00B010I

00B010I

Project Numbers: JTO 0001 - 43

JTO 0002

JTO 0003

Cost Effectiveness Analysis of Prostate Cancer Treatments

An Interactive Qualifying Project Report

submitted to the Faculty

of the

WORCESTER POLYTECHNIC INSTITUTE

in partial fulfillment of the requirements for the

Degree of Bachelor of Science

by

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Abstract

Medical care costs are escalating rapidly in the United States and confusion concerning optimal treatment protocols contributes to the waste of medical resources. In this project an analysis of prostate cancer treatments was performed. This analysis was accomplished by examining each treatment alternative in terms of its complications, cost, and effectiveness—by cancer stage. In localized prostate cancer radiotherapy and prostatectomy are more cost effective than other treatments. After prostate cancer has metastasized, hormone therapy is the most cost effective option.

Authorship

This page denotes the individual who originally wrote the indicated section of the project. However, in virtually all sections all team members have contributed new material during the rewrite process.

1 Introduction

Prostate cancer is one of the most common types of cancer in men, second only to skin cancer (Walsh 1997, 25). Until recently, very little research was being performed on this type of cancer even though it causes as many deaths annually as breast cancer in women (Association for the Cure of Cancer of the Prostate, 1999).

When faced with the decision of choosing some form of medical procedure, it is important to research that procedure in terms of its effectiveness, comfort, and cost. Such an approach allows the patient to make an informed decision on which treatment is best for his or her specific needs and preferences.

The object of this project is to research existing treatments for prostate cancer—as well as newer, experimental treatments—and to analyze their results in terms of their effectiveness, complications and cost. Such analyses enable us to establish a general protocol to assist a prostate cancer patient in deciding which treatment is best for him depending on his specific disease characteristics and preferences. For example, the optimal treatment for a fifty-year-old man with extremely extensive cancer of the prostate might well be different than the optimal treatment for a seventy-year-old man with the beginning stages of prostate cancer.

This project was written to fulfill the degree requirement of the Interactive Qualifying Project (IQP) at Worcester Polytechnic Institute (WPI). The purpose of the IQP is to challenge students to examine how "science or technology interacts with societal structures and values" (WPI Undergraduate Catalog 2001, 37).

Researching the latest technologies associated with prostate cancer treatment meets this requirement because efficiency in health care is becoming a major concern.

Health care costs are continually rising as new and more expensive medical technologies are used in treatment (Stoll, 1988, 1). Society must take steps to justify the added expenses of new technologies. Researchers must demonstrate that the added cost is adding proportional benefits. Investing a large amount of resources on a new technique that is only slightly better than the older methods is not practical.

The second chapter of this paper presents the background. This chapter emphasizes important information for understanding prostate cancer and the different forms of treatment available. The chapter starts with a discussion of the anatomy of the prostate, its function in the male human body, and Prostate-Specific Antigen (PSA)—an antigen whose level in the blood stream has been found to be related to prostate cancer. The next section discusses cancer of the prostate and the stages into which it is separated. This is followed by a description of the different methods used to detect prostate cancer. Common treatments for prostate cancer are then discussed, including a description of the treatments and possible complications resultant from these treatments. Experimental treatments are also presented.

Chapter 3 presents the methodology of the paper. It first discusses economic analysis as it applies to health care. Then the different sources pursued in order to obtain the information needed for the paper are discussed. An overview of the different medical studies used as sources in this paper is presented next. Finally, an explanation of the particular procedures used for implementing this project is also given.

Chapter 4, the results chapter, is categorized into sections based on treatment and presents the data compiled in the course of this project. These include data on complications, cost and effectiveness of each treatment.

Chapter 5 presents a suggested model for patients to follow to help them determine the “best” treatment at each stage of prostate cancer. This chapter is categorized into sections by cancer stage. For each stage, relevant treatments are discussed. The three dimensions of each treatment (i.e. cost, complications and effectiveness of the treatment) are then discussed, and a suggestion for the most appropriate treatment is given. It must be noted that this chapter simply offers a strategy, as well as data, for finding a treatment plan; it is only suggestive. The patient and physician must decide together on the best treatment plan; these suggestions would merely aid in that decision. All cases are different and should be evaluated individually by a physician.

Chapter 6 presents the conclusions that may be drawn from the project as a whole. Such conclusions discussed include treatment recommendations that are made given all the presented data in the project and summarizes Chapter 5. This chapter also includes a discussion on the problems encountered while working on this project and a discussion on possible future work that can be undertaken to extend this project.

2 Background

This chapter presents important information for understanding prostate cancer and the different forms of treatment available. The chapter starts with a discussion of the anatomy of the prostate, its function in the male human body, and Prostate-Specific Antigen (PSA)—an important antigen found in the blood stream which, as will be discussed, is important in the detection of prostate cancer. The next section discusses cancer of the prostate and the stages into which it is separated. This is followed by a description of the different methods used to detect prostate cancer, such as the digital rectal examination, the PSA test, biopsies, and imaging techniques.

Common treatments for prostate cancer are divided into three sections: Surgery, Hormone Therapy and Radiation Therapy. The surgery section gives an overview of the two most commonly used prostatectomy procedures, radical retropubic prostatectomy and perineal prostatectomy, as well as transurethral resection of the prostate. Radiation therapy describes external beam radiation and interstitial brachytherapy. Hormone therapy discusses physical and chemical castration. Procedures currently under experimental review are briefly outlined as well. Finally, complications that result from these different treatment methods are presented.

2.1 Anatomy of the Prostate

The male pelvis has several organs and ducts that are used in the biological systems involved in waste disposal and reproduction. In front of the pelvis are the penis and the scrotum. Testes within the scrotum supply sperm to the prostate through the ductus deferens and ejaculatory duct. Two seminal vesicles, small sacs that act as a kind of semen reservoir, are positioned with bilateral symmetry on either side of the prostate in the middle of the pelvis. Above the prostate and seminal vesicles is the bladder, which stores urine. The prostate surrounds the urethra, the pathway for urine (from the bladder) and semen (from the ductus deferens) to the penis. Behind the prostate and seminal vesicles is the rectum. See figure in Appendix C (Atlas of Normal Anatomy 1956, 46).

The prostate is a chestnut-sized gland, which is divided into two halves called the lobes. This gland is also composed of an inner layer and an outer layer. The inner layer, which surrounds both left and right lobes, produces a secretion to keep the urethra moist. The outer layer, which surrounds the inner layer, secretes a liquid that is part of a male's semen. Sperm and this liquid secretion make up what is called semen, with the secretion acting to protect the sperm from the acidic urine along the urethra.

One of the important chemicals associated with the prostate gland is Prostate-Specific Antigen (PSA). It is unclear exactly where PSA is manufactured in the human body (Catalona, William J, 1996, 64-69; Morgan, Ted O., et al., 1996, 58-63; Partin, Alan W, et al., 1996, 35-39). PSA exists naturally in a male's blood in relatively small amounts when the prostate is healthy and normal. Antigens attack foreign materials in the body and PSA in the prostate is no exception. When foreign material is introduced into the prostate, PSA is produced in an attempt to destroy this material. PSA levels are known to rise for reasons such as an enlargement of the prostate, ejaculation, or the presence of invasive surgical instrumentation or invasive diagnostic instrumentation (such as a needle biopsy). PSA may reach levels of 4-10 ng/mL, or higher, of blood content while "attacking" a cancerous tumor compared to a normal level of about 2.5

ng/mL (Catalona 1996, 65) (the unit ng is an abbreviation of nanogram, which is one trillionth of a gram and the unit mL is an abbreviation for a milliliter). Here one can see how PSA level can be used to detect prostate cancer. When the PSA level is suspiciously high (4-10 ng/mL, or even higher) then it is possible that the patient has prostate cancer. If the PSA level is below 4ng/mL, then the patient most likely has a healthy prostate.

