surgery or radiation therapy
4. Summary
3b. Your preferences
You have read the information about the treatment options. Your personal feelings are just as important as the medical facts.
Think about what matters most to you in this decision. Show how you feel about the following statements by moving the blue dots on the slider scale.
Reason for: Surgery
Reason for: Radiation therapy
I want all tumour cells to be removed from my body
I want all tumour cells to die and stop growing
More important
Equally important
More important
I find bowel problems are worse than incontinence
I find incontinence is worse than bowel problems
More important
Equally important
More important
I feel reassured that I can still have radiation if surgery is not sufficient
I find it acceptable that surgery is more difficult after radiation therapy
More important
Equally important
More important
I don't feel anxious about surgery
I feel anxious about surgery
More important
Equally important
More important
Previous step
Next step



Chapter 5

Longitudinal regret and information satisfaction after deciding on treatment for localized prostate cancer with or without a decision aid. Results at one-year follow-up in the PCPCC trial

M. Cuypers, R.E.D. Lamers, P.J.M. Kil, L.V. van de Poll-Franse, M. de Vries

Patient Education and Counseling
2019 Mar; 102(3):424-428

Abstract

Objective To investigate the effect of including an online decision aid (DA) during prostate cancer treatment counseling on decisional regret and information satisfaction in a one-year follow-up.

Methods Within a cluster RCT, 18 Dutch hospitals were randomized to DA counseling or care-as-usual, patients (n = 382) initially completed questionnaires directly after treatment decision making. Six and twelve months later regret (Decisional Regret Scale) and information satisfaction (SCIP-B) were assessed. Anxious and depressive symptoms (HADS) was included as possible covariate.

Results After 12 months, 43 participants (15%) regretted their treatment choice and 105 participants (36%) were dissatisfied with the information that was received at the time of decision-making, regardless of being exposed to the DA. Anxious and depressive symptoms at follow-up were associated with regret and information dissatisfaction.

Conclusion No long-term beneficial effects emerged from DA usage compared to patients who underwent standard counseling.

Practice implications During PCa treatment counseling, healthcare providers should be aware of anxious and depressive symptoms.

Background

A novel Dutch web-based prostate cancer (Pca) treatment decision aid (DA) with values clarification exercises (VCEs) has been developed and tested in a pragmatic, cluster randomized trial (1,2). In contrast to what was hypothesized, no positive effects from this DA on decisional conflict, decision preparation, or information satisfaction were noted immediately after treatment was chosen, and the DA was evaluated less positively by patients with anxious and depressive symptoms (3). Given these unexpected initial findings, we aimed to study regret and information satisfaction in a 12-months follow-up.

The concern of post-Pca treatment regret has been addressed in a limited number of previous DA trials, of which two studies reported modest positive effects (4–9). One study has reported beneficial effects from values clarification exercises (VCEs) included in a Pca DA on regret at a 12-months follow-up, while no differences were found 3-months post- decision, suggesting positive DA effects can still emerge long after the decision is made (10). In line with these findings we hypothesized positive DA effects on regret and information satisfaction after 12 months, also for DA

Methods

Design

The Prostate Cancer Patient Centered Care (PCPCC) trial was set up as a cluster randomized controlled trial, with eighteen Dutch hospitals randomly assigned to either include the DA in their counseling routine, or to provide information and counseling as usual (1). Randomization at hospital level was chosen to avoid contamination of usual counseling with components of the DA. The regional Medical Ethics Review Board waived the need for formal ethical approval (reference: NW2014-03), and the study protocol was approved by all participating hospitals. The study was pre- registered in the Dutch Trial Register (NTR4554) (1). We report following the Consolidated Standards of Reporting Trials (CON- SORT) guidelines (11).

Participants and procedure

All patients newly diagnosed with localized low- or intermediate risk prostate cancer (T1-T2N0M0), and a minimum of two treatment alternatives (including AS), were eligible for participation (12). Exclusion criteria were mental or cognitive impairment, or inability to complete a questionnaire in Dutch. Patients were recruited at diagnosis, and informed that the topic of the study was to evaluate information provision and treatment decision-

making in Pca care. On the consent form, patients indicated the date of the subsequent consultation during which the treatment decision was planned to be finalized. The first questionnaire was sent after this indicated date (T1), which was on average two weeks after receiving diagnosis. Follow-up questionnaires were sent 6 (T2) and 12 months (T3) later. Patients were unaware of assignment to trial arm as the DA was not mentioned as subject of this study. Care providers and researchers were not blinded of trial assignment (1).

Intervention

In addition to all information provided as part of usual care, patients in the intervention arm were invited by their care provider to access the DA online. The DA included information about all treatments, values clarification exercises (VCEs), and a summary that could be taken to the next consultation (2). Implementation results and patients evaluations after DA usage within the intervention arm of the current trial have been reported earlier (13).

Measures

Age, marital status, and education level were obtained from the questionnaire. The treatment that was received by the patients was verified through their medical record. Regret after the treatment decision was assessed with the five-item Decision Regret Scale (DRS) (14). Information satisfaction was assessed with the Satisfaction with Cancer Information Profile - part B (SCIP-B) (15). Both measures had 5-point answer scales, of which scores were transformed to a 0–100 scale.

To further aid clinical interpretation, regret and information satisfaction were dichotomized using cutoff scores of >25 and ≤75, respectively (16–19). The presence of anxious or depressive symptoms was assessed at all-time points with the Hospital Anxiety and Depression Scale (HADS), consisting of seven-item subscales for both aspects (20). Answers (score ranging from 0-not at all to 3-very much) were summed, with scores 8 representing substantial levels of anxiety or depression (20). Internal consistency for all scales was good ($\alpha \leq 0.80$).

Statistical analysis

Intention-to-treat analysis included all patients from both arms. Descriptive statistics are presented as means (and SDs) for continuous variables and frequencies (and percentages) for categorical variables. Differences in participants' characteristics

between trials arms, and between responders and non-responders were compared with t-tests for continuous variables and chi- square tests for categorical variables.

To assess determinants of clinically relevant levels of regret and information satisfaction, the dichotomized scores served as outcome variables in multivariable logistic regression analyses that included age, education, marital status, received treatment, trial arm, and anxious and depressive symptoms as covariates. The association between these factors and the outcome variables are presented as odds ratios (with 95% confidence intervals). Statistical analyses were conducted using SPSS 22.0 (Statistical Package for Social Sciences, Chicago, IL). Tests were two-sided and considered statistically significant if $p < .05$.

Results

In total, 384 patients were enrolled in this study (DA: n = 273, control: n = 111) and received the initial questionnaire after treatment decision-making (T1, response rate 88%). Follow-up questionnaires after 6 months (T2) were sent to 336 patients (DA: 235, control: 101, response rate 92%), and to 308 patients after 12 months (T3, DA: 214, control: 94, response rate 95%) (Fig 1). Completion rates were comparable across participants from all hospitals. Men without a partner and men with low education were more often lost-to-follow-up (Table 1).

No differences were observed in socio-demographic- or clinical characteristics (PSA, Gleason) between participants from both trial arms, but a different pattern in selected treatments was noted in the DA and control arm. Fewer patients were recruited for the control group, and patient enrolment varied across hospitals (Table 1), resulting in sufficient power (>80%, post-hoc) for comparing trial arms, but low power for subgroup comparisons (<38%).

After 12 months, 43 participants (15%) regretted their treatment choice and 105 participants (36%) reported information dissatisfaction, with no statistically significant differences between trial arms or time points (Table 2). Receipt of the DA had no statistically significant association with lower odds of reporting regret (OR 0.61, 95% CI 0.27–1.37) or information dissatisfaction (OR 1.06, 95% CI 0.27–1.37) after 12 months. Participants who reported anxious or depressive symptoms at T3 were more likely to report regret (OR 1.13, 95% CI 1.06–1.20) and information dissatisfaction at follow-up (OR 1.13, 95% CI 1.07– 1.19). None of the other covariates had a statistically significant association with regret or information dissatisfaction (data not shown).

Figure 1: Flow diagram of patients included in the Prostate Cancer Patient Centered Care (PCPCC) trial.

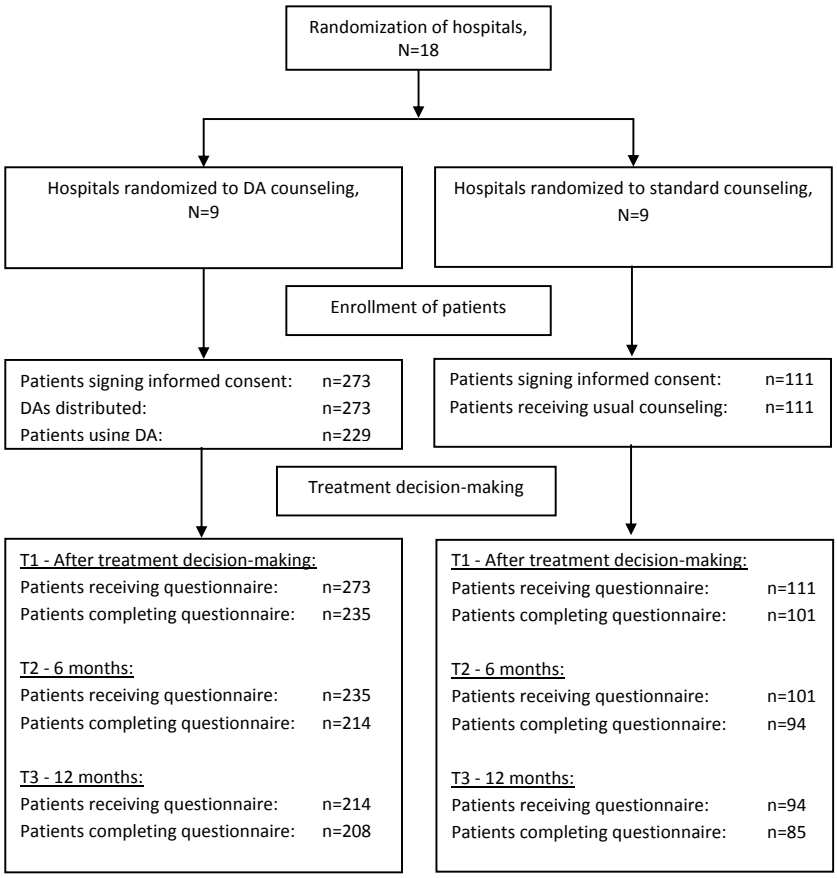


Table 1: Patient characteristics

	DA group	Control group	*P*-value	Complete participation	Lost to follow-up	*P*-value
	N= 235	N=100		N=270	N=65	
Patients						
Age at informed consent						
Mean (SD)	64.9 (6.0)	66.2 (5.7)	.06	65.6 (5.8)	64.2 (6.4)	.09
Marital Status, n (%)						
Married/together	208 (89%)	87 (86%)	.54	244 (90%)	51 (60%)	<.001
Other	27 (11%)	14 (14%)		27 (10%)	34 (40%)	
Education, n (%)						
Low	76 (33%)	36 (36%)	.41	81 (30%)	31 (48%)	.02
Medium	54 (23%)	28 (28%)		69 (26%)	13 (20%)	
High	101 (44%)	36 (36%)		117 (44%)	20 (31%)	
Gleason sum, n (%)						
6	134 (61%)	44 (69%)	.25	141 (61%)	37 (71%)	.16
7	86 (39%)	20 (31%)		91 (39%)	15 (29%)	
PSA level, mean (SD)						
≤10.0, n (%)	180 (78%)	72 (75%)	.92	203 (77%)	49 (79%)	.94
10.1-20.0, n (%)	50 (22%)	24 (25%)		61 (23%)	13 (21%)	
Number of eligible treatments						
2	49 (21%)	25 (28%)	.51	59 (23%)	21 (27%)	.74
3	115 (50%)	42 (46%)		130 (50%)	37 (47%)	
4	65 (29%)	24 (26%)		71 (27%)	20 (26%)	
Treatment received						
Active surveillance	68 (31%)	19 (19%)	<.001	63 (24%)	26 (36%)	.11
Surgery	87 (39%)	29 (29%)		98 (37%)	26 (36%)	
Radiotherapy	67 (30%)	52 (52%)		101 (39%)	21 (28%)	
Other/unknown	13	1		9	6	
Hospitals						
1	20 (7%)		<.001	9 (3%)	6 (7%)	.26
2	1 (1%)			0 (0%)	1 (1%)	
3	50 (18%)			37 (14%)	10 (12%)	
4	34 (13%)			19 (7%)	12 (15%)	
5	16 (6%)			10 (4%)	5 (6%)	
6	21 (8%)			13 (5%)	4 (5%)	
7	72 (25%)			53 (20%)	13 (16%)	
8	38 (14%)			31 (11%)	6 (7%)	
9	21 (8%)			18 (7%)	3 (4%)	
10		6 (6%)		6 (2%)	0 (0%)	
11		20 (18%)		13 (3%)	1 (1%)	

Table 1: (Continued)

	DA group	Control group	*P*-value	Complete participation	Lost to follow-up	*P*-value
	N= 235	N=100		N=270	N=65	
12		10 (9%)		8 (3%)	1 (1%)	
13		10 (9%)		8 (3%)	2 (2%)	
14		24 (22%)		19 (7%)	5 (6%)	
15		8 (7%)		5 (2%)	3 (4%)	
16		23 (21%)		17 (6%)	3 (4%)	
17		8 (7%)		5 (2%)	3 (4%)	
18		Merged with hospital 14				

Table 2: Patient reported outcomes per trial arm in the first year after treatment was chosen

	All treatment groups	
	DA N=207	Control N=96
Decision regret (0-100), Mean (SD)		
T2	17.4 (20.6)	13.4 (14.5)
T3	13.5 (16.9)	12.7 (15.4)
Information satisfaction (0-100), Mean (SD)		
T1	70.8 (20.1)	77.8 (15.8)**
T2	76.2 (17.2)	78.5 (19.6)
T3	76.4 (17.2)	78.2 (18.7)
Anxious and depressive symptoms (0-44)		
T1	7.4 (6.5)	7.2 (5.5)
T2	6.8 (6.4)	6.1 (5.7)
T3	6.5 (5.5)	6.2 (5.1)

Note: T1 was before treatment start; decision regret was not surveyed at that time point.

P-values represent comparisons between trial arms of unadjusted means according to independent samples t-tests.

** $p<.001$

Discussion

This study longitudinally assessed regret and information satisfaction in a sample of Pca patients who chose treatment with or without being provided with an online treatment DA. Previously, no positive effects from the DA on patient-reported decision process parameters were observed directly after decision- making (3). The current study showed that after a 12-months follow-up no long-term effects on regret or information satisfaction from the current DA emerged. Anxious and depressive symptoms were associated with the odds of reporting regret and information dissatisfaction at follow-up, regardless of expo- sure to the DA.

Overall regret was lower than what is generally found in Pca survivors, while the degree of information dissatisfaction was comparable to what has been reported earlier (19,21). In spite to what was found with a comparable Pca DA with VCEs, this study found no evidence that beneficial DA effects emerged past the moment of actual DA usage (10). In line with our initial finding that anxious and depressive symptoms moderated DA satisfaction immediately after treatment decision-making, the current study also found a relation with regret and information satisfaction at follow-up (3).

Limitations of the current study include the unbalanced sampling in both trial arms and therefore potentially including caregiver effects or sampling error into this study. Due to the limited number of patients, low power prevented further investigation of hospital and treatment specific effects. In particular, enrolment of patients on AS in the control arm was low, leading to an underrepresentation of patients on AS in the control arm. Single and lower educated men were lost-to-follow- up more often, although, given the low drop-out level, this does not seem to have impacted the results.

Future research should look in to possibilities to tailor the DA and Pca counseling to the presence of anxious and depressive symptoms (i.e. timing, explanation, and usage of the DA). The current study focused on patient-reported outcomes in the first year after treatment decision-making. A longer follow-up period (up to 36 months) including clinical data about possible tumor recurrences (or tumor progression in case of AS) could provide insight if the patients from the DA group adjusted better due to more accurate risk perceptions (22).

Conclusion

Exposure to a Dutch online PCa DA with VCEs during decision- making did not lead to differences in regret or information satisfaction 12 months after treatment was chosen, compared to a control group who selected treatment after standard counseling. In both patient groups, the odds of reporting regret or information dissatisfaction was associated with anxious and depressive symptoms.

