Health Related Quality of Life

Tailored Internet Support for Cancer Patients

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Master Thesis

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Foreword

Considering topics for my master thesis, I was offered the opportunity to use data from a randomised controlled trial of a web based tool for shared decision-making (WebChoice) performed by the research team at the Center for Shared Decision Making and Nursing Research. I was generously given the data set on quality of life (15D scores) and demographics. The study was designed and undertaken from 2006 to 2008. My involvement began in November 2008, and I received the data in January 2009.

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My supervisor was Ivar Sønbø Kristiansen, MD PhD MPH, at The Institute of Health Management and Health Economics, University of Oslo. My co-supervisor was Cornelia Ruland, RN PhD, director of the Center for Shared Decision Making and Nursing Research at Rikshospitalet University Hospital HF.

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Katrine Schia Fjære

Abstract

Background

Cancer places a considerable burden on patients' health-related quality of life (HRQOL). Information on own disease can both help patients to cope with symptoms and side-effects, and make them more competent participants in shared decision-making with clinicians. In this context the Center for Shared Decision Making and Nursing Research developed a tailored Internet support system called WebChoice. This thesis is a partial economic evaluation of the effects of WebChoice, where its impact on HRQOL is explored.

Methods

The research team randomised breast cancer and prostate cancer patients into two groups, a WebChoice group and a control group. The patients' HRQOL was measured three times during the intervention period of one year. HRQOL weights were measured with the multi attribute health status classification system, 15D. This thesis measures the health outcome and WebChoice effects by statistical methods. The health outcome was measured in quality adjusted life years (QALYs). Data were analysed with *t*-tests and multiple linear regressions.

Results

In total, 445 patients were recruited and randomised to WebChoice groups or control groups. This thesis presents data for 234 patients who filled in the 15D questionnaire at baseline, at 6 months and at 12 months. Among 130 breast cancer patients included in this study, the mean 15D score at baseline was 0.85 in the WebChoice group and 0.88 in the control group, while the respective means were 0.85 and 0.88 by the end of the trial. Among 104 prostate cancer patients included in this study, the mean 15D score at baseline was 0.87 in the WebChoice group and 0.87 in the control group, while the respective means were 0.84 and 0.84 by the end of the trial. Adjusted for baseline 15D, the mean QALYs gained for WebChoice compared to the control group, was -0.03 for the breast cancer group and -0.01 for the prostate cancer group. HRQOL score at baseline was the only variable which had a significant impact on this result.

Interpretation/conclusion

The results of this study indicate that WebChoice has no impact on HRQOL for breast cancer and prostate cancer patients. However, the conclusion must be made with the following reservations: The result does not necessarily apply to patients with a recent diagnosis, or with little education or with a low HRQOL.

Contents

1. Introduction

1.1 Shared decision-making

Physicians have been seen as paternalistic in their professional conduct, making decisions with great consequences without involving the patient's values (Wulff et al., 2001). A traditional paternalistic view is that the physicians are the only ones who know what is best for the patient. A consequence is that historically, patients have only to a limited extent been involved in the decision-making process. More recently, shared decision-making has been introduced. This decision type is a different way of thinking about how clinicians, and especially physicians, should communicate with patients and approach treatment options.

The following definition of shared decision making has been proposed by the Department of Biomedical Informatics at the Colombia University:

> [I]nvolvement of patients with their providers in making health care decisions that are informed by the best available evidence about treatment / screening / illness management options, potential benefits, and harms, and that consider patient preferences (*Patient preferences in Health Care Decision Making. Shared Decision Making*, 2009).

Shared decision-making is present when the patient together with the physicians and other clinicians make informed decisions about the patient's health care. The main arguments for introducing shared decision-making are autonomy and patient preferences. Patient autonomy in a treatment perspective can be viewed as a fundamental right to decide over one's own health. The extent of autonomy is an ethical question and beyond the scope of this thesis.

Patient autonomy and patient preferences are two sides of the same matter. In an ever growing arsenal of treatment options with radically different consequences, it is impossible for the physician to decide the "best" option (Hunink & Glasziou, 2001). The "impossibility" is not in terms of complex professional evaluation, but more in terms the patients' wide array of preferences. The physician can simply not decide what treatment (with its consequences) is best for the particular patient without having detailed information about the patient's preferences. Patient autonomy implies that patients are best suited to value process and outcome from diagnostics and treatments.

Although the patient's own views and values are crucial in the choice of diagnostics and treatment, the patient must still have the option to leave the decision to the clinician. For instance, clinical experience indicates that young and/or relatively healthy patients want to take great part in the decisions, while older and/or sicker patients often prefer to leave

decisions to the physician (Hunink & Glasziou, 2001). However, shared decision-making still implies that physicians should base their decisions on the patient's preferences.

A premise for shared decision-making is that the patient has received information relevant to the decision he or she is about to make. It is the clinicians' (especially the physicians' and nurses') task to ensure that the patient gets reliable and up-to-date information about the specific disease he or she suffers from and the different treatment options. Internet support, both tailored and general, have proven valuable for informing patients and thereby making them better qualified to take part in a shared decision-making process (Brennan et al., 2001, Fleischer et al., 2002 and Gustafson et al., 1999 & 2001).

Shared decision making can improve health-related quality of life (HRQOL), as HRQOL is sensitive to the patient's preferences. HRQOL will be discussed later. Even though there has been limited focus on the practice of shared decision making in Norway, the principles do apply. This master thesis will explore the consequences of one of the aspects in shared decision-making: Information provided through tailored Internet support and its effect on cancer patients' HRQOL.

In the following, I will first describe two types of cancer and their potential consequences for HRQOL. Subsequently, the concept of health-related quality of life and how it can be measured will be explored. The thesis will then describe a clinical trial of tailored Internet support to enhance shared decision-making, and test empirically whether it influences cancer patients' HRQOL.

1.2 Cancer

1.2.1 The cell

The cell is the principle building unit of the human body. There are different types of cells, and similar types of cells together make up one type of tissue. The main types of tissues are epithelium tissue, muscle tissue, connective tissue, nerve tissue and liquid tissue (Bjålie et al., 1998). Every cell consists of cytoplasm, a liquid inside the cell, surrounded by a cell membrane. In the cytoplasm there are different types of cell organelles, and in the centre of most cells is the nucleus which "administrates" the protein synthesis. The nucleus contains DNA molecules which store genetic information. The DNA governs the production of proteins.

Figure 1: The cell
Description:
1. Nucleolus
2. Nucleus
3. Ribosome
4. Vesicle
5. Rough endoplasmic reticulum
6. Golgi apparatus (or "Golgi body")
7. Cytoskeleton
8. Smooth endoplasmic reticulum
9. Mitochondrion
10. Vacuole
11. Cytosol
12. Lysosome
13. Centriole

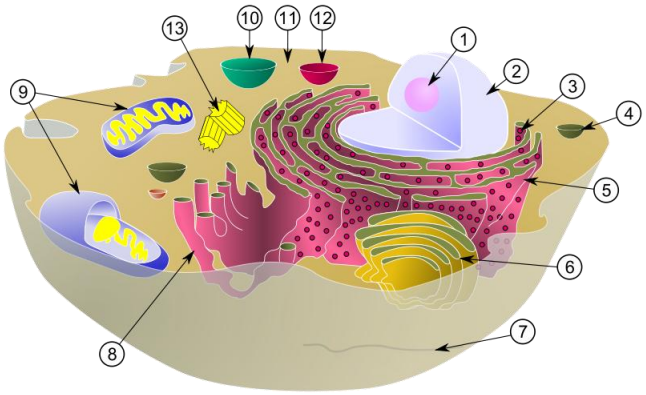
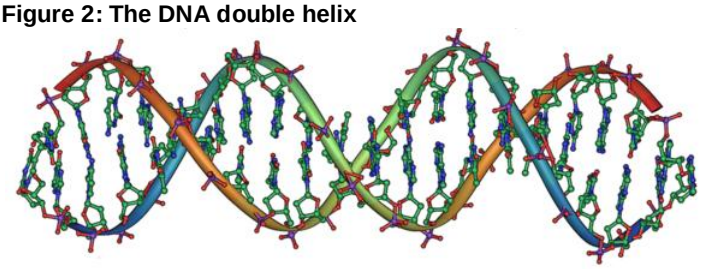


Illustration “biological_cell_svg” with explanation, is from Wikipedia.org, and used with permission under a Creative Commons licence.

Each DNA molecule consists of two nucleotide chains which are coiled up beside each other. The two nucleotide chains are linked through hydrogen connections. The chains consist of single nucleotides, and each nucleotide consists of a monosaccharide, a phosphate group and a nitrogen base. There are four different nitrogen bases: Adenine (A), guanine (G), cytosine (C) and thymine (T), and each nucleotide consist of a combination of two bases. The sequence of nucleotides in the DNA-chain represents the genetic information, in other words the genetic code. Three nucleotides in a row, a triplet, decide one type of amino acid. A gene contains the number of triplets (or the number of amino acids) which is necessary to code for a specific protein.

Figure 2: The DNA double helix



The illustration “DNA overview.png” by Michael Ströck is from Wikipedia.org, used with permission under a GNU Free Documentation Licence.

The human body grows and is maintained through cell growth. The cell itself grows until a certain point where it starts the process of dividing, a process which is called mitosis. The first step in mitosis is that all DNA in the nucleus is replicated. During the division process, one set of DNA is transferred to each of the two new cells with identical DNA. When the DNA is replicated, on special occasions an error called a mutation occurs. Errors or mutations could be that a nitrogen base changes place, that nitrogen bases are exchanged or

that more nitrogen bases are added. The consequence of a mutation is that the new DNA contains the code for a new protein. Amino acid sequence changes could either be no change in the cell, change in the cell, but it cannot grow or that the cell dies. A factor that increases the probability of mutations is mutagens. The mutagens break down the chemical bindings in the DNA. This results in disturbance of the process of division of the cell and a possible change of the nucleotides.

1.2.2 Cancer

Cancer is a disease of the regulation of tissue growth (*Cancer*, 2009). The cells keep growing even though the stimulation, which started the growing process, is absent (Næss, 2002). The cluster of cells that emerges is called a tumour. The reason for the abnormal growth of the cancer cells is alteration of the genes in the DNA of these cells (*Cancer*, 2009). Because of this error, the cell is dividing independently of the bodies' normal mechanisms for regulation (Næss, 2002). The change in the genes can occur at several levels, from mutation that affects only one DNA nucleotide, to loss or gain of one or more chromosomes (*Cancer*, 2009). The change in the genes in cancer cells are most often due to mutations or changes in the nucleotide sequence. The loss or gain of a chromosome because of an error in the mitosis can also be the cause of the development of cancer cells.

Oncogenes and tumour suppressor genes affect the cell growth in opposite directions. Oncogenes promote cell growth and predispose for cancer. The genes alter the normal cell cycle regulation and make it possible for an uncontrolled growth of the cell. Oncogenes are usually dominant and promote the malignant phenotype of cancer cells. Cancer promoting oncogenes are always activated in a cancer cell. They give the cell new properties, which lead to abnormal growth such as hyperactivity, invasion of other tissue, the cell's ability to grow in different locations consisting of different tissue, and so on.

The tumour suppressor genes are genes that inhibit the growth of a cell, both its survival and the cell division. These genes are often disabled, when changes in cancer-promotion genetic occur (DNA damage). The tumour suppressor genes are recessive.

Cancer develops when the abnormal cells are growing rapidly and/or do not die, and when they infiltrate the surrounding tissue (Næss, 2002). Further, cancer spreads when the abnormal cells start to grow into the lymph vessels and veins, and are transported as satellites (metastases) to other areas of the body where they keep growing. The extent of cancer spread, including the number and location of metastases, represents the basis for staging of cancer diseases.

1.2.3 Breast cancer

Breast cancer is the most frequent type of cancer for women in Norway, but men can also get the disease (Næss, 2002). For women below 20 years the disease is rare. In 2006, 2687 (2673 women and 14 men) persons were diagnosed with the disease. The number of persons who died from it was 679 (675 women and 4 men) (*Brystkreft*, 2009 and *Kreftstatistikk*, 2009). In 2006, no women between 0 to 14 years had the diagnosis breast cancer, while the numbers were 49 for women between 15 and 29 years, 4513 for women between 30 to 54 years, 6245 for women between 55 to 74 and 2967 for women 75 years and older. This shows that the disease is nearly absent at ages below 30 years and that it increases with age.

Most of the tumours in a breast arise from passage structures, while a few of the tumours arise from the milk glands. The tumours arising from the milk glands sometimes simultaneously arise in both breasts. The size of a tumour indicates the stage of the cancer. Normally, the smaller a tumour is when detected, the greater the chance is to survive from the cancer disease. A tumour in a woman's breast can be detected by palpating the breast when it has reached a certain size (Næss, 2002). Another way to detect tumours is by mammography, which is an X-ray examination. With this technique or other imaging techniques smaller tumours can also be detected. The use of mammography has increased in recent years. Smaller tumours are therefore more frequently discovered today, but the impact of mammography screening on survival has been debated (Jørgensen et al., 2007).

Symptoms

Tumours at early stages are usually not painful and are therefore hard to detect without medical attention. Symptoms in addition to observable lumps are pain in the breast, eczema like outbreaks of the breast and suppuration from the breast.

Staging

For breast cancer the most used staging tool is the TNM system (T = primary tumour, N = regional nodes, M = distant metastasis) (*Breast Cancer*, 2009). The TNM system has four (five) main stages, where the first stage describes a condition where the breast cancer tumour shows no sign of invasion into other tissue or metastasis and the last stage describes a condition where the breast cancer has distant metastasis.

Table 1: Description of the TNM system for breast cancer (Breast cancer, 2009)

Stage	Description
Stage 0	Carcinoma in situ
Stage I	Tumour (T) does not involve axillary lymph nodes (N)
Stage II A	Tumour of 2 to 5 centimetres in diameter and tumour does not involve axillary lymph nodes, or tumour of less than 2 centimetres in diameter and tumour involve initial axillary lymph node.
Stage II B	Tumours of more than 5 centimetres in diameter and tumour does not involve axillary lymph nodes, or tumour of 2 to 5 centimetres in diameter and tumour can involve as much as 4 axillary lymph nodes
Stage III A	Tumour is either more than 5 centimetres in diameter and involves axillary lymph nodes, or tumour is from 2 to 5 centimetres and involves 4 or more axillary lymph nodes
Stage III B	Tumour has penetrated the chest wall or chest skin, and involve more than ten axillary lymph nodes
Stage III C	Tumour involve more than 10 axillary lymph nodes and one or more supraclavicular or infraclavicular lymph nodes are present, or initiary mammary lymph nodes
Stage IV	Distant metastasis

There are more ways to stage breast cancer, however (*Breast cancer*, 2009). One classification system is based on hormone receptors. Two thirds of postmenopausal breast cancer tumours are progesterone receptor positive – PR+, and oestrogen receptor positive – ER+. Such breast cancers are sensitive to hormonal therapy. Another system is based on the presence or absence of human epidermal growth factor receptor 2 (HER2, erbB2 or neuB2). HER2 is a protein which is involved in cell development. The stage of the breast cancer has implications for the choice of treatment.

Treatment

Surgery is the main treatment for breast cancer at the earliest stages (*Breast Cancer*, 2009). Earlier the whole breast would be removed during surgery, but now the usual method is breast conserving surgery. Also, in the earliest stages sometimes surgery is not enough to remove all of the tumour tissue. In such cases supplementary treatment is normal praxis. One type of adjuvant therapy is radiation. Especially for patients who have late stage cancer with metastases, the lymph node in the armpit is removed through radiation therapy. Pharmaceuticals are another type of treatment to cure breast cancer (*Nasjonale faglige retningslinjer. Nasjonal handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av pasienter med brystkreft*, 2007). One pharmaceutical treatment is adjuvant hormonal therapy. This treatment is only given to patients who have cancer tumours that are affected by hormones. The reason for this is that tumours which are affected by hormones have receptors that the pharmaceuticals attach to. Another pharmaceutical treatment is adjuvant non- hormonal therapy, which is also called chemotherapy or cytostatica. There are several types of cytostatica, and for breast cancer patients, a combination of different cytostaticas is often more effective than the use of only one.

Side-effects of treatment

The treatments for breast cancer are effective, but they all have side-effects. Which treatment to choose primarily depends upon the type of breast cancer a patient has, but also on patients preferences, because the choice of treatment may imply trade-off between effects and side-effects. Shared descision-making therefore requires that the patient patient is properly informed about effects and side-effects.