PSA exists in two forms, free and bound. Free PSA means that the PSA molecule exists without any other protein molecules bound to it. Bound PSA means that PSA molecules are bound to other protein molecules. Total PSA refers to the combination of free and bound PSA. Tests exist that can measure the amount of PSA in the bloodstream and these tests have the ability to indicate the presence of either free PSA or total PSA. This ability to distinguish between the two forms of PSA is important because research shows that free PSA is a better indicator of prostate cancer than bound PSA (Partin, et al., 1996, 37; Morgan, et al., 1996, 61).

2.2 Adenocarcinoma of the Prostate Gland

There are several ailments of the prostate that may occur. These ailments include prostatitis, prostatic infarction, benign prostatic hyperplasia and prostate cancer (Catalona, 1996, 64). Prostatitis is the inflammation of the prostate gland. Prostatic infarction is a condition in which prostate tissue dies as a result of lack of blood flow to the tissue.

One of the more common disorders of the prostate is benign prostatic hyperplasia, hereafter referred to as BPH. BPH is characterized by an inflammation of the prostate. BPH is also characterized by pain and poor urinary flow because the swelling of the prostate gland, which surrounds the urethra, starts to "choke" the urethra. The symptoms of BPH are very similar to those of prostate cancer, such as incontinence and a rise in the PSA level. So, if a patient is diagnosed with BPH, further tests must be performed to rule out the possibility of that patient having prostate cancer (Walsh, 1997, 277-378).

Adenocarcinoma of the prostate, more commonly referred to simply as prostate cancer, is also an affliction of the prostate gland. This is the prostate ailment with which this paper is most concerned.

Adenocarcinoma of the prostate is a malignant tumor developing in the prostate gland. Although there are several staging systems for prostate tumors, the most standard system is the one developed by the American Joint Committee on Cancer (AJCC) (Fondorulia, 1999, 7). The stages of prostate cancer development according to the AJCC system are outlined below. In this classification system there are four stages (T1, T2, T3 and T4), with three substages (a, b and c) in each stage. T4 is an exception having only substages a and b.

In the first stage, T1, the cancer is virtually undetectable. In the T1 stage the tumor is very small and confined to the inner layer of the prostate. As noted above, T1 consists of T1a, T1b and T1c. T1a denotes a very small tumor that grows in the middle of the prostate around the urethra. A tumor in T1b is larger than a T1a tumor and it is also located around the urethra in the middle of the prostate. Stage T1c is slightly different in that the tumor is small, but not in the middle of the prostate. Rather, it is located closer to the surface of the prostate.

Stage T2 tumors are larger than T1 tumors, but still confined to the inner layer of the prostate. T2a and T2b are characterized by a tumor occupying almost half of one lobe of the prostate, with T2b tumors being larger than T2a tumors. T2c tumors occupy both lobes of the prostate, but are still within the inner layer.

Starting in stage T3, the cancer is no longer confined to the inner layer of the prostate gland. Stage T3a tumors have spread in one direction into or beyond the outer layer of the prostate. T3b tumors have spread bilaterally through the outer layer of the prostate. T3c tumors have spread into at least one of the seminal vesicles.

Stage T4 is divided into substages T4a and T4b. T4 prostate tumors have spread into neighboring organs. Stage T4a is characterized by spreading into the bladder neck, the external sphincter, or the rectum. Stage T4b has spread into the muscles surrounding the inside of the pelvis or attached to the pelvic wall.

One should note that this staging system is categorical and not continual. That is, it places tumors in their stages by size and location rather than by chronological development. Under the AJCC system, a T2a tumor may not be as severe as a T1b tumor because the type and location of tumors vary greatly.

2.3 Prostate Cancer Detection Methods

Several detection methods exist for diagnosing prostate cancer. There are two common methods: the digital rectal exam (DRE), and the PSA test. The DRE is an examination that can be performed in the physician's office. The patient lies on a table and the physician searches for irregularities, such as lumps or inflammation, using his or her finger inserted into the patient's rectum. Recall that the rectum is directly behind the prostate; a digit inserted into the rectum may feel around the prostate area for tumors (Walsh, 1997, 45). This test can only detect tumors that have progressed to at least T2 in size. This test is usually coupled with another test, the PSA test, for more accurate and early detection of cancer.

The PSA test is a simple blood test to measure the level of PSA in the bloodstream. An elevated level of PSA may denote the existence of a tumor, making PSA an excellent marker for prostate cancer. A PSA level below 4ng/mL is considered safe. A level of 4-10ng/mL indicates PSA is possibly elevated to attack foreign matter; this level or anything higher is enough to make a physician suspicious that the patient may have prostate cancer. It is important to remember that PSA levels may rise for reasons other than prostate cancer, so a physician cannot make a diagnosis on a PSA test alone.

Recall that physicians are able to measure free PSA and total PSA. Free PSA is a more accurate detector of prostate cancer than total PSA. The free PSA test is not accurate for low PSA levels (less than 4ng/mL), in which case there is a low risk of a tumor being present. It also does not work well for very high levels of PSA (greater than 10ng/mL), but methods such as the DRE are usually able to detect tumors in this case, depending on the tumor location as well as size (Catalona, 1996, Partin et al., 1996, Morgan et al., 1996). For total PSA levels between 4-10 ng/mL, the percent of free PSA may be used as an indicator for prostate cancer. Biopsies should be performed on only those patients at the cutoff of 25% or less of free PSA in the total PSA. Using this cutoff, 95 percent of cancers would be detected and 20 percent of those patients with elevated PSAs—who would ordinarily undergo prostate biopsies—would be spared from that procedure (Catalona et al., 1998, 1545). PSA and DRE tests are usually used together to evaluate the patient's condition.

A third important method for prostate cancer detection is needle biopsy. A needle biopsy involves the insertion of a needle into the rectal end of the prostate and removal of samples of prostate tissue. The end of the needle is designed to tear away a small piece of tissue and hold it while the needle is removed. The samples are analyzed in a lab and searched for cancerous material. Several samples, perhaps four or five, are taken to insure accuracy. It is difficult to detect small tumors with this method because the chance of the needle hitting the small tumor and removing a piece of it is low (Resnick and Thompson, 1998, 21-29; Walsh, 1997, 65).

Special guiding techniques are usually used to ensure accurate targeting of the needle. One of these techniques employs the use of cameras. In this case, an incision is made at the front of the pelvis and a camera is inserted. With this camera in place, the physician may see where the needle is being positioned with precision. This technique is called a laparoscopic biopsy (Resnick and Thompson, 1998, 61). Another technique involves ultrasound imaging to see inside the patient while maneuvering the needle to the prostate gland. Both are effective guiding techniques, but the technique that is used depends on the preference of the physician.

A needle biopsy may be performed on a patient who has BPH in an attempt to rule out the possibility that the patient has prostate cancer. The physician may find cancerous cells in the sample. In this way, prostate cancer can be diagnosed at an early stage (Fondurulia, 1999, 10). Depending on the amount of cancerous tissue found, the cancer is categorized in the appropriate stage according to the AJCC system. However, because a needle biopsy causes the PSA level to rise, it is recommended that PSA tests be performed at least six weeks after a needle biopsy. This effect is important to keep in mind because PSA tests are also used to monitor progress of the condition of BPH or prostate cancer in a patient.

From biopsies a number representation of the seriousness of the cancer is assigned. This number representation is called the Gleason score. The Gleason score is a means by which the grade of the prostate tumors can be classified on the basis of the cancer cells' differentiation. Cell differentiation refers to the appearance of the cell. If the cancer cells are well differentiated, it means that they have well-defined boundaries and clearly visible centers. These cells usually grow slowly and predictably. Poorly differentiated cancer cells appear more like blobs that run into each other, with poorly defined boundaries. These cells usually grow rapidly and unpredictably. A Gleason score range of about 2-4 is assigned to low grade or well-differentiated cancer cells. A Gleason score of about 8-10 is assigned to high grade or poorly differentiated cancer cells. Cancer cells that fall in the middle range of about 5-7 are considered unpredictable. The lower the Gleason score the better the prognosis (Walsh, 1997, 75, Resnick and Thompson, 1998, 13).