Practice implications

During PCa treatment counseling, healthcare providers should be aware of anxious and depressive symptoms.

Declarations of interest

This research is funded by CZ Fund, a Dutch not-for profit health insurer (Grant 2013-00070) and Delectus Foundation, a Dutch non-profit foundation aimed to initiate and stimulate research into shared decision making. The funding agreements ensured the authors' independence in designing, conducting, and analyzing the results. MdV obtained funding from CZ, PK is chairman of Delectus Foundation. The authors declare that they have no further conflicts of interest.

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Part 2

Chapter 6

Development of a decision aid for the treatment of benign prostatic hyperplasia: A four stage method using a Delphi consensus study

R.E.D. Lamers, M. Cuypers, M.M. Garvelink, M. de Vries,
J.L.H.R. Bosch, P.J.M. Kil

Patient Education and Counseling
2016 Jul;99(7):1249-56

Abstract

Objective To develop a web-based decision aid (DA) for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS/BPH).

Methods From February–September 2014 we performed a four-stage development method: 1: Two- round Delphi consensus method among urologists, 2: Identifying patients' needs and expectations, 3: Development of DA content and structure, 4: Usability testing with LUTS/BPH patients.

Results 1 (N = 15): Dutch urologists reached consensus on 61% of the statements concerning users' criteria, decision options, structure, and medical content. **2** (N = 24): Consensus was reached in 69% on statements concerning the need for improvement of information provision, the need for DA development and that the DA should clarify patients' preferences. **3:** DA development based on results from stage 1 and stage 2. **4** (N = 10): Pros of the DA were clear information provision, systematic design and easy to read and re-read.

Conclusion A LUTS/BPH DA containing VCEs** was developed in cooperation with urologists and patients following a structured 4 stage method and was stated to be well accepted.

Practice Implications This method can be adopted for the development of DAs to support other medical decision issues.

** Values Clarification Exercises.

Introduction

BPH is a common problem among older men worldwide and the incidence of BPH increases with age (1,2). In 2012, the percentage of Dutch citizens aged >65 was 16%, in 2040 this is estimated to increase to 26% (3). Unfortunately, indications for various treatment options for LUTS/BPH are not sharply demarcated in Dutch and European guidelines (4,5). Hence, there are strong differences in doctors' interpretations which may lead to treatment variation (6). Decision aids (DAs) are tools to assist patients in the decision-making process and the use of DAs may influence treatment variation, lower decisional conflict, bring more accurate expectations of possible benefits and harms and help to align choices with their informed values (7–9).

Since no structured LUTS/BPH DA development has been described before, most DAs are outdated, did not involve patients and/or urologists or did not clarify patient preferences our objective is to structurally develop an interactive web-based DA for the treatment of LUTS/BPH to improve and standardize information provision and involve patients in decision-making (10–16). By involving urologists and patients in development we aim to facilitate implementation since clinicians may find that offering DAs will not fit in their workflow, are concerned that patients are not able to process the DA information or because they report a lack of confidence in DA content (17,18).

Methods

From February–September 2014 we developed a Dutch web- based DA in accordance with the International Patient Decision Aid Standards (IPDAS) (19,20). Development took place in the southern part of the Netherlands and consisted of four stages, each described below (Fig. 1).

Stage 1: Two-round Delphi consensus method among experts

We conducted a two-round Delphi questionnaire consensus procedure among a random panel of 15 urologists to identify the medical DA content and structure (21–23).

Round 1

Thirty-one experts received an invitation for participation by email including a direct link to the questionnaire wherein 41 statements were presented. They indicated the level of agreement with each statement using a 5-point Likert scale. Experts added items which they considered important but which were not included in the questionnaire in open comment fields. Consensus outcomes were classified using median scores.

Round 2

Statements on which no consensus was reached were presented again. A 7-point Likert scale was used to allow more variance in answers (23–25). The Dutch association of urology (NVU) has created a working group consisting of 10 experts in the field of urology and/or decision-making. Comments made in round 1 were included in round 2 when evaluated as relevant by this working group. The degree of consensus was classified based on medians and Inter Quartile Deviations (IQD's). The IQD equals the difference between the 25th and the 75th percentile, an IQD <1 is categorised as good consensus (22–24). The working group decided on statements on which no consensus had been reached.

Stage 2: Identify patients' needs and expectations

A cross-sectional needs assessment was performed among 26 patients using online questionnaires to determine patient information needs and expectations. Patients were recruited by clinicians from the working group in 5 Dutch hospitals in the southern part of the Netherlands. Open comment fields were used to determine expected pros and cons about the DA. Statements were rated on a 5-point Likert scale.

Stage 3: Development of content and structure of the DA

The final content of the DA was decided upon by the working group based on guidelines and the results of stages 1 and 2 (Fig. 1) (4,5). To clarify patients' preferences the working group composed VCEs to elicit patients' preferences towards all treatment alter- natives (26).

Stage 4: Usability testing among BPH patients

We invited all participating patients from stage 2 to run the DA and complete an online usability questionnaire afterwards. The questionnaire consisted of 5 open questions to assess first impressions and positively and negatively evaluated aspects and 10 statements about DA usability.

Results

Stage 1: Two round Delphi consensus method among experts

Round 1
Response rate was 48% (N = 15). Mean age was 48 years, with a median of 11–15 years of clinical experience. Consensus was reached on 80% (33/41) of the statements (Table 1).

Round 2
For round 2 we created 23 new statements based on the comments given via the open comment fields and statements on which no consensus was reached in round 1. Consensus was reached on 61% of the statements. (Table 2).

Stage 2: Identify patients' needs and expectations

Response rate was 92% (N = 24) and 83% wanted to be involved in their medical decision-making (Table 3). The expected pros of the DA were related to clarification of the disease and treatment choice, simplification of the decision, lower decisional conflict, patient-tailored treatment, shared decision-making, preparation for the treatment and improvement of information provision (N = 18, by open comment fields). Expected cons of the relevant DA concerned impersonal approach, higher decisional conflict and making the wrong decision (N = 15, by open comment field). Consensus was reached on 69% of the statements (Table 4).

Stage 3: Development of content and structure of the DA

After analysing the previous stages the working group consented to develop a web-based DA including an IPSS- questionnaire (International Prostate Symptom Score, a standardized urinary symptom score) that calculates outcome scores and written information fields supported by medical images followed by VCEs. The DA contains routing depending on the individual patient's use of medication. Medication-naïve patients can read information and clarify personal preferences by filling in VCEs about the treatment options watchful waiting vs. medication followed by the options (other) medication vs. surgery whereas patients who already used medication for LUTS/BPH directly start at the medication vs. surgery field. Finally, the DA provides a printable summary including patients' treatment preferences to discuss with their urologist.

Stage 4: Usability testing among BPH patients

Response rate was 42% (N = 10, Table 5). First impressions of the DA were indicated as clear and concise, forces you to think about various cases, difficult, neat and balanced. Pros of the DA were clear information provision, systematic design and easy to read and re-read (N = 10, by open comment field).

Figure 1: Flow-diagram

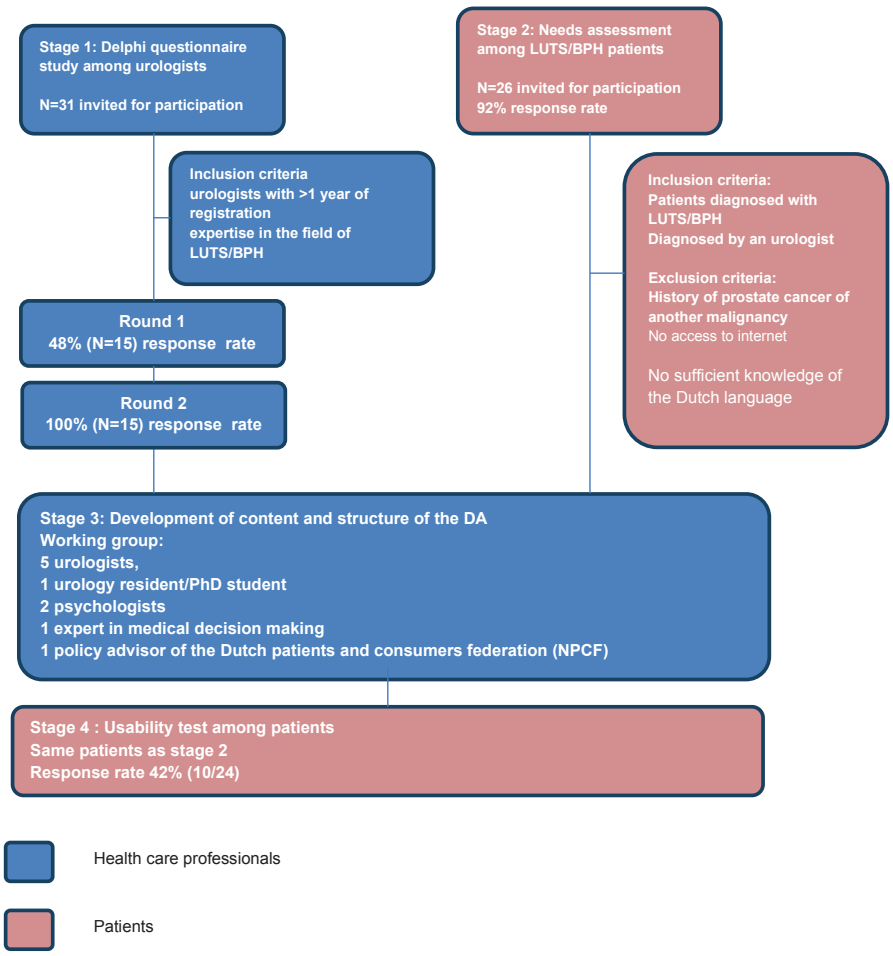

Table 1: Stage 1, Two round Delphi consensus method among experts, round 1

Statements stage 1, round 1	***Median***	***Consensus level***
Inclusion criteria (N=15)		
The DA should be offered to…		
…only medication naïve LUTS/BPH patients	2	Consensus on disagreement
…only patients with an IPSS score >7	3	No consensus
…only patients who already use an alpha-blocker	2	Consensus on disagreement
…only patients with a PSA value > 1.5ug/L	1	Consensus on disagreement
…all patients referred to an urologist with LUTS/BPH	5	Consensus on agreement
In case of a PSA level >4, malignancy should be ruled out histopathological	3	No consensus
Decision options (N=15)		
The DA should…		
…overview the option watchful waiting vs. medication when a patient is medication naïve.	4	Consensus on agreement
…overview the option medication vs. surgery when a patient already used an alfablocker	5	Consensus on agreement
...only overview the option medication vs. surgery	2	Consensus on disagreement
…always show the option surgery, even if the patient is medication naïve	4	Consensus on agreement
Structure (N=15)		
The DA should be offered to all patients referred to an urologist with LUTS/BPH	5	Consensus on agreement
* I think it's important that…		
…the DA helps to clarify patients preferences	4	Consensus on agreement
…there are different DAs for patients with and without medication)	4	Consensus on agreement
…the DA provides an end summary of the given responses	4	Consensus on agreement
…the DA provides a treatment advice based on the given patient answers	4	Consensus on agreement
…patients can skip information fields/ steps in the DA	3	No consensus
…after reading the information fields, patients will be tested if they understand the ridden information (e.g. with test questions)	4	Consensus on agreement

Table 1: (Continued)

Statements stage 1, round 1	*Median*	*Consensus level*
IPSS (International Prostate Symptom Score) (N=15)		
* I think it's important that…		
…the DA starts with the IPSS score	4	Consensus on agreement
…the IPSS results are displayed as a label (e.g. you have "mild-moderate-severe complaints")	4	Consensus on agreement
…the IPSS results are displayed as a number (e.g. "Your IPSS is 30")	4	Consensus on agreement
…the IPSS is filled in, but the results aren't shown for the patient.	2	Consensus on disagreement
…the possible treatment options are determined by IPSS score	3	No consensus
…the IPSS is displayed in the end summary	4	Consensus on agreement
Time expectations (N=15)		
I think that the use of a DA may save time for my consult	2	Consensus on disagreement
I think that the use of a DA may requires more time for my consult	3	No consensus
Medical content- treatment options (N=15)		
* I think it's important that		
…only common surgical treatment options in the Netherlands are displayed in the DA	4	Consensus on agreement
…experimental treatment options (e.g. stent, dilatation etc.) are also described.	2	Consensus on disagreement
…transurethral electrovaporisation (TUVP) is mentioned as a treatment option for LUTS/BPH	3	No consensus
…the options "Millin and Hryntchack (open prostatectomy) are mentioned in the DA as a possible treatment option	4	Consensus on agreement
Medical content- medical options (N=15)		
For moderate/severe LUTS/BPH and predominantly storage LUTS/"overactive bladder symptoms" (prostate volume <30 and no residual volume), an alphablocker combined with a antimuscarin drug is an appropriate treatment.	4	Consensus on agreement
A combination of an alphablocker and a 5-ARI is an appropriate treatment for moderate/severe LUTS/BPH and a prostate volume > 30cc-40cc.	4	Consensus on agreement
Surgery should be offered to medication naïve patients.	4	Consensus on agreement
A 5-ARI should not be offered to patients with a prostate volume < 40cc.	4	Consensus on agreement
A phosphodiesterase 5 (PDE-5) inhibitor should be mentioned as an appropriate drug treatment for LUTS/BPH.	3	No consensus

Table 1: (Continued)

Statements stage 1, round 1	*Median*	*Consensus level*
Medical content- side effects (N=15)		
* I think it's important that…		
… side effects occurring in less than 1% should not be mentioned.	4	Consensus on agreement
… dizziness is mentioned as a possible side effect of an alphablocker	4	Consensus on agreement
… retrograde ejacultation is mentioned as a possible side effect of an alphablocker	4	Consensus on agreement
…erectile dysfunction is mentioned as a possible side effect of a 5-ARI	4	Consensus on agreement
... loss of amount in semen volume is mentioned as a possible side effect of a 5-ARI.	4	Consensus on agreement
… in case of surgery, incontinence is mentioned as a possible side effect.	4	Consensus on agreement
… in case of surgery, erectile dysfunction is mentioned as a possible side effect.	4	Consensus on agreement

1= totally disagree, 2= disagree, 3= do not disagree/ do not agree, 4= agree, 5= totally agree
median > 3: consensus on agreement with a statement
median = 3: no consensus on agreement with a statement
median < 3: consensus on disagreement with a statement

Table 2: Stage 1, Two round Delphi consensus method among experts, round 2

Statements stage 1, round 2	***Median***	***IQD***	***Consensus level***
** How important are the following items for the LUTS/BPH DA?*			
- The treatment choice watchful waiting versus medication in medication naïve patients.	6	1	consensus on importance
- The necessary examinations prior to the diagnosis LUTS/BPH	6	1	consensus on importance
- Information about the natural course of the disease.	6	1	consensus on importance
- Success rates of different treatment options.	6	1	consensus on importance
- Percentages of complications/side effects	6	1	consensus on importance
Cons of the DA (N=15)			
You and your colleges filled in what kind of disadvantages you expect of a LUTS/BPH DA. Please indicate the degree to which you agree with the following possible disadvantages.			
* I expect…			
… too much information for the patient	5	3	no consensus
… more confusion for the patient	4	3	no consensus
… a large time load for the patient	2	3	no consensus
… a decrease in personal attention	2	3	no consensus
… incorrect information (content) in the DA	4	3	no consensus
Inclusion criteria (N=15)			
In case of a PSA level >4, malignancy should be ruled out histopathological	4	2	no consensus
The DA should be offered to only patients with an IPSS score >7	5	3	no consensus
The DA should be offered to only patients who already use an alphablocker	3	4	no consensus
Medical content- treatment options (N=15)			
I think it's important that the DA always show the option surgery, even if the patient is medication naïve	6	1	consensus on agreement
A phosphodiesterase 5 (PDE-5) inhibitor should be mentioned as an appropriate drug treatment for LUTS/BPH	5	4	no consensus
Values Clarification Exercises (N=15)			
How important do you think it is to include these VCMs in the DA? (watchful waiting vs. medication)			
I'm not willing to take medication on a daily basis vs. I'm willing to take medication on a daily basis.	4	1	consensus less to moderately important
I think it's sufficient to learn how to deal with my symptoms vs. I just want to reduce my symptoms	4	1	consensus less to moderately important
I suffer from my complaints but I'd like to defer the use of medication vs. I suffer from my complaints so I'm willing to try medication.	4	0	consensus less to moderately important
I'm willing to accept progression when not taking medication vs. I'm willing to accept side effects when taking medication.	4	0	consensus less to moderately important