For breast surgery, several post-operative problems could occur like infections, fluid leakage from the drain and seromas, which are fluid collection beneath the surgical site (Lynn, 1999). Signs of infections are fever, swelling around the drain site or incision. Pain in the body is also a normal side-effect from breast surgery. Discomfort in the axilla and pain connected to specific exercises recommended after surgery is particulary normal. Depression is not an unusual side-effect, because parts or all of the breast is removed during the surgery. Side-effects from hormonal therapy are hot flashes, decrease in libido, depression, vaginal dryness and irregularity in the menstrual cycle. Other possible side-effects from hormonal therapy are eye problems such as cataracts, corneal scarring and retinal changes. For premenopausal women, the tamoxifen stimulates the ovaries, which in turn increases progesterone and estrogen levels, and this could lead to an increase in the incidence in ovarian cysts and stimulate ovulation while blocking the estrogen in the breast. Vaginal dryness is also a common side-effect of hormonal therapy. For chemotherapy the fast-growing cells are affected. Therefore, side-effects attached to this treatment are hair loss and low level of white blood cells. Patients who have low levels of white blood cells are more susceptible to infection. Another side-effect of the chemoterapy is that patients can sometimes feel constant hunger and gain weight while they are on chemotherapy. Other important side-effects from chemoterapy are nausea and alterations in taste of food and odors.

1.2.4 Prostate cancer

Prostate cancer is the most frequent type of cancer in men, and the frequency increases with increasing age (Næss, 2002). In 2006, there were 1042 fatal cases caused by prostate cancer in Norway (*Kreftstatistikk*, 2009). In 2006, 3815 men had the diagnosis prostate cancer. In 2006, no men between 0 to 29 years had the diagnosis, while the number was 577 for men 30-54 years, 9960 for men 55-74 years and 6932 for men older than 75 years.

Prostate cancer is slow-growing (Næss, 2002). It arises in the peripheral parts of the prostate gland, and starts developing from semen-secreting cells (*Prostate cancer*, 2009).

The primary metastases from a prostate tumour are found in the bone marrow, mostly in the pelvis and columna. The growth of the tumour and the metastases is triggered by male hormones.

Staging

For prostate cancer, as for breast cancer, the most frequently used staging system is the four-stage TNM system (Tumour Node Metastases) (*Prostate cancer*, 2009).This system takes into account the size of the tumour, the number of lymph nodes involved and the presence of distant metastases. In stage level I and II, the cancer is located in the prostate gland only, while in stage III and IV, the tumour has spread to other parts of the body (Silva & Abdel-Wahab, 2008):

Table 2: Description of the TNM system for prostate cancer

Stage	Description
Stage I: T1a N0, M0, G1	Tumour incidental histologic finding ≤ 5% of resected tissue. The histologic grade is "well differentiated", G1.
Stage II: T1a N0, M0, G2/ G3-4	Tumour incidental histologic finding ≤ 5% of resected tissue. The histologic grade is from "moderate differentiated" to "poorly differentiated or undifferentiated", from G2 to G3-4.
T1b, N0, M0, G1 – G3-4	Tumour incidental histologic finding >5% of resected tissue. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T1c, N0, M0, G1 – G3-4	Tumour is identified by needle biopsy. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T1, N0, M0, G1 – G3-4	Clinically inapparent tumour neither palpable nor visible by imaging. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T2, N0, M0, G1 – G3-4	Tumour is confined within the prostate. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T2a, N0, M0, G1 – G3-4	Tumour involves one-half of one lobe or less. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T2b, N0, M0, G1 – G3-4	Tumour involves more than one-half of one lobe, but not both lobes. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T2c, N0, M0, G1 – G3-4	Tumour involves both lobes. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
Stage III: T3, N0, M0, G1– G3-4	Tumour extends through the prostate capsule. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T3a, N0, M0, G1 – G3-4	Extracapsular extension (unilateral or bilateral). The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
T3b, N0, M0, G1 – G3-4	Tumour invades seminal vesicle(s). The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
Stage IV: T4, N0, M0, G1 – G3-4	Tumour is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
Any T, N1, M0, G1 – G3-4	Tumour is from "incidental histologic finding is equal to, or less than 5% of resected tissue" to "fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall,"- from T1a to T4. Regional lymph nodes are "metastasis in regional lymph node(s) – N1. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated", from G1 to G3-4.
Any T	Tumour is from "incidental histologic finding is equal to, or less than 5% of resected tissue" to "fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall,"- from T1a to T4. Regional lymph nodes is from "no regional lymph node metastasis" to "metastasis in regional node(s) - from N0 to N1. Distant metastasis is "distant metastasis" – M1. The histologic grade is from "well differentiated" to "poorly differentiated or undifferentiated" - from G1 to G3-4.

Staging is an important part of evaluating prostate cancer in order to choose therapy. A prostate biopsy reveals if there is cancer in the sample, and at which stage it is. The Gleason staging system rates prostate tumours from 2 to 10, where 10 is the most sever type of cancer. At this level the tumour has the most abnormalities. For this system the decision of the level of the tumour is made in two steps. First, the pathologist examines the tumour under a microscope and gives the most common pattern of the tumour a number from 1 to 5. Then the pathologist gives the second most common pattern a number, and the sum of these two numbers is the Gleason score. A third staging system is the Whitmore-Jewett system.

Detection

Different investigation methods can be used to identify the stage of the cancer (Silva & Abdel-Wahab, 2008). The different methods are specialised to detect different stages of the cancer development. They are computer tomography (CT) and magnetic resonance imaging (MRI), bone scanning radioactive isotopes, endorectal coil magnetic resonance imaging and prostate biopsy. The computer tomography is used to examine the size of the primary tumour and potential spread within the pelvis. The bone scan is used to examine whether the cancer has spread to the bones and to reveal possible osteoblastic appearances, which occur because of an increased bone density in the areas of bone metastasis. The endorectal coil magnetic resonance imaging is used to closely examine the prostatic capsule and the seminal vesicles.

Treatment

There are several treatment options for prostate cancer, and the choice of treatment basically depends upon two factors: the stage of the tumour and the patient's preferences for side-effects of the treatment. Different types of treatments can be used either alone or in combination.

Because prostate cancer is a disease which develops slowly, watchful observation is one option for early prostate cancer (*Prostate Cancer*, 2009). For patients without metastases, there are three active treatments: radical prostatectomy, external beam radiation and brachytherapy. Removal of the prostate through surgery, prostatectomy, is the most common treatment when the tumour has developed and is at an early stage, or if the cancer has failed to respond to radiation therapy. Both radical prostatectomy and laparoscopic radical prostatectomy are methods used to remove the prostate. Radiation therapy kills prostate cancer cells with ionising radiation, and is a treatment used at all stages of prostate cancer. There are two types of radiation therapy, external beam radiation therapy and brachytherapy.

Chemotherapy is used for metastatic prostate cancer and uses pharmaceuticals. All types of chemotherapy acts by killing cells that divide rapidly. This is why chemotherapy is used only on late stage prostate cancer tumours, since tumours at an early stage divide relatively slowly and are affected by the chemotherapy only to a lesser extent.

Prostate cancer is stimulated by androgens. To stop androgen stimulation, patients may have surgical removal of the testicles (orchiectomy) or pharmaceutical treatment. LHRH agonists are one of the most commonly used pharmaceutical therapies (*Prostate Cancer Info. Hormone therapy*, 2009). Such pharmaceuticals block the release of the LHRH, which is released before the testosterone is produced. This restrains the growth of the tumour.

Cryotherapy is a treatment which uses cold to treat the prostate cancer. Needles which produce cold temperature are inserted into the prostate gland. At freezing temperature the needles destroy the whole prostate.

High Intensity Focused Ultrasound (HIFU) is a treatment which destroys tissue by rapid heat elevation (*What Is High Intensity Focused Ultrasound (HIFU)?*, 2009). Ultrasound waves are focused on the cancer tissue, which is rapidly heated up to 90 degrees Celsius and then destroyed.

For all stages of prostate cancer, the passage for urine may be blocked, and this blocking has to be opened. This is done by a transurethral resection (TUR).

Symptoms

There are usually no symptoms for prostate cancer at an early stage (*Prostate cancer*, 2009). Symptoms for prostate cancer at more advanced levels are frequent urination (especially at night), difficulties with starting and maintain a steady stream of urine, painful urination and bloody urine. Sexual function problems such as difficulties achieving erection and painful ejaculation are also normal. Fatigue and especially pain are frequent symptoms with metastases.

Side-effect of treatment

Side-effects of the different treatments of prostate cancer are many, and the most common ones are impotence, erectile dysfunction and incontinence (*Prostate cancer*, 2009). For surgery the most common complications are impotence and loss of urinary control. Radical prostatectomy can give preoperative complication and sexual and urinal dysfunctions. External beam radiotherapy and brachytherapy may cause diarrhoea, rectal bleeding, urinary incontinence and impotence.

The external beam radiotherapy carries the risk of long-term troublesome bowel problems, while brachytherapy can give acute urinary symptoms and long-term risk of proctitis.

For therapies which blocks androgen stimulation, side-effects encompass psychological problems, weight gain, enlargement of the breasts, hot flashes, osteoporosis, impotence and loss of libido. The severe and chronic side-effects of therapies, even with curative goals, means that patients involvement in choice of therapy is critical.

1.3 Tailored Internet support

Tailored Internet support is one solution to provide patients with reliable and up-to-date information about their own disease, which is one of the criteria for shared decision-making. The support system can improve a patient's self-efficacy, which is a person's level of confidence that he or she can perform specific health behaviour (Merluzzi et al., 2001). The level of self-efficacy is an indicator for how well a person can improve his functional status.

WebChoice is a tailored Internet support system developed at the Center for Shared Decision Making and Nursing Research at Rikshospitalet University Hospital in Oslo. In addition to WebChoice there are other examples of Internet support systems such as CHESS, ComputerLink and HeartCare. CHESS is an Internet-based health promotion system. It provides information, decision-making support and emotional support services. It was developed by a group of scientists at the University of Wisconsin in Madison and was initially called the Wisconsin project (Schwitzer, 2002). ComputerLink was especially designed for patients with HIV/AIDS (Gustafson et al., 1999). The system provides information, communication and self-care guidance services. HeartCare was especially designed for patients recovering from Coronary Artery Bypass Surgery (Brennan et al., 2001). The support system provides information and support services.

1.4 WebChoice

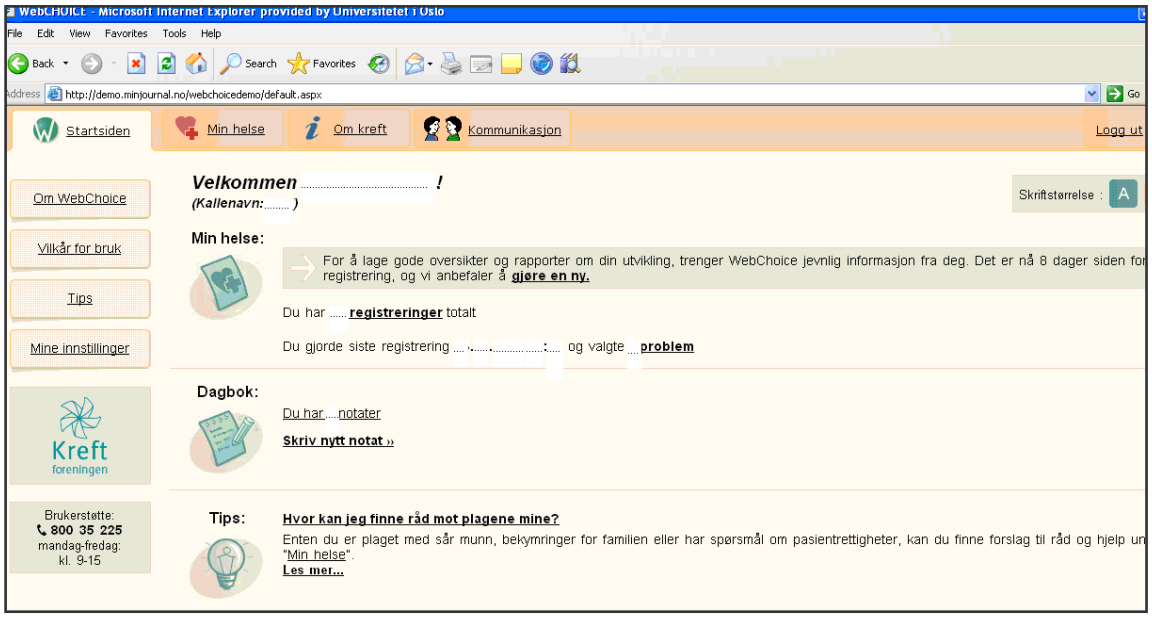
WebChoice is a tailored Internet support system and is the intervention to be tested in the randomised controlled trial presented in this thesis. The core of WebChoice is an Internet site, and username and password are needed for access. It was designed for individually tailored illness management for cancer patients and is especially created to assist cancer outpatients in their everyday life (*WebChoice – internettjeneste for kreftpasienter*, 2009 and

Ruland, 2006). WebChoice is an extension of a system called CHOICE (= Creating better Health Outcomes by Improving Communication about patients' Expectations). CHOICE is a support system for preference-based care planning based on handheld-computers. Today CHOICE is available for inpatients at one clinic at Rikshospitalet University Hospital.

WebChoice provides patient-centred information both at an individual level and a general level, and gives the patients an opportunity to communicate with other cancer patients and a nurse specialised in cancer care. The patients cannot communicate with a physician through WebChoice. The web site WebChoice has three components: an assessment component, an information component and a communication component. All three components consist of several pages or links to other underlying pages, or other sites on the Internet.

WebChoice's start page is depicted below (figure 3). It consists of eight links, one of them to the Norwegian Cancer Society. Three of the links provide information about WebChoice, one link provides advice, one link points to the patient's personal diary and one link guides the patient to one of the three main parts of WebChoice, the link "Min helse" ("My own health"- my translation).

Figure 3: The front page of WebChoice



1.4.1 Assessment component

The assessment component consists of a patient assessment tool for symptoms and problems that are typical for cancer patients. The symptoms and problems are both for functional,

physical and psychosocial conditions that could arise for cancer patients. The assessment component consists of three parts: one part where patients can register their problems, a second part where patients can get advices on how to deal with their specific problems and where they can register which solutions they choose for the problems, and a third part where the information the patients have registered in the two first parts is summarised in three different reports, which all have different aims.

One report is for the patient only and her or his relatives. The purpose of this report is to make it easier for the patient to remember what action were taken to deal with different problems. A second report is intended for the physician. The purpose of this report is to receive up-to-date information about the patient's condition and what has been done to ease any problems in the last period. A third report is a trend report which shows the development of the patient's health condition during the whole period from the start of the registration. All in all this part of WebChoice consists of five main links, and several links from the three links.

1.4.2 Information component

The information component gives the patient information about the disease and information about other Internet resources that are reliable and relevant to the patient's condition. The information component is divided into four parts. One part provides information about the patient's cancer type (in this case either prostate cancer or breast cancer): about the nature of the cancer, about the causes of the cancer, about the different examination methods and treatments, about the side-effects of the treatments, about the follow-up after treatment, about alternative- or complimentary treatments and national statistics of cancer.

Another part provides information about how to deal with the cancer in everyday life: about diet and nutrition, about physical activity, about how to talk about the cancer disease, about sexuality, about job-related issues, about when to contact the physician, about pharmaceuticals and how to use them, about relapse and spread of cancer, about how to be a relative and about fatigue. A third part provides information about patient rights. A fourth part gives information about other web sites which have relevant and reliable information concerning cancer. All in all, the information component consists of 28 links.

1.4.3 Communication component

The communication component consists of two parts. One part is a discussion forum where everyone who has access to WebChoice can join. In this forum everybody can ask questions

and reply to questions. When needed, a nurse joins the forum and gives advice, or starts a discussion which could be of relevance for cancer patients. There are also forums where only either breast cancer patients or prostate cancer patients are intended to join, or the discussion is not relevant for other cancer patient group. The other part of the communication component is a private one-on-one communication with a nurse.

1.4.4 Experiences with WebChoice

Patients have actively used all functions of WebChoice and several patients have used the program several times per week. A tendency has been that patients, who were recently diagnosed, frequently use the information component. Another tendency has been that patients who have had the disease for some time frequently use the communication component. An analysis of the first six months conducted by the research team has shown that patients actively make use of the possibility to personally contact a cancer nurse (Ruland, 2007).