Other methods of prostate cancer detection include the transrectal ultrasound (TRUS) and magnetic resonance imaging (MRI). In a TRUS, ultrasonic waves are bounced off the prostate to get an image of the organ. It works the same way as an ultrasound used to see a prenatal baby. As mentioned above, the ultrasound imaging involved in TRUS is also a technique that is used in guiding a needle biopsy to its target for accurate sampling as an alternative to laparoscopic biopsy (Resnick and Thompson, 1998, 21-29). MRIs bounce a beam off the prostate looking for different water concentrations. Water concentration differs between tumor tissue and normal tissue.

Both the TRUS and MRI are limited in their abilities to detect small tumors that would be in the T1 or T2 stages.

2.4 Common Prostate Cancer Treatments

2.4.1 Surgery

Surgery as a treatment for prostate cancer consists of removal of all or part of the prostate in an attempt to rid the body of cancerous tissue. Surgery is usually performed when the tumor is still confined to just the prostate, T1 and T2 stages (Resnick and Thompson, 1998, 90-93). Radical prostatectomy procedures (RP) or transurethral resection of the prostate (TURP) are two types of procedures used for prostate surgery. A radical prostatectomy is the complete removal of the prostate, and a TURP is the removal of the portion of the prostate surrounding the urethra (Walsh, 1997,123).

If the cancer is not within the confines of the prostate, T3 or T4 cancer, radical prostatectomy is not performed to treat the cancer because it would not be effective in ridding the body of all the cancer. There is no need to cause the patient unnecessary complications due to a RP if the procedure will not result in an effective treatment (Resnick and Thompson, 1998, 90-93).

TURP is most often related to prostate cancer treatment as a diagnostic tool. It is also used as a symptom reliever for patients practicing watchful waiting or patients with cancer beyond the T2 stage.

2.4.1.1 Radical Prostatectomy

The majority of men who undergo a radical prostatectomy are between the ages of fifty and seventy years (Schwartz, Lepor, 1999, 1185). Men undergoing treatment for prostate cancer must weigh the benefits of the procedure against the complications and inconveniences of the procedure—based on their individual preferences and personal lifestyles. Given their prognosis, men may choose an alternative to surgery for treatment, because maintaining their current lifestyles is more important to them than the outcome, cost or complications due to surgery. For example, a man who is 80 years old may decide that the complications and cost of a prostatectomy are too severe for a procedure that would not necessarily prolong his life.

A radical prostatectomy involves the complete removal of the prostate gland and the tissue located close to the prostate known as the seminal vesicles (Resnick and Thompson, 1998, 90-98). As noted above, there are currently two different procedures commonly used for RP: the perineal approach and the retropubic approach.

2.4.1.1.1 Radical Perineal Prostatectomy

Radical perineal prostatectomies (RPP) require the patient to be placed on his back in stirrups—with his back supported at the base of the spine with either rollers or sand bags to elevate the pelvis. This position elevates the lower portion of the patient's body and places the knees of the patient over his upper abdominal area. Figure 2-2 illustrates this position. Notice how deeply the patient's knees are curled in toward the chest. This procedure is particularly not recommended for overweight men, because of the way the patient must be positioned for the procedure (Resnick and Thompson, 1998, 137).

The RPP involves a small incision above the anus. Figure 2-1 shows the positioning of this incision as a dashed line curving about the anus of the patient. The location of the incision allows for a quick and comfortable recovery and avoids the major veins in the pelvic area (Resnick and Thompson, 1998, 131). There is little bleeding because a major vein does not have to be removed. Unfortunately, the surgeon cannot see as much of the tissue as he or she is interested in seeing from this direction. For this reason, it is difficult to see and protect neurovascular bundles on the side of the prostate, which are responsible for erections (Walsh, 1997, 154).

As mentioned above and as shown in Figure 2-1, with RPP surgery is performed through a curved incision made around the patient's anal opening, between two parts of the pelvis known as the ischial tuberosities (Thomas, 1996, 1). The ischial tuberosities can best be described as the part of the pelvis that comes in contact with a surface when sitting upright in a chair. Figure 2-3 shows a view of the mail pelvis angled from the front left of the pelvis. The left ischial tuberosity is labeled on the figure. One can picture the right ischial tuberosity being positioned on the right side of the pelvis in the same manner as the left ischial tuberosity.

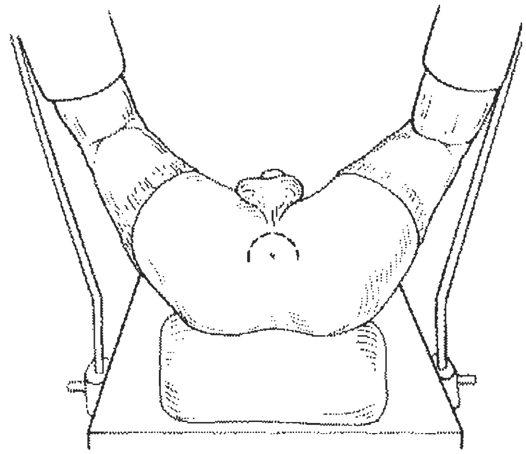

Figure 2-1 Location of the incision for radical perineal prostatectomy

Resnick, Martin I., Thompson, Ian M., eds. Surgical Skills: Surgery of the Prostate.
New York: Churchill Livingston Inc., 1998, p137

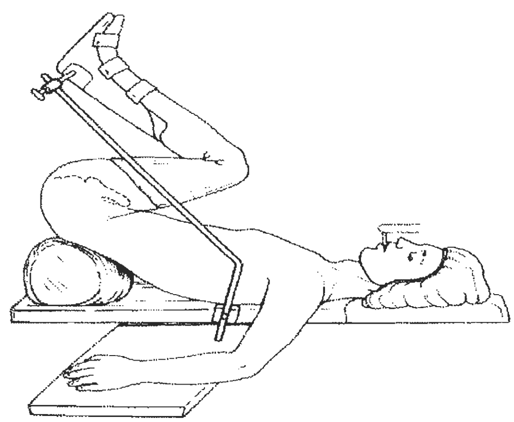

Figure 2-2 Positioning of the patient for radical perineal prostatectomy

Resnick, Martin I., Thompson, Ian M., ed. Surgical Skills: Surgery of the Prostate.
New York: Churchill Livingston Inc., 1998, p137

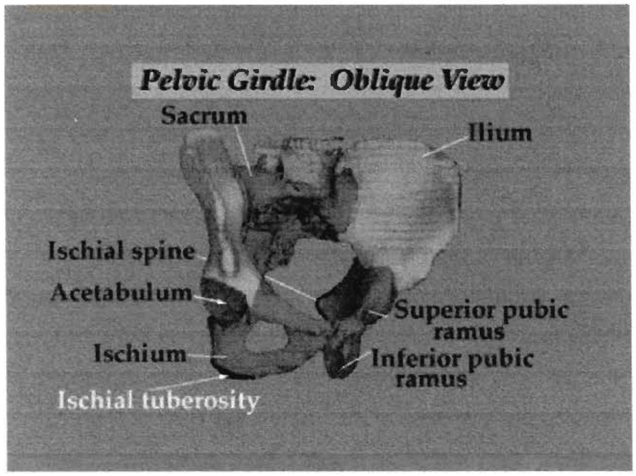

Figure 2-3 View of the pelvis and the ischial tuberosities

Busick, Natisha B.S.,Brandser, Eric M.D. Anatomy of the Pelvis and Perineum: A Multimedia Textbook and Teaching Module. Virtual Hospital. http://www.vh.org/Providers/Textbooks/pelvis/PelvisOblique10.html

At the beginning of the surgical procedure, an instrument called a retractor is positioned inside of the urethra to help position the prostate properly for dissection. The membranes holding the urethra to the prostate are cut, and the ridge separating the neck of the bladder to the prostate is made visible. Then the prostate is separated from the neck of the bladder. A catheter to aid in drainage and help with retraction of the prostate replaces the retractor after surgery.

As the prostate is completely removed from the patient through the incision made above the anus, the surgeon must be sure to protect the rectum from tearing. This is a problem because the prostate sits right on the top of it. Special care is also taken to protect the delicate neurovascular bundles at the sides of the prostate in order to prevent impotence.