Table 2: (Continued)

Statements stage 1, round 2	*Median*	*IQD*	*Consensus level*
How important do you think it is to include these VCMs in the DA? (medication vs. surgery)			
I'm willing to take medication on a daily basis vs. I'm not willing to take medication on a daily basis.	4	1	consensus less to moderately important
I do not suffer from side effects of my medication vs. My side effects from medication bother me too much	4	1	consensus less to moderately important
I suffer from my urinary symptoms but it's acceptable vs. My urinary symptoms bother me so much that I want to undergo surgery.	4	1	consensus less to moderately important
I do not think it's important to improve my urinary stream force vs. I think it's important to improve my urinary stream force.	4	1	consensus less to moderately important

Concerning importance:
1=very unimportant, 2=unimportant, 3=slightly unimportant, 4= not unimportant/ not important, 5=slightly important, 6=important, 7= very important
Concerning agreement:
1= totally disagree, 2= disagree, 3= slightly disagree, 4= do not disagree/do not agree, 5= agree, 6 slightly agree, 7=totally agree
1. consensus on agreement with a statement/ consensus that a statement is important (IQD ≤ 1 and median score ≥ 6)
2. no consensus on agreement with a statement/ no consensus on importance (IQD >1)
3. consensus on disagreement with a statement/ consensus that a statement is less to moderately important (IQD ≤ 1 and median score ≤ 5)

Table 3: Stage 2, Patient characteristics

Patient characteristics stage 2	***N (%)***	***Mean (SD)***
Age, years	24 (92)	70 (5.3)
Education*		
Low	2 (8)	
Medium	12 (50)	
High	10 (42)	
Urinary symptoms		
Increased frequency	12 (50)	
Nocturia	15 (63)	
Interrupted urinary stream	8 (33)	
Weak urinary stream	14 (58)	
Post voiding residual volume	16 (67)	
Straining for urination	5 (21)	
Received LUTS/BPH treatment		
Medication	18 (75)	
Surgery	1 (4)	
None/Lifestyle advices	5 (21)	
Preferred decision role		
Active	1 (4)	
Active shared	6 (25)	
Collaborative	13 (54)	
Passive shared	3 (13)	
Passive	1 (4)	

*Low (no or primary school), medium (lower general secondary education or vocational training), High (pre-university education, high vocational training, university)

Table 4: Stage 2, Identify patients' needs and expectations

Statements stage 2	***Median***	***Consensus level***
Received information provision (N=23)		
I'm satisfied about the information about urinary symptoms received via my urologist	4	Consensus on agreement
I would have like to receive more information about my treatment options	3	No consensus
I didn't feel like I had a say in my treatment choice	2	Consensus on disagreement
I didn't know that there were multiple treatment options	3	No consensus
I knew well what the risks and complications of medication contain	3	No consensus
I knew well what the risks and complications of surgery contain	3	No consensus
I would have like to have some more time for my treatment decision	3	No consensus
Information provision in general (N=23)		
Information provision about LUTS/BPH treatment should be improved.	4	Consensus on agreement
I think it's important that a LUTS/BPH DA will be developed	4	Consensus on agreement
I think a website in general won't contribute to patients' information provision	2	Consensus on disagreement
I think it's important that patients can print their information about their treatment options from the internet and discuss this with their clinician	4	Consensus on agreement
It's important that patients can indicate their preferences in a DA	4	Consensus on agreement
It's important that patients' preferences are clear for their clinician	4	Consensus on agreement
A clinician does not need to reckon with patients' preferences	2	Consensus on disagreement
The clinician's opinion may not play a role in information provision	3	No consensus
Usability (N=23)		
I'm willing to spend a maximum of 30 minutes on a DA	3	No consensus
I'm willing to spend over 30 minutes on a DA	4	Consensus on agreement
I think it's important that patients cannot skip information fields/ steps in the DA	4	Consensus on agreement
Patients should be able to determine by themselves which parts of the DA they go through.	3	No consensus
I think that the use of a DA may save time for a consult	4	Consensus on agreement
I think that the use of a DA may requires more time for a consult	2	Consensus on disagreement

Table 4: (Continued)

Statements stage 2	*Median*	*Consensus level*
IPSS (International Prostate Symptom Score) (N=22)		
* I think it's important that…		
…the possible treatment options are determined by the IPSS (e.g. no surgery in case of a very low IPSS)	4	Consensus on agreement
…the IPSS results are displayed as a number (e.g. "Your IPSS is 30")	4	Consensus on agreement
…the IPSS results are displayed as a label (e.g. you have "mild-moderate-severe complaints")	4	Consensus on agreement
Treatment advice (N=22)		
I think it's important that…		
…the DA provides a treatment advice based on the given patient answers	4	Consensus on agreement
…the DA clarifies patients' preferences, but doesn't provide a treatment advice	4	Consensus on agreement

1. consensus on agreement with a statement (median > 3)
2. no consensus on agreement with a statement (median = 3)
3. consensus on disagreement with a statement (median <3)

Table 5: Stage 4, Usability testing among BPH patients

Statements stage 4	*Median*	*Consensus level*
Usability (N=10)		
If I was facing a new treatment choice, I would use the DA.	4.5	Consensus on agreement
The DA was unnecessarily difficult.	2	Consensus on disagreement
The DA was easy to use.	3	No consensus
I need more instructions to use the DA.	2	Consensus on disagreement
The various DA components were well synchronised (e.g. diagnosis, information, preferences).	4	Consensus on agreement
The DA contained to much inconsistencies.	2	Consensus on disagreement
I think most people can easily learn how to use the DA.	4	Consensus on agreement
The DA was very cumbersome to use.	2	Consensus on disagreement
I felt very familiar with the DA.	4	Consensus on agreement
I needed to learn a lot before I could use the DA.	2	Consensus on disagreement

1. consensus on agreement with a statement (median > 3)
2. no consensus on agreement with a statement (median = 3)
3. consensus on disagreement with a statement (median < 3)

Discussion and Conclusion

Discussion

We developed and described a structured four-stage method for the development of a LUTS/BPH DA. Urologists in our sample population reached consensus on statements concerning users' criteria, decision options, structure and medical content. In 83%, patients wanted to be involved in their medical decision-making. Most consensus among patients was reached on statements concerning the need for information provision improvement, the need for DA development and that the DA should clarify patients' preferences. Pros of the DA according to patients were clear information provision, systematic design and easy to read and re-read.

In line with other research, our patients who had generally high education levels indicated to prefer an active or collaborative role in decision-making (27). This may also explain their high satisfaction rates with our DA. Additionally, the fact that they were relatively old (mean age 70) did not lead to a preference for more passive roles in decision making, as found by others (27). This might be due to selection bias resulting from non-response by the more passive patients.

Limitations

In stage 4 we achieved a response rate of 42%. The duration of 2 months between the needs assessment and usability test may have been too long so that patients' motivation was too low to delve into the DA again. The burden may also have been too high because patients were asked to fully run the DA as well as fill in a DA usability questionnaire. Secondly, some IPDAS criteria (3/44) regarding review by professionals not involved in production, used quality of research evidence, and readability levels were not met (20,28).

Conclusion

Since no structured LUTS/BPH DA development method has been published before we described a structured four-stage method for the development of a LUTS/BPH DA well accepted by urologists and patients. By involving patients and urologist, we aim to facilitate implementation.

Practice implications

This method could be adopted for the development of DAs to support other medical decision problems considering the fact that this method is in line with earlier published

recommended methods, followed a systematic, patient-centered process and involved stakeholders (19,20,29).

I confirm all patient/personal identifiers have been removed or disguised so the patient/person(s) described are not identifiable and cannot be identified through the details of the story.

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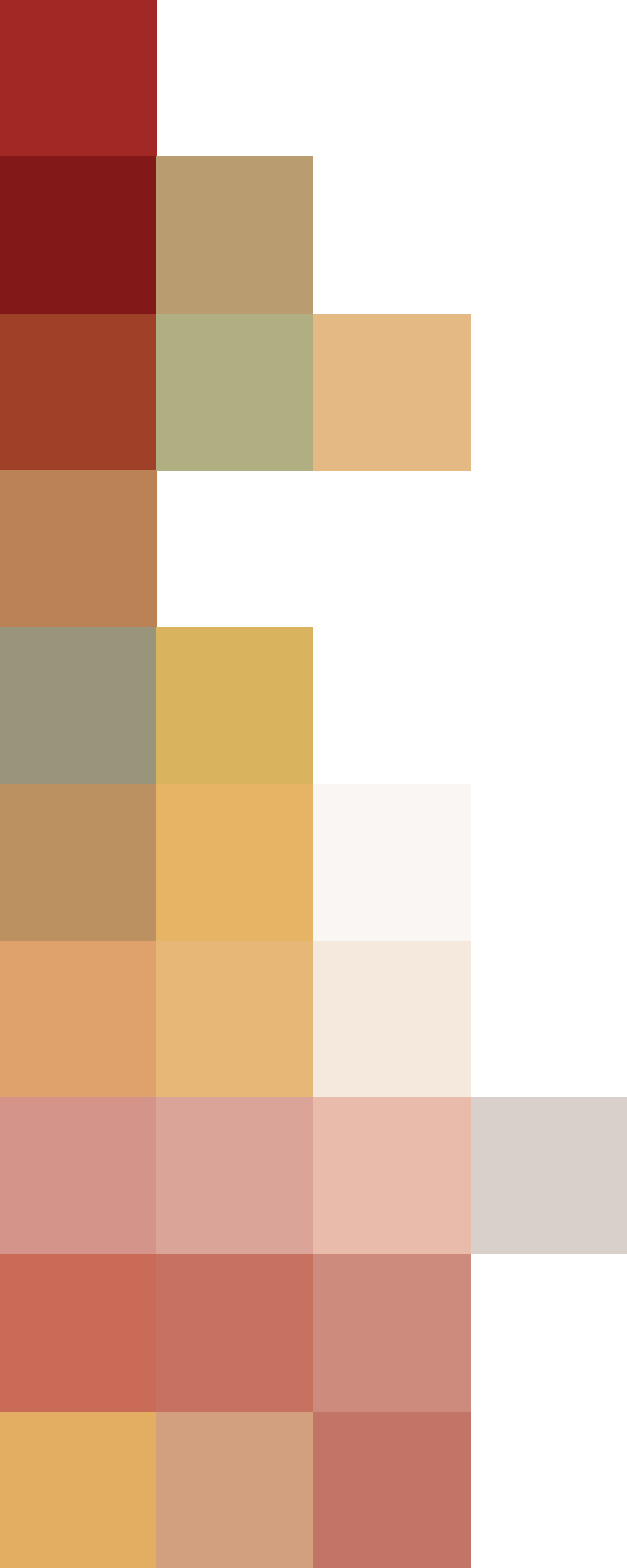


Chapter 7

Treatment preferences of patients with benign prostatic hyperplasia before and after using a web-based decision aid

R.E.D. Lamers*, F.C. van der Wijden*, I.B. de Angst, M. de vries, M. Cuypers, H.H.E. van Melick, J.S. de Beij, D.J.A.J. Oerlemans, C. van de Beek, J.L.H.R. Bosch, P.J.M. Kil

**Both authors contributed equally to this work and should be considered as shared first author*

Submitted

Abstract

Objectives To evaluate treatment preferences of patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) before and after using a web-based decision aid (DA). Furthermore, to evaluate the feasibility of the DA use in clinical practice among patients and their healthcare providers.

Patients and Methods Between July 2016 and January 2017 patients were invited to use a web-based LUTS/BPH DA. Treatment preferences (for lifestyle advices, medication or surgery) before and after DA use and responses on values clarification exercises (VCEs) were extracted from the DA. To evaluate the feasibility of the DA use, questionnaires were administered among patients and their healthcare providers.

Results In total, 126 patients were included in the analysis. Thirty-four percent (43/126) did not use medication for LUTS and was eligible for lifestyle advices or medication. Sixty-six percent (83/126) did use medication and was eligible, either for continuing medication or surgery. Before DA use, 67 patients were undecided (53%) and 59 patients already had an initial treatment preference (47%). Half of the patients who were initially undecided were able to indicate a preference after DA use (51%). Of the patients with an initial preference, 80% confirmed their initial preference after DA use. Five out of seven VCEs used in the DA were discriminative between final treatment preferences. In 79%, the treatment preferred after DA use matched the received treatment. Overall, patients and healthcare providers were positive about DA content and its usefulness in treatment decision-making.

Conclusion Our findings suggest that a LUTS/BPH DA may help patients make well-informed decisions and support them in forming a treatment preference even if they did not have an initial preference. Both patients and their healthcare providers are positive about its usefulness in clinical practice.

Introduction

Prevalence rates of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) range from 50% to 75% among men over the age of 50 years and increase with age (1). These symptoms can have substantial impact on quality of life (2-4). Treatment options are watchful waiting, lifestyle advice, pharmacotherapy or surgery. Indications for the various treatment options are not well defined in Dutch and European guidelines. Preferences and values of the individual patient are important factors in disease management, next to well-established factors like results of diagnostic tests, the estimation of disease progression and ability of treatments to reduce symptoms, preferences and values of the individual patient matter in disease management. Trade-offs must be made between expected benefits, side effects, risks and burden of treatments, and disease burden (5,6). Misconceptions about preferences and expectations about LUTS/BPH treatment are common both in patients and physicians and differ between these two groups (7-9). Given the preference-sensitive elements of this treatment decision, patient involvement is important and may reduce unwarranted practice variations (10,11).

Structural implementation of shared decision-making (SDM) in daily practice is challenging (12). The majority of patients wants to be involved in decision-making; and once patients are well informed, the need to be involved even increases (13,14). However, observational research shows that a minority of healthcare providers consistently involves patients in the decision-making process (15).

To support SDM, decision aids (DAs) have been developed to assist patients and physicians in exploring patients' preferences, values and expectations. DAs provide standardized information in understandable language for patients (16). Previous research has shown that DA users feel more knowledgeable, are clearer about their values, play a more active role in decision-making and have more accurate risk perceptions regarding treatment options compared to patients who receive usual care. There is increasing evidence that DAs improve congruence between the chosen option and patients' values (17-19).

Despite the high prevalence rate of LUTS/BPH, attention for the development and evaluation of DAs is far less than for other (oncological) conditions. Available DAs are outdated and conclusions are limited by variations in outcome measures (20-28). We therefore developed a web based DA with values clarification exercises (VCEs) to clarify patients' preferences and support SDM in the treatment of LUTS/BPH (29, 30). Recently, we performed a questionnaire study and showed that DA users make well–informed and

value congruent decisions more often than non DA users (29). This recently published study also showed that DA users had less decisional conflict (29).

As a part of the above described study, the aim of the current study is to zoom in on DA users by assessing their treatment preference before and after DA use, as well as the match with their received treatment. In addition, we analyzed the level of congruence of VCEs with received treatment and the feasibility of DA use among patients and their healthcare providers.

Patients and Methods

Study population

Between July 2016 and January 2017 patients from five hospitals in the Netherlands, who consulted the urologist because of LUTS/BPH, were invited to use a web-based DA. Patients were eligible for inclusion if they had the choice between the treatment options watchful waiting/lifestyle advices versus medication (decision A) and (continuing) medication versus surgery (decision B). Patients had to have access to a desktop, laptop, or tablet with internet connection. Patients with prior prostate surgery, an absolute medical indication for surgery, prostate cancer, cognitive impairment or insufficient Dutch language were excluded (29).

Intervention

The DA contains the following two treatment tradeoffs: treatment decision A (watchful waiting/lifestyle advices versus medication) and treatment decision B (continuing medication or undergo surgery) (29). After the urologists discusses the treatment options, he/she indicates which decision applies to the patients' individual situation. Then, the DA guides the patient through the decision process step-by-step. All information was accessible for patients, even when it was not considered primarily suitable for the patient at that moment by the urologist.

The DA contains general information about LUTS/BPH, diagnostics, and the various treatment options according to current guidelines (6). Furthermore, patients are invited to respond to VCEs to obtain their individual preferences. The VCEs used in the DA are shown in Figure 1. With a pointer on a slider scale, patients could indicate the strength of their preference towards one of the treatment options. All VCEs used were developed by a team of patients, urologists, psychologists and engineers (30). Finally, patients were asked to indicate their final treatment preference.