1.5 Health related quality of life

When evaluating health interventions, there is a need to measure health. But how can health be defined and measured? The Constitution of the World Health Organization gave the following definition in 1948: "A state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity." The concept of well-being calls for an emphasis on a person's own experience of a health state, which is increasingly recognised in professional health care and politics (Brazier et al., 2007). When measuring health, it is in other words not enough to just count nights spent in hospitals or to solely rely on the physician's examination. The patient must evaluate his own health.

The following section will describe how health can be measured and how health-benefits can be evaluated. HRQOL is the main endpoint for this randomised controlled trial on the effects of WebChoice.

1.5.1 Economic evaluation

In a context of limited resources, output must always be measured and compared with input to evaluate options. Economic evaluation can be described as "the comparative analysis of alternative courses of action in terms of both their costs and consequences" (Drummond et al., 2005, p. 9, italics in original removed). The core aspects are inclusion of both input and

output, and a comparison of at least two interventions. When these aspects are included, it is possible to make choices that maximise desired outcome within limited resources.

A partial economic evaluation only evaluates one alternative and/or is only concerned with either costs (inputs) or consequences (outputs). Depending on different "combinations", the following types of partial economic evaluation can be identified (Drummond et al. 2005):

- Outcome description: Examines the consequences of one alternative.
- Cost description (Cost of illness): Examines costs of one alternative.
- Cost-outcome description: Examines costs and consequences of one alternative.
- Cost analysis: Examines costs of two or more alternatives
- Efficacy or effectiveness evaluation: Examines consequences of two or more alternatives.

Consequences can be put in three categories: Natural units, monetary units and utility. This gives three different main types of full economic evaluations:

- Cost-benefit analysis: Costs and effects are measured in monetary units.
- Cost-effectiveness analysis: Costs are measured in monetary units, and effects are measured in natural units.
- Cost-utility analysis: Costs are measured in monetary units and effects are measured in QALYs.

The cost-utility analysis is by some seen as a subgroup of cost-effectiveness analysis, since the two methods are similar in several aspects. The main difference between the two is that cost-utility analysis uses a generic measure of the outcome and is therefore in principle comparable across all diseases and patient groups, while the cost-effectiveness uses a measure of outcome which is specific to the program under study.

This master thesis is a partial economic evaluation of WebChoice: It can be classified as an effectiveness evaluation, since it only measures consequences of two alternatives. The consequences are measured in utility (HRQOL and quality adjusted life years - QALYs), so the study can be part of a later cost-utility analysis.

1.5.2 Preferences

Preference is an umbrella term which covers values and utilities (Drummond et al. 2005): Values are preferences under certainty, while utilities are preferences under uncertainty. Certainty concerning future health outcome can only be found at a theoretical level, which

means that all preferences concerning health are in general referred to as utilities in health care terminology.

The concept of utility in a strict economic sense was first developed in 1944, by John von Neumann and Oscar Morgenstern, a mathematician and an economist respectively (Drummond et al., 2005). Through their theory of rational decision-making under uncertainty, they constructed the concept of utility. This theory is today known as utility theory or von Neumann-Morgenstern utility theory. They developed a normative model where they described how rational individuals "ought" to make decisions when faced with uncertain outcomes. For this purpose they defined what they meant by rational behaviour under uncertainty. This was expressed through different axioms which defined preferred options under different scenarios of uncertainty. These axioms provide the foundation for modern decision theory and for specific preference measurements in health care.

Measuring health preferences

There are several methods to measure preferences for health states. The three most widely used techniques are the category rating/ scaling, the standard gamble (SG) and the time trade-off (TTO) (Drummond et al., 2005).

When using category rating, the patient ranks different health outcomes. The scale may include numbers, and the numbers may be presented in categories (category scaling). In a visual analogue scale (VAS), the scale just consists of a line. The different scaling techniques can be combined.

The standard gamble is the classical method for measuring cardinal preferences, and it is based directly on the fundamental axioms of the utility theory of von Neumann and Morgenstern. The respondent is offered two alternatives, where the first alternative is treatment with two outcomes: perfect health or death, and the second alternative is no treatment with a certain health status lower than perfect health, for the rest of the patient's life. The outcomes in the treatment-alternative have to include their probability, and the introduction of risk makes this method a measurement of utility in economic terms.

The time trade-off was developed specifically for use in health care. The time trade-off is a method for measuring preferences were the patient has to choose between two alternatives: a) Stay in a specific health state for a specific time period *t* followed by death, or b) Have perfect health for a time period *x*, which is less than the time period *t*. Then the time period *x* is varied until the patient values the alternatives as equal.

Multi-attribute health status classification systems with preferences scores

The use of the rating scales, the time trade-off and the standard gamble is time consuming and complex. For instance, the standard gamble and TTO often requires face-to-face interviews to ensure that the respondent fully understand the concept of probability (Drummond et al., 2005). In this context, faster and more simplistic methods have been introduced to measure preferences in large-scale surveys.

Pre-scored multi-attribute health status classification systems are tools to measure preferences for health outcomes or HRQOL and are meant for surveys with a large number of respondents. The requirements for a useful generic classification system are: Feasibility and general applicability, reliability, validity and sensitivity.

The most frequently used systems are the Quality of Well-Being, Health Utilities Index, EQ-5D and Short Form 6D. Other systems are 15D and Assessment of Quality of Life (Drummond et al., 2005).

All classification systems consist of a descriptive system in a questionnaire and a summary index. The questionnaire has different numbers of questions or dimensions, according to different types of systems. System-names often indicate the number of dimensions, like five dimensions in the EQ-5D and fifteen in the 15D.

Each dimension has a set of predetermined levels, and the number of levels differs across the systems. The levels are classified with an ordinal number: 1 is the best health state for the dimension and the highest number is the worst.

The summary index is an index where 0 represents death and 1.0 represents perfect HRQOL. Some multi attribute systems have index values below 0 (e.g. EQ-5D). The summary index is created on the basis of the respondent's scoring on the dimensions, using an algorithm to incorporate preferences. The basis of the algorithm is typically TTO or VAS values from interviews of representative samples of the general population. The results from complex and time consuming preference surveys are hence incorporated in pre-scored multi-attribute systems, which make them adequate for large scale surveys.

1.5.3 The 15 D

The 15D is a multi-attribute health status classification system (Brazier et al., 2007). It is generic, multi-dimensional, standardised and self-administrated (Sintonen, 1994). The 15D was designed to meet the requirement for a useful generic measure as far as possible.

The 15D consists of two parts. The first part is the health state descriptive system, which is formed as a questionnaire. It consists of fifteen questions with five alternative

response categories for each question. The dimensions cover most of the content in any preference-based measure (Brazier et al., 2007). For each question, response category 1 indicates no problems with the dimension in question, and 5 indicates severe problems. In the questionnaire, the respondent tick off only the answer to each question which best describes his or her present health state. The fifteen dimensions are:

- Mobility
- Vision
- Hearing
- Sleeping
- Eating
- Speech
- Elimination
- Usual activities
- Mental function
- Discomfort and symptoms
- Depression, distress
- Vitality
- Sexual activity

The second part of the 15D is a valuation system which is based on a simple, additive algorithm. The system puts a health state value on each of the five dimensions for each of the fifteen questions. The method used to calculate the values is a variant of VAS. 15D has been evaluated in five population based samples in Finland and one in Denmark.

1.5.4 Quality-adjusted life years (QALYs)

In a cost-utility analysis the measure of benefit is QALYs, which is based on HRQOL and the length of time of the health benefit (Drummond et al., 2005). When measuring HRQOL in the context of health economics, the idea is that the respondents express the preference for different health states. This is typically done with a method that forces the respondent to make a trade-off between HRQOL and another good (e.g. length of life or money). This means that HRQOL, and consequently QALYs, express preferences for health improvements.

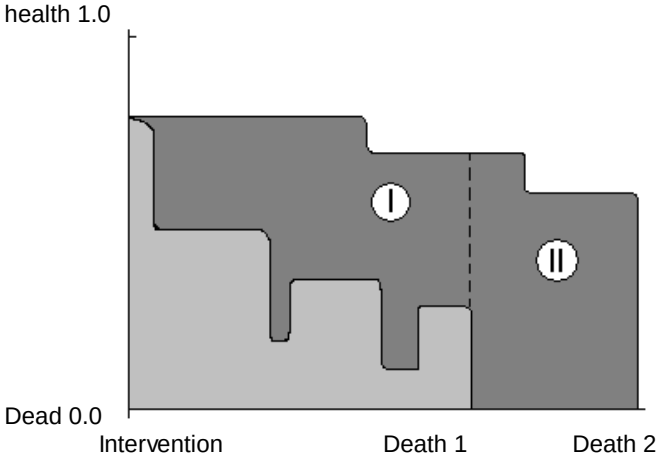
The concept of QALYs was introduced by Herbert Klarman and his colleagues in 1968 (Drummond et al., 2005). The QALY captures time and a person's health state, and it is based on the relative desirability of different outcomes. The QALY consists of a combination of two dimensions: time and health state, or quantity and quality. This indicates that the QALY simultaneously captures health gains from reduced morbidity and reduced

mortality. For an individual, his/her total QALYs will be given by the sum of quality-adjusted time periods (Manca et al., 2005). This can be expressed as:

$$QALYs = {}^{n}\Sigma_{j=1} = Q_j * t_j$$

Q is the 15D index score, t is time, j is the interval number, n is the number of subintervals. Depicted in a figure, the QALYs gained is the area between the expected life curve without the intervention and the expected life curve with the intervention.

Figure 4: A person's QALYs with and without the intervention



Dark grey = with intervention. Light grey = without intervention

The expected QALY for a person is calculated as the sum of each pathway weighted by its respective probability. This is called the area under the curve (AUC) method.

To measure change in QALYs in randomised clinical trials, three different methods may be used: Linear change, earlier level maintained and change at midpoint. Of the three, the linear change is most used in such contexts (Manca et al., 2005).

1.5.5 How to achieve the highest possible HRQOL

Patients with breast cancer or prostate cancer at an early stage do usually not have severe symptoms, but the treatments may give severe side-effects (see section 1.2.3 and 1.2.4). It is therefore a trade-off between treatment effectiveness and side-effects, which in many cases is equivalent to a trade-off between to live longer with more pain versus to live shorter with less pain (Brazier et al., 2007). In such cases, shared decision-making is especially important because it is the patient himself who knows best what his preferences are, and the patient cannot make such trade-offs unless they are properly informed. When the patient participates in the decision-making process, this will likely lead to better outcomes for the patient and hence the highest possible HRQOL score for the patient.

1.6 Epidemiology and study design

Epidemiology is the science and practice of detecting and explaining disease patterns in populations (Bhopal, 2002 and Thelle, 2004). The objective is to prevent and control disease, and to improve health by analysing effects of different medical or non-medical interventions.

When measuring these aspects, the two core measures are prevalence and incidence. Prevalence is defined as the number of persons who, at a specific point in time, have a given disease. While prevalence measures the distribution of a disease, incidence incorporates a time factor and is a measurement for development: Incidence is defined as the number of new cases of a disease during a specified period of time.

Within epidemiology there are different types of study design which fit different types of research situations. The four main types of epidemiologic study designs are *cross-sectional study*, *case-control study*, *cohort study* and *trials* (Thelle, 2004). It possible to add *case series* in this line up, but since case series typically are used as background for the other studies, it will not be discussed here (Bhopal, 2002). The following description of designs is largely based on Thelle (2004) and Bhopal (2002).

A cross-sectional design studies health and disease states in one or more populations at a defined time and place. As the name indicates, this type of study is a "slice" of time and place which explores prevalence of a disease or other exposures. Cross-sectional studies can test hypotheses by identifying correlating results. The study can be repeated to measure change. This is called *repeated cross-sectional design* or *panel design*. The problem with a cross-sectional design is difficulties in detecting causality and development, since there is no randomisation and the respondents will in principle be new in each new study.

A case-control design compares a group with a specific disease (case group) to a similar group without the disease (control group). The researcher identifies differences and similarities between the two groups, for instance that lung cancer patients smoke more tobacco than persons without lung cancer. These types of studies typically involve collecting extensive medical and social background data for the respondents.

A cohort design follows a specific group of people over a time period. The group, or cohort, is defined by common characteristics, for instance that all of the members have a given disease or take part in a specific lifestyle. The measure of interest is often incidence, where the study seeks to measure the number of new cases. The cohort can be compared to a control cohort. It is possible to link exposure (e.g. alcohol use, use of drugs) to outcomes (e.g. liver problems) in cohort studies.

The participants in a trial are divided into two (or more) groups, where one group is exposed to an intervention and the other is not. A trial design has many similarities with a cohort design, but with one important difference: The exposure is deliberately changed and controlled. When the intervention group has been selected on the basis of randomisation, the design is called *randomised controlled trial* (RCT). The randomisation process prevents *confounding*, since the groups, in principle, are equal in all respects except for the exposure. Any difference in outcome can then be attributed to the exposure, and hence such trials are typically used to test hypotheses of causality. In epidemiology, randomised controlled trials can be used to analyse treatments, but is rarely used to investigate exposures with presumed negative health effects, due to ethical issues.

A problem in all study designs is the risk of *bias*. Bias can be defined as systematic errors, both intentional and unintentional, that favour certain outcomes (Bhopal, 2002 and Thelle, 2004). Confounding is a major cause of bias, and may lead to a wrong conclusion about the relationship between exposure and outcome. A high level of exposure (e.g. non-fat milk) may correlate with outcome (e.g. overweight and obesity), but the cause may be a hidden, third factor (historical example in Thelle (2004): non-fat milk did not cause obesity, but obese persons had the highest consumption of non-fat milk because they were on a diet). Two other main biases are information bias and selection bias. A selection bias is a systematic difference between the intervention and control group in terms of more than the exposure. This bias derives from the method of data collecting, for instance that the recruitment process was flawed. Information bias is one or more errors in interpretation, collection and/or analysis of data. This type of bias ranges from false assumptions in the hypotheses (e.g gender affects intelligence), or manipulation of the results by the respondents, both deliberate and unintentional.

1.7 Research questions and hypotheses

Cancer is likely to impact HRQOL negatively (Juver & Vercosa, 2008). However, information and advice from WebChoice may relieve several of the problems patients encounter and may consequently reduce the negative impact of the disease.

When capturing health related quality of life with the 15D instrument, I would, on the basis of the previous presentation (see section 1.2 - 1.5), expect that WebChoice may improve HRQOL along 8 of the 15 dimensions of 15D:

- The patients in the intervention group have less problems with their sleep because they receive advice about how to avoid sleeping disorders.
- The patients in the intervention group have less problems with eating because they learn about which effects different cancer treatments can have on their appetite, and how some cancer treatments can change the taste of food.
- The patients in the intervention group have less problems with their bladder function and bowel function because they get advice on how to ease problems with these functions.
- The patients in the intervention group have less symptoms and less problems with their mental function because they learn how to deal with symptoms and because they can discuss problems with other patients who have experienced the same problems as themselves, and with nurses.
- The patients in the intervention group experience less depressions because they discuss problems concerning the cancer disease with other patients and with nurses.
- The patients in the intervention group are less distressed because they have more knowledge about the disease and side-effects of different treatments and because they know that if they are worried about something, they can ask a nurse about it and be sure that they will get an answer the same day.
- The patients in the intervention group are healthier and more energetic, because they can ask for help about the best way to deal with an illness and what the best nutrition is for a cancer patient who gets a specific treatment and suffers from specific side-effects.
- The patients in the intervention group have less problems with their sexual functions because they receive much information about how the disease impacts the sexual function.

WebChoice may also provide information which makes the patients more competent to participate in shared decision-making, hence assure them treatment according to their preferences. This, in turn, may improve the patients' HRQOL, as it is sensitive to patient preferences.

The main hypothesis is therefore that patients using WebChoice score better on 8 out of 15 HRQOL dimensions and hence have a better 15D summary score (index) after one year of intervention, compared to "usual care" (the control group).

2. Methods

The design, patient recruitment and execution of the trial were performed by the research team. During the rest of this methods section, I will describe how the study was designed and implemented by the research team, and how data were subsequently analysed by myself.

2.1 The WebChoice randomised clinical trial

The Centre for Shared Decision Making and Nursing Research at Rikshospitalet University Hospital in Norway carried out a randomised controlled trial of WebChoice during 2007 and 2008. The head of the research centre and the principal investigator was Professor Cornelia M. Ruland, and Laura Slaughter was the co-investigator.

The participants in the trial were prostate cancer patients and breast cancer patients from all parts of Norway. They were recruited through advertisement on the Internet, in national newspapers, in weekly magazines, on national television programmes and through flyers handed out in outpatient clinics across the country. The recruited patients were randomised into two different groups, the intervention group, or WebChoice group, and the control group.