After the RPP, the patient is immediately started on clear liquids and antibiotics to prevent infection; and the patient must avoid long periods of sitting. Discharge from the hospital usually occurs two to three days after surgery. A catheter is left in place for roughly 2 weeks after the procedure to drain urine and to allow the urethra to heal before normal urination is resumed (Resnick and Thompson, 1998, 138-147).

Dr. Hugh Hampton Young of John Hopkins University developed the perineal approach to radical prostatectomy in 1904 (Walsh, 1997, 132). After the retropubic approach was developed the 1940's, the perineal approach was abandoned, but it is now becoming more popular again. The main reason for its regain in popularity is due to the ability to use laparoscopic techniques for performing the dissection of lymph nodes immediately before the surgery.

Laparoscopic surgery is presently becoming more and more popular because it is less invasive to the body than traditional forms of surgery. The surgeon makes small incisions in the patient and inserts a camera into one and surgical tools in others. The camera allows the surgeon to operate by watching the tools inside the body on a monitor.

Figure 2-4 shows the placement of incisions for the tools used to perform laparoscopic prostate surgery. The small incisions allow for faster healing and greater comfort during the healing process as compared to more invasive surgeries involving larger incisions. Surgeons perform laparoscopic surgical biopsies to ensure that the cancer has not spread out of the prostate and thus to spare the patient the unnecessary major surgery of an RP. Use of laparoscopic technique—combined with the location and size of the incision used for RPP—results in less blood loss, a shorter hospital stay, and a more comfortable recovery (Resnick and Thompson, 1998 , 62-64).

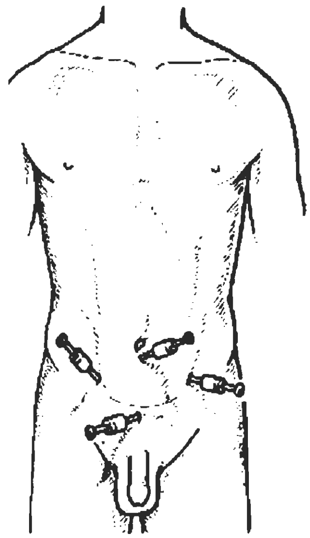

Figure 2-4 The positioning of laparoscopic tools to perform a lymphotic dissection
Resnick, Martin I., Thompson, Ian M., eds. Surgical Skills: Surgery of the Prostate.
New York: Churchill Livingston Inc., 1998, p63

2.4.1.1.2 Radical Retropubic Prostatectomy

The second approach to radical prostatectomy that can be used is called the retropubic approach, which was developed in the 1940's (Walsh, 1997, 123). The retropubic approach uses an incision in the abdomen rather than one around the anus. One advantage of radical retropubic prostatectomy (RRP) over RPP is better visibility of the prostate and the surrounding tissue. Because the surgeon can see the prostate more clearly from an abdominal incision, he or she can be surer that enough tissue has been removed to get all of the cancer. The neurovascular bundles can also be seen more clearly. The surgeon also does not have to worry about an incision so close to the sensitive area of the rectum (Walsh, 1997, 152-154). However, the surgeon does have to be cautious when dealing with the major veins in the lower abdominal area to prevent major blood loss (Resnick and Thompson, 1998, 111).

During a radical retropubic prostatectomy, the patient can be placed in a variety of different positions. The most extreme is the "Trendelenburg" position (Resnick and Thompson, 1998, 310). This means that the patient is placed face up on a table that is tilted with the head lower than the feet. Shoulder braces prevent the patient from slipping off the table. This position causes the abdominal organs to be pushed towards the chest by gravity and out of the way of the surgeon (Clayton, 1970, T-63).

Figure 2-5 illustrates the Trendelenburg position for radical retropubic prostatectomies. This picture helps to visualize the angle at which the patient is tipped for the procedure. Other positions have the patient placed in stirrups without the steep slope of the Trendelenburg position (Resnick and Thompson, 1998, 110).

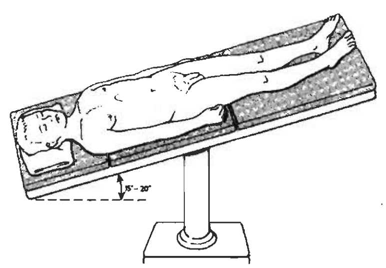

Figure 2-5 The Trendelendburg position

Resnick, Martin I., Thompson, Ian M., eds. Surgical Skills: Surgery of the Prostate. New York: Churchill Livingston Inc., 1998, p64

At the beginning of this surgery, a catheter with a balloon tip is inserted into the urethra to aid with the positioning of the bladder and urethra. The neurovascular bundles are carefully isolated from the prostate in an attempt to prevent impotence. The bladder and the prostate are separated and the prostate is removed using the catheter as a guide. Then the seminal vesicles are removed, and reconstruction of the urethra to the bladder proceeds.

Common concerns after performing any RP procedure are incontinence and impotence (caused by damage of nerves) and urethral stricture (scar tissue blocking the urethra) (National Cancer Institute, 1999, 1). Though there is some indication that the perineal approach may promote complete recovery of continence more quickly and effectively than the retropubic approach, both approaches appear to be equally reliable in terms of preserving continence. It should be noted that neither procedure completely eliminates incontinence (Gray, Petroni, Theodorescu, 1999, 881).

2.4.1.2 Trans Urethral Resection of the Prostate

TURP is generally not a procedure used to cure the body of prostate cancer. It is usually used to relieve problems with urination caused by inflammation of the prostate due to benign prostatic hyperplasia. After a TURP is performed, the removed tissue is analyzed to see if it is cancerous. Because cancerous tissue is sometimes found this way, TURP is an indirect form of cancer detection.

Similar inflammation problems associated with BPH occur for men with prostate cancer. Men who choose to carefully monitor cancer progression rather than treat it, and men whose cancer has progressed beyond the stage where full removal of the prostate would be beneficial, can have a TURP performed to relieve problems with urination (Walsh, 1997, 318).

During a TURP only the portion of the prostate surrounding the urethra is removed. This is achieved by using a device called a resectoscope. The device has a camera attached to it, and can have either a laser attachment or an electro-surgical unit to cut the tissue. The resectoscope is inserted through the urethra into the section of the urethra lining the inside of the prostate called the prostatic urethra. This tissue can be removed by chipping away at the prostate. As the surgeon removes the pieces of tissue, they are placed in the bladder and then flushed out using an irrigation fluid after the chipping away is completed (Walsh, 1997, 318). Figure 2-6 shows the configuration of the cutting edge of a resectoscope in the top two pictures and the shape of the chip of tissue that the resectoscope cuts in the two bottom pictures.

Figure 2-6 The shape of a resectoscope and a chip of prostate tissue
Blandy, John, Notley, Richard. Transurethral Resection. ed. 4. Oxford: Isis Medical Media Ltd., 1998, 63.

Figure 2-7 shows what the prostate looks like in stages as the tissue is being removed. The first picture on the left shows the prostate before the start of the surgery. The dashed lines indicate how the resectoscope will remove the portions of the prostate little by little—starting with the center dashed lines. The middle picture shows the first portion of the prostate removed. The surgeon would then start at the center of the portion of the prostate still there and again remove it little by little. The last picture shows the end of the process, with all but the outermost portion of the prostate removed.