To facilitate discussion with the urologist during the next consultation, it was possible to print the summary or access the summary.

Procedure

The pragmatic aspect of this study allowed participating hospitals to integrate the introduction of the DA with their own standard information provision routines, leading to different time points of offering the DA between hospitals.

After written informed consent, patients received online or paper questionnaires. Results from the questionnaires were linked to patients' DA data. Patients who did not return their informed consent form still had the opportunity to use the DA without participating in the study.

Outcome measures

To assess the preferred role in decision-making, the Control Preference Scale was used prior to DA use and before treatment decision was made. Patients could respond on a 5-point Likert scale. Scores were summarized into three groups: active/active shared, collaborative and passive/passive shared (31).

Patients had to indicate if they used medication for their urinary symptoms at time of this study. To quantify patients' LUTS, the validated International Prostate Symptom Score (IPSS) was used (32). Level of education and age were obtained from completed questionnaires and patient records.

Treatment preferences and responses on VCEs were extracted from the DA. To analyze if the separate VCEs matched with final preferences in DA, median scores were used and responses were demonstrated in box-and-whisker plots.

To assess the association between final preference in the DA and the treatment received, information about treatment decisions was collected from patient records. To investigate the match between responses on VCEs and the treatment received, patients' mean VCE scores were calculated for decision A (3 VCEs) and B (4 VCEs). For decision A and B, a mean VCE score of 0-39 indicated a preference for watchful waiting/lifestyle advices or (continuing) medication respectively, a mean VCE score of 40-60 was not clearly pointing towards one particular treatment option and a score of 61-100 indicated a preference for starting medication or surgery.

Due to the lack of a brief questionnaire assessing non-oncological patients' satisfaction with information provision, the Satisfaction with Cancer Information Profile part B (SCIP-B) was used to assess patient satisfaction with usefulness and understandability of information presented in the DA with scores ranging from very dissatisfied to very satisfied (33). Three study specific items were used to assess patients' satisfaction with the content of the DA and one assessed patients' attitude towards future use of the DA. Patients could respond on a 5-point Likert scale, ranging from "strongly disagree" to "strongly agree".

The Preparation for Decision Making scale was used to assess usefulness of the DA in preparing patients for communication with their urologist about the treatment decision (34). Patients could respond on a 5-point Likert scale, ranging from "not at all" to "a great deal".

To evaluate healthcare professionals' satisfaction with the use of the DA, they were invited to complete an online questionnaire in April 2017. The questionnaire was based on the measurement instrument for determinants of innovations (MIDI) (35). Questions about procedural factors were asked. Healthcare professionals could respond on a 5-point Likert scale, ranging from "never" to "every time". More questions were asked about the content of the DA, advantages and disadvantages of DA use in daily routine, patient outcomes and attitude towards future use. Healthcare professionals could respond on a 5-point Likert scale, ranging from "mostly disagree" to "mostly agree". Finally, respondents were asked to rate the overall quality of the DA on a scale from zero to ten.

Statistical analysis

This study is a sub analysis of a prospective observational study on the effectiveness of the implementation of this DA in patients with LUTS/BPH, were the DA group was compared with a historical control group (29). For this sub analysis, only patients who used the DA were included, regardless of the moment the DA was provided to them.

For continuous data, descriptive statistics were presented as means with standard deviations (SD) and box-and-whisker plots. Categorical data were presented as frequencies with percentages. Quantitative variables were examined with ANOVA and t-tests when normality and homogeneity assumptions were satisfied. Non-normally distributed data were examined with a non-parametric test (Mann Whitney U). To compare proportions we used the Pearson chi-square test.

All analyses were conducted using the IBM Statistical Package for the Social Sciences (SPSS), version 24.0 (SPSS Inc., Chicago, IL, USA), with a P <0.05 considered statistically significant.

Results

A total of 210 patients were invited for participation of whom 73% (154/210) returned the informed consent form. Eleven percent of these patients (17/154) were excluded based on exclusion criteria. After extraction of the DA user log data, 8% (11/137) patients appeared not to have used the DA and were excluded from analyses. Enrollment numbers and flowchart of the study are shown in Figure 2.

Treatment preferences of 126 patients were obtained from DA log data both before and after DA use. Thirty-four percent (43/126) of these patients did not use medication for their LUTS and were eligible for decision tradeoff A. Sixty-six percent (83/126) did use medication and were eligible for decision B. Response rate on questionnaires was 65% (126/193).

Most patients were offered the DA by the urologist before or directly after the diagnostic process (hospital A,B,C,E). In hospital D, the DA was offered when patients visited a nurse for an intake consultation. In hospital C, patients received the DA by e-mail before consulting the urologist. Baseline characteristics are described in Table 1.

Treatment preference before and after DA use

Of all DA users, 53% (67/126) did not indicate an initial treatment preference. Fifty-one percent (34/67) of these patients were able to indicate a preference after DA use. Forty-nine percent (33/67) remained unable to decide after DA use.

In total, 47% (59/126) of patients indicated their initial preference before DA use. Of these patients 80% (47/59) stayed with their initial treatment preference and 19% (11/59) did not indicate a specific final treatment preference or were left undecided after DA use. Only 1 patient changed his initial treatment preference from medication to surgery after DA use (1/59).

Responses on VCEs and final preference in DA

Used VCEs are demonstrated in Figure 1. For decision A, median scores of VCE 1 and 2 were congruent with final treatment preferences and were significantly different between preferences (P<0.05). Median scores of VCE 3 were only congruent with final preference for ‘watchful waiting/lifestyle advices’ after DA use. Median scores of VCE 3 were not significantly different (P=0.28) between final treatment preferences.

For decision B, median scores of VCE 4 and 5 were congruent with final treatment preferences and were significantly different between final treatment preferences (P<0.05). Median score of VCE 6 was only congruent with final treatment preference for '(continuing) medication'. Median scores on this VCE were not significantly different between the final preferences (P=0.35). Median score of VCE 7 was only congruent with final treatment preference 'surgery'. However, median scores of VCE 7 differed significantly between patients with final preference for '(continuing) medication' and 'surgery' (P<0.05). Responses on all VCEs are illustrated in box-and-whisker plots (Figure 3).

Concordance between final treatment preference and treatment received

Sixty-five percent (82/126) of the patients were able to indicate a preferred treatment option after DA use. At decision A, patients' final preferences for watchful waiting/lifestyle advices or starting medication, matched with their received treatment in 67% (14/21) and 100% (9/9) respectively. At decision B, 92% (33/36) of the final preference for (continuing) medication matched the treatment received. Patients with a preference for surgery, underwent surgical treatment in 56% (9/16) of the cases. From all study participants, their preferred treatment option after DA use matched with their received treatment in 79% (65/82) of the cases.

Twenty-one percent (17/82) of the DA users received another treatment than indicated as final preference after DA use. Patients with a final preference for watchful waiting/ lifestyle advices were prescribed medication in 24% (5/21) of the patients and underwent surgery in 9% (2/21) of the patients. Three per cent (1/36) received lifestyle advices and 5% (2/36) of the patients underwent surgery, in spite of their preference for (continuing) medication. Moreover, patients who preferred surgical treatment received medication in 44% (7/16) of the cases. In only 29% (5/17) of these patients the mean calculated VCE score matched with their received treatment. Patients who received a treatment which did not match with their final preference in the DA, nor with calculated mean VCE score (7/17) reported that they wanted to have more information and wanted to know the physician's opinion (N=1), wanted to try other medication first (n=1) or wanted to avoid side effects of medication or surgery (N=3).

From all study participants, 35% (44/126) was not able to indicate a final preference after DA use. Of these patients 11% (5/44) received watchful waiting/lifestyle advices as treatment, 14% (6/44) received medication, and 5% (2/44) underwent surgery in decision A. In decision B, 2% (1/44) received watchful waiting/lifestyle advices as treatment, 59% (26/44) continued medication and 9% (4/44) underwent surgery. In these patients the

calculated mean VCE score matched their received treatment in only 25% (11/44) or was not clearly associated with one treatment option in 57% (25/44).

Patients of whom their treatment received did not match with their responses on VCEs (8/44), reported that they wanted to have more information and to know their physician's opinion (N=4) or wanted to avoid side effects of medication or surgery (N=2).

Data on final treatment decisions are presented in Table 2.

Patients' satisfaction with DA

Table 3 presents patients' satisfaction with the explanation about the DA, the usability of the DA, the different aspects of information presented in the DA, and the usefulness in preparing them for the final treatment decision. Eighty-one per cent (101/126) would recommend this DA to other patients with LUTS. Lower level of education or age older than 70 years was not associated with less satisfaction with information in DA (education: P=0.09, age>70: P=0.80), perception of usefulness of DA in preparation for final treatment decision (education: P=0.27, age>70: P=0.41) or a larger portion patients who remained undecided after DA use (education: P=0.65, age>70: P=0.77). Also, no relation was found between perception of usefulness of DA in preparing for decision and participating study site (P=0.11). Numbers were too low to analyze differences between different preferred role in decision-making and previously mentioned items.

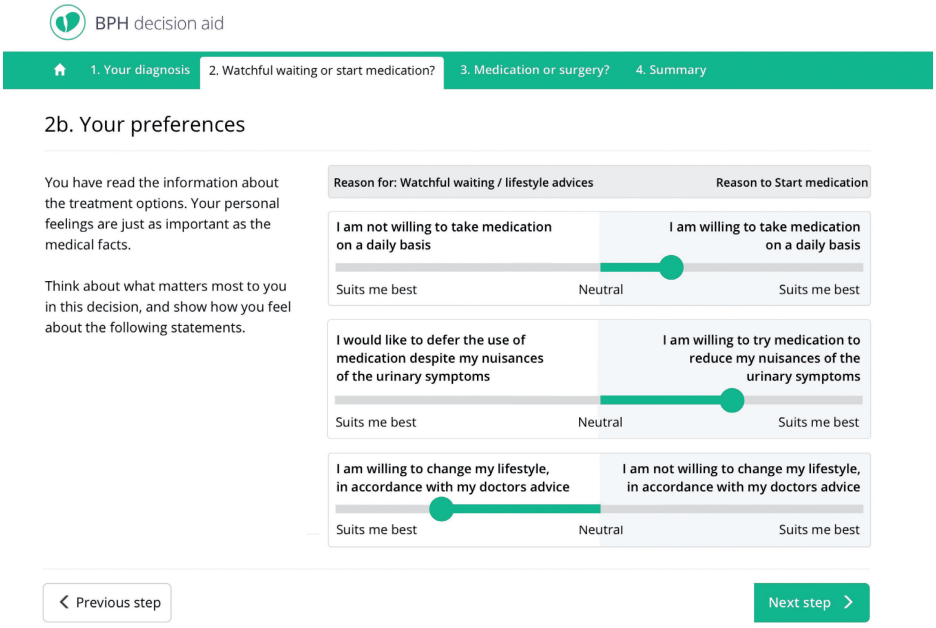
Healthcare professionals' satisfaction with the DA

Healthcare professionals' response rate to online questionnaires was 45% (29/65). Three participants indicated that they did not use the DA, because functional urology was not part of their field of interest. Therefore, these respondents were excluded from analysis. (Table 4)

Overall, healthcare professionals were positive about procedural factors, instrument related factors, subjective patient outcomes and attitude towards future use. Seventy-seven percent (20/26) would recommend this DA to their colleagues and 69% (18/26) want to continue using this DA in the future. Mean number of overall satisfaction was 7.4 (SD 1.0). (Supplementary Table 1)

Figure 1: Values clarification exercises used in the DA. Decision A: watchful waiting/lifestyle advices versus medication, decision B: Continuing medication versus surgery

Decision A



Decision B

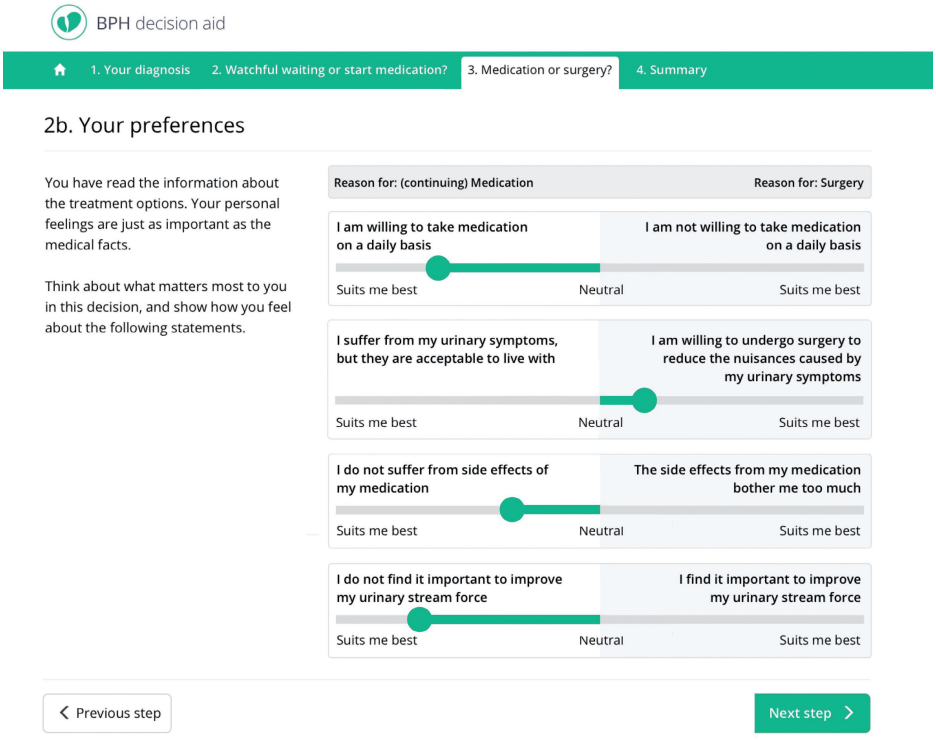

BPH decision aid
1. Your diagnosis
2. Watchful waiting or start medication?
3. Medication or surgery?
4. Summary
2b. Your preferences
You have read the information about the treatment options. Your personal feelings are just as important as the medical facts.
Think about what matters most to you in this decision, and show how you feel about the following statements.
Reason for: (continuing) Medication
Reason for: Surgery
I am willing to take medication on a daily basis
I am not willing to take medication on a daily basis
Suits me best
Neutral
Suits me best
I suffer from my urinary symptoms, but they are acceptable to live with
I am willing to undergo surgery to reduce the nuisances caused by my urinary symptoms
Suits me best
Neutral
Suits me best
I do not suffer from side effects of my medication
The side effects from my medication bother me too much
Suits me best
Neutral
Suits me best
I do not find it important to improve my urinary stream force
I find it important to improve my urinary stream force
Suits me best
Neutral
Suits me best
Previous step
Next step