During the trial period, the intervention group had access to the website WebChoice in addition to normal care, while the control group received only normal care (see section 1.2). The trial period was one year. Five times during this period (at baseline, after three months, after six months, after nine months and after twelve months) both groups received a data collection package from the research team. Both groups received the same package for each period, but the content was not identical at every dispatch.

All of the packages included a information letter and a registration form for symptoms and pain called the memorial symptom assessment scale (MSAS). Most packages also contained one of the following registration forms where the patients could register their choice of actions taken to handle the disease: The Cancer Behaviour Inventory (CBI), the social support (MOS), a form for registration of depression (CES-D) and the diary.

In three of the five packages, the form Patient Preferences in participating in Decision Making (Degner) and the HRQOL questionnaire 15D were included. The following elements were included in only one package: the informed consent form, the Buypass form which was the registration form for access to WebChoice, a demographics form, a

questionnaire about ease of use of WebChoice, and a form for health related information use and usage, which was different for the WebChoice group and the control group.

2.1.1 Inclusion criteria and exclusion criteria

There were several criteria for inclusion of the participants in the randomised control trial, and one exclusion criterion.

Inclusion criteria:

- Written informed consent
- Age 18 or over
- Mentally healthy
- Able to talk and write Norwegian
- Access to Internet and a computer with Microsoft Windows operating system (version 98 or later)
- For breast cancer patients: Had received or planned to receive surgery, and received or planned to receive one adjuvant therapy, except for radiation therapy only
- For prostate cancer patients: Had received or received treatment for the disease

Exclusion criterion:

- Metastases of the brain, treated with radiation therapy

2.1.2 Recruitment

Interested persons were invited to contact the research team for participation in the randomised controlled trial. Relatively few people showed interest in joining the randomised controlled trial, and the research team made several attempts to recruit participants over a time period of more than a year. The start of the recruitment period was in May 2006 when an advertisement was put in the national Norwegian newspaper *VG*. In June, an attempt to recruit patients was carried out by an advertisement in the weekly magazine *Se og Hør*. Also, an article in the regional newspaper *Aftenposten* about a patient from the pilot study was used to recruit patients. The same patient was presented in a morning program on the Norwegian national television channel *TV 2*.

In July 2006, both written and spoken information about the randomised controlled trial was given to clinics that treat breast cancer and prostate cancer patients. In September, a description of the randomised controlled trial and a request for people to participate, were given in a member magazine for Prostatakreftforeningen (The Prostate Cancer Society – my translation), and at the WebChoice webpage. In November, a description of the randomised controlled trial and a request for participants was made in the member magazine for Foreningen for brystkreftopererte (Society of Breast Cancer Post Operatives – my

translation), along with advertisements in the two national papers *Dagbladet* and *VG*. In February 2007, attempts at recruitment were made by advertising at Sammen mot Kreft's webpage (United Against Cancer – my translation) and in their periodical. Prostatakreftforeningen, Foreningen for brystkreftopererte and Sammen mot Kreft are all subdivisions of the Norwegian Cancer Society.

The Cancer Registry of Norway provided national patient lists which were used in direct recruitment through letters from the research team. In May 2007, final advertisements were made in the two national papers *VG* and *Dagbladet*.

The last patient was recruited on the 15th of June 2007. At this time the number of patients included was well below the estimated need, but the recruitment process was finished for practical reasons.

2.1.3 Registration

Individuals who showed interest in the WebChoice project, but did not participate, were not registered. Apparently, a great number of patients contacted the research team, but relatively few participated because of lack of interest or because they did not have breast or prostate cancer.

2.1.4 The inclusion process

In total, 445 breast and prostate cancer patients who contacted the research team met the inclusion criteria and were interested in participation. These persons received the "baseline" package which included:

- Information letter
- Informed consent form
- BuyPass form
- Registration form about socio-demographic variables
- Memorial Symptom Assessment Scale
- Patient Preferences in Participating in Decision-Making
- Cancer Behavior Inventory
- 15D Quality of Life questionnaire
- Social support (MOS)
- Depression (CES-D)
- The use of health care diary

In total, 325 patients returned this first package. Nine of the respondents informed that they did not want to participate after all. After three months, 316 persons received the next package, and 265 returned it. At this point, 8 of the 316 persons had informed that they did not want to participate in the study anymore. After 6 months, 308 persons received the

package and 257 returned it. At this point an additional 26 participants among the 308 withdrew from the study. The fourth package was sent after 9 months to 282 persons and 242 returned it. At this point seven more patients withdrew. The last package was sent after 12 months to 275 persons and 245 returned it. Among the 325 who returned the initial package, a total of 80 persons did not complete the study.

Among the 245 patients who participated till the end, 9 did not fill in the 15D questionnaire sent after 6 months (but they filled in at baseline and after twelve months). This leaves 236 patients for analysis. Of the 236 patients, two patients had more than four missing values in the last questionnaire, which made it difficult to include them in analyses of the 15D.

In total, 325 patients returned the 15D questionnaires, once, twice or three times, but the subsequent analyses are based on information from the 234 patients who filled in the all three 15D questionnaires completely or almost completely. The reason for participants to drop out of the study is not known, because a premise for the patients to join the study was that they could withdraw from the study at any time without explanation.

2.1.5 Randomisation

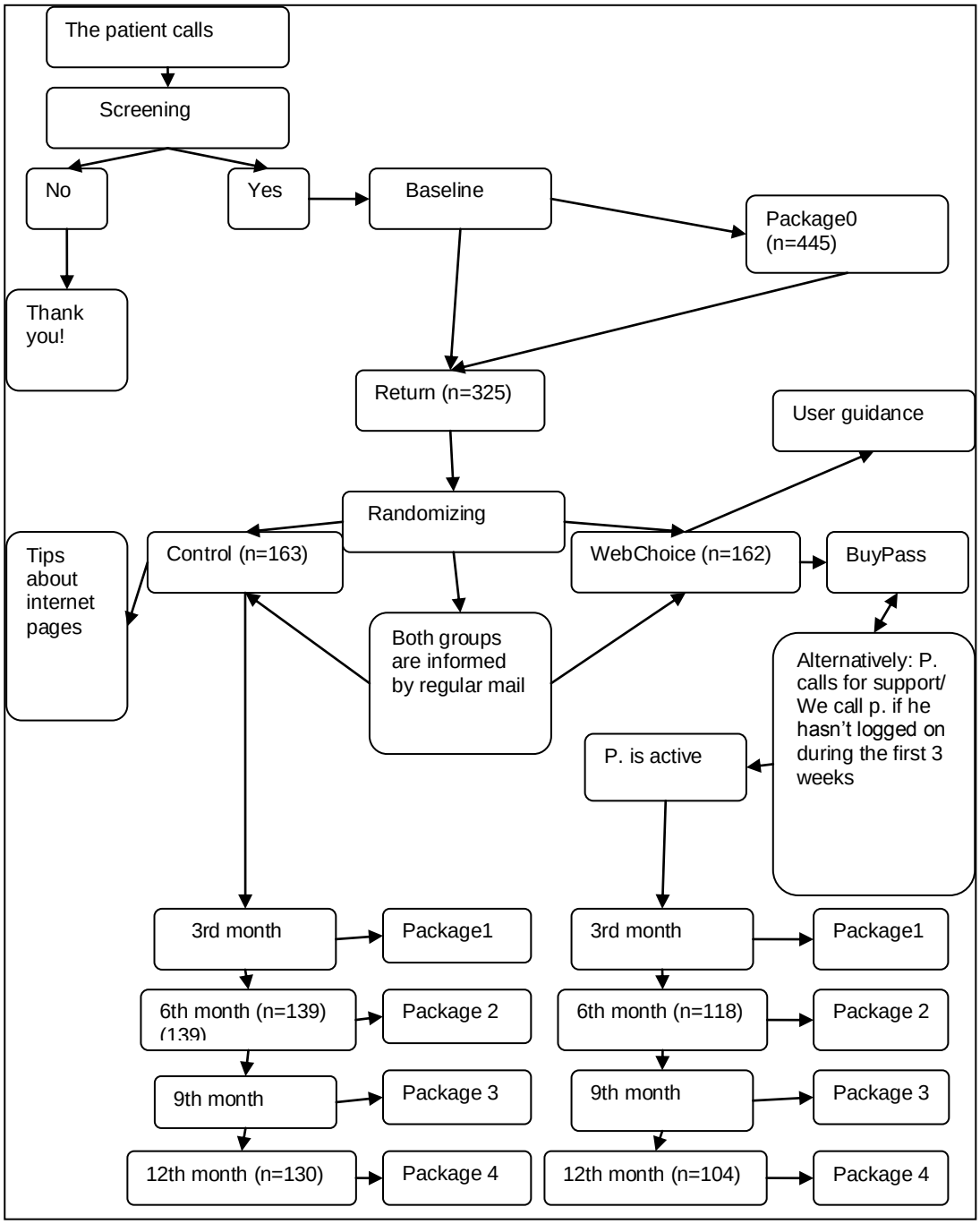
The inclusion process ended with 325 patients. These patients were randomised into the two groups, the WebChoice group and the control group. The randomisation method used was the minimisation method to balance covariates (Zeller et al., 1997). The randomisation system R-Tool was used for this purpose.

2.1.6 Endpoints and power

The primary endpoint of the WebChoice study was symptom distress measured by MSAS. Secondary endpoints were self-efficacy, decision-making skills, social support, depression, 15D and resource use.

Using symptom distress as the endpoint for power calculation, the research team made the assumption based on previous work, that the difference would be 0.3 between the WebChoice and the control group. The statistical power was set at 0.80, and the significance level at 0.05. The study would then require 140 patients in each group. To allow for subgroup analyses, the group sizes were increased to 200. Additionally, the attrition rate was expected to be 50 percent, and the research team aimed to recruit 500 patients in each group.

Figure 5: The inclusion/exclusion process (from the research team)



2.1.7 Approval

The study was approved by the Norwegian Data Inspectorate and by REK, the Regional Ethics Committee.

2.1.8 Literature search

A literature search was carried out by the research team prior to the start of the study period.

2.2 Statistical methods

2.2.1 Exclusion and inclusion of variables

I received the data as four SPSS files from the research team (three data sets for the 15D scores and one set for demographics). The patients/respondents had answered a large amount of questions concerning health, age, income, education, family and so on (see Appendix). I had to exclude certain variables in my analysis, due to time limitations. The following considerations were made:

Socio-economic variables and skills

This study measures the effect of web-based advice and information, so information about the patients pre-existing knowledge, skills and ability to acquire and deal with complex information is vital. Such data are best acquired through interview tests, but such tests were not conducted by the research team. Socio-economic variables can indicate levels of skills and are relevant in this study. These types of variables are also important in order to evaluate how representative the sample is. I therefore included education, household income and age as background variables.

I did not include the number of children. This variable could have been interesting, since teenagers and adult children can provide help and assistance with a tool like WebChoice. However, this variable does not provide information on the children's age or skills, so I excluded this variable.

I also excluded marital status. It could not be used to control household income, since it is impossible to specify the income of the spouse. And as with the children variable, it does not indicate skills in an "assistance" perspective.

The patients had answered a question about their experience with computers, but I excluded this variable because I found WebChoice so accessible and user-friendly that computer experience should have little relevance. The self-evaluation of own experience is also not very reliable, as the respondents classify themselves relative to what they consider to be "normal". The exclusion of this variable might have been a mistake in a post-perspective, as it could have helped to explain the results.

Time since the cancer diagnosis is an important background variable. It indicates the patient's experience and hence knowledge about own disease. The data set contained the date of diagnosis for each patient. The time since diagnosis varied considerably among the patients, so I calculated the number of months since diagnosis and divided these into four

intervals: 0 - 6 months, 7 - 12 months, 13 - 18 months and 19+ months. The latter interval was the reference level when the variable was expressed in terms of three dummies in the regression analysis. The precision level of four categories was unnecessary except for the regression analysis, so a variable for "new" and "old" cancer diagnoses was constructed. New diagnosis was from 0 to 6 months before the start of the survey, and old diagnosis was from 7 months or more.

Health variables

The patients had answered questions concerning each of the 15D variables. All of these were included since these variables are what measure the effect(s) of the intervention. The 15D variables at baseline serve as background variables. Eight of the 15D variables were analysed separately to address the eight research questions concerning sleeping, eating, elimination, mental function, discomfort and symptoms, distress, vitality and sexual activity. Additional analysis on the remaining seven 15D-variables are presented in the Appendix.

Detailed variables describing the patients' cancer and treatments were excluded. The inclusion criteria had to some extend defined the patients' cancer and treatments, and I found the 15D variables more relevant to describe their health.

I calculated the QALY variable, based on the method of linear interpolation and the regression based adjustment described by Manca et al. (2005). The method I used adjusts for possible difference in baseline utility.

2.2.2 Statistics

Differences between the groups were tested by the chi-square test for categorical variables. The variables age and mean QALY were tested by the *t*-test for independent samples. All these tests are two-sided, with a significance level set to 5 percent. Linear regression and regression based adjustment were used to estimate the difference in one year QALY between the WebChoice and the control group (Manca et al., 2005). I used the statistical tool SPSS for the statistical tests.

2.2.3 Calculations

Three main types of calculations were done: Replacing missing 15D values through imputation based on linear regression, transforming 15D variables into a summary score and finally calculating the number of QALYs for each patient during the study period through linear interpolation. The patients were somewhat unbalanced at baseline with respect to the 15D score, so when I calculated QALYs, I used multiple linear regression to adjust the

differences (Manca, 2005). The formula is based on Manca, but was expanded due to more groups of interest: $QALY_i = \beta_0 + \beta_1 * t_i + \beta_2 * k_i + \beta_3 * Q_i^b$

i is the ID of the respondent. t_i is the treatment arm dummy variable, where 1 is WebChoice and 0 is the control group. k_i is a cancer group dummy variable, where 1 is prostate cancer and 0 is breast cancer. Q_i^b is the patient specific 15D score at baseline. Through a multiple linear regression where 15D score at 12 months were the dependent variable, and intervention group, type of cancer and the patient's specific 15D score at baseline were the independent variable, I found the values for β_1, β_2 and β_3. Then I constructed the new variable QALYs.

To be able to calculate the 15D indexes for the patients, the missing values had to be replaced before they were translated into 15D scores. The first operation was carried out by the means of two methods explained at the homepage of the 15D (*Replacing missing data*, 2009). The main method uses linear regression to replace the missing values. In some cases the missing data had to be replaced by the use of the optional method: I removed the independent variables which also have missing data for the specific ID, and then I had to run the regression once more. This replaced the rest of the missing data in the 15D questionnaires, and all the 234 15D indexes were calculated. To translate the 15D values into 15D score, I used a syntax file available at the 15D homepage.

2.2.4 Procedure

The following table is a short description of the procedures during the statistical analyses

Prior to analyses	- Remove empty IDs in all sets
Demographics	- Select/exclude variables - Separate analyses according to cancer type - Analyses on dropout - t-tests on age - Chi-square tests on income and education (crosstabs) - Construct new variables for time since diagnosis - Separate analyses of time since diagnosis - Chi-square tests (crosstabs) on time since diagnosis
Quality of life	- Separate analyses on each of the eight variables according to cancer types - Chi-square tests (crosstabs)
15D index	- Create new data files with demographics, cancer types, intervention/control and all 15D variables for each of the three measurement points. - Replace missing values - Transform variable values into 15D scores - t-tests - Manual input of constructed time variables - Separate analyses on mean scores according to groups and time since diagnosis - Linear regression analyses on variables' impact
QALYs	- Linear interpolation and regression-based adjustment to calculate QALYs - Regression analyses on different variables' impact - t-tests of difference in mean QALYs

3. Results

This chapter presents the results of the analyses of this thesis. In total 325 patients were included in the randomised controlled trial. Of the 325 patients, 234 filled in the 15D questionnaire all three times. The analyses presented in the results section are mainly based on the 234 patients who answered all three times.

3.1 Descriptives

The characteristics of the 325 patients are given in the table below (table 3).