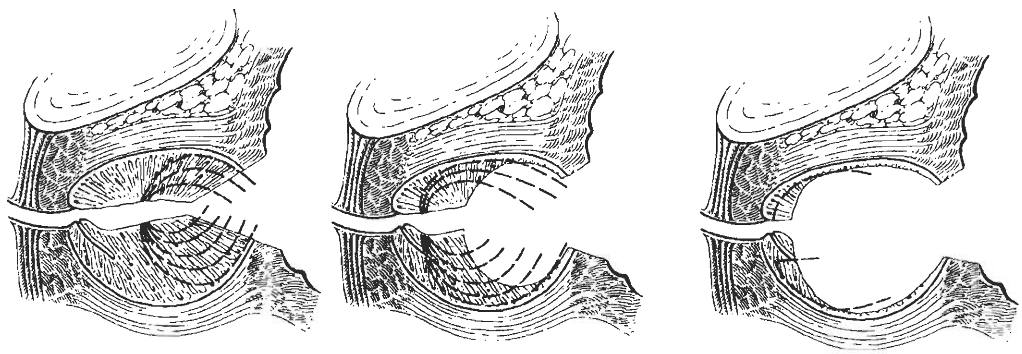

Figure 2-7 Transurethral resection of the prostate
Resnick, Martin I., Thompson, Ian M., eds. Surgical Skills: Surgery of the Prostate.
New York: Churchill Livingston Inc., 1998, p246

This procedure incurs the possibility of the same risks as RP, as well as "post-TURP syndrome." Post-TURP syndrome is caused by absorption of large volumes of the irrigation fluid that is used for flushing away chips in the bladder during the procedure. Post-TURP syndrome consists of a decrease in sodium concentration in the blood (hyponatremia), coma, blindness, and cardiorespiratory depression (Agarwal and Emmet, 1994, 1).

2.4.2 Hormone Therapy

Hormonal therapy is based on the fact that prostate cancer usually requires male sex hormones (which are called androgens) in order to grow. One familiar example of an androgen is testosterone. Hormonal therapy seeks to block or remove androgens from the prostate. Since this type of therapy only prevents the formation of new cancer cells, it can only slow, and at best stop, cancer growth; it never eliminates cancer in the patients on which it is used. The tumor remains in the prostate, though its spread may be slowed or ceased (Margolis, 1997, 38). Accordingly, it is used to prolong the life of patients whose cancer is too advanced for either surgery or radiation therapies to correct. Impotence and loss of libido are almost always side effects of hormonal therapies (Margolis, 1997, 41).

The prostate consists of both androgen-dependent cells (which require androgens), and androgen-independent cells (which will grow even in the absence of male sex hormones). The ratio of dependent to independent cancerous cells in a given patient determines the effectiveness of hormonal treatment (ibid.). The amount of androgen-independent cells in a tumor tends to increase over time, making hormonal therapy less effective as the cancer progresses (ibid.).

The oldest form of hormonal therapy is the surgical removal of the testicles, which is known as bilateral orchiectomy. This is classified as a hormonal and not a surgical treatment because the removal of the testicles has no direct influence on the cancer; it simply removes the source of the androgens. Since the testicles are largely responsible for the production of testosterone, an androgen, their removal often slows the growth of prostate cancer.

Even though bilateral orchiectomy is an effective form of hormonal therapy, psychological concerns about body image often lead the patient to select an alternative, noninvasive treatment. The side effects and benefits are roughly equivalent, but many prefer a reversible alternative.

One option for noninvasive hormonal therapy is the use of Diethylstilbestrol, or DES. DES is a synthetic form of estrogen which blocks production of lutenizing hormone (LH), a hormone that triggers the production of testosterone. A daily DES pill is considered to be as effective as surgical castration, although it carries an increased risk of cardiovascular complications (Margolis, 1997, 41).

Other drugs used in hormonal therapy are the lutenizing hormone-releasing hormone (LH-RH) analogs. These drugs also attempt to block lutenizing hormone production, just as DES does. These drugs cause an initial rise in LH production, but after a short while they block further release of LH, causing testosterone levels to fall. LH-RH analog treatments take the form of monthly injections, and are considered to have roughly the same effectiveness as surgical castration (Margolis, 1997, 42).

There are also drugs known as antiandrogens, which, in the case of prostate cancer treatment, prevent androgens from stimulating the cancerous prostate cells. To stimulate prostate cells, androgens must 'bind' to a certain part of the cell, which is called an androgen 'receptor.' Antiandrogens bind to these receptors in the place of androgens. This interception at the binding site prevents the androgens from reaching the portion of the cell it must stimulate. Because they do not stop the production of androgens, antiandrogens preserve potency in 87 percent of patients, but are not considered to be effective enough alone to treat advanced cancer (Margolis, 1997, 43).

Since the adrenal glands produce small amounts of androgens, it was once thought that combining antiandrogens with surgical castrations would block all androgens produced by the body. This is known as total androgen blockade. Trials now show that antiandrogens have little to no benefit over surgical castration alone (Margolis 1997, 43). These findings indicate that the amount of androgen produced outside the testes is so low that prostate cancer growth is not affected (ibid.).

2.4.3 Radiation Therapy

Radiation therapies are used when a patient is either too old to withstand the physical stresses of surgery or has some medical illness that rules out a surgical treatment. Cancer that has advanced too far to be fully removed by surgery is also a cause for the use of radiation. Radiation therapy is often used as a follow up to surgery as well.

Radiation therapy uses radiation to damage or destroy cancer cells in the targeted area. In many cases it damages non-cancerous tissue as well, but the healthy cells are more able to heal than the cancerous ones. Radiation treatments are often spaced out over time to provide time for the healthy cells to heal themselves between applications of radiation.

The standard in radiotherapy is external beam radiation, in which the radiation is projected into the cancerous growth in an effort to kill the cancer cells. Recently, systems that are able to target the radiation more effectively have been developed (Margolis, 1997, 38). Called three-dimensional conformal radiation therapy (3D CRT), this version of radiation treatment allows the delivery of a higher dose of radioactivity to the cancer while lessening the impact of radiation on the surrounding tissue. Conventional radiotherapy considers the prostate two dimensionally. A 'beam' of radiation is shot at the prostate, and incidentally damages tissues in front of and behind the cancer tissue. Consequently, the radiation dosage is limited to what these other tissues can withstand—which reduces the effectiveness of the radiation in damaging the cancer cells. With 3D CRT, a computerized topography (CT) scan is used to target the radiation three dimensionally. Rather than shooting a beam though the general area of the patient's pelvis, the radiation can be focused on a single point—the location of the cancer.

Another method of delivering radiation to the cancerous growth is through implanting radioactive 'seeds' in the prostate tissue. Called interstitial brachytherapy, this technique is not considered to be as effective as the external beam treatment. For the best result, it is necessary for the seeds to be implanted very close to the location of the cancer in the prostate. Recent improvements in placing the seeds for greater effectiveness have led to a resurgence of interest in this form of therapy (Margolis, 1997, 38). The newer techniques rely on using TRUS or CT scans which generate a 3D 'map' of the prostate that can be used to plan the placement of the seeds.

2.5 Experimental Treatments for Prostate Cancer

With the current rise in research relating to prostate cancer there are many different approaches to treatment and cures taking place. Cryosurgery is new in the treatment of prostate cancer, though it has been used to treat other forms of tumors—especially benign tumors—in the past. It is used as a form of radical prostatectomy where the prostate and cancerous tissues are first frozen and then removed (Wong, 1997, 968).

It was mentioned earlier in this chapter that laparoscopic techniques could be used to perform a biopsy of the prostate before the actual prostatectomy. This is done to prevent unnecessary invasive surgery. For this reason, procedures where the prostatectomy is performed with laparoscopic techniques are also being examined as a possibility. The main goal of this approach is to decrease the chance of infection and the length of hospital stay because of the minimal invasiveness of the procedure (Guillonneau and Vallancien, 1999, 74).

Immunotherapies harvest cells from the patient's own blood and then alter them to fight the cancer cells. Special cells called dendritic cells are infused with a protein specific to cancer cells. The dendritic cells are then injected back into the body where they swarm to the tumor and cause the immune system to fight the tumor (Association for the Cure of Cancer of the Prostate, 1999, 1).

It has also been recently discovered that the PSA is more than a diagnostic tool. Studies have shown that mice that have had PSA applied to their tumors actually show signs of slowed tumor growth than mice whose tumors did not have PSA application. So, PSA may be used in the future to fight the cancer cells (Associated Press, 1999).

2.6 Complications Due To Prostate Cancer Treatments

The set of cancer treatments discussed in this chapter, though offering the benefit of treating the cancer and its symptoms, also present some unfortunate complications. Some of these complications include impotence, incontinence, bowel dysfunction, urethral stricture, hot flashes and loss of libido. However, most of these complications are treatable.