Figure 2: Flowchart

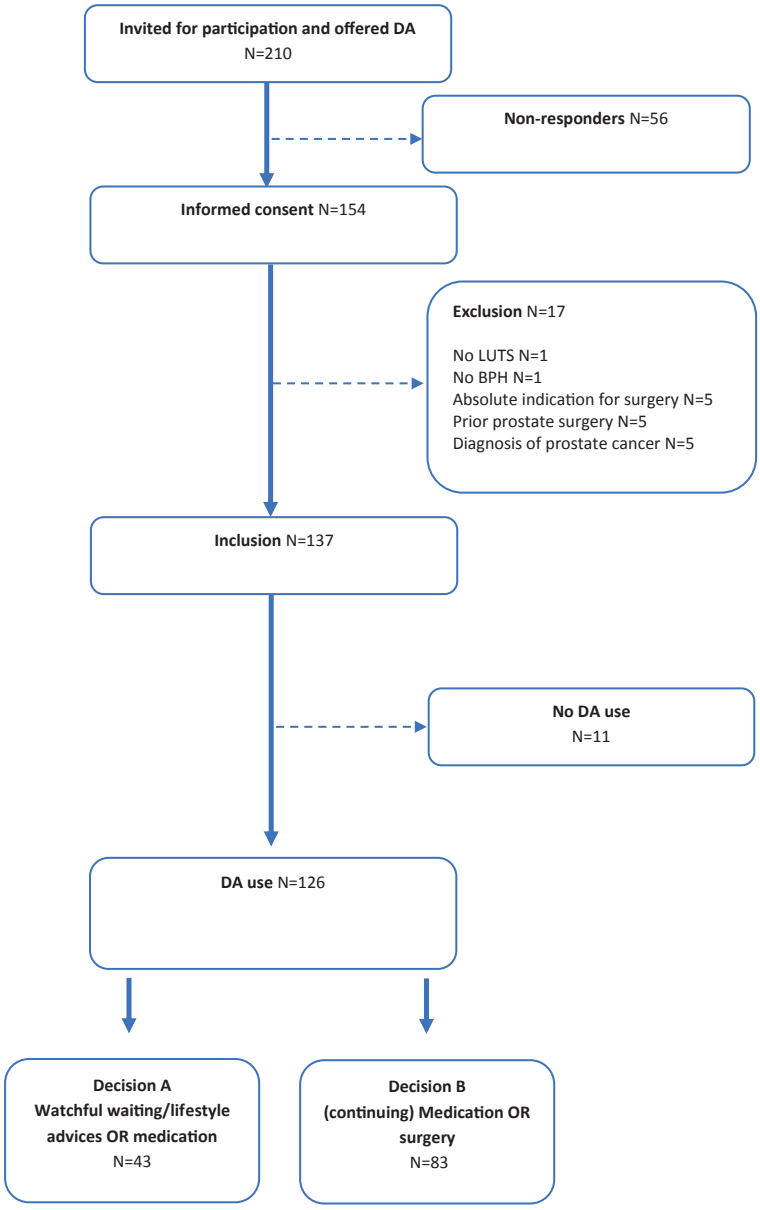
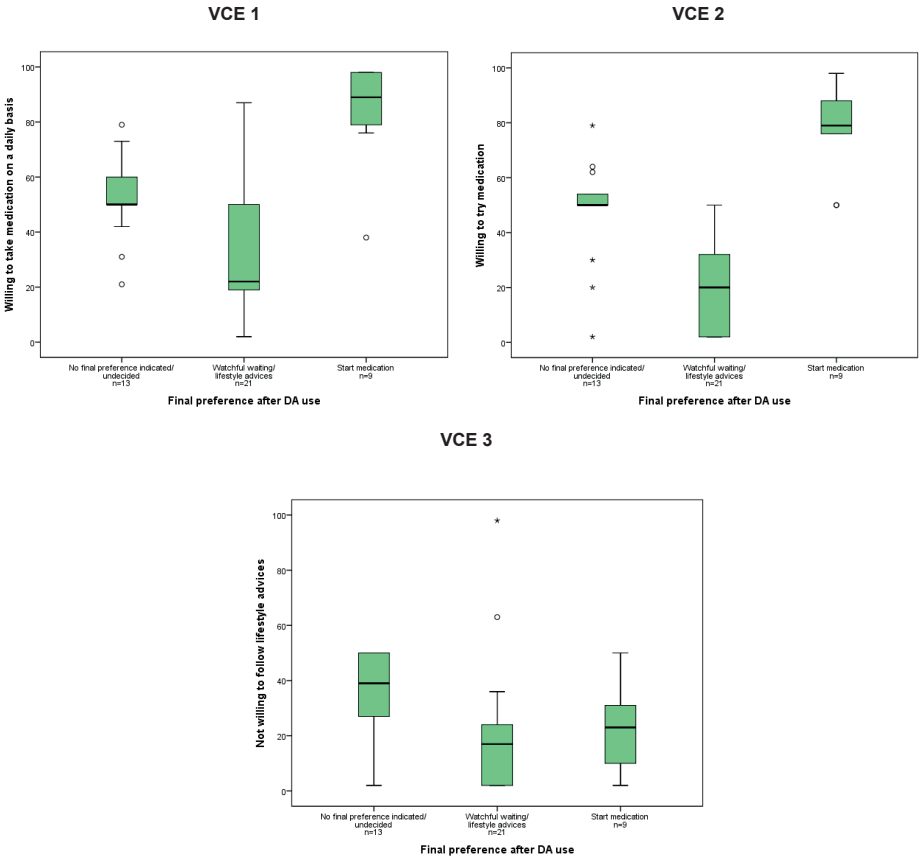
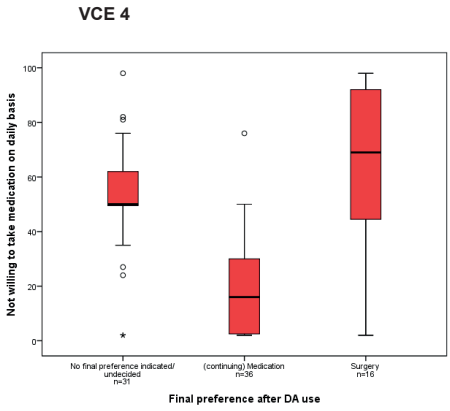


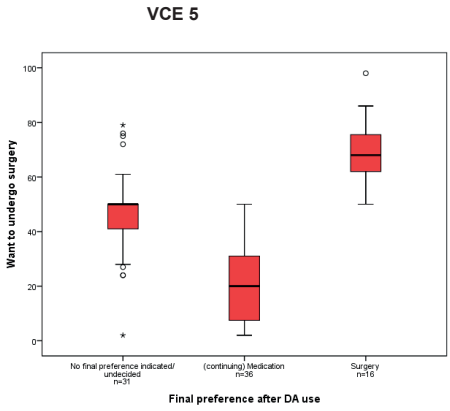
Figure 3: Patients' responses on VCEs. VCEs are named after the 'active treatment' (decision A: towards medication and decision B: towards surgery). High scores correspond to concordance between statement and treatment option. Box represents 50% of the scores and the whiskers illustrate the minimum and maximum value. The horizontal line in the box represents the median. Dots(°) are outliers and asterisks (*) are extremes.

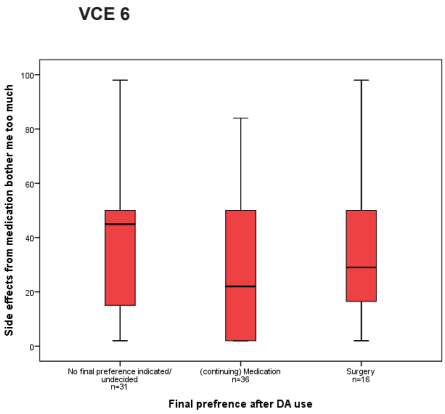
Decision A



Decision B


VCE 4
Not willing to take medication on daily basis
100
80
60
40
20
0
No final preference indicated/ undecided n=31
(continuing) Medication n=36
Surgery n=16
Final preference after DA use


VCE 5
Want to undergo surgery
100
80
60
40
20
0
No final preference indicated/ undecided n=31
(continuing) Medication n=36
Surgery n=16
Final preference after DA use


VCE 6
Side effects from medication bother me too much
100
80
60
40
20
0
No final preference indicated/ undecided n=31
(continuing) Medication n=36
Surgery n=16
Final prefrence after DA use

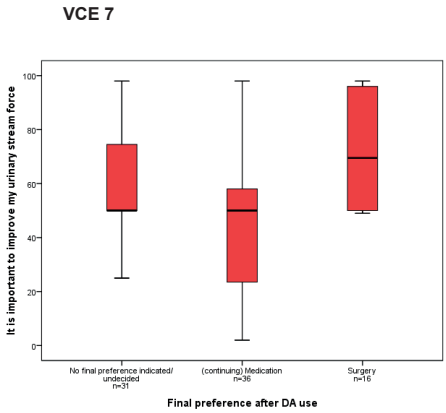

VCE 7
It is important to improve my urinary stream force
100
80
60
40
20
0
No final preference indicated/ undecided n=31
(continuing) Medication n=36
Surgery n=16
Final preference after DA use

Table 1: Patient-related characteristics of DA users (N=126)

		N (%)
Age, in years mean ± SD	67.8 ± 7.0	
Inclusion per hospital	A	50 (40)
	B	34 (27)
	C	21 (17)
	D	12 (9)
	E	9 (7)
Education*	Low	42 (35)
	Medium	29 (25)
	High	48 (40)
LUTS (IPSS score)	Mild (0-7)	12 (10)
	Moderate (8-19)	67 (55)
	Severe (20-35)	43 (35)
Preferred role in decision-making	Active	55 (44)
	Collaborative	63 (50)
	Passive	8 (6)

Percentages do not include missing values.
*Education: low (no primary school, lower general secondary education or lower vocational training), medium (higher general secondary education, vocational training), high (high vocational training and university)

Table 2: Treatment preferences before and after DA

Decision A: choice between watchful waiting/lifestyle advices vs. medication			
	Initial treatment preferences		
Final treatment preferences	Watchful waiting/ lifestyle advices N=15 N ,(%)	Medication N =11 N ,(%)	No initial preference N =17 N ,(%)
Watchful waiting/lifestyle advices	12 (80)	-	9 (49)
Medication	-	9 (82)	-
Not indicated/ undecided	3 (20)	2 (18)	8 (47)
Decision B: choice (continuing) medication vs. surgery			
	Initial treatment preferences		
Final treatment preferences	(continuing) Medication N =20 N ,(%)	Surgery N =13 N ,(%)	No initial preference N =50 N ,(%)
(continuing) Medication	17 (85)	-	19 (38)
Surgery	1 (5)	9 (69)	6 (12)
Not indicated/ undecided	2 (10)	4 (31)	25 (50)

Table 3: Patients' satisfaction with DA (N=126)

	(mostly) Disagree N, (%)	Neutral N, (%)	(mostly) Agree N, (%)
Explanation about the DA			103 (72)
I received enough explanation about the DA	8 (6)	8 (6)	
Accessibility of DA			102 (82)
The DA was easy to access	3 (2)	14 (11)	
Attitude towards future use			101 (80)
I would recommend the DA to other patients with LUTS/BPH	5 (4)	13 (10)	
Information in DA			97 (77)
Usefulness of information to you	3 (2)	19 (15)	87 (69)
Usefulness to your partner/family	3 (3)	29 (23)	92 (73)
Detail of information in DA	6 (5)	21 (17)	105 (83)
Understanding of DA	3 (2)	11 (9)	97 (77)
Written information	5 (4)	17 (14)	91 (72)
Verbal information	4 (3)	24 (19)	88 (80)
Timing of DA	3 (2)	15 (12)	
Total mean score (range 1-5)		3.87 (SD 0.48)	
Usefulness in preparing for decision	**Not at all**	**A little - some what**	**Quite a bit - a great deal**
The DA helped me to:	N, (%)	N, (%)	N, (%)
recognize that a decision needs to be made	-	13 (10)	106 (84)
prepare you to make a better decision	-	17 (13)	102 (81)
think about pros and cons of each option	-	14 (11)	105 (83)
think about which pros and cons are most important	-	13 (10)	106 (84)
know that the decision depends on what matters most to me	-	10 (8)	109 (87)
organize my own thoughts about the decision	-	15 (12)	104 (82)
think about how involved I want to be in this decision	-	11 (9)	108 (86)
identify questions I want to ask my doctor	-	14 (11)	105 (83)
prepare me to talk to my doctor about what matters most to me	-	12 (10)	107 (85)
prepare me for a follow-up visit with my doctor	-	14 (12)	104 (82)
Total mean score (range 1-5)		3.66 (SD 0.79)	
Balanced information	**Yes** N, (%)	**No, more information on medication** N, (%)	**No, more information on surgery** N, (%)
The information in the DA was neutrally presented	112 (89)	5 (4)	2 (2)

Missing N =7, percentages do not include missing values

Table 4: Healthcare providers' characteristics (N =26)

	N, (%)
Profession	
Urologist	13 (50)
Resident	11 (42)
Nurse	2 (8)
Hospital	
A	9 (35)
B	4 (15)
C	4 (15)
D	4 (15)
E	5 (20)
Are you familiar with the content of the DA?	
Not familiar	-
I know the DA, but I have read not read it (yet)	-
I know the DA and I briefly read it	9 (35)
I know the DA and I reviewed it completely	17 (65)
To how many patients did you offer the DA?	
No patients	-
1-5 patients	4 (15)
6-10 patients	11 (42)
>10 patients	11 (43)

Discussion

The use of this LUTS/BPH DA in clinical practice demonstrates that it supports the majority of patients in forming and indicating a treatment preference after using the DA. Moreover, when patients did not have an initial preference, they were able to indicate a preferred treatment after DA use. Furthermore, it supports patients in confirming their initial preference in 80% of the cases. Most VCEs used in this DA discriminated well between treatment options and matched with patient's final treatment preference. In the majority of the patients their preferred treatment matched their received treatment. Overall, patients and their healthcare providers were satisfied with the use of the DA in clinical practice with 80% of the patients recommending the DA to other patients with LUTS and an overall value of 7.4 given by healthcare providers.

Our results are in line with previous studies, showing that DAs are able to support patients in forming and indicating preferences about the treatment decision of LUTS/BPH.(21, 22, 24) Also, patients who indicated one specific preference before DA use, were in most cases (80%) confirmed in their initial treatment preference.(24,28) Confirmation of the initially preferred treatment option is relevant, because patients gained more knowledge about possible risks, side effects and alternative treatment options. Perception of feeling more informed and clearer about personal values could be increased, which may result in lower decisional conflict.(17,29) However, it might be possible that these patients read and interpreted the DA content in a selective way that confirmed their preexisting preference, resulting in confirmation bias.

In agreement with our results, Piercy et al. demonstrated that a DA was not able to alter treatment preferences in most patients who had an initial preference for the treatment of LUTS/BPH.(24) However, few studies observed shifts in treatment preferences after DA use. One study showed that 38.8% of patients changed their preferences at least once while watching an educational decision aid videotape about LUTS/BPH. These changes were equally balanced between watchful waiting and medication, with changes to surgery occurring only about 1/3 as frequently.

Several studies implicate a shift towards more conservative treatments than surgery after using a DA and that the use of DAs lowered elective surgical rates.(17,19,21,28,36) Similar to these studies, our results show that patients were more inclined towards the more conservative treatment options.(21,28)

After DA use one third of the patients remained or became undecided. One could argue that these patients gained more knowledge about the different treatment options and risks

which could have resulted in high decisional conflict scores indicating that they became more aware of the difficulty of the decision after DA use. However, it is not clear if these patients were truly undecided or just did not indicate a final preference (missing data).

Compared with previously developed DAs for LUTS/BPH, VCEs were used to clarify patients' preferences.(30) Analysis of VCEs was done to indicate their discriminative power between treatment options. Most VCEs in the DA were discriminative between final treatment preferences and congruent with final treatment preferences. Since two VCEs (VCE 3 and VCE 6) did not discriminate between the treatment options, replacement of these VCEs could be considered.

In most patients, who indicated a preferred treatment option after DA use, their final preference matched their received treatment. Previous studies showed concordance rates between 67% and 93% in post-DA preference and received treatment.(37-41) In the present study, in 21% of the patents their final treatment preference did not match with received treatment. Of this group, discrepancies between responses on VCEs, final treatment preference, and treatment received were observed, meaning that 29% had responses on VCEs which did match their treatment received but did not match their final treatment preference. Despite the fact that most of the VCEs discriminated well between treatment options, one can argue that the attributes (characteristics of treatment) of available treatments relevant to the individual patient were not included in the VCEs. Also, it could be possible that these patients may not have fully understood the use of the VCEs which resulted in discordance between their responses on VCEs and their final treatment preference. In 41% of the patients of whom their final preference did not match with their treatment received, their responses on VCEs neither matched with their treatment received nor with their final treatment preference. A possible explanation could be that their preferences were not discussed during consultation or that results of performed diagnostics changed their final treatment decision. Also, additional information provided by clinicians about side-effects and complications of treatment options may have influenced patients' final treatment decision. Clinicians could affect the decision on unwarranted grounds as well, such as their personal preference and experience with different treatment options and bias in risk perception. Overall, patients with a mismatch between final treatment preference and received treatment reported that they first needed more information and wanted to know their clinicians' preference before making a final treatment decision.

The participating hospitals were allowed to integrate the DA with their own standard information provision routines, with the aim to facilitate structural implementation of DA usage in routine clinical care.. This may have resulted in the overall positive attitude of

healthcare providers towards the usability of the DA in the decision-making process. They reported that procedural steps were clear and believed that DA use fitted in their daily practice. Thus, with this study (procedure) we demonstrated that some barriers for DA usage (e.g. lack of confidence in the DA, concerns of fitting in the workflow) were no longer an issue. Still, opinions are divided on the applicability of this DA to all LUTS/BPH patients. Possibly, because of patient's personality or health literacy levels.