Table 3: Characteristics of all patients (n = 325) who accepted to participate and were randomised to type of intervention, according to type of cancer and intervention type

	Breast cancer (n = 189)		Prostate cancer (n = 136)	
	WebChoice	Control	WebChoice	Control
Mean age (SD)	50.6 (7.5)	50.3 (9.4)	66.1 (7.5)	64.9 (8.3)
Median age	50.0	50.0	66.5	63.5
Age range	32 (35 – 67)	45 (32 – 77)	33 (47 – 80)	38 (45 – 83)
Level of education: Secondary school or less High school University/college 4 years or less University/college more than 4 years	 6.2% 35.4% 43.8% 14.6%	 7.5% 31.2% 35.5% 25.8%	 6.1% 27.3% 40.9% 25.8%	 15.9% 31.9% 31.9% 20.3%
Level of income: Less than 200 000 NOK 200 000 – 400 000 NOK 400 000 – 600 000 NOK 600 000 – 800 000 NOK More than 800 000 NOK	 1.1% 24.2% 28.6% 20.9% 25.3%	 3.4% 18.4% 25.3% 26.4% 26.4%	 3.0% 34.8% 27.3% 22.7% 12.1%	 0.0% 31.9% 29.0% 24.6% 14.5%

Within each type of cancer, the randomisation of the 325 patients included in the trial was relatively successful in that the groups were relatively well balanced with respect to age, education and income within each of the disease groups (table 3).

The characteristics of the 234 patients who are included in the 15D analyses are given in the table below (table 4).

Table 4: Characteristics of the patients (n = 234) who responded to the 15D questionnaire all three times according to type of cancer and type of intervention

	Breast cancer (n = 130)		Prostate cancer (n = 104)	
	WebChoice	Control	WebChoice	Control
Mean age (SD)	52.2 (7.4)	50.9 (9.6)	65.6 (7.1)	66.37 (7.5)
Median age	51.0	50.0	66.0	65.0
Age range	31 (36-67)	45 (32-77)	30 (50-80)	27 (55-82)
Level of education: Secondary school or less High school University/college 4 years or less University/college more than 4 years	 5.5% 38.2% 40.0% 16.4%	 8.0% 33.3% 32.0% 26.7%	 2.0% 26.5% 44.9% 26.5%	 20.0% 32.7% 27.3% 20.0%
Level of income: Less than 200 000 NOK 200 000 – 400 000 NOK 400 000 – 600 000 NOK 600 000 – 800 000 NOK More than 800 000 NOK	 0.0% 24.5% 26.4% 28.3% 20.8%	 4.2% 19.4% 22.2% 29.2% 25.0%	 2.0% 30.6% 26.5% 28.6% 12.2%	 0.0% 33.3% 33.3% 18.5% 14.8%

Within each type of cancer, the randomisation was relatively successful in that the groups were relatively well balanced with respect to age, education and income within each of the disease groups.

To test for selection bias, I compared characteristics of the 91 participants who filled in the 15D form less than three times with the 234 participants who filled in the 15D form three times. Table 5A shows the difference for the breast cancer patients and table 5B shows the difference for the prostate cancer patients.

Table 5A: Characteristics of breast cancer patients (n = 189) who responded to the 15D questionnaire all three times (n = 130), and those who responded less than three times (n = 59), according to intervention type, WebChoice (n = 96) and control group (n = 93)

	WebChoice (n=96)			Control (n=93)		
	Answered all (n=55)	Not answered all (n=41)	*p-value*	Answered all (n=75)	Not answered all (n=18)	*p-value*
Mean age(SD)	52.2 (7.4)	48.4 (7.2)	0.012	50.9 (9.6)	48.2 (8.4)	0.281
Median age	51.0	48.0		50.0	48.0	
Age range	31 (36-67)	29 (35-64)		45 (32-77)	31 (32-63)	
Level of Education: 1.Secondary school or less 2.High school 3.University/college 4 years or less 4.University/college more than 4 years	 5.5% 38.2% 40.0% 6.4%	 7.3% 31.7% 48.8% 12.2%	 0.777 	 8.0% 33.3% 32.0% 26.7%	 5.6% 22.2% 50.0% 22.2%	 0.547
Level of income (NOK): Less than 200 000 200 000 – 400 000 400 000 – 600 000 600 000 – 800 000 More than 800 000	 0.0% 24.5% 26.4% 28.3% 20.8%	 2.6% 23.7% 31.6% 10.5% 31.6%	 0.200 	 4.2% 19.4% 22.2% 29.2% 25.0%	 0.0% 13.3% 40.0% 13.3% 33.3%	 0.415

In the breast cancer WebChoice group, the non-respondents were significantly younger than the respondents. This was only a tendency in the control group. When it comes to income, the tendencies were somewhat unclear. In both groups, the non-respondents were less represented with medium/high income patients, but on the other hand, more of them had high income. Educational level was equally distributed between respondents and non-respondents in the WebChoice group. This was not the case in the control group, where the non-respondents tended to be more educated. The WebChoice group had a higher dropout rate than the control group (43 percent versus 19 percent).

Table 5B: Characteristics of prostate cancer patients (n=136) who responded to the 15D questionnaire all three times (n=104), and those who responded less than three times (n =32), according to intervention type, WebChoice (n=67) and control group (n=69)

	WebChoice (n=66)			Control (n=70)		
	Answered all (n=49)	Not answered all (n=17)	*p-value*	Answered all (n=55)	Not answered all (n=15)	*p-value*
Mean age(SD)	65.6 (7.1)	67.65 (8.7)	0.341	66. 6(7.4)	59.1 (9.1)	0.002
Median age	66.0	68.0		65.0	57.5	
Age range	30 (50- 80)	32 (47- 79)		27 (55- 82)	38 (45 - 83)	
Level of Education: 1.Secondary school or less 2.High school 3.University/college 4 years or less 4.University/college more than 4 years	 2.0% 26.5% 44.9% 26.5%	 17.6% 29.4% 29.4% 23.5%	 0.117 	 20.4% 33.3% 27.8% 18.5%	 0.0% 28.6% 50.0% 21.4%	 0.197
Level of income (NOK): Less than 200 000 200 000 – 400 000 400 000 – 600 000 600 000 – 800 000 More than 800 000	 2.0% 30.6% 26.5% 28.6% 12.2%	 5.9% 47.1% 29.4% 5.9% 11.8%	 0.343 	 34.0% 34.0% 17.0% 15.1%	 26.7% 13.3% 46.7% 13.3%	 0.098

In the prostate cancer group, the non-respondents in the WebChoice group tended to be older, have less education and lower household income than the respondents. In the control group, the non-respondents were statistically significantly younger, and they tend to have more education and higher household income. The latter difference was close to statistically significant. There were only small differences in dropout between the WebChoice group and the control group.

Time since diagnosis

The results of a comparison for the variable time since diagnosis between the WebChoice group and control group according to cancer group within the 234 patients who answered all three times, are presented in the table below (table 6).

Table 6: The distribution of time since diagnosis at inclusion to the trial, according to cancer type and type of intervention.

	Breast cancer (n =130)		**Prostate cancer (n = 104)**	
	WebChoice (n=55)	Control (n=75)	WebChoice (n=49)	Control (n=55)
0-6 months	9.1%	6.8%	10.9%	5.7%
7-12 months	7.3%	13.5%	13.0%	24.5%
13-18 monts	32.7%	43.2%	21.7%	18.9%
19 + months	50.9%	36.5%	54.3%	50.9%
p-value	0.285		0.445	

For both disease groups the tendency was that the WebChoice group had a few more patients with more recent diagnosis, but the difference was not statistically significant.

The result of a comparison for a second variable of time since diagnosis between the WebChoice and control group according to type of cancer is given in the table below (table7).

Table 7: The distribution of time since diagnosis at inclusion into the trial, according to cancer type and type of intervention.

	Breast cancer (n=130)		**Prostate cancer (n=104)**	
	WebChoice (n=55)	Control (n=75)	WebChoice (n=49)	Control (n=55)
New: 0-6 months	9.1%	6.8%	10.9%	5.7%
Old: 7+ months	90.9%	93.2%	89.1%	94.3%
p-value	0.624		0.343	

Within both disease groups, a tendency was that the WebChoice group had a higher percentage of patients with the recent diagnosis. There were no statistically significant differences between the WebChoice group and control group.

3.2 Health related quality of life

3.2.1 Analyses of the eight relevant 15D dimensions.

The results for the eight relevant 15D dimensions will be presented in the tables below. The first tables (A tables) will present the distribution of the responses to the eight questions for all cancer patients in the WebChoice and the control group. In the next two tables (B tables and C tables) the 15D scores are presented for each of the cancer types. Number of "stars" (*) marks missing values: *) One missing value, **) Two missing values, ***) Three or more missing values.

Table 8A: 15D scores for the fifth dimension (sleep) for all patients (n=234).

Sleeping						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months*	Baseline	6 months*	12 months
Valid responses	104	104	103	130	129	130
1.Sleeping normally	28.8%	24.0%	30.1%	25.4%	30.2%	33.8%
2.Slight problems sleeping	45.2%	46.2%	39.8%	51.5%	39.5%	38.5%
3.Moderate problems sleeping	13.5%	21.2%	20.4%	15.4%	20.9%	18.5%
4.Great problems sleeping	12.5%	8.7%	9.7%	7.7%	8.5%	9.2%
5.Suffer severe sleeplessness	0.0%	0.0%	0.0%	0.0%	0.8%	0.0%
Chi-square test (*p*)	0.524	0.698	0.940			

Table 8B: 15D scores for the fifth dimension (sleep) for breast cancer patients (n=130).

Sleeping						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months*	Baseline	6 months	12 months
Valid responses	55	55	54	75	75	75
1.Sleeping normally	23.6%	23.6%	27.8%	25.3%	28.0%	32.0%
2.Slight problems sleeping	45.5%	43.6%	38.9%	49.3%	40.0%	40.0%
3.Moderate problems sleeping	16.4%	21.8%	20.4%	14.7%	20.0%	17.3%
4.Great problems sleeping	14.5%	10.9%	13.0%	10.7%	10.7%	10.7%
5.Suffer severe sleeplessness	0.0%	0.0%	0.0%	0.0%	1.3%	0.0%
Chi-square test (*p*)	0.900	0.891	0.920			

Table 8C:15D scores for the fifth dimension (sleep) for prostate cancer patients (n=104)

Sleep						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months
Valid responses	49	49	49	55	54	55
1.Sleep normally	34.7%	24.5%	32.7%	25.5%	33.3%	36.4%
2.Slight problems sleeping	44.9%	49.0%	40.8%	54.5%	38.9%	36.4%
3.Moderate problems sleeping	10.2%	20.4%	20.4%	16.4%	22.2%	20.0%
4.Great problems sleeping	10.2%	6.1%	6.1%	3.6%	5.6%	7.3%
5.Suffer severe sleeplessness	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.306	0.719	0.962			

For the dimension sleep, there was little difference between the WebChoice groups and the control groups (Tables 8A to C), and the differences were not statistically significant.

Table 9A: 15D scores for the sixth dimension (eat) for all patients (n=234).

Eating						
	WebChoice (n=104)			Control (n=130)		
	Baseline*	6months**	12 months**	Baseline	6 months	12months
Valid responses	103	102	102	130	130	130
1. Eat normally	99.0%	98.1%	98.0%	100.0%	100.0%	100.0%
2. Eat with minor difficulty	1.0%	1.9%	2.0%	0.0%	0.0%	0.0%
3. Eat with some help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. Unable to eat by myself	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Unable to eat at all	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.263	0.112	0.109			

Table 9B: 15D scores for the sixth dimension (eat) for breast cancer patients (n=130).

Eating						
	WebChoice (n=55)			Control (n=75)		
	Baseline*	6 months	12 months*	Baseline	6 months	12 months
Valid responses	54	55	54	75	75	75
1. Eat normally	98.2%	96.4%	98.1%	100.0%	100.0%	100.0%
2. Eat with minor difficulty	1.8%	3.6%	1.9%	0.0%	0.0%	0.0%
3. Eat with some help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. Unable to eat by myself	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Unable to eat at all	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.241	0.096	0.237			

Table 9C: 15D scores for the sixth dimension (eat) for prostate cancer patients (n=104).

Eating						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6months	12 months*	Baseline	6 months	12months
Valid responses	49	49	48	55	55	55
1. Eat normally	100.0%	100.0%	97.9%	100.0%	100.0%	100.0%
2. Eat with minor difficulty	0.0%	0.0%	2.1%	0.0%	0.0%	0.0%
3. Eat with some help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. Unable to eat by myself	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Unable to eat at all	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	Equal	equal	0.282			

For the dimension eating, there were some differences between the WebChoice groups and the control groups, in that the WebChoice groups for both cancer groups had a higher level of worse conditions (tables 9 A, B and C). However, the differences were not statistically significant.

Table 10A: 15D scores for the eighth dimension (elimination) for all patients (n=234)

Elimination						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months*	Baseline*	6 months*	12 months
Valid responses	104	104	103	129	129	130
1.Bladder/bowel work normally	51.9%	50.0%	49.5%	51.9%	64.3%	53.8%
2.Slight problems with bladder/bowel	41.3%	41.3%	42.7%	46.5%	31.0%	43.8%
3.Marked problems with bladder/bowel	4.8%	5.8%	5.8%	1.6%	2.3%	0.8%
4.Serious problems with bladder/bowel	1.0%	1.0%	1.0%	0.0%	.8%	0.8%
5.No control over bladder/bowel	1.0%	1.9%	1.0%	0.0%	1.6%	0.8%
Chi-square test (*p*)	0.302	0.230	0.270			

Table 10B: 15D scores for the eighth dimension (elimination) for breast cancer patients (n=130)

Elimination						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months*	Baseline*	6 months	12 months
Valid responses	55	55	54	74	75	75
1.Bladder/bowel work normally	67.3%	67.3%	68.5%	62.2%	76.0%	69.3%
2.Slight problems with bladder/bowel	30.9%	27.3%	31.5%	37.8%	24.0%	30.7%
3.Marked problems with bladder/bowel	1.8%	5.5%	0.0%	0.0%	0.0%	0.0%
4.Serious problems with bladder/bowel	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5.No control over bladder/bowel	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.385	0.102	0.921			

Table 10C: 15D scores for the eighth dimension (elimination) for prostate cancer patients (n=104)

Elimination						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months
Valid responses	49	49	49	55	54	55
1.Bladder/bowel works normally	34.7%	30.6%	28.6%	38.2%	48.1%	32.7%
2.Slight problems with bladder/bowel	53.1%	57.1%	55.1%	58.2%	40.7%	61.8%
3.Marked problems with bladder/bowel	8.2%	6.1%	12.2%	3.6%	5.6%	1.8%
4.Serious problems with bladder/bowel	2.0%	2.0%	2.0%	0.0%	1.9%	1.8%
5.No control over bladder/bowel	2.0%	4.1%	2.0%	0.0%	3.7%	1.8%
Chi-square test (*p*)	0.497	0.488	0.337			

For the dimension elimination, there were some differences between the WebChoice groups and the control groups, in that the WebChoice groups had a greater proportion of patients in the worse conditions than the control groups. The differences were not statistically significant (tables 10 A, B and C).

Table 11A: 15D scores for the tenth dimension (mental function) for all patients (n=234)

Mental function						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months*
Valid responses	104	104	104	130	129	129
1.Think clearly and logically	70.2%	62.5%	62.5%	76.9%	72.1%	68.2%
2.Slight difficulties thinking clearly and logically	28.8%	34.6%	35.6%	23.1%	27.1%	30.2%
3.Marked difficulties thinking clearly and logically	1.0%	2.9%	1.0%	0.0%	.8%	1.6%
4.Great difficulties thinking clearly and logically	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%
5. Permanently confused and disoriented	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.308	0.189	0.535			

Table 11B: 15D scores for the tenth dimension (mental function) for breast cancer patients (n=130).

Mental function						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months
Valid responses	55	55	55	75	74	75
1.Think clearly and logically	60.0%	49.1%	54.5%	70.7%	64.9%	66.7%
2.Slight difficulties thinking clearly and logically	38.2%	45.5%	43.6%	29.3%	33.8%	30.7%
3.Marked difficulties thinking clearly and logically	1.8%	5.5%	0.0%	0.0%	1.4%	2.7%
4.Great difficulties thinking clearly and logically	0.0%	0.0%	1.8%	0.0%	0.0%	0.0%
5. Permanently confused and disoriented	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.264	0.124	0.167			

Table 11C: 15D scores for the tenth dimension (mental function) for prostate cancer patients (n=104).

Mental function						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months	12 months*
Valid responses	49	49	49	55	55	54
1.Think clearly and logically	81.6%	77.6%	71.4%	85.5%	81.8%	70.4%
2.Slight difficulties thinking clearly and logically	18.4%	22.4%	26.5%	14.5%	18.2%	29.6%
3.Marked difficulties thinking clearly and logically	0.0%	0.0%	2.0%	0.0%	0.0%	0.0%
4.Great difficulties thinking clearly and logically	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Permanently confused and disoriented	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.599	0.588	0.551			

For the dimension mental function, there were some differences between the WebChoice groups and the control groups, in that the WebChoice groups had a greater proportion of patients in the worse conditions than the control groups (tables 11 A, B and C). The difference was most present in the breast cancer group. The differences were not statistically significant.