Impotence is the severely decreased ability to maintain an erection for normal male sexual function. It should be pointed out that impotence following a prostate cancer treatment might be a result not only of nerve damage during the treatment, but also mental or emotional stress accompanying thoughts of the treatment or of having prostate cancer. Data presented in this paper for incidence of impotence refer specifically to patients who reported a significant decrease in their sexual function after treatment, regardless of the cause.

Patients who suffer impotence as a result of their cancer treatments can be treated in a number of different ways. One method is the insertion of a penile implant. This implant is used to give the penis enough rigidity to be used in intercourse. Another option is the use of a vacuum pump. This pump may be used to artificially draw blood into the penis, resulting in an erection. The blood can then be held in the penis long enough for intercourse by applying a rubber band to the base of the penis. There are also studies underway to evaluate the effectiveness of Viagra in treating impotence brought on by prostate cancer treatments (Zippe CD, et al., 2000, 244).

Incontinence is the severely decreased ability to control time of urination. The severity of this problem corresponds to the amount of unwanted urinary flow. For example, one patient may leak urine only when laughing or coughing. Another patient may have to wear pads because of significant daily urinary leakage.

Urinary incontinence can also be treated in a variety of ways. Methods of treating incontinence include the use of pads or other collection devices for less severe incontinence and the implantation of an artificial sphincter for more severe incontinence. An artificial sphincter is a device that consists of a circular cuff, which is implanted around the urethra. The cuff is connected to a bulb that is placed within the scrotum; squeezing the bulb will cause the sphincter to open and close, giving the patient control of the flow of urine.

Bowel dysfunction includes increased diarrhea, a feeling of urgency, pain, or rectal bleeding. Any of these symptoms in any form are considered bowel dysfunction for the purpose of this paper.

Urethral stricture is the narrowing or blockage of the urethra. This may result in inflammation of the urethra, decreased urinary flow, or pain during urination. This problem is often correctable with surgery.

Should a urinary stricture result from a prostate cancer treatment, it can be treated through the use of a procedure known as dilation. A balloon is inserted into the urethra and is inflated at the location of the stricture. This widens the urethra and increases the ability of urine to flow. Dilation can also be accomplished by inserting progressively larger diameter rods into the urethra. Another treatment option for urethral stricture is urethroplasty. During the course of this procedure, the section of the urethra that contains the stricture is cut out, and the two resulting ends are joined back together—sometimes with a skin graft.

Hot flashes are the sudden onsets of a physical feeling of being hot, which is due to a hormone imbalance. They are often treated with supplementary hormones.

Finally, loss of libido is the absence of sexual drive or desire to perform sexual functions. This does not mean that there is no desire for physical contact. Loss of libido may be due to a hormone imbalance. As with impotence, loss of libido may also be due to mental or emotional stress. Hormone replacement therapy is usually the means to treat loss of libido. The problem with using hormone replacement therapy is that loss of libido is a complication of hormone therapy, the goal of which is to block the production of sex hormones. So, the cure for loss of libido negates the effects of the treatment that caused that complication.

3 Methodology

This chapter is divided into four sections. The first section discusses economic analysis as it applies to health care. The second section explains the different sources pursued in order to obtain the information needed for the paper. The third section is a discussion of the different medical studies used as sources in this paper. This section also explains how these studies could and could not be compared to each other. Finally, the last section explains the procedure used for implementing this particular project.

3.1 Economic Analysis in Health Care

Economic analysis has become very important in health care. The costs of the newest high technology treatments have been rising rapidly, and the organizations that must bear these costs have become interested in measuring what specific improvements these high cost therapies are providing. These increased costs can often be justified by conducting an economic analysis. There are two main types of economic analysis that are used in health care. They are cost effectiveness analysis and cost benefit analysis.

3.1.1 Cost Effectiveness Analysis

Cost effectiveness analysis is a relatively easy and simple type of economic analysis that is often used in medical care. Imagine two distinct treatments that share the exact same benefits. Here "benefit" is used to encompass both length of life and quality of life measures. If these benefits are exactly the same, then the cheapest procedure is clearly the best one. Funds should be allocated to the cheaper of the two treatments, since the more expensive one does not give any added value for the increased price.

This type of analysis can also be used as a starting point for comparing two procedures with similar benefits, where further refinements in the analysis are made later. Initially it is assumed that two similar treatments provide benefits that are in fact equal, and adjustments are made later.

In reality, the assumption that two treatments share the exact same benefits—or even similar benefits—is often not a valid one. Therefore, a more complex and realistic type of economic analysis is called for as an alternative to cost effectiveness analysis.

3.1.2 Cost Benefit Analysis

Cost benefit analysis is a more comprehensive type of economic analysis. When utilizing cost benefit analysis, common cost and benefit units are usually assigned to all of the treatment's costs and benefits. One very common unit used in the U.S. is the U.S. dollar. All of the costs would be enumerated in U.S. currency, and all of the benefits would be assigned a dollar value as well. The costs are then subtracted from the benefits. If the resulting sum is greater than zero, the treatment is considered to be "cost beneficial".

Cost benefit analyses are desirable because they are complete and relatively easy to interpret, since all of the numbers involved in the analysis share the same unit. However, these analyses are also difficult to perform because while costs may be easy to express in dollar amounts—benefits often are not. There are significant issues involved in simply assigning a dollar amount to a reduction in a person's physical limitations, pain and suffering. Similarly, judging what the dollar value of an additional year of a person's life should be can be problematic as well.

3.1.3 Modified Cost Benefit Analysis

This section discusses a modified version of cost benefit analysis. This version is a more specific and restricted form of economic analysis than the usual cost benefit analysis.

Modified cost benefit is a way to analyze treatments that differ in their benefits. In this case, benefits must be measured in a way that has meaning for all treatments. The most commonly used measure of benefit is years of extended life. Other benefit measures could be used as well, such as a five-year survival rates.

When conducting a modified cost benefit analysis, the difference in costs is compared to the difference in benefits between the two options. For example, the difference in costs may be divided by the difference in life expectancy. This would give an additional cost per year of life expectancy. For example, consider one procedure that costs $200 and has a five-year survival rate of 25 percent. Assuming that the distribution of patients' survival times is linear, this five-year survival rate can be called expected survival time of 1.25 years. This calculation is accomplished by multiplying the time span by the percentage of survivors. Consider as well a second option that costs $500 and has a five-year survival rate of 50 percent. It can be assumed that this is equivalent to an added 2.5 years of life expectancy. Should the second option be used, essentially the cost is $300 ($500 - $200) for one and one quarter additional years of life (2.5 – 1.25).

The consensus in American society seems to be that treatments that cost less than about $50,000 per year of life saved are acceptable (Hayman et al., 1996, 829).

3.1.4 Use of Present Value Techniques in Economic Analysis

Some of the costs and benefits that pertain to decisions made today lie in the future. Many medical treatments are balancing an expenditure made today versus an improvement in the patient's condition that will occur at a later time. When considering costs and benefits that occur at different points in time it is very helpful to be able to convert these values into their present time equivalents.

Capital budgeting is a system of financial planning. Using one of capital budgeting's common techniques one can equate an amount of money paid out in the future with their dollar value of today. For instance, a sum of $100 dollars to be paid out in a year would be worth less in today's dollars. Knowing $100 must be spent in a year, a smaller amount of money can be invested now to have the $100 available later. If only $80 must be invested today to get that $100, then that $80 can be considered the present value of that $100 future cost. The process of converting future sums of money into their present values is called discounting, a commonly used capital budgeting technique.

In a medical scenario, present value techniques may be used to convert the long-term costs or benefits of purchasing medical technology or offering medical services into today's terms. For instance, if a patient is put on a medication, the future costs of that medication should be discounted in order to determine what amount must be set aside today to meet those future costs.

Present value techniques played a role in this project whenever continuing care costs were evaluated. For example, hormone therapy treatments can go on for years, and the value of those future costs in today's terms must be considered. Also, there are further PSA testing and follow up costs after the various prostate cancer treatments to monitor the status of the patient. These follow up visits and testing go on for a long span of time, and, therefore, their costs must be discounted using present value techniques.