Some limitations should be addressed. First, 56 of the 210 invited DA users did not sent informed consent and therefore we were not able to obtain DA data and questionnaires from all DA users. Second, when interpreting results, it has to be taken into account that the moment of DA use could be different between patients due to differences in standard information provision routines between participating hospitals. It may be possible that patients who received the DA before visiting the urologist were less satisfied with the usability of the DA due to lack of explanation. Furthermore, selection bias may have occurred since it is possible that healthcare professionals were selective in providing the DA to e.g. younger patients or patients with higher literacy levels or higher levels of education. However, patient characteristics (age and level of education) were not significantly related with satisfaction with DA or with not indicating a treatment preference after DA use.

Conclusion

Our findings suggest that this DA does not only help patients make well-informed decisions, which reflect their personal preferences, but also supports them in forming a treatment preference even if they did not have an initial preference. Both patients and their healthcare providers are positive about its usefulness in clinical practice which may improve clinical implementation.

Acknowledgments

We would like to thank ZorgKeuzeLab and the Dutch Association of Urology for their contribution to the development of this decision aid. Furthermore, we would like to thank Y. de Vuijst and PROFILES for their contribution to the data collection and M. van den Brink for her contribution to the data analysis.

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Supplementary Table 1: Healthcare providers' satisfaction with the DA (N =26)

	Never/ Sometimes N, (%)	Regularly N, (%)	(almost) Every time N, (%)
Procedural factors			
When I offer the DA, I perform the following activities:			
Indicating all treatment options, each with their pros and cons	-	-	25 (96)
Indicate for which treatments the patient is eligible	-	-	25 (96)
Stimulate patient to weigh pros and cons	-	1 (4)	24 (92)
Login in DA together with my patient	25 (96)	-	1 (4)
Ask for patients' preferences after using the DA	2 (8)	3 (12)	20 (77)
	(Mostly) disagree N, (%)	**Neutral** N, (%)	**(Mostly) agree** N, (%)
Instrument related factors			
The DA is based on factual, correct knowledge			
The information in the DA is complete	-	-	26 (100)
The DA offers all information needed to work with	1 (4)	2 (8)	23 (88)
It is clear to me which activities should be executed in what order	1 (4)	-	25 (96)
The DA is too complicated for clinicians to work with	2 (8)	5 (19)	19 (73)
The DA fits with my workflow	21 (81)	2 (8)	3 (11)
The DA fits in current guidelines and procedures	1 (4)	8 (31)	17 (65)
The DA is suitable for every patient with LUTS/BPH with a choice	1 (4)	3 (11)	22 (85)
between 2 treatment options	8 (31)	10 (38)	8 (31)
Advantages and disadvantages of DA use in daily routine			
When patients use the DA, I expect the following effects:			
- *Using the DA saves me time*	7 (27)	18 (69)	1 (4)
- *Using the DA is stressful to patients*	17 (65)	7 (27)	2 (8)
- *It is more easy to talk about treatment options with my patient*	2 (8)	7 (27)	17 (65)
- *Patients are more satisfied with information provision*	1 (4)	11 (42)	14 (54)
- *Patients are more knowledgeable about LUTS/BPH*	2 (8)	6 (23)	18 (69)
- *Patients are more involved with the treatment decision*	2 (8)	8 (31)	16 (61)
Patient outcomes			
When patients use the DA, I expect the following effects:			
- *Patients are able to make a good comparison between treatment alternatives*	-	1 (4)	25 (96)
- *Patients have insight in pros and cons of the treatment alternatives*	-	3 (12)	23 (88)
- *Patient's treatment preference is clear*	-	10 (39)	16 (61)
- *Patient's doubt about treatment choice will be reduced*	1 (4)	5 (19)	20 (77)
Attitude towards future use			
Patients will be satisfied if I offer the DA	1 (4)	4 (15)	21 (81)
Patients will use the DA	2 (8)	8 (31)	16 (61)
I want to use the DA in the future	2 (8)	6 (23)	18 (69)
I would recommend the use of this DA to colleagues	1 (4)	5 (19)	20 (77)
Overall satisfaction with DA (1= not at all, 10= very much) Mean (SD)		7.4 (1.0)	

Percentages do not include missing values

Chapter 8

General Discussion

General Discussion

This chapter summarizes the key findings and reviews the strengths and weaknesses of the studies performed. Finally, implications for clinical practice and future research are proposed.

Summary of key findings

On average, four years after a prostate cancer (PC) diagnosis, 34% of the men who participated in a cross-sectional study indicated that they were dissatisfied with the information received (**Chapter 2**). The patients who indicated dissatisfaction scored lower on quality of life (QoL) subscales and indicated worse illness perception compared to patients who indicated that they were satisfied with the information received.

In **Chapter 3**, we examined responses to values clarification exercises (VCEs) in relation to a decision aid (DA). The VCEs revealed the PC treatment benefits/harms that patients consider when they are choosing their preferred treatment. Of the men who chose active surveillance (AS) after DA use, 97% preferred to postpone unnecessary treatment. For radical prostatectomy (RP), 91% of the patients valued the possibility of tumour removal. For brachytherapy (BT), 88% valued incontinence worse than bowel complaints. Of the patients who could not indicate a treatment preference before DA use, about 50% were able to decide on a treatment preference after DA use. Furthermore, most patients chose the treatment in accordance with their treatment preference after DA use and to a lesser extent in accordance with urologists' preference.

A cluster randomized controlled trial was performed among 18 hospitals in the Netherlands to examine differences between patients receiving a DA after PC diagnosis compared to patients receiving care as usual. **Chapter 4** shows that patients who use the DA after PC diagnosis more often choose AS than patients who receive usual care during the decision-making process. After 12 months of follow up, no difference was found in information satisfaction and decisional regret between the groups (**Chapter 5**). Also, patients with anxiety or depressive symptoms were more likely to report regret and information dissatisfaction.

Lower urinary tract symptoms due to bladder outlet obstruction (BOO) as a result of benign prostatic hyperplasia (LUTS/BPH) indicate a benign prostatic disorder that is a common problem in older men. Despite the high prevalence rate of LUTS/BPH and the need for appropriate decision making because expectations about the disease and treatments are often inaccurate, far less attention is paid to the development and

evaluation of DAs for this condition than for other (oncological) conditions (1-3). Therefore, we developed a LUTS/BPH DA containing VCEs and accurately described a 4-stage development method (**Chapter 6**). **Chapter 7** reports treatment preferences before and after DA use and DA feasibility. Half of the patients who were initially undecided were able to form a treatment preference after DA use. We found that most patients confirmed their initial preference after DA use, and, overall, patients and healthcare providers were positive about DA content and usefulness in treatment decision making for LUTS/BPH.

Methodological considerations

Recall bias

Prior to reflecting on the key findings, we should consider the methods used in this thesis. In **Chapter 2**, we described a cross-sectional study conducted among 999 patients between 2006 and 2009. The study's major strength is the large population-based approach and the well-organized data collection using the PROFILES registry (4). PROFILES is a registry for the study of the physical and psychosocial impact of cancer and its treatment on a dynamic, growing population-based cohort of both short- and long-term cancer survivors (4). Another main strength of this study is the use of internationally validated questionnaires for determining QoL and illness perception, making it possible to compare results with other studies (5-8). The main limitation of the cross-sectional study design is possible recall bias, as patients had, on average, been diagnosed four years previously. As previously reported, breast cancer survivors underestimated their baseline QoL after more than six years in almost all QoL dimensions (9). A higher negative effect and lower current QoL may contribute to this recall bias (9). It is unknown whether this applies for PC survivors, but they also may experience a discrepancy between actual experienced QoL at diagnosis and remembered QoL. For future cross-sectional research it is therefore important to determine current (and if available historical) QoL and effect, as this may influence patient-reported outcomes.

There may be a discrepancy between actual information satisfaction at time of diagnosis and remembered information satisfaction. For PC survivors, this discrepancy concerning information satisfaction is not described thoroughly. However, high overall satisfaction with care seems to be associated with receiving more information, better functional outcomes, and high-quality information among PC survivors (10). As done in our study, it is therefore recommended to adjust for functional outcomes when information satisfaction is being determined some years after diagnosis.

Design considerations

A cluster randomized controlled trial was conducted among patients in 18 hospitals in the Netherlands to investigate the effect of patients using a DA after PC diagnosis compared to patients receiving care as usual after PC diagnosis (**Chapters 4 and 5**). A statistician not involved in the study randomized the hospitals to either the DA group (intervention group) or the usual care group (control group). Hence, after PC diagnosis, healthcare providers did not need to randomize patients and thus did not need to switch from DA counselling and usual counselling. With cluster randomization, we aimed to prevent contamination of shared decision making (SDM) components in the control group; this is a major strength of this study (11). Randomization at patient level is difficult in clinical practice because the clinician then should apply 'SDM with DA use' for intervention patients and 'standard of care' for controls. In such situations, contamination with SDM in the control group is a serious risk. Therefore, a cluster-controlled trial is preferred when comparison between decision-making styles is the goal. Another strength of this study design is the natural fit of the DA in clinical practice because, in this way, clinicians do not need to change their way of decision making per patient. Another advantage is that patients are not aware of randomization in a cluster randomized controlled trial (11). However, the study design may be a cause of imbalanced patient enrolment. In the current study, fewer control than intervention patients were included, causing a lower level of power for subgroup analyses. Possibly, healthcare providers in the control group were not as motivated as intervention group clinicians to include patients as they felt that they had nothing to offer (only intervention group clinicians could offer a DA). Perhaps an alternative study design, e.g. a stepped-wedge design, is a solution for this imbalance. It is important that clinicians in the control group are motivated to include patients. If patients have the possibility to cross over and participate in the intervention group after a certain period, this may enhance the number of controls included (12).

Response rate

In **Chapter 4**, patient inclusion numbers varied from 1 to 64 patients per hospital, resulting in an imbalanced inclusion between hospitals. This implies that DA implementation, as known from the literature, needs to overcome barriers (13, 14). In our opinion, we need doctors who believe in SDM to convince colleagues to use SDM support tools such as DAs. A recommendation in current guidelines that advocates DA use may help to overcome implementation barriers. In the current chapter, implementation barriers and strategies are discussed in more detail.

In **Chapter 6**, we introduced a 4-stage development method for a LUTS/BPH DA. Patients and urologists were included to identify patients' needs and determine the content of the DA. By involving patients and urologists, we aimed to facilitate clinical implementation, which is known to be a significant barrier to DA use (14). For agreement on medical content, we used the Delphi consensus method, a well-accepted questionnaire procedure, which is a group facilitation technique designed to transform expert opinions into group consensus (15, 16). Although this is a strong method for achieving consensus, the experts' response rate was only 48%. In comparable focus group studies, similar response rates (46%) and comparable numbers of experts are described, indicating low but sufficient numbers for expert opinion retrieval (17, 18).

Decision aid data analyses

Chapter 3 shows interim data obtained from the cluster randomized trial. We zoomed in on DA users only, extracting DA data. The main advantage of this study was that we were able to analyse patient treatment preferences pre and post DA use in 175 patients. Additionally, we could analyse the trade-offs regarding the VCEs. The main limitation of this chapter is the amount of missing data regarding patient characteristics and final treatment decisions consequent to informed consent refusal (N=47).

Chapter 7 describes how LUTS/BPH data were extracted from the DA to gain insight into shifts in treatment preferences before and after DA use. As done in Chapter 3, we also determined trade-offs analysing VCE responses. This is a reliable method because patients are not biased using the DA as they were not aware of these analyses.

Patient population

In the current literature, no clear conclusions can be drawn regarding the effect of a DA on treatment choice because not all studies included AS or even combined watchful waiting and AS as deferred treatment options (19-21). Other studies included high risk patients, thereby leading to a heterogeneous/different patient population, making comparison between studies difficult (22, 23). In our study, we examined all current treatment options – AS, RP, EBRT, and BT – for low and intermediate risk PC. Hence, our study consisted of a homogeneous group, analysed all current treatment options, and therefore contributes to the current literature. The majority of patients diagnosed with PC are low or intermediate risk prostate cancer patients (24). Therefore, our results may be suitable to extrapolate to a large patient group.

Future perspectives

The objectives of this thesis were:

1. to study the level of information satisfaction after prostate cancer diagnosis
2. to describe how the use of a decision aid affects the shared decision-making process with regard to treatment decision making, values clarification, and (information) satisfaction among patients diagnosed with both low and intermediate risk PC and LUTS/BPH.

In the following sections, we reflect on the key findings, with special emphasis on future perspectives and clinical implications.

Considerations about information provision among patients diagnosed with prostate cancer

We found that, four years after a PC diagnosis, a third of PC patients indicated that they were dissatisfied with the information received. This study was conducted between 2006 and 2009, and it is very possible that the level of information provision has improved in more recent years. Nowadays, SDM is a frequently discussed topic, and special (oncology) nurses are more often trained to support clinicians and patients with their medical process. Access to these nurses seemed to be associated with higher overall satisfaction with care among localized PC patients, and 85% of the patients recommended a particular nurse (10, 25). As overall satisfaction with care is associated with information provision, it is conceivable that information satisfaction has increased over the past years (10). We hypothesized that the use of a DA could improve satisfaction with information provision. However, in our study (**Chapter 4**), we found no differences in level of satisfaction with information provision between patients using a DA and patients receiving care as usual 12 months after diagnosis. Therefore, we can conclude that our PC DA did not demonstrate superiority on information provision compared to no DA use (mean information satisfaction 76.4 vs. 78.2, respectively). As mentioned above, oncology nurses inform patients about PC after diagnosis, and sometimes hospital information meetings are organized for patients. In some hospitals, a radiation oncologist provides information after the urologist's visit. Patients are more likely to report 'being informed' after a visit with both a urologist and a radiation oncologist (25). Ideally, all patients should be offered a visit with a radiation oncologist.

Hence, information provision in usual care is perhaps already very good; this makes it hard to achieve DA superiority on information satisfaction (26). To make a solid

comparison with our results presented in **Chapter 3**, we should therefore assess the level of information satisfaction among the patients enrolled in the cluster randomized controlled trial four years after inclusion. The question is, is the proportion of patients who indicate that they are dissatisfied with information provision less than a third, considering improved overall information provision in the Netherlands? QoL and treatment side effects should be measured as well, as these characteristics can bias the patient-reported outcomes on satisfaction with information provision (**Chapter 2**) (9).

Lastly, Cuypers et al. reported that 16% of the DA users participating in our study preferred a printed DA version over the web-based version (27). A preference for the printed version was negatively associated with satisfaction and conflict scores (27). This implies that this web-based DA is not suitable for every patient and patients should not be burdened with a web-based DA when this may increase dissatisfaction or decisional conflict.

Hence, some patients may benefit from a printed version of the DA. Therefore, not only should future research focus on the way information is provided to determine factors that can influence satisfaction with information provision, but also information needs should be determined prior to consultation to provide tailored information provision (e.g. paper-based information, web-based interactive DA, no DA aid) (28). An information needs tool/questionnaire may improve satisfaction with information provision. Depending on patient characteristics (e.g. education, health numeracy/literacy, preferred role in decision making, information needs, depressive symptoms), information provision could be tailored to improve decision making and lower decisional distress (26, 29-31).

Considerations about prostate cancer decision aid use

DA use can support SDM positively, even without a significant impact on satisfaction with information. A large Cochrane review recently showed that the benefits of DA use can be found in other attributes such as values-congruent choices, values clarification, and a more active role in decision making (26). Therefore, values clarification exercises and treatment choices were analysed as well, since there is growing evidence that decision aids may improve value–congruent choices (26). It is therefore recommended that clinicians not only inform patients, but also support patients to elicit preferences and make choices that match their preferences (32). In our opinion, the focus for future research should not only be on the level of satisfaction with information provision.

The use of the PC DA enabled 50% of the patients who were initially undecided to form a treatment preference (**Chapter 3**). Moreover, agreement between treatment preference

after DA use and final treatment was high. In line with the current literature, this showed that the DA helps patients to form a treatment decision (26, 32). This agreement seemed to be higher than the level of agreement with the urologist's preference, indicating an active shift in treatment decision making regardless of the urologist's opinion. This may be a positive finding, as healthcare providers may overestimate their level of SDM and misinterpret patients' preferences (22, 33-36). These findings are in line with current literature assuming that DA use in cancer-related issues may reduce clinician-controlled decision making (37). Consequently, the use of DAs may reduce unwanted practice variance caused by urologists' preferences.