Table 12A: 15D scores for the eleventh dimension (discomfort and symptoms) for all patients (n=234).

Discomfort and symptoms						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months*
Valid responses	104	104	104	130	129	129
1.No physical discomfort or symptoms	46.2%	43.3%	51.9%	41.5%	48.1%	46.5%
2.Mild physical discomfort or symptoms	43.3%	45.2%	35.6%	50.8%	42.6%	38.0%
3.Marked physical discomfort or symptoms	10.6%	9.6%	8.7%	7.7%	8.5%	14.7%
4.Severe physical discomfort or symptoms	0.0%	1.0%	3.8%	0.0%	0.0%	0.8%
5.Unbearable physical discomfort or symptoms	0.0%	0.0%	0.0%	0.0%	0.8%	0.0%
Chi-square test (*p*)	0.472	0.788	0.192			

Table 12B: 15D scores for the eleventh dimension (discomfort and symptoms) for breast cancer patients (n=130).

Discomfort and symptoms						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months*
Valid responses	55	55	55	75	74	74
1.No physical discomfort or symptoms	40.0%	40.0%	43.6%	33.3%	48.6%	41.9%
2.Mild physical discomfort or symptoms	45.5%	41.8%	38.2%	56.0%	39.2%	41.9%
3. .Marked physical discomfort or symptoms	14.5%	14.5%	12.7%	10.7%	10.8%	14.9%
4.Severe physical discomfort or symptoms	0.0%	1.8%	5.5%	0.0%	0.0%	1.4%
5.Unbearable physical discomfort or symptoms	0.0%	1.8%	0.0%	0.0%	1.4%	0.0%
Chi-square test (*p*)	0.481	0.676	0.584			

Table 12C: 15D scores for the eleventh dimension (discomfort and symptoms) for prostate cancer patients (n=104).

Discomfort and symptoms						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	49	49	55	55	55
1.No physical discomfort or symptoms	53.1%	46.9%	61.2%	52.7%	47.3%	52.7%
2.Mild physical discomfort or symptoms	40.8%	49.0%	32.7%	43.6%	47.3%	32.7%
3. Marked physical discomfort or symptoms	6.1%	4.1%	4.1%	3.6%	5.5%	14.5%
4.Severe physical discomfort or symptoms.	0.0%	0.0%	2.0%	0.0%	0.0%	0.0%
5.Unbearable physical discomfort or symptoms	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.826	0.943	0.221			

For the dimension discomfort and symptoms, there was almost no difference between the WebChoice and the control groups (tables 12 A, B and C). A tendency was that the WebChoice groups scored slightly higher at the best condition. This was especially present for the prostate cancer group. There were no statistically significant differences.

Table 13A: 15D scores for the thirteenth dimension (distress) for all patients (n=234).

Distress						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months*
Valid responses	104	104	104	130	129	129
1. Not at all anxious	44.2%	44.2%	46.2%	49.2%	48.1%	51.2%
2. Slightly anxious	46.2%	47.1%	42.3%	42.3%	41.9%	40.3%
3. Moderately anxious	7.7%	6.7%	11.5%	8.5%	7.8%	6.2%
4. Very anxious	1.9%	1.9%	0.0%	0.0%	2.3%	2.3%
5. Extremely anxious	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.385	0.881	0.197			

Table 13B: 15D scores for the thirteenth dimension (distress) for breast cancer patients (n=130).

Distress						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months	Baseline	6 months*	12 months*
Valid responses	55	55	55	75	74	74
1. Not at all anxious	36.4%	32.7%	40.0%	48.0%	40.5%	50.0%
2. Slightly anxious	52.7%	56.4%	50.9%	45.3%	47.3%	43.2%
3. Moderately anxious	7.3%	9.1%	9.1%	6.7%	8.1%	5.4%
4. Very anxious	3.6%	1.8%	0.0%	0.0%	4.1%	1.4%
5. Extremely anxious	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.251	0.666	0.485			

Table 13C: 15D scores for the thirteenth dimension (distress) for prostate cancer patients (n=104).

Distress						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	49	49	55	55	55
1. Not at all anxious	53.1%	57.1%	53.1%	50.9%	58.2%	52.7%
2. Slightly anxious	38.8%	36.7%	32.7%	38.2%	34.5%	36.4%
3. Moderately anxious	8.2%	4.1%	14.3%	10.9%	7.3%	7.3%
4. Very anxious	0.0%	2.0%	0.0%	0.0%	0.0%	3.6%
5. Extremely anxious	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.892	0.655	0.378			

For the dimension distress, there were no statistically significant differences between the two groups (tables 13 A, B and C).

Table 14A: 15D score for the fourteenth dimension (vitality) for all patients (n=234).

Vitality						
	WebChoice (n=104)			Control (n=130)		
	Baseline	6 months	12 months*	Baseline*	6 months	12 months*
Valid responses	104	104	103	129	130	129
1. Healthy and energetic	30.8%	29.8%	25.2%	31.8%	35.4%	36.4%
2. Slightly weary	51.9%	40.4%	53.4%	52.7%	47.7%	45.0%
3. Moderately weary	11.5%	20.2%	9.7%	15.5%	11.5%	16.3%
4. Very weary	5.8%	8.7%	11.7%	0.0%	5.4%	2.3%
5. Extremely weary	0.0%	1.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.043	0.184	0.005			

Table 14B: 15D scores for the fourteenth dimension (vitality) for breast cancer patients (n=130).

Vitality						
	WebChoice (n=55)			Control (n=75)		
	Baseline	6 months	12 months*	Baseline*	6 months	12months*
Valid responses	55	55	54	74	75	74
1. Healthy and energetic	23.6%	23.6%	27.8%	29.7%	41.3%	44.6%
2. Slightly weary	49.1%	34.5%	44.4%	54.1%	42.7%	40.5%
3. Moderately weary	16.4%	27.3%	7.4%	16.2%	8.0%	12.2%
4. Very weary	10.9%	12.7%	20.4%	0.0%	8.0%	2.7%
5. Extremely weary	0.0%	1.8%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.034	0.012	0.005			

Table 14C: 15D scores for the fourteenth dimension (vitality) for prostate cancer patients (n=104).

Vitality						
	WebChoice (n=49)			Control (n=55)		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	49	49	55	55	55
1. Healthy and energetic	38.8%	36.7%	22.4%	34.5%	27.3%	25.5%
2. Slightly weary	55.1%	46.9%	63.3%	50.9%	54.5%	50.9%
3. Moderately weary	6.1%	12.2%	12.2%	14.5%	16.4%	21.8%
4. Very weary	0.0%	4.1%	2.0%	0.0%	1.8%	1.8%
5. Extremely weary	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.377	0.617	0.537			

For the dimension vitality, there were some differences between the WebChoice groups and the control groups, in that the WebChoice groups had a greater proportion of patients in the worse conditions than the control groups (tables 14 A, B and C). This difference was statistically significant for the breast cancer group, but not for the prostate cancer group.

Table 15A: 15D scores for the fifteenth dimension (sexual activity) for all patients (n=234).

Sexual activity						
	WebChoice (n=104)			Control (n=130)		
	Baseline***	6 months*	12 months***	Baseline*	6 months**	12 months
Valid responses	101	103	99	129	128	130
1. Health has no adverse effect on	16.8%	14.6%	11.1%	15.5%	18.0%	19.2%
2. Health has slight effect on	24.8%	19.4%	23.2%	37.2%	31.2%	26.2%
3. Health has considerable effect on	28.7%	33.0%	27.3%	27.1%	23.4%	25.4%
4. Health makes sex almost impossible	9.9%	7.8%	11.1%	5.4%	7.0%	9.2%
5. Health makes sex impossible	19.8%	25.2%	27.3%	14.7%	20.3%	20.0%
Chi-square test (*p*)	0.260	0.197	0.392			

Table 15B: 15D scores for the fifteenth dimension (sexual activity) for breast cancer patients (n=130).

Sexual activity						
	WebChoice (n=55)			Control (n=75)		
	Baseline**	6 months	12 months***	Baseline*	6 months	12 months
Valid responses	53	55	52	74	75	75
1. Health has no adverse effect on	30.2%	25.5%	21.2%	23.0%	29.3%	33.3%
2. Health has slight effect on	37.7%	36.4%	44.2%	51.4%	45.3%	42.7%
3. Health has considerable effect on	24.5%	32.7%	26.9%	25.7%	24.0%	21.3%
4. Health makes sex almost impossible	5.7%	1.8%	3.8%	0.0%	1.3%	1.3%
5. Health makes sex impossible	1.9%	3.6%	3.8%	0.0%	0.0%	1.3%
Chi-square test (*p*)	0.113	0.350	0.452			

Table 15C: 15D scores for the fifteenth dimension (sexual activity) for prostate cancer patients (n=104).

Sexual activity						
	WebChoice (n=49)			Control (n=55)		
	Baseline*	6 months*	12 months**	Baseline	6 months**	12 months
Valid responses	48	48	47	55	53	55
1. Health has no adverse effect on	2.1%	2.1%	0.0%	5.5%	1.9%	0.0%
2. Health has slight effect on	10.4%	0.0%	0.0%	18.2%	11.3%	3.6%
3. Health has considerable effect on	33.3%	33.3%	27.7%	29.1%	22.6%	30.9%
4. Health makes sex almost impossible	14.6%	14.6%	19.1%	12.7%	15.1%	20.0%
5. Health makes sex impossible	39.6%	50.0%	53.2%	34.5%	49.1%	45.5%
Chi-square test (*p*)	0.699	0.166	0.548			

For the dimension sexual activity, there were some differences between the WebChoice groups and the control groups, in that the WebChoice groups had a greater proportion of patients in the worse conditions than the control groups (tables 15 A, B and C).The differences were not statistically significant.

Summary of the eight relevant dimensions

There was a tendency that the control group had a slightly higher quality of life than the WebChoice group for both cancer groups, but the difference was significant only for the fourteenth dimension, vitality (Tables 8A – 15C). The significantly different result is both present in the comparison of all patients and in the comparison within the breast cancer group.

3.2.2 Analysis of the 15D index

In the table below (table 16A), the mean index for each group of patients and each group of intervention is presented.

Table 16 A: Mean (SD) 15D scores at 0, 6 and 12 months according to cancer type and intervention type (n = 234)

	Breast (n=130)		*p-value*	Prostate (n=104)		*p-value*
Months follow-up	WebChoice (n=55)	Control (n=75)		WebChoice (n=49)	Control (n=55)	
Baseline	0.85 (0.09)	0.88 (0.07)	0.059	0.87 (0.08)	0.87 (0.08)	0.882
6 months	0.84 (0.10)	0.88 (0.10)	0.032	0.85 (0.08)	0.86 (0.08)	0.864
12 months	0.85 (0.10)	0.88 (0.09)	0.131	0.84 (0.10)	0.84 (0.10)	0.801

For the breast cancer group, the 15D index was slightly lower in the WebChoice group than in the control group at baseline, 6 months and 12 months, but the difference was statistically significant only at 6 months. For the prostate cancer group there was no difference at any point in time.

A comparison of respondents and non-respondents according to 15D summary scores at baseline is given in the table below (table 16B).

Table 16 B: Mean (SD) 15D-scores at baseline for patients who responded to the 15D-questionnaire all three times (n=234) and those who answered less than three times (n=91)

	Breast (n=189)			Prostate (n=136)		
	Answered all (n=130)	Not answered all (n=59)	*p-value*	Answered all (n=104)	Not answered all (n=32)	*p-value*
Baseline	0.87	0.84	0.043	0.87	0.85	0.104

The breast cancer patients who answered less than three times had a statistically significant lower 15D-score at baseline. The same difference is a tendency for the prostate cancer patients.

Time since diagnosis

In the table below (table 17), the mean index for each group of patients and each group of intervention according to the second variable of time of diagnosis, are presented.

Table 17: Mean (SD) 15D scores at 0, 6 and 12 months according to cancer type, intervention type and time since diagnosis

Months follow-up	Breast cancer				Prostate cancer			
	WebChoice (n=55)		Control* (n=74)		WebChoice*** (n= 46)		Control** (n=53)	
	New (n=5)	Old (n=50)	New (n=5)	Old (n=69)	New (n=5)	Old (n=41)	New (n=3)	Old (n=50)
Baseline	.87 (.06)	.85 (.10)	.87 (.08)	.88 (.07)	.85 (.11)	.87 (.08)	.92 (.03)	.87 (.08)
6 months	.85 (.09)	.84 (.10)	.90 (.11)	.87 (.09)	.85 (.11)	.85 (.08)	.92 (.07)	.85 (.08)
12months	.90 (.05)	.85 (.10)	.88 (.14)	.88 (.09)	.81 (.06)	.84 (.10)	.85 (.12)	.83 (.09)

When "new" and "old" breast cancer WebChoice groups are compared, there were some differences between the two groups in that the "new" WebChoice group had higher 15D score than the "old". The opposite was present for the prostate cancer patients within the WebChoice groups. When comparing WebChoice and control groups, the WebChoice breast cancer patients with a recent diagnosis had a better score than those in the control group at 12 months. At 6 months, the difference was opposite in the same patient group. The opposite was present for the prostate cancer patients within the WebChoice groups compared to the control group.

Variables impact on the 15D index score

The table below (table 18) shows the effect of independent variables on 15D summary score at 12 months. Type of intervention (WebChoice versus control) and baseline 15D summary score were entered as independent variables.

Table 18: Linear regression analysis of the 15D score at 12 months

	Unstandardised Coefficients B	*p-value*
Constant	0.170	0.001
Intervention group	0.000	0.932
15Dscore at baseline	0.789	0.000

Type of intervention group had almost no impact on the 15D-score at 12 months, and it was not significant. The 15D score at baseline had much effect of the outcome of the 15D score at 12 months, and it was statistically significant.

In an additional linear regression analysis of the 15D summary score at 12 months, time since diagnosis was added as independent variable (table 19).

Table 19: Linear regression analysis of 15D summary score at 12 months

	Unstandardised Coefficients B	*p-value*
Constant	0.169	0.001
Intervention group	0.001	0.921
15Dscore at baseline	0.779	0.000
0-6 months	0.013	0.492
7-12 months	0.021	0.147
13-18 months	0.014	0.196
19+ months (reference)	0	

Time since diagnosis had no impact on the 15D summary score. The 15D summary score at baseline was the only variable which was statistically significant, and implicitly affected the dependent variable.

3.2.3 QALYs

For each patient, the one year of QALYs was calculated using linear interpolation combined with regression-based adjustment, which adjusts for baseline differences. In linear regression of one year QALY, baseline 15D score and type of intervention were used as explanatory variables (table 20) (Manca, 2005). QALY was the dependent variable.

Table 20: Linear regression of one year QALYs

	Unstandardised Coefficients B	*p-value*
Constant	0.131	0.000
Intervention group (WebChoice = 1, control = 0)	-0.004	0.478
Patient group (prostate cancer =1, breast cancer = 0)	-0.013	0.035
15D score at baseline	0.848	0.000

There was a very small and negative impact of WebChoice on the one year QALY value (table 20).

QALYs gained for the WebChoice group according to cancer groups is presented in the table below (table 21). The difference of one year QALYs were analysed with t-test for each disease type separately.

Table 21: The mean QALYs adjusted for baseline differences, for each cancer group according to type of intervention, and QALYs gained for the WebChoice group.

	Breast cancer			Prostate cancer		
	WebChoice (n=55)	Control (n=75)	*p- value*	WebChoice (n= 49)	Control (n=55)	*p- value*
QALY	0.8490	0.8767	0.028	0.8775	0.8834	0.650
QALYs gained	- 0.028			- 0.006		

The difference in QALYs was statistically significant for the breast cancer group, with a negative gain of QALYs (in the WebChoice group). There was no difference within the prostate cancer group.

QALYs gained for the WebChoice group for both cancer groups is presented in the table below (table 22).

Table 22: The mean QALYs adjusted for baseline differences for both cancer group according to type of intervention, and QALYs gained for the WebChoice group.

	Both cancer groups		
	WebChoice	Control	*p- value*
QALY	0.8624	0.8795	0.060
QALYs gained	- 0.017		

The difference between the WebChoice group and control group in QALYs was not statistically significant.