3.1.5 Type of Economic Analysis in this Project

As noted above, it is not easy to place a dollar amount on a human life. However, cost benefit analysis requires that this be done. It is beyond the scope of this IQP to address the ethical issues involved in placing monetary values on the duration and quality of human life. For this and other reasons, this project has employed cost effectiveness analysis and modified cost benefit analysis, rather than 'full' cost benefit analysis.

Cost effectiveness analysis allows a researcher to consider only the cost of the therapy required to treat the patient. Cost effectiveness analysis seeks only to achieve the goal of saving the patient's life or reducing the patient's morbidity through the most cost efficient method available.

Modified cost benefit analysis can be used to compare those treatments that have very different outcomes. This type of analysis can be used, for example, when two treatments have a significant difference in survival rates. This project only examines easily quantifiable measures of benefits, such as differences in increased life expectancy. The differences in quality of life are mentioned, but a dollar value is not placed on them.

This gives readers the responsibility to decide which procedure is best using their own views on what is important.

3.2 Sources Used in this Project

3.2.1 The Medline Database

Research for this project began with the online medical database, Medline. This is an Internet version of the Index Medicus, a database including virtually all the latest medical articles published worldwide. Medline may be accessed from any computer in the world that has an Internet connection. The U.S. National Library of Medicine is the source of this publication. This database indexes approximately 400 journals from around the world. Medline was used to examine abstracts regarding the study of prostate cancer—its diagnosis and its treatment.

3.2.2 Libraries

The Gordon Library at WPI and the Lamar Soutter Library at the University of Massachusetts Medical School were used to find sources for this project. In these libraries, computers were used to search the card catalog, search for Internet materials or search online databases such as Medline.

After using Medline, the relevant articles were retrieved from the Lamar Soutter Library at the University of Massachusetts Medical School (UMMS) in Worcester. The Gordon Library at WPI was not as well suited for finding medicine-related materials. The Lamar Soutter Library was also helpful in acquiring books regarding cost analysis, as well as on other subjects relative to prostate cancer.

A particularly helpful source during this project has been the book The Prostate: A Guide for Men and the Women Who Love Them, by Dr. Patrick C. Walsh, M.D. Dr. Walsh is one of the leading experts on the diagnosis and treatment of prostate cancer. In addition to being a good source of information, Dr. Walsh's book has been a guide in terms of how a paper on this topic should be presented.

3.2.3 Sources of Cost Data

The reimbursement levels provided by Medicare to hospitals and to physicians are used in this project to approximate the costs of the various procedures considered in this project. The reimbursement provided by Medicare is often used as an estimate for costs in medical care.

Medicare provides reimbursement levels through a system known as a Prospective Payment system (PPS). Medicare's PPS is used to provide a standard reimbursement level for medical care received by patients covered by Medicare. Patients covered by Medicare include the elderly, the disabled, and certain other groups. A set amount of money is paid for each type of medical treatment, which is required by the patient, from a flu shot to a liver transplant. In practice, the actual costs per patient vary with each individual case, as some people have more severe conditions than others, some have more complications, etc. The assumption behind this PPS system is that the cost of treating a certain condition will, on average, be Medicare's PPS set amount.

Medicare's hospital prospective payment system is categorized according to a system called Diagnosis Related Groups (DRGs). The Diagnosis Related Groups are a comprehensive set of categories for hospital-related medical treatments. All hospital treatments covered by Medicare fall into a DRG. When Medicare wishes to provide coverage for something not already a part of the DRG system, a new category is added.

Medicare sets a standard amount of money for each DRG payment unit and that amount is reevaluated regularly to correct for inflation. Reimbursement rates vary by geographic region. Medicare sets a standard Medicare payment amount per DRG unit for all the regions of the U.S.

This standard DRG unit amount is multiplied by a weight that is associated with a given DRG. Each DRG has an associated unit weight. These weights vary according to the amount of resources used on average in treating a given diagnosis. A DRG with a weight of 2 receives twice the Medicare standard DRG unit payment, while a DRG with a weight of .5 would receive only one half. When the standard DRG unit payment is multiplied by the applicable DRG weight, their product is the reimbursement Medicare will pay out to the hospital providing care. This system of weights and payments that are associated with each DRG comprise Medicare's hospital prospective payment system.

Medicare provides a standard for medical reimbursement rates across the country, since it is a truly national system that is utilized by every hospital that wishes to accept Medicare patients. Therefore, most hospitals use the Medicare system, for a large percentage of their charges.

3.3 The Use of Medical Studies

The data used in this project was obtained from study results that were published in medical journals. Such studies are conducted by researchers to investigate the effectiveness of a certain treatment, to determine the natural progress of a certain disease, etc. When evaluating a treatment, the standard method is to measure the effectiveness of the new treatment and at the same time measure the effectiveness of a more conventional treatment. The effectiveness of the two treatments can then be compared. The effectiveness of a treatment may also be measured in comparison with a placebo.

There are many relevant factors in evaluating the significance of a particular prostate cancer study. These factors, which will be discussed, include: patient ages, ethnicity and geographical location; the follow up period; number of patients in the study; method of collecting study data; clinical stages of the cancer that the patients had; treatments studied; symptoms studied, and; the results or conclusions of the study. If these factors are not addressed by a prostate cancer study, then the study loses some of its value. Appendix A lists the studies used in this project and gives the details on these study dimensions.

Factors such as patient ages, ethnicity and geographical location describe the study's target population. Prognoses and presenting conditions are different for patients of different ages, ethnicity or geographical location, so it is important to account for these factors in describing the study being presented. For example, many prostate cancer studies show that there is a higher occurrence of prostate cancer in Africans and African Americans than in Caucasians (Cassel, 1997, 308). For this reason, a prostate cancer study should describe its study group in these terms. Also, many prostate cancer studies show a difference in cancer metastasis rates for patients of different ages (Cassel, 1997, 310; Walsh, 1997, 35). A prostate cancer study therefore should present the age of the patients in its data set. If a prostate cancer study does not describe these population identification factors, then the relevance of the study to particular individuals may be lost.

In general, the accuracy and reliability of the data are clearly important in a study. Factors that establish the accuracy and reliability of a prostate cancer study include the number of patients in the study, the method by which data were collected (questionnaire, interview, etc.) and the follow up period. Generally, the more data points there are the better the accuracy in estimating the frequency of a phenomenon. For example, if a prostate cancer study looks at two patients who both had a prostatectomy and both of them develop incontinence after the procedure, then the study might claim that 100 percent of patients who have had a prostatectomy also developed incontinence as a complication. In actuality, the average occurrence of this complication from a prostatectomy is much smaller (see Results chapter). All of the studies used in this project involve a large number of patients in the data pool.

In prostate cancer studies several methods are used to gather data, including a mailed out questionnaire, a nurse- or physician-administered questionnaire, physician observation or data gathered from patient files. The method of gathering data is important because it may reflect the biases and accuracy of data reported in a medical study. Biases may occur when a researcher wants to interpret information a certain way. The researchers may try to get the data to fit a curve to prove their theory, which may result in inaccurate study conclusions. Disagreements may even arise between what a patient observes and what a physician observes.

Questionnaires and patient files are most commonly used to collect data. The problem with a patient questionnaire is that the patient may exaggerate his or her condition; or, if a female nurse administers the questionnaire, the patient may be too embarrassed to answer accurately. Also, the data often cannot be standardized because different patients have different interpretations of complication severity. In a prostate cancer study, one patient may report as severe incontinence what another reports as mild incontinence, while in reality their conditions are the same. This problem of data standardization may sometimes be avoided by using patient files. However, reading patient files to gather data requires a physician to interpret the patient's condition, which may be problematic. A patient file may be incomplete or the physician may judge the patient's condition inaccurately. All of the studies used in this project used either questionnaires or patient files to collect data.

The follow up period is important because it describes the time after a treatment in which data were collected on a patient in the prostate cancer study. Ideally, a patient in a prostate cancer study should be followed to his ultimate death in order to gather the maximum amount of data, especially since much of the necessary data concern the effectiveness of a procedure. Some prostate cancer studies have only a follow up period of a few years. Such a time duration may not be long enough to help in predicting the true effectiveness of a treatment. Many of the studies used in this project follow the patients to their death.