VCEs are used in decision support tools to elicit preferences, but the value of VCE use in relation to knowledge improvement is not clear (38). However, the literature shows that the use of VCEs does encourage patients to consider all eligible treatment options and that it facilitates the comparison of options (39). In our study also, we found that the DA clarified patients' preferences, enabling patients to make trade-offs between treatment options using VCEs. Most patients indicated the VCEs in accordance with their final treatment decisions (AS: 97% preferred to postpone unnecessary treatment, RP: 91% valued tumour removal, BT 88% valued incontinence worse than bowel problems) (**Chapter 3**). These results imply that the VCEs used in the DA are congruent with particular treatment options. When participating in the VCEs, patients were unconsciously forced to think about risk and harm profiles, and this supports value-based treatment decision making (26, 37). At the end of the DA, a summary of all VCEs and treatment preferences can be printed and given to the relevant urologist. In this way, urologists can view patients' preferences at a glance. Consequently, patients' preferences are clear for both patient and urologist. In short, the use of VCEs in the DA enables patients to clarify their values and to consider treatment options, and it clarifies patients' preferences for their urologist. In this era of SDM and DA development, it is important that explicit VCEs are included in order to elicit patient preferences and enable patients to make value-based treatment choices (39).

In **Chapter 4**, we showed that PC patients who used the DA chose AS significantly more often than patients receiving usual care. This may imply that our PC DA oriented treatment decision making towards the most conservative treatment option, if AS was eligible. This is in line with earlier published research showing more conservative treatment options when a DA is used compared to no DA use; this is known for malignant and non-malignant conditions (23, 32, 40). With regard to AS, it is known that patients on AS need more information and need to participate more in decision making than they currently do (10). The finding that patients who used the DA chose AS more often than

control group patients may imply that the DA provided sufficient information for them to be confident enough to pursue AS.

However, if AS was not an eligible treatment option, we found that more than half of the patients using the DA chose RP over radiation therapy. This contrasts with the hypothesis that DA use affects treatment decision making in favour of more conservative treatment options. It is possible that the DA helped patients to choose between extremes, and therefore this result was found. Counselling by both a urologist and a radiation oncologist may optimize information provision regarding all other possible treatment options, thereby potentially balancing these treatment choices. To prevent bias towards one of the treatment options, we involved radiation oncologists in the DA development; however, we cannot rule this bias out (41). Therefore, it is recommended to involve all relevant parties in DA development and clinical SDM.

Another remarkable finding of our study is that some of the patients who were eligible for AS chose active treatment over AS. So why did patients choose active treatment with risks and side effects while AS was an eligible option? This tendency towards active treatment has been described before, as few people can imagine standing by and doing nothing after a cancer diagnosis, regardless of the risks (42). The main reason for not choosing AS is the fear of disease progression (43). This is in line with the VCE results from the PC DA: most patients choosing AS were *confident enough that they would be treated on time, if necessary* (N=33/38). Patients who pursued RP or BT (while eligible for AS) *did not want to postpone treatment because they did not want to be too late* (N=7/10 and N=7/8, respectively) (**Chapter 3**). Patients who are eligible for AS, but choose active treatment, might be more neurotic/anxious, as these characteristics are associated with PC-specific anxiety (44). Unfortunately, our patients' subgroups were too small to analyse these issues.

Future researchers are recommended to take into account patient characteristics regarding anxiety/neuroticism with their treatment preferences when looking at shifts in PC treatment following the use of a DA. Afterwards, information knowledge should be assessed by validated questionnaires to confirm whether patients did understand the received information well. This is important, because patients may overestimate the risk of requiring active treatment after AS and patients may not understand the comparable mortality rates following AS, RP,EBRT, and BT (31).

Considerations about LUTS/BPH decision aid use

Similar to PC, LUTS/BPH concerns the ageing male (45). However, in contrast to PC, LUTS/BPH concerns a benign prostatic disorder, which also can negatively affect QoL (46-48). In collaboration with patients and healthcare providers, we described a structured 4-stage development method for a LUTS/BPH DA to support the treatment decision-making process. Patients were involved to investigate needs and expectations about the DA. After DA use in clinical practice (**Chapter 7**), patients would recommend the DA to other patients. Furthermore, patients indicated that the DA helped them to think about the pros and cons and to organize their thoughts about the decision. These are important findings, as these items are essential for making trade-offs in medical decision making.

Known problems with existing DAs for LUTS/BPH are that they were developed years ago, are not up-to-date, are not accepted by healthcare providers, and are therefore not used (1, 13, 49, 50). Thus, DAs are often developed and evaluated in studies, but not implemented in daily clinical practice. It is important to prevent the proliferation of DAs that are outdated and not well implemented in clinical practice.

By involving healthcare professionals, we aimed to overcome known DA implementation barriers such as ‘a lack of confidence in the DA content’ and ‘concern about disruption in workflow’ (13). Healthcare providers in our study valued the LUTS/BPH DA overall very well and indicated that the LUTS/BPH DA fits their workflow (65% almost every time), and 85% indicated that it fits current guidelines (**Chapter 7**). These are positive results regarding DA implementation in clinical practice. Naturally, the DA should fit clinical practice in order to achieve wide implementation.

Moreover, the DA is up-to-date thanks to the web-based design, which makes adjustments easy to incorporate after guideline changes and/or the introduction of new treatment strategies. Therefore, web-based DAs are less prone to becoming outdated. By involving a working group from the Dutch association of urology (NVU), we gained professional support and achieved implementation in 18 hospitals in the Netherlands (15 hospitals currently use the PC DA, 3 hospitals still use the LUTS/BPH DA).

To achieve long-term DA use/implementation, it is highly important that adjustments are made continuously to ensure the most accurate information in line with current guidelines. At this time, both DAs are reviewed by the NVU and updated in accordance with recent guidelines and clinical practice. For instance, the PC DA has been updated with information about hypofractionation (EBRT).

In our opinion, the development method as described in **Chapter 7** can be adapted for other oncological and non-oncological medical treatment decisions as it provides a structured method both for content development and for usability testing. DA development should be undertaken in collaboration with healthcare providers, professional associations, and patients to fit clinical practice and facilitate implementation. Moreover, DAs should include VCEs as they elicit patient preferences in order to make medical trade-offs (**Chapter 7**) (39). It is recommended to involve an expert in the SDM field to advise clinicians with regard to SDM principles and VCE development, as VCEs should be discriminative towards one of the eligible treatment options.

Prostate cancer versus LUTS/BPH: similarities and differences in presented studies

Two different prostatic disorders are studied in this thesis, one malignant and one benign. It is remarkable that, in both DA studies (**Chapter 3** and **Chapter 7**), 50% of the undecided patients could form a treatment preference after DA use. Consequently, after forming a final treatment decision, the majority of the patients received their preferred treatment. These are comparable outcomes indicating similarity in DA use among patients with a malignant and a benign disease.

Another finding is that PC patients formed an initial treatment preference (before DA use) more often than patients diagnosed with LUTS/BPH (74% versus 47%, respectively). However, similar proportions formed a final treatment preference after DA use (67% vs 65%, respectively). These results may imply that patients diagnosed with LUTS/BPH are not sure what to choose after counselling and therefore do not form an initial treatment preference. It seems that they are less pre-informed compared to patients diagnosed with PC. This might imply that, among patients with LUTS/BPH, the DA provided new information given that the proportion of patients who indicated a final preference was 65%, an increase of 18%.

On the other hand, the proportion of PC patients who indicated a final preference after DA use was 67%; this is a decline of 7%, indicating that they were possibly in doubt after DA use. One could argue that the DA therefore increased decisional conflict; this contrasts with the literature, because most studies showed less decisional conflict after DA use (26). Regarding our population, Cuypers et al. described no differences in decisional conflict between patients using the PC DA compared to patients receiving care as usual (29). Additional research is needed to understand this decline in the ability to indicate a preference. This could be done, for instance, in a qualitative research study (e.g. patient interviews). This information could clarify why patients who formed an initial

treatment preference were undecided after DA use (e.g. decisional conflict, inaccurate initial expectations, new information).

Unanswered questions

The best way to measure DA efficacy is still unknown as there is a large variety in DAs (e.g. web-based DAs, clinical programmes, videos, paper DAs) in review studies, and single outcome measures are not always discriminative for DA use satisfaction (21). Ideally, after treatment decision making, patients should experience the health outcomes that they prefer and avoid the outcomes that they dislike (26). Single-use outcome measures such as satisfaction with information provision, decisional conflict, self-reported outcomes, and knowledge are not always discriminative for DA effectiveness. In our opinion, the DA is effective if it can elicit patient preferences and makes clear that a decision has to be made; subsequently, these items can be discussed with the clinicians in order to make a value-congruent decision.

Furthermore, DAs are not helpful for all patients. It is still unknown how to select patients who can benefit from a DA. In our opinion, information needs should be assessed to provide information adjusted to patients' preferences. In this way, DAs can be provided to patients who can be supported by a DA and other decision support tools to patients who cannot be helped by a DA. Future research should focus on how to determine information needs and whether adjusted information provision supports SDM positively.

General conclusion

In this chapter, we reflected on key findings, and we have made suggestions for future research for patients with both PC and LUTS/BPH. Naturally, besides considerations and future research recommendations, some conclusions can be drawn in response to the key findings as presented in this thesis.

First, on average four years after PC diagnosis, a third of patients indicated that they were dissatisfied with the information received at the time of diagnosis.

Secondly, the results showed that the DAs for the treatment of low and intermediate risk PC and LUTS/BPH support undecided patients to indicate a treatment preference. Consequently, after DA use, the majority of the patients studied received their preferred treatment, and most VCEs used in the DAs were discriminative for the corresponding treatment options.

Thirdly, patients who used the PC DA chose AS more often than patients who did not use the DA, indicating that the PC DA may affect treatment decision making in favour of the most conservative treatment option. Furthermore, after 12 months of follow up, no difference was found in information satisfaction and decisional regret between groups

Epilogue

In this thesis, information satisfaction among prostate cancer survivors and the effect of decision aid use for the treatment of low and intermediate risk prostate cancer and LUTS/BPH are studied, and the results are thoroughly discussed in this chapter. As known however, new research questions originate from studies performed. These questions are the basis for further research.

In this thesis, we found that decision aids may support shared decision making in order to make preference-based treatment decisions. However, decision aids are not suitable for all patients. In our opinion, shared decision making should be stimulated in clinical practice and decision aids are helpful for selected patients. However, it is still unclear how to determine which patients may benefit from decision aids and which patients do not. In our opinion, future research should focus on how to support value-based decision making, with a special emphasis on information needs.

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Appendices

Nederlandse samenvatting

Het doel in dit proefschrift is om de waarde van het gebruik van keuzehulpen te onderzoeken bij de behandeling van patiënten met prostaatkanker en patiënten met plasklachten door een goedaardige vergroting van de prostaat. Gedeelde besluitvorming is het proces waarin de arts en de patiënt gezamenlijk bespreken welk medisch beleid het beste bij de patiënt past, waarbij alle opties, voor- en nadelen, patiëntvoorkeuren en omstandigheden worden meegenomen (definitie Federatie Medisch Specialisten). Er is onderzocht hoe keuzehulpen gedeelde besluitvorming kunnen ondersteunen ten aanzien van informatievoorziening, het verhelderen van persoonlijke voorkeuren, en het maken van behandelkeuzes.

In de inleiding (**Hoofdstuk 1)** worden er twee prostaataandoeningen geïntroduceerd waar mannen mee geconfronteerd kunnen worden: prostaatkanker en een goedaardige vergroting van de prostaat (met als gevolg plasklachten). Beide aandoeningen worden ongeveer vanaf de leeftijd van 50 jaar gediagnosticeerd.

Voor prostaatkanker zijn vaak verschillende behandelopties mogelijk met gelijkwaardige oncologische uitkomsten. Omdat elke behandeling zijn eigen voor- en nadelen (risicoprofiel) heeft is de beste behandeling afhankelijk van de persoonlijke voorkeuren van een patiënt.

Ook mannen met plasklachten door een goedaardige vergroting van de prostaat (LUTS/BPH genoemd in dit proefschrift) hebben meerdere behandelopties waar zij uit kunnen kiezen, ondanks het gegeven dat de uitkomsten bij deze behandelingen wel kunnen wisselen. Net als bij prostaatkanker geldt bij deze goedaardige prostaataandoening dat elke behandeling verschillende voor- en nadelen heeft en dat persoonlijke voorkeuren hierin een rol spelen.

Om mannen met prostaatkanker en LUTS/BPH zo goed mogelijk te helpen bij het maken van een behandelkeuze dienen een aantal stappen ondernomen te worden, namelijk: informeren, voorkeuren verhelderen en vervolgens een behandelvoorkeur vormen.

Op deze manier kan dan (vaak samen met de arts) een weloverwogen behandelkeuze gemaakt worden, aangepast aan de voorkeuren van de patiënt.

Een keuzehulp is een goed instrument om patiënten ondersteunen in de besluitvorming doordat door het gebruik van een keuzehulp de patiënt betrokken wordt in de besluitvorming, de kennis kan verbeteren en voorkeuren verhelderd kunnen worden.

Het is echter nog niet geheel duidelijk wat de waarde van een keuzehulp specifiek voor prostaatkanker patiënten en LUTS/BPH patiënten is. Het doel van dit proefschrift was om te onderzoeken:

1. Hoe tevreden patiënten met prostaatkanker zijn met de standaard informatie-voorziening die zij hebben ontvangen ten tijde van diagnose
2. Hoe keuzehulpen de gedeelde besluitvorming beïnvloeden bij patiënten met prostaatkanker en LUTS/BPH met betrekking tot de behandelkeuze, het verhelderen van persoonlijke voorkeuren en tevredenheid over de informatievoorziening.

DEEL 1: Prostaatkanker

De eerste studie, **Hoofdstuk 2**, beschrijft een onderzoek dat uitgevoerd is onder prostaatkanker patiënten die gemiddeld 4 jaar geleden de diagnose prostaatkanker hebben gekregen. Er is onderzocht hoe de tevredenheid met informatievoorziening was ten tijde van de diagnose. Tussen 2006 en 2009 zijn er vragenlijsten verstuurd naar prostaatkanker patiënten, 697 patiënten hebben deze vragenlijst ingevuld. Van deze patiënten gaf 34% aan ontevreden te zijn met de informatie die zij ten tijde van de diagnose hebben ontvangen. Deze studie toonde aan dat de patiënten die ontevreden waren met de informatievoorziening ook vaker een lagere kwaliteit van leven hadden en een lagere ziekteperceptie dan patiënten die aangaven wel tevreden te zijn met de informatievoorziening.

Er blijkt dus onvrede te zijn met de standaard informatievoorziening over prostaatkanker. Dat is niet wenselijk wanneer patiënten op basis van deze informatievoorziening een behandelkeuze moeten maken. Bij patiënten met een laag- en middelmatig risico prostaatkanker zijn er meerdere behandelopties mogelijk: afwachten (active surveillance, AS), opereren (radicale prostatectomie, RP) uitwendige bestraling (EBRT) en inwendige bestraling (brachytherapie, BT). Om patiënten te ondersteunen bij de besluitvorming voor een behandelplan na de diagnose prostaatkanker is er een keuzehulp ontwikkeld. Deze keuzehulp is gebaseerd op een bestaande Amerikaanse keuzehulp aangepast aan de Nederlandse cultuur, richtlijnen en praktijk. De keuzehulp is een website waar patiënten kunnen inloggen en vervolgens informatie kunnen lezen over de diagnose prostaatkanker en hun behandelopties (*web-based keuzehulp*). Ook worden stellingen gepresenteerd waarbij patiënten op een schuifbalk kunnen aangeven welk van de stellingen het meest bij hun passen (Values Clarification Excercises, VCEs genoemd). De stellingen hebben betrekking op de mogelijke behandelopties (bv: *Ik vind incontinentie voor urine erger dan darmklachten* (reden voor bestralen) *vs. Darmklachten vind ik erger dan incontinentie*

voor urine (reden voor opereren) . Hierdoor worden persoonlijke preferenties verhelderd en krijgen patiënten inzicht in wat voor hen belangrijk is.