Variables' impact on QALYs

Finally, the one year 15D summary scores were analysed as dependent variable in a linear regression, where intervention group, patient group, 15D score at baseline, age and time since diagnosis were independent variables (table 23). The variables' impact on QALYs are tested in the table below.

Table 23: The variables intervention group, patient group, 15D score at baseline, age and time since diagnosis impact on QALYs.

	Unstandardised Coefficients B	*p-value*
Constant	0.134	0.000
Intervention group (WC=1, C=0)	-0.004	0.540
Patient group (PC=1, BC=0)	-0.016	0.059
15Dscore at baseline	0.837	0.000
Age	0.00	0.810
0-6 months	0.012	0.289
7-12 months	0.010	0.264
13-18 months	- 0.001	0.876
19+ months (reference)	0	

The one year QALY was slightly lower in the prostate cancer group, while age and time since diagnosis had no impact. 15D score at baseline was the only variable which was statistically significant.

4. Discussion

The results in the previous section seem to indicate that WebChoice has very little, if any, impact on HRQOL for cancer patients. However, such a conclusion does not take the strengths and weaknesses of this study into consideration. This section is first and foremost a discussion of core aspects of internal and external validity: Are there any systematic errors in the study that have influenced the results (internal validity), and can the results be applied to the population (external validity) (Thelle, 2002)?

4.1 Strenghts

The research team applied a well tested method and measurement index to gain knowledge about the effects of WebChoice. When choosing a randomised controlled trial to investigate the effect, the study both gained control of cause and effect and a low risk of selection bias since patients are assigned to type of intervention by chance. Other types of study designs would not have given the same degree of control (see section *1.6 Epidemiology and study design*). As in all surveys the problem of bias is still inherent, an aspect which is discussed later under representativeness.

15D is a sensitive instrument which measures several relevant aspects that affect the HRQOL for a person. The use of this instrument gives a good and valid measurement of the patients' health conditions. The algorithm for the index is validated both in Finland and in Denmark, and these countries have approximately the same population composition as Norway according to age, health level and so on. This indicates that it should be valid to employ the 15D index on Norwegian patients.

Randomisation

The randomisation of the patients in general was good. Differences in demographics were small, but there was a specific problem for the breast cancer group at baseline: The WebChoice group had lower HRQOL than the control group. This could imply that the randomisation process was unsuccessful. The baseline problem has been compensated for in the final analysis.

The variable time since diagnosis was almost equally distributed, but a trend was that the WebChoice group consisted of a few more patients with more recent diagnoses, though it

was not significant. A regression analysis showed that this variable had little or no effect on the HRQOL after twelve months. Hence, the difference had little impact on the study since more than 80 percent of the participants have had the diagnosis for more than one year.

4.2 Weaknesses

4.2.1 Characteristics

What characterises the respondents? This is both a question relevant for evaluating representativeness and to determine whether or not there are some special characteristics of the sample which makes the results not valid for patients with other characteristics (for different types of bias – see section *1.6 Epidemiology and study design*). The latter is the concern of this section, and representativeness will be discussed later.

Socio-economic charateristics

The respondents who answered all three times had the following characteristics that can be compared with statistics on the Norwegian population in general.

The respondents were well educated: Approximately 60 percent (breast) and 70/50 percent (prostate intervention/control group) of the respondents had a college degree or more (table 4). In 2007, 25 percent of the Norwegian population had a college degree or more (*Utdanningsnivå i befolkningen*, 2009). This must of course be adjusted for age, but the result is quite the same: 27 percent of the Norwegian population above 30 years had a college degree or more in 2007.

The respondents had medium to high income: Approximately 70 percent of the respondents had a household income of 400 000 NOK or more (table 4). In 2007, the median household income in Norway was 366 000 NOK (*Inntekt*, 2009).

Education and income are indicators of skills concerning gathering and coping with complex information, so the characteristics could indicate high levels of skills in the sample. This is relevant since WebChoice is a tool for providing patients with information on their own disease. The special characteristic of the respondents implies that results in this study do not necessarily apply to patients with little or no education and/or low income.

Time since diagnosis

The recruitment problems led the research team to omit one important inclusion criterion first stated in the protocol: Time since diagnosis must be within the last 12 months. The consequence of omitting this criterion was a quite different sample than originally planned:

More than 70 percent of the participants who joined have had the diagnosis for *more* than one year (table 6).

Since cancer patients are in a situation with a high information need and are often intensively seeking information, it is relevant that most of the participants were well experienced with their own disease (Luker et al., 1995). Most of the respondents had received the diagnosis for more than twelve months ago, which probably gave them time to gain extensive information. Most likely, there is a difference between being unfamiliar and inexperienced with the disease and its consequences, and being a patient who has had time to get information and experience. To put inexperienced and experienced patients in the same trial without the necessary numbers to make sub-analyses, is to mix two groups that could be incomparable. The consequence is that this study primarily concerns patients with experience and therefore with knowledge on their own disease, and hence the results cannot necessarily be applied to patients with a recent diagnosis.

Health

The respondents had a 15D-score at baseline of approximately 0.85 (table 16 B). Could it be that the respondents only to a limited extent suffered from burdens of the disease? The 15D score implies that many respondents had set their health states at level 1 or 2 for many of the dimensions, at baseline. A control analysis shows that the average level for almost all of the dimensions is between 1 and 2 (see Appendix). The first two levels in each dimension are typically described as "no problems" or "minor problems". From this, it is possible to assume that the patients only to a limited extend suffered from the problems related to the disease. WebChoice addresses problems for many different health states and problems, so the results are not necessarily valid for patients who suffer severe problems from the disease.

4.2.2 Representativeness

Do the respondents differ from the population of breast- and prostate cancer patients in Norway? Internal validity of this study is threatened by various types of selection bias and few participants. The problem with selection bias and few participants is that the sample may not represent the population it was supposed to represent and therefore have a weakened external validity.

The characteristics of the sample should be compared with the population (breast cancer and prostate cancer patients) to determine representativeness. A full scale comparison of the characteristics requires an extensive gathering and adapting of statistical findings of

others, which would be beyond the scope of this thesis. However, the following considerations concerning representativeness of the characteristics can still be made:

When it comes to age, the respondents are middle aged: approximate mean ages are 50 years and 65 years (breast/prostate). As outlined in section 1, these cancer types typically strikes at middle age, so the sample appears to be representative in this aspect. However, it could be that the respondents had an overrepresentation of "younger" patients.

The representativeness of the patients' education and income is difficult to measure. I have no directly comparable data on educational and income levels for prostate cancer and breast cancer patients, but high levels of education increases the risk of both prostate cancer and breast cancer (*Kreft*, 2009 and Green et al., 2005). This implies that persons with education above the national average could be overrepresented for both cancer types. The overrepresentation of persons with high education in the sample indicates that the sample probably is representative for the population under study.

I have not been able to find any average on time since diagnosis for breast cancer and prostate cancer patients under treatment, so the representativeness of the sample concerning this aspect cannot be exactly measured. However, the survival rate is high (over 80 percent) after five years since diagnosis for both cancer types (*Prostatakreft*, 2009 and Småstuen et al., 2008). This could indicate that many prostate cancer and breast cancer patients have had their diagnosis for an extended period of time. Hence, the overweight of respondents with old diagnosis does not necessarily lower the representativeness of the sample.

To my knowledge, there is little data on the average HRQOL score for breast cancer and prostate cancer patients in Norway. A comparison of the health of the respondents in sample and the population is therefore not possible.

Recruitment

The research team was unable to collect the pre-planned and desired number of participants. While this should be kept in mind when dealing with the results, the number of respondents is still high enough for a valid analysis. Unfortunately, it is not high enough for sub-analyses.

The respondents joined through advertisements, and the recruitment process could have impact on the representativeness of the group. Self-recruitment tends to favour those who have a special interest in the subject (Chambelis & Schutt, 2006). This is a common problem for many surveys. The self-recruitment could in itself have lead to a selection bias, because certain types of persons could be more eager to join the study than others. The

recruitment problems led the research team to repeat the same recruitment procedure several times, and this may have led to an increased number of "special-interest" respondents (Chambelis & Schutt 2006).

Another aspect of self-recruitment of patients is the risk of recruiting only those with relatively good health. Cancer patients have a potentially life threatening disease, and not all have the mental and/or physical energy needed to join a survey. Self-recruitment requires initiative from the patient, and those with bad health could be less likely to join. Experienced patients may also find it easier to participate in a survey, since they probably have had time to deal with some of the mental trauma of the diagnosis.

It should also be mentioned that Internet access was an inclusion criterion that could have excluded some patients from joining the survey. In Norway, 84 percent of all households had Internet access in 2008 (*IKT i husholdningene*, 2008). Since some of the population in Norway does not have access to Internet, the inclusion criterion could lead to a selection bias. Patients with Internet access, but other operative systems than Microsoft Windows, were also excluded, which could have created another selection bias. However, it is hard to see how this could have had any impact on the results.

Dropout

Dropout was a problem during the trial period. Especially during the period from 0 to 6 months, the number of patients who dropped out was relatively high (figure 5). A problem with high dropout rates is selection bias. In addition, the matter that patients were not obliged to reveal the reason why they dropped out, could make it harder to detect a possible selection bias.

27 percent of the respondents dropped out from inclusion to baseline. It could be a number of reasons for this dropout, but there is no data on the 120 respondents who chose to leave the study. However, there is data on the dropouts of the next two rounds, and it is likely that the same mechanisms took place all three times.

In total, 234 of 445 patients filled out the 15D questionnaire all three times. This gives an answer rate of 53 percent and a dropout rate of 47 percent. This is a high dropout rate, but it is as expected by the research team who predicted an attrition rate of 50 percent (Chambelis & Schutt, 2006). The patients who dropped out had a lower HRQOL score at baseline than the ones who answered the questionnaire all three times (table 16B). This difference was statistically significant for the breast cancer patients and a tendency for the

prostate cancer patients. This indicates that the dropout lead to an overrepresentation of patients with higher HRQOL scores.

Socio-economic differences between respondents and dropouts must also be examined. In the breast cancer group (table 5A), differences in age, education and income points in different directions. In the breast cancer WebChoice group, the non-respondents were statistically significantly younger than the respondents. This was only a tendency in the control group. When it comes to income, it is somewhat unclear. In both groups, the non-respondents were less represented with medium/high income, but on the other hand, more of them had high income. Education level was equally distributed between respondents and non-respondents in the WebChoice breast cancer group. This is not the case in the control group, where the non-respondents tended to be more educated. The socio-economic variables do not reveal a clear pattern of systematic differences with impact on the representativeness, or which can explain the dropout.

The picture of the non-respondents is equally unclear in the prostate cancer group (table 5B). The non-respondents in the WebChoice group tended to be older, they had less education and they had lower household income than the respondents. In the control group, the non-respondents were statistically significantly younger, and they tended to have more education and higher household income. The latter difference was close to statistically significant. Socio-economic differences are opposite between non-respondents in the WebChoice and in the control group. Why well educated and high income individuals drop out of the control group remains unanswered, but a plausible explanation on WebChoice non-respondents is that they find the web tool challenging due to their higher age and less extensive education.

To sum up, health seems to be the only systematic difference between the non-respondents and the respondents. A more difficult health situation may be the dropout reason for many of the participants. To fill out a questionnaire during the cancer could have been difficult, and to both fill out questionnaires and use a new web-tool, was perhaps simply too much. This corresponds with a higher dropout rate in the WebChoice group than in the control group for breast cancer patients. Socio-economic differences are not coherent when it comes to dropout and should be used with caution to explain the dropout or to lower the representativeness.

Concluding on representativeness

As outlined above, the recruitment process could have led to respondents who have extensive knowledge on own disease and who have "minor" disease related problems. The dropout rate can be considered as high, and it may have led to a further concentration of patients with high HRQOL score. Both of these mechanisms make the sample less representative, but it is difficult to determine to what extent. In all, the sample is representative enough for a valid analysis with some reservations. The results in this study must be used with caution on patients with low HRQOL, as they could be underrepresented.

It is difficult to judge whether or not this sample is representative for similar patients in other countries, but it is likely that an intervention such as WebChoice may be sensitive for cultural factors and differences in health care systems.

4.2.3 Response

Since fewer cancer patients than pre-planned were included in the study (445 versus 1000), the randomised controlled trial was underpowered according to number of participants (234 versus 400). No power calculation was done for 15D, and the trial may have been underpowered for this endpoint. Underpowering may increase the risk of committing an error of type 2: There is a risk of neglecting a real difference between the WebChoice and control group because the number of patients was too low. However, the likelihood of a type-2 error seems small since there was not even a tendency for impact of WebChoice on the number of QALYs.

Missing values made the 15D questionnaires incomplete, and they had to be replaced to calculate the 15D summary indexes. The number of missing values per questionnaire increased with time, and the sexual activity value had the most missing values. This could have an adverse effect on the result for prostate cancer patients, because this variable (together with the elimination variable) is probably the one which is most affected by prostate cancer, and because the functional problems often increase with time.

A problem with replacing missing values is uncertainty. As more values are missing and are replaced, the more uncertain the 15D index becomes, which indicates the health-related quality of life for the patient it concerns. There is a certain probability that the replaced value is not the true one.

4.3 The results

4.3.1 The main result

There was no difference in health-related quality of life between the WebChoice group and the control group, neither in the breast cancer group nor prostate cancer group.

Little or no differences between the intervention and control groups are found when health related quality of life is transformed into QALYs. The intervention had no effect, since the only variable with significant impact on QALY was the 15D score at baseline. Other variables, such as time since diagnosis, cancer type and intervention type had only a minor and non-significant effect on the one-year number of QALYs.

4.3.2 Other results and tendencies

There was no statistically significant difference at twelve months for the 15D index, but there was a tendency that the WebChoice groups had a slightly lower HRQOL than the control groups. Especially the score that derives from the dimension vitality was statistically significant lower for the WebChoice groups.

When split into the different cancer groups, the statistically significant difference only occurred for the breast cancer group, and it was statistically significant at all times. Other dimensions had nearly statistically significant different results, which pointed in the same direction for the breast cancer group. These were the dimensions eating, elimination and mental function. The differences can partly be explained by differences at baseline. The prostate cancer group had no statistically significant different results.

Baseline differences were adjusted when calculating QALYs, but the results remained the same. The WebChoice breast cancer group had a statistically significant lower QALY than the control group. The difference was small.

4.3.3 Possible explanations

The results of this study do not confirm the main hypothesis, which was that WebChoice improves patients' HRQOL. One possible interpretation of the study is that WebChoice in fact has no effect on cancer patients' HRQOL. A premise for the main hypothesis, however, was that WebChoice provided new and relevant information, so there are several possible explanations as to why no difference was found between the two groups in this trial:

The patients were well experienced: Most of the patients included in the trial had received the diagnosis more than 12 months before inclusion. This could lower the impact of the intervention, because the patients have had an extended period of time to gain much of the knowledge accessible in WebChoice. For this group, the available information could already be known and therefore be "useless". If WebChoice were to be tested on patients with a recent diagnosis, the effect on HRQOL could be positive.

The patients had high competence: As outlined in the discussion on recruitment and dropout, the participants were both well educated and perhaps especially interested. Combined with their experience, the patients are likely to have already gained much of the information accessible in WebChoice, prior to the trial.

The patients were of good health: The HRQOL for the patients was relatively high in general. Perhaps a large amount of the information and advice was not relevant and was intended for patients with more severe side-effects and symptoms. If WebChoice were tested on patients with more severe health problems, it is possible that the effect on HRQOL would be positive.

Other explanations are more speculative. For instance, WebChoice could have both positive and negative effects that nullify each other: More knowledge about the disease could make cancer patients more anxious, because they become aware of what different treatments and what the cancer itself can do to their health. This explanation is unlikely, since there was almost no effect on any of the 15D values when they were analysed separately.

4.4 Findings of others

WebChoice is a new application designed to assist patients in symptom management, while previous network-based computerised home support systems have been more focused on improving self-efficacy. Several surveys concerning Internet-based support for outpatients with cancer or other diseases indicate a positive relationship with patients' well-being and self-efficacy, but few of these surveys actually measure patients' HRQOL.

Internet support provides tailored and accessible information and more remote nursing services (Brennan, 2001). This correlates well with the findings in a previous study: Internet based support for HIV-positive patients improved quality of life, in terms of a more active life and less negative emotions (Gustafson, 1999). The patients were also more efficient in their use of health care services.

Significant improvements in psycho-social quality of life were also found in a survey studying online self-help groups for breast cancer patients (Lieberman & Goldstein, 2005).