Factors such as cancer stage, treatments used and symptoms studied are very important in making a prostate cancer study significant. Most prostate cancer studies examine the effects of a particular procedure on a patient, usually with respect to complications and the effectiveness of the treatment. It is important to know at what cancer stage a treatment was used in order to understand its effectiveness. For example, a particular treatment may be found to be more effective at one cancer stage than another.

3.4 Method of Procedure for this IQP

In this project, several different prostate cancer treatments were researched and then assessed with a cost effectiveness analysis. Particular attention was given to the costs associated with each treatment, the costs involved in maintaining treatment for the patient after the initial treatment, and the costs associated with remedying the common side effects of a treatment.

Measures of quality of life are concerned with the comfort and functional ability of the patient. A procedure that greatly increases the life span of a patient—but at the expense of damaging psychological and physiological side effects—may not be as desirable to a particular patient as a form of therapy that is not quite as effective but has considerably fewer side effects. As noted above, the common side effects of different prostate treatments that physicians seek to minimize include incontinence, impotence, loss of libido, and damaged body image. Because the perceived seriousness of these side effects will vary with different individuals, this report does not attempt to categorize them in terms of importance or desirability.

Effectiveness and quality of life data were found in a multitude of different medical studies. Because many different organizations and individuals conduct these studies, the results are often reported in different ways. Some statistical analysis of the data points was necessary to place all of the effectiveness information into the common units that are required by our analysis. Survival rates, for instance, are commonly reported as the percentage of patients who live a certain number of years after the specified treatment. Some analysis was required to correct for the difference in time spans of the survival rates.

Through evaluating these factors and conducting comparisons between available forms of prostate cancer therapies, a system to provide recommendations for treatment of patients was reached. Also discussed are new treatments and other possibilities for improving prostate cancer outcomes in the future.

4 Results

This chapter presents the data associated with effectiveness, quality of life, and costs related to the various prostate cancer treatments which were compiled in the course of this project.

Throughout this chapter, a survival time span of five years is typically used to measure treatment effectiveness. The five-year span is something of a standard in cancer studies, and this allows one researcher's data to be comparable to another researcher's data.

This chapter also presents the average costs to treat cancer with the different treatments that are available. The way in which these costs were calculated requires some explanation.

Computing the complete cost of a treatment is not a trivial task. First, the initial cost of the therapy has to be considered. There will be "up-front" spending involved in any treatment. For example, this cost could be associated with the surgery that actually removes the prostate. This is an initial, one time expenditure.

This initial cost is often only the first step in finding total cost. In addition, the costs of treating any side effects and complications of the treatment need to be considered. These 'secondary' costs, which are associated with complications, are not spent on every patient. Adding the cost for treating every complication in full to the total cost of the procedure would produce a large overestimate. Instead, in this project the cost has been multiplied by the incidence rate of that complication. For instance, a complication that costs $1000 to treat and occurs in half of the treated patients would be calculated to have an expected cost of $500. If a large number of randomly selected patients are treated with this therapy, allocating $500 per patient for treating this complication should account for all of those patients who actually suffer from the complication.

Finally, there are the continuing costs associated with a treatment. All of the treatments studied in this project require, at a minimum, regular PSA testing to monitor the effectiveness of the treatment. In some cases the continuing costs are much greater than the price of PSA testing. For example, hormone therapy requires continuous spending to purchase more medications for the patient. The future costs associated with a particular treatment have all been discounted so as to compute their present value (see Methodology chapter).

In order to obtain the cost of a procedure, the initial cost is considered first. To this initial cost, the adjusted complication costs are added. Adjusted costs are computed by multiplying the cost to treat a complication by the incidence rate of that complication.

Then to generate a more complete cost, a time span needs to be established. In this project a five-year span was used. The continuing costs are followed and discounted within this time span. The continuing costs are then added to the initial and complication costs. This computation results in the average full cost associated with treating one patient.

The rest of this chapter is divided into discussions of each of the treatments considered in this project. In each of these discussions the effectiveness of the treatment is presented; then the quality of life that the patient can expect after treatment is discussed. Finally, the costs associated with each of the treatments are detailed.

4.1 Prostatectomy

Ideally, information and calculations for each different type of prostatectomy procedure would be used for a complete analysis of prostatectomy procedures. Unfortunately, data for effectiveness, complications, and costs that are categorized by type of prostatectomy procedure are not available. Therefore, for the sake of this discussion, this project must assume that the radical retropubic prostatectomy procedure is the same as the perineal prostatectomy procedure in terms of outcomes and costs.

4.1.1 Effectiveness

Survival rates in terms of disease specific survival and disease free survival were used in this project. Disease free survival rates describe the percentage of treated patients who did not show any signs of prostate cancer within the time span studied. Disease specific survival rates describe the percentage of patients who may have prostate cancer after treatment but did not die of prostate cancer within the time span.

The data show that only 23 percent of men who underwent prostatectomy to treat their prostate cancer died from prostate cancer within 10 years after the procedure was performed (Margolis, 1997, 37). Fifty two percent of patients who received a prostatectomy were free of prostate cancer 10 years after the procedure (ibid.). These survival rates are expressed over a 10-year span, so they will need to be adjusted to fit the more commonly used 5-year time span.

4.1.2 Quality of Life

Aspects of quality of life for prostatectomy treatments were typically discussed in studies by stating the number of men who had difficulties with impotence, incontinence (that did and did not require surgical treatment), bowel dysfunction, and urethral stricture, and death during the procedure. Table 4-1 gives a breakdown of the occurrence of each of these complications as discussed for prostatectomy.

Of the complications mentioned in the studies, Table 4-1 shows that sexual dysfunction was the most frequent complication for men after undergoing a prostatectomy. An average of 66.7 percent of men polled answered that they had some difficulty maintaining an erection within about a year after their procedure was performed (McCammon, 1999, 506-519).

Incontinence was the next most common complication. The information collected on it allowed a division to be made between men who had severe incontinence requiring surgery and men who had no more than a few drops of uncontrolled urine per day. Notice that there were far fewer patients who required surgery to aid their problems with incontinence than there were men who had less severe difficulties.

Urethral stricture occurred more than bowel dysfunction. Both complication rates are considerably lower than the complication rates of impotence and incontinence. Roughly 10.5 percent of the men surveyed reported bowel dysfunction (McCammon, 1999, 506-519). Urethral stricture was reported in 15 percent of patients (Macdonagh et al., 1997, 401-408).

Reports of death during the actual prostatectomy procedure do not appear to be common, but they are worth mentioning. Table 4-1 shows that 2 percent of men in a particular case study died from complications during the procedure (Macdonagh, et al., 1997, 406). The specific cause of these deaths is not known. If this percentage is accurate, then it is highly uncommon that a man undergoing a prostatectomy will die during the surgery.

Complication Rates For Prostatectomy Procedures						
Complication	Sexual Dysfunction (Impotence)	Incontinence		Bowel Dysfunction	Urethral Stricture	Death During Procedure
		General	Surgery Required			
Mean %	66.7 %	31 %	11 %	10.5 %	15 %	2 %

Table 4-1 Complication Rates For Prostatectomy Procedures

Source: Macdonagh, R.P. et al. "The Use of Generic Measures of Health-Related Quality of Life In the Assessment of Outcome from Transurethral Resection of the Prostate." British Journal of Urology. 79 (1997): 401-408. McCammon, Kurt A. et al. "Comparative Quality-of-Life Analysis After Radical Prostatectomy or External Beam Radiation For Localized Prostate Cancer." Urology. 53:4 (1999): 509-516. Shrader-Bogen, Cheryl L., et al., "Quality of Life and Treatment Outcomes" Cancer. 79:10 (1997): 1977-1986.

4.1.3 Cost of Treatment

The initial cost of performing a prostatectomy as obtained from 1995 Medicare DRG reimbursement rates is about $8,500 (U.S. Congress Office of Technology Assessment, 1995, 61).

The complication costs depend on both the costs to treat the complication and the incidence rate of the complication. The cost for a penile implant to treat impotence is about $11,350 (U.S. Congress Office of Technology