In **Hoofdstuk 3** zijn resultaten gepresenteerd betreffende behandelvoorkeuren en preferenties (VCEs) bij het gebruik van een keuzehulp. In deze studie hebben 181 prostaatkanker patiënten de keuzehulp doorlopen. Vooraf aan het doorlopen van de keuzehulp had 74% van de patiënten al een behandelvoorkeur en 67% bleef ook bij deze keuze. De helft (50%) van de patiënten die aanvankelijk nog geen behandelvoorkeur hadden, kon wel een behandelvoorkeur aangeven na het doorlopen van de keuzehulp. Uit analyses van de stellingen bleek dat patiënten die kozen voor afwachten met name geen onnodige behandeling wilden ontvangen. Patiënten die kozen voor operatie hechtten met name belang aan het verwijderen van prostaatkankercellen, voor patiënten die kozen voor inwendige bestraling gold dat zij met name incontinentie erger vonden dan darmklachten. De meeste patiënten ontvingen ook daadwerkelijk de behandelkeuze van voorkeur na het doorlopen van de keuzehulp. De behandelvoorkeur van de uroloog bleek in mindere mate een relatie te hebben met de ontvangen behandeling.

In het volgende hoofdstuk, **Hoofdstuk 4**, zijn prostaatkanker keuzehulp gebruikers (273 patiënten) vergeleken met patiënten die de keuzehulp niet hadden ontvangen na de diagnose prostaatkanker (109 patiënten). In dit cluster gerandomiseerd gecontroleerd onderzoek is onderzocht of er een verschil is in behandelkeuze tussen keuzehulp gebruikers en niet-keuzehulp gebruikers (controlegroep). Er blijkt uit dit onderzoek dat keuzehulp gebruikers vaker een afwachtend beleid (active surveillance) kozen vergeleken met patiënten die de keuzehulp niet hadden gebruikt. Patiënten zonder keuzehulp kozen juist vaker voor inwendige bestraling in vergelijk met keuzehulp gebruikers. De resultaten uit dit onderzoek tonen aan dat het gebruik van een keuzehulp de behandeling bij prostaatkanker kan beïnvloeden. Het blijkt dat er vaker een afwachtend beleid wordt gekozen bij het gebruik van een keuzehulp vergeleken met een groep patiënten zonder keuzehulp.

Vervolgens wordt in **Hoofdstuk 5** geconcludeerd dat de mate van tevredenheid met informatievoorziening en spijt van behandelkeuze 12 maanden na diagnose prostaatkanker niet verschilt tussen patiënten met keuzehulp en zonder keuzehulp. De resultaten tonen tevens dat patiënten die meer angstig zijn en meer depressieve kenmerken hebben vaker spijt hebben en onvrede uiten over de informatievoorziening. Hieruit werd geconcludeerd dat door het gebruik van de keuzehulp de tevredenheid met informatievoorziening niet beter was dan bij de patiënten die de keuzehulp niet hadden gebruikt. Tevens dient er bij diagnose rekening gehouden moet worden met angstige en depressieve patiënten.

DEEL 2: Plasklachten bij een goedaardige vergroting van de prostaat (LUTS/BPH)

Net als bij prostaatkanker zijn voor de behandeling van LUTS/BPH zijn verschillende behandelopties mogelijk: leefstijlveranderingen, medicijnen en opereren. Elk van deze behandelopties hebben een eigen risicoprofiel en uitkomsten. Het is dus van belang dat patiënten goed geïnformeerd worden over deze voor- en nadelen en dat de wensen van de patiënt zelf ook worden uitgevraagd.

Om patiënten te ondersteunen in het proces van gedeelde besluitvorming is er een web-based keuzehulp ontwikkeld. In **Hoofdstuk 6** is de ontwikkeling van deze keuzehulp uitvoerig beschreven. De ontwikkeling van de keuzehulp bestaat uit 4 fasen waarbij patiënten en zorgverleners zijn betrokken. De keuzehulp is een website met een persoonlijke inlogcode waar informatie over LUTS/BPH wordt gegeven, de ernst van de plasklachten wordt geobjectiveerd, voorkeuren worden uitgevraagd en behandelinformatie wordt verstrekt. Voor de (medische) inhoud en structuur van de keuzehulp is een expert consensus studie uitgevoerd (Delphi methode). De keuzehulp bevat VCEs waardoor de persoonlijke voorkeuren/preferenties van patiënten verhelderd worden.

De gestructureerde keuzehulp ontwikkelmethode (**Hoofdstuk 6**) kan ook voor andere ziektebeelden gebruikt kunnen worden. Op deze manier komt er een keuzehulp tot stand met betrouwbare medische informatie welke door zorgverleners en patiënten wordt ondersteund.

De keuzehulp is uitgereikt aan 126 patiënten die de diagnose LUTS/BPH hadden gekregen en een keuze hadden tussen verschillende behandelopties. In **Hoofdstuk 7** is aangetoond dat 53% van de patiënten nog geen behandelvoorkeur hadden vooraf aan het doorlopen van de keuzehulp. Van deze patiënten was ongeveer de helft (51%) in staat na het doorlopen van de keuzehulp wel een behandelvoorkeur te vormen. In bijna 80% werd de behandelvoorkeur na het doorlopen van de keuzehulp ook de daadwerkelijk uitgevoerde behandeling.

Ook laat dit hoofdstuk zien dat 5 van de 7 VCEs (stellingen om persoonlijke voorkeuren te verhelderen) in de keuzehulp een goede correlatie tonen tussen de antwoorden op de VCEs en de daarbij behorende behandelingen (bv *Ik heb last van mijn plasklachten, maar kan hiermee leven* (reden voor medicatie) *vs. Ik heb zoveel last van mijn plasklachten dat ik mij wil laten opereren* (reden voor operatie)). Patiënten en zorgverleners bleken tevreden over de inhoud en gebruiksvriendelijkheid in het proces van besluitvorming.

In het laatste hoofdstuk, **Hoofdstuk 8**, wordt gereflecteerd op de verschillende onderzoeksresultaten beschreven in dit proefschrift. Er worden suggesties gedaan voor nieuwe onderzoeken en worden de huidige resultaten bediscussieerd.

Uit dit proefschrift blijkt dat:

1. gemiddeld 4 jaar na diagnose prostaatkanker, een derde van de patiënten onvrede uit over de (standaard) ontvangen informatie ten tijde van de diagnose.
2. de keuzehulpen voor prostaatkanker en LUTS/BPH patiënten in staat stellen een behandelkeuze te vormen wanneer zij dit vooraf aan de keuzehulp nog niet konden. Tevens blijkt dat de behandelvoorkeur na doorlopen van de keuzehulp vaak ook de daadwerkelijk ontvangen behandeling is. De antwoorden op de VCEs in de keuzehulpen blijken goed te correleren met de bijbehorende behandelkeuzes.
3. patiënten die na de diagnose prostaatkanker de keuzehulp doorlopen vaker voor AS kiezen dan patiënten die de keuzehulp niet hebben ontvangen. Na 12 maanden follow-up werd er geen verschil gevonden in tevredenheid met informatievoorziening en spijt van behandelkeuze tussen beide groepen.

In dit hoofdstuk wordt gesteld dat een keuzehulp de patiënt goed kan ondersteunen bij de besluitvorming om vervolgens een behandelkeuze te maken welke past bij de persoonlijke voorkeuren. Er zijn echter ook tekortkomingen die worden belicht. Het is nog niet geheel duidelijk hoe dit keuzehulp effect het best te meten is en de keuzehulp lijkt ook niet voor iedereen geschikt. Gedeelde besluitvorming moet gestimuleerd worden in de praktijk en keuzehulpen kunnen hierbij helpen. Om goed te kunnen onderzoeken welke patiënten baat kunnen hebben bij het gebruik van een keuzehulp wordt de aanbeveling gedaan om informatiebehoeften en persoonlijke kenmerken (depressie, angst, opleiding, vermogen om informatie te verwerken) bij patiënten te onderzoeken. Op deze manier zou informatievoorziening op maat geleverd kunnen worden (bv juist geen keuzehulp, een web-based keuzehulp, een keuzehulp op papier). Zo kan de patiënt optimaal ondersteund worden om de beste behandeling te kiezen, aangepast op de wensen van de patiënt.

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List of abbreviations

BPE	benign prostatic enlargement
BOO	bladder outlet obstruction
BPH	benign prostatic hyperplasia
LUTS	lower urinary tract symptoms
LUTS/BPH	lower urinary tract symptoms caused by bladder outlet obstruction due to benign prostatic hyperplasia
IPSS	international prostate symptom score
TURP	transurethral resection of the prostate
PC	prostate cancer
Pca	prostate cancer
DA	decision aid
PSA	prostate specific antigen
TNM	tumour node metastasis
EAU	European Association of Urology
AS	active surveillance
RP	radical prostatectomy
EBRT	external beam radiation therapy
BT	brachytherapy
QoL	quality of life
HRQoL	health related quality of life
SDM	shared decision making
VCE	values clarification exercise
ECR	Eindhoven cancer registry
CCCN	comprehensive cancer centre the Netherlands
PROFILES	patient reported outcomes following initial treatment and long term evaluation of survivorship
SCQ	self-administered co-morbidity questionnaire
EORTC	European organisation for research and treatment of cancer
EORTC QLQ-INFO25	EORTC quality of life questionnaire information provision
EORTC QLQ-C30	EORTC quality of life questionnaire Core (prostate cancer survivors)
EORTC QLQ-PR25	EORTC quality of life questionnaire prostate cancer survivors (side effects)
BIP-Q	brief illness perception questionnaire
RCT	randomized controlled trial
CRCT	cluster randomized controlled trial
PCPCC	prostate cancer patient centered care
NPCF	Dutch patients and consumers federation

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Dankwoord

Dit proefschrift heeft tot stand kunnen komen doordat heel veel collega's, patiënten, familie en vrienden mij hebben bijgestaan en gesteund gedurende dit project. Heel graag wil ik iedereen hiervoor bedanken, met een paar in het bijzonder.

Allereerst Paul, zonder jou was dit proefschrift er niet geweest. Toen ik als coassistent in Tilburg kwam ontfermde jij je over mij en bood je mij de mogelijkheid om ANIOS urologie te worden. Al snel werden er plannen gemaakt om samen met de Universiteit van Tilburg (UvT) een promotietraject op te starten. Jij hebt mij alle kansen geboden die een jonge arts nodig heeft, veel dank hiervoor. Ik bewonder jouw energie en enthousiasme voor het vak. Zoals jij zijn er niet veel! Uiteraard zal ik onze onderzoekuitstapjes missen, hoop dat we in de toekomst nog eens chateaubriand gaan eten bij die grote vogel. Dank voor alle leermomenten en levenslessen, ik heb heel veel van je geleerd.

Marieke, dank dat je ook mijn copromotor wilde zijn. Jij had altijd een luisterend oor voor problemen en maakte veel tijd vrij om mijn artikelen tot in detail te beoordelen. Wanneer ik er een beetje doorheen zat bij de afronding van mijn proefschrift kon jij lekker relativeren en bood je oplossingen, heel waardevol.

Maarten, wij zijn samen dit onderzoeksproject gestart. Jij als psycholoog vanuit de UvT en ik als arts, dit bleek al snel een gouden combinatie. Dank voor alle steun die jij mij hebt geboden tijdens ons onderzoek, met z'n tweeën was het veel leuker! Wat hebben we een mooie tijd gehad tijdens congres in Miami! Ik kijk met heel veel plezier terug op onze onderzoeksperiode en ben daarom vereerd dat jij mijn paranimf bent.

Beste prof. Bosch, beste Ruud, dank dat u mijn promotor wilde zijn. Altijd bereid mee te denken en naar Tilburg af te reizen voor overleg. Dank voor de kritische klinische blik.

Beste prof. van de Poll-Franse, beste Lonneke, dank dat jij tweede promotor wilde zijn. Jouw kritische blik, rake feedback en epidemiologische expertise waren een waardevolle aanvulling op de artikelen.

Prof. Horenblas, prof. Geenen, prof. De Wit, prof. Roobol en prof. Aaronson, dank voor het plaatsnemen in de beoordelingscommissie. Met gezonde spanning kijk ik uit naar 21 november.

Uiteraard wil ik ook graag alle urologen en (oncologie/research)verpleegkundigen bedanken van de deelnemende ziekenhuizen. Zonder jullie inspanningen was dit proefschrift er niet geweest. Dank voor jullie vertrouwen in de studies.

Willeke en Yvon, secretaressen urologie, wij waren jaren lang een hecht drietal. Alle actualiteiten werden uitgebreid besproken! Ik mis deze tijd met jullie hoor.

Margo Fabrie, secretaresse Hoogleraar UMCU, dank voor al jouw hulp bij onze MyPhD perikelen en praktische zaken rondom de afronding van mijn promotie.

Maatschap urologie, Herman, Rob, Bart, Yvette, Anton en Paul. Als echt Tilburgs product ga ik straks mijn opleiding afronden in Utrecht. Jullie hebben mij de mogelijkheid geboden om onderzoek te combineren met mijn opleiding, veel dank hiervoor. Dank voor de fijne periode in Tilburg waar gezelligheid, opleiding en openheid hoog in het vaandel stonden.

Isabel, jij hebt mij opgevolgd als promovendus bij Paul. Je hebt in korte tijd ontzettend veel voor elkaar gekregen, heel knap. Ik ben ontzettend blij dat jij met zoveel passie het onderzoek voortzet.

Regina en Klemens, samen met Paul en Maarten hebben we de eerste keuzehulpen ontwikkeld met jullie ZorgKeuzeLab. Inmiddels zijn er vele keuzehulpen voor diverse specialismen ontwikkeld en hebben jullie een prachtig bedrijf. Dank voor de fijne, gezellige en professionele samenwerking.

Marian Bakker, statisticus, dank voor jouw hulp bij de (multilevel)statistiek.

Collega A(N)IOS, Marlies, Aukje, Belle, Alex, Michelle, Robert, Simone, Linn en Nieck. Wat hebben we met elkaar gelachen in het Tilburgse, dank voor de fijne tijd. Ik kijk er naar uit om weer met sommigen van jullie te gaan samenwerken in het UMCU. *#dedokterdrinktgeenpennen*

Jasmijn, drie jaar geleden stond ik aan jouw zijde als paranimf. Nu sta jij aan mijn zijde, met een dikke buik! Wat hebben wij sinds de middelbare school al veel meegemaakt. Hoop dat wij nog vele mooie reisjes, etentjes en dwaze momenten mogen meemaken. Ik zou me geen betere paranimf kunnen wensen, dank dat jij er weer bent voor mij.

Tenslotte mijn familie, papa en mama, ik ben jullie ontzettend dankbaar voor de onvoorwaardelijke steun die jullie mij altijd bieden. Jullie staan altijd voor ons klaar en nooit is iets teveel. Ik hoop dat wij onze kinderen net zoveel liefde en steun kunnen geven als dat jullie ons altijd geven.

Lieve Martin, al 15 jaar ben jij mijn steun en toeverlaat. Jij laat mij lachen, stimuleert mij om mijn ambities waar te maken en trapt op de rem waar nodig. Wij genieten van het leven en van elkaar, ik hoop dat wij dit nog heel lang kunnen doen.

Isabella, kleine meid, wij genieten elke dag van jou! Jij bent het mooiste wat ons is overkomen en in januari word jij een grote zus. Met z'n vieren staat ons hopelijk een mooie toekomst te wachten.

A

Curriculum Vitae

Rosalia Eleonora Désideria (Romy) Lamers (1988, Dordrecht) attended high school at the Gymnasium Camphusianum, Gorinchem. In 2006 she graduated and subsequently started to study medicine at the Erasmus University Rotterdam. In 2012 she graduated Cum Laude from medical school and started her first job as a ship's doctor on Tall Ship the 'Wylde Swan', crossing the ocean from the Canaries to Dominica.

The next year, she started working at the urology department in the Elisabeth hospital, Tilburg and in parallel, started a research project. From January 2014 she worked part-time as a researcher on her PhD project 'Treatment decision making in prostatic disorders' (this thesis) and part time as a resident not in training. Her research focused on the effect of decision aids for the treatment of prostate cancer and LUTS/BPH and was conducted in close cooperation with Tilburg University.

In 2016, she started her urological residency training program at the department of general surgery and subsequently at the department of urology in the Elisabeth-Tweesteden hospital, Tilburg. She will continue her residency program at the urology department of the University Medical Center Utrecht in 2020.

Romy is happily married to Martin de Vlaam and proud mother of Isabella. Martin and Romy are expecting their second child in January 2020.

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