Two other studies conclude that access to information improved patients' self-efficacy and gave them more confidence to both ask questions and discuss treatment options with their physicians (Gustafson et al., 2001 and Fleischer, 2002). The patients became more involved in the decision-making process. The benefits were greatest for patients with less income and education (Gustafson et al., 2001).

Gustafson et al. went deeper into the latter aspect in a survey concerning low-income women with breast cancer and the Internet-based eHealth System CHESS in the United States of America (Gustafson et al., 2005). Access to the system improved quality of life.

The findings of Gustafson et al. (2001 and 2005) support the "high competence" explanation for no positive effects in this study of WebChoice. Demographic differences combined with differences in health care system also have an impact on the effect of online support. Free and accessible advice probably makes a statistically significant difference for a low income group with little education, in a high cost health care system. In this study, the situation is opposite: The participants are well educated, with medium to high income in a low-cost health care system.

Patients in three of the mentioned surveys were all inexperienced in their situation, either with a new diagnosis or on recovery from an operation (Gustafsson et al., 2001, Fleischer, 2002 and Brennan, 2001). This is an important difference from the patients in this study of WebChoice, and it confirms that the results from this study are not necessarily valid for newly diagnosed patients.

4.5 Conclusion

The results of this study show that WebChoice had no effect on the patients' health-related quality of life, and no QALYs were gained. Hence, the main hypothesis which stated that WebChoice improves the 15D summary score (index), can be rejected. The hypotheses for each of the eight dimensions can also be rejected, since no positive effects for WebChoice were found.

However, these conclusions must be reached with some reservations: The results do not necessarily apply to patients with a recent diagnosis, to patients with little education or to patients with low HRQOL.

The respondents in this trial were well educated, well experienced with the disease and were of relatively good health. This indicates that the patients had probably gained much of the information accessible in WebChoice through different channels prior to the trial, and that some of the information was irrelevant. If another study tests WebChoice on patients with opposite characteristics than the respondents in this trial, the result could be a positive effect and a fundamentally different result from the one in this study.

Appendix

Variables included in the trial

Variable name	Explanation	Type
ID	Patients unique ID number	Numeric
MTIME	Time at measurement	Nominal
GROUP	Group assignment	Numeric
DATE	Date of measurement	Date
AGE	Age	Numeric
MARITAL	Marital status	Nominal
CHILD	Number of children	Nominal
ED	Level of education	Ordinal
INCOME	Household total yearly income	Numeric
DIA	Cancer diagnosis	Nominal
TIMEDIA	When diagnosis was given	Date
FIRSTDIA	First diagnosis	Nominal
CBACK	The cancer has returned	Nominal
METASTASIS	Metastasis	Nominal
SURGERYuns	First participants kind of surgery is not known	Nominal
REMbreast	Removed breast	Nominal
SAVBREAbreast	Scale- Numeric: 0 (“no -not checked”), 1(“yes – checked”)	Nominal
OPLYMPHbreast (Removed lymphnodes)	Surgery sparing breast	Nominal
RADIOTHbreast	Radiotherapy breast and or lymphnodes	Nominal
CHEMObreast	Chemotherapy	Nominal
ANTIHbreast	Anti hormone treatment	Nominal
HERCEPTbreast	Herceptin	Nominal
REMPROprostate	Removed prostate	Nominal
RADIOTHprostate	Radiotherapy prostate	Nominal
HORMON_unspecified	First participants kind of hormon is not known	Nominal
HORMTABprostate	Hormone treatment (tablets)	Nominal
HORMINJECTprostate	Hormone treatment (injections)	Nominal
REMTESTprostate	Removed testicles	Nominal
CHEMOprostate	Chemotherapy	Nominal
OTHTREAT	Other treatment for current cancer	Nominal
WHATTREAT	What other treatment for current cancer	Nominal
OTHERILL	Other illnesses	Nominal
WHATILL	What illnesses	Nominal
COMPEX	Experience using computers	Ordinal
15D: QL1mobil	Mobility	Ordinal
15D: QL2sight	Vision	Ordinal
15D: QL3hear	Hearing	Ordinal
15D: QL4breath	Breathing	Ordinal
15D: QL5sleep	Sleeping	Ordinal
15D: QL6eat	Eating	Ordinal
15D: QL7speech	Speech	Ordinal
15D: QL8urin	Elimination	Ordinal
15D: QL9activ	Usual activities	Ordinal
15D: QL10ment	Mental function	Ordinal
15D: QL11symp	Discomfort and symptoms	Ordinal
15D: QL12depr	Depression	Ordinal
15D: QL13stress	Distress	Ordinal
15D: QL14qol	Vitality	Ordinal
15D: QL15sex	Sexual activity	Ordinal

Uncommented 15D results

1A: 15D scores for the first dimension for all patients (n= 234).

Moving						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	103	102	104	130	130	128
1.Walk normally indoors and outdoors	88.3%	84.3%	88.5%	89.2%	86.9%	82.8%
2.Slight difficulties outdoors/stairs	10.7%	14.7%	8.7%	10.8%	12.3%	14.8%
3.Considerably difficulty outdoors/stairs	1.0%	1.0%	2.9%	0.0%	0.8%	2.3%
4. Walk indoors only with help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5.Completely bed-ridden	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.531	0.852	0.350			

1B: 15D scores for the first dimension for breast cancer patients (n=130).

Moving						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	55	75	75	74
1.Walk normally indoors and outdoors	90.9%	87.3%	90.9%	92.0%	89.3%	86.5%
2.Slight difficulties outdoors/stairs	9.1%	12.7%	9.1%	8.0%	10.7%	12.2%
3.Considerably difficulty outdoors/stairs	0.0%	0.0%	0.0%	0.0%	0.0%	1.4%
4. Walk indoors only with help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Completely bed-ridden	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.825	0.716	0.581			

1C: 15D scores for the first dimension for prostate cancer patients (n=104).

Moving						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	48	47	49	55	55	54
1.Walk normally indoors and outdoors	85.4%	80.9%	85.7%	85.5%	83.6%	77.8%
2.Slight difficulties outdoors/stairs	12.5%	17.0%	8.2%	14.5%	14.5%	18.5%
3.Considerably difficulty outdoors/stairs	2.1%	2.1%	6.1%	0.0%	1.8%	3.7%
4. Walk indoors only with help	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Completely bed-ridden	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.542	0.935	0.282			

2A: 15D scores for the second dimension for all patients (n= 234).

Vision						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	103	103	130	130	129
1. Read without difficulty	93.3%	88.3%	87.4%	92.3%	90.0%	90.7%
2. Read with slight difficulty	5.8%	10.7%	10.7%	7.7%	10.0%	8.5%
3. Read with considerable difficulty	1.0%	1.0%	1.9%	0.0%	0.0%	.8%
4. Cannot read, but can walk without guidance	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Almost or completely blind	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.457	0.521	0.621			

2B: 15D scores for the second dimension for breast cancer patients (n=130).

Vision						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	55	75	75	74
1. Read without difficulty	92.7%	87.3%	87.3%	92.0%	89.3%	90.5%
2. Read with slight difficulty	7.3%	12.7%	9.1%	8.0%	10.7%	8.1%
3. Read with considerable difficulty	0.0%	0.0%	3.6%	0.0%	0.0%	1.4%
4. Cannot read, but can walk without guidance	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Almost or completely blind	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.878	0.716	0.676			

2C: 15D scores for the second dimension for prostate cancer patients (n=104).

Vision						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	48	48	55	55	55
1. Read without difficulty	93.9%	89.6%	87.5%	92.7%	90.9%	90.9%
2. Read with slight difficulty	4.1%	8.3%	12.5%	7.3%	9.1%	9.1%
3. Read with considerable difficulty	2.0%	2.1%	0.0%	0.0%	0.0%	0.0%
4. Cannot read, but can walk without guidance	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Almost or completely blind	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (p)	0.453	0.558	0.576			

3A: 15D scores for the third dimension for all patients (n= 234).

Hearing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	103	104	130	130	129
1. Hear speech normally	92.3%	88.3%	88.5%	91.5%	90.0%	89.1%
2. Hear speech with a little difficulty	7.7%	10.7%	11.5%	7.7%	9.2%	9.3%
3. Hear speech with considerable difficulty	0.0%	1.0%	0.0%	0.8%	0.8%	1.6%
4. Hear even loud voices poorly	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5.Completely deaf	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.669	0.920	0.388			

3B: 15D scores for the third dimension for breast cancer patients (n=130).

Hearing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	55	75	75	74
1. hear speech normally	98.2%	90.9%	94.5%	96.0%	93.3%	94.6%
2. hear speech with a little difficulty	1.8%	9.1%	5.5%	4.0%	6.7%	5.4%
3. hear speech with considerable difficulty	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. Hear even loud voices poorly	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Completely deaf	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.477	0.608	0.990			

3C: 15D scores for the third dimension for prostate cancer patients (n=104).

Hearing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	48	49	55	55	55
1. hear speech normally	85.7%	85.4%	81.6%	85.5%	85.5%	81.8%
2. hear speech with a little difficulty	14.3%	12.5%	18.4%	12.7%	12.7%	14.5%
3. hear speech with considerable difficulty	0.0%	2.1%	0.0%	1.8%	1.8%	3.6%
4. Hear even loud voices poorly	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Completely deaf	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.626	0.995	0.365			

4A: 15D scores for the fourth dimension for all patients (n= 234).

Breathing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	102	104	129	130	128
1. Breathe normally	60.6%	52.0%	49.0%	64.3%	52.3%	53.1%
2. Shortness of breath during heavy work	32.7%	41.2%	42.3%	28.7%	40.8%	34.4%
3. Shortness of breath walking on flat ground	3.8%	5.9%	6.7%	6.2%	5.4%	10.2%
4. Shortness of breath after light activity	1.9%	0.0%	1.9%	.8%	1.5%	2.3%
5. Breathing difficulties almost all the time	1.0%	1.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.577	0.579	0.579			

4B: 15D scores for the fourth dimension for breast cancer patients (n=130).

Breathing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	55	74	75	73
1. Breathe normally	54.5%	47.3%	52.7%	64.9%	56.0%	56.2%
2. Shortness of breath during heavy work	36.4%	43.6%	40.0%	29.7%	37.3%	31.5%
3. Shortness of breath walking on flat ground	5.5%	9.1%	7.3%	5.4%	5.3%	11.0%
4. Shortness of breath after light activity	1.8%	0.0%	0.0%	0.0%	1.3%	1.4%
5. Breathing difficulties almost all the time	1.8%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.452	0.540	0.589			

4C: 15D scores for the fourth dimension for prostate cancer patients (n=104).

Breathing						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	47	49	55	55	55
1. Breathe normally	67.3%	57.4%	44.9%	63.6%	47.3%	49.1%
2. Shortness of breath during heavy work	28.6%	38.3%	44.9%	27.3%	45.5%	38.2%
3. Shortness of breath walking on flat ground	2.0%	2.1%	6.1%	7.3%	5.5%	9.1%
4. Shortness of breath after light activity	2.0%	0.0%	4.1%	1.8%	1.8%	3.6%
5. Breathing difficulties almost all the time	0.0%	2.1%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.670	0.470	0.876			

5A: 15D scores for the dimension for all patients (n= 234).

Speech						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	104	103	130	130	130
1. Speak normally	94.2%	94.2%	92.2%	96.9%	93.1%	93.8%
2. Slight speech difficulties	5.8%	5.8%	7.8%	3.1%	6.9%	6.2%
3. Can make myself understood	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. People have great difficulty understanding my speech	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Only make myself understood by gestures	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.312	0.720	0.629			

5B: 15D scores for the seventh dimension for breast cancer patients (n=130).

Speech						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	54	75	75	72
1 Speak normally	92.7%	92.7%	96.0%	94.7%	90.7%	96.0%
2. Slight speech difficulties	7.3%	7.3%	4.0%	5.3%	9.3%	4.0%
3. Can make myself understood	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. People have great difficulty understanding my speech	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Only make myself understood by gestures	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.649	0.677	0.222			

5C: 15D scores for the seventh dimension for prostate cancer patients (n=104).

Speech						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	47	47	49	55	55	55
1. Speak normally	95.9%	95.9%	93.9%	100.0%	96.4%	90.9%
2. Slight speech difficulties	4.1%	4.1%	6.1%	0.0%	3.6%	9.1%
3. Can make myself understood	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
4. People have great difficulty understanding my speech	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5. Only make myself understood by gestures	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.130	0.906	0.571			

6A: 15D scores for the dimension for all patients (n= 234).

Usual activities						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	104	103	129	129	130
1 Perform my usual activities	43.3%	50.0%	49.5%	47.3%	51.2%	51.5%
2. Perform usual activities with minor difficulty	37.5%	31.7%	35.0%	41.9%	34.9%	34.6%
3. Usual activites with considerable difficulty	13.5%	11.5%	5.8%	5.4%	10.9%	9.2%
4. Small proportion of usual activities	5.8%	6.7%	8.7%	5.4%	3.1%	4.6%
5. None of my usual activities	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.202	0.611	0.450			

6B: 15D scores for the seventh dimension for breast cancer patients (n=130).

Usual activities						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	55	55	75	74	75
1 Perform my usual activities	32.7%	40.0%	43.6%	41.3%	54.1%	52.0%
2. Perform usual activities with minor difficulty	36.4%	34.5%	32.7%	45.3%	31.1%	37.3%
3. Usual activites with considerable difficulty	21.8%	16.4%	10.9%	6.7%	10.8%	5.3%
4. Small proportion of usual activities	9.1%	9.1%	12.7%	6.7%	4.1%	5.3%
5. None of my usual activities	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.070	0.328	0.264			

6C: 15D scores for the seventh dimension for prostate cancer patients (n=104).

Usual activities						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	49	48	54	55	55
1. Perform my usual activities	55.1%	61.2%	56.2%	55.6%	47.3%	50.9%
2. Perform usual activities with minor difficulty	38.8%	28.6%	37.5%	37.0%	40.0%	30.9%
3. Usual activites with considerable difficulty	4.1%	6.1%	.0%	3.7%	10.9%	14.5%
4. Small proportion of usual activities	2.0%	4.1%	4.2%	3.7%	1.8%	3.6%
5. None of my usual activities	0.0%	0.0%	2.1%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.965	0.382	0.072			

7A: 15D scores for the twelfth dimension for all patients (n= 234).

Depression						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	104	103	104	130	128	129
1. Not at all sad	43.3%	46.6%	51.0%	48.5%	53.9%	52.7%
2. Slightly sad	48.1%	41.7%	39.4%	45.4%	35.9%	35.7%
3. Moderately sad	7.7%	10.7%	8.7%	5.4%	4.7%	10.1%
4. Very sad	1.0%	1.0%	1.0%	.8%	5.5%	1.6%
5. Extremely sad	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.818	0.065	0.912			

7B: 15D scores for the twelfth dimension for breast cancer patients (n=130).

Depression						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	55	54	55	75	74	74
1 Not at all sad	36.4%	35.2%	45.5%	50.7%	50.0%	52.7%
2 Slightly sad	52.7%	53.7%	47.3%	44.0%	37.8%	33.8%
3. Moderately sad	9.1%	11.1%	7.3%	4.0%	2.7%	12.2%
4. Very sad	1.8%	0.0%	0.0%	1.3%	9.5%	1.4%
5. Extremely sad	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.341	0.007	0.351			

7C: 15D scores for the twelfth dimension for prostate cancer patients (n=104).

Depression						
	WebChoice			Controls		
	Baseline	6 months	12 months	Baseline	6 months	12 months
Valid responses	49	49	49	55	54	55
1 Not at all sad	51.0%	59.2%	57.1%	45.5%	59.3%	52.7%
2 Slightly sad	42.9%	28.6%	30.6%	47.3%	33.3%	38.2%
3. Moderately sad	6.1%	10.2%	10.2%	7.3%	7.4%	7.3%
4. Very sad	0.0%	2.0%	2.0%	0.0%	0.0%	1.8%
5. Extremely sad	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Chi-square test (*p*)	0.848	0.678	0.853			

Average level on the answers of the 15D questionnaire at baseline

Average level on the answers of the 15D questionnaire at baseline, both cancer groups and both intervention groups together.

	Average level of answer	Average total
Mobility	1.1	1.5
Vision	1.1	
Hearing	1.1	
Breathing	1.5	
Sleeping	2.1	
Eating	1.0	
Speech	1.0	
Elimination	1.5	
Usual activities	1.8	
Mental function	1.3	
Discomfort and symptoms	1.7	
Depression	1.6	
Distress	1.6	
Vitality	1.9	
Sexual activity	2.8	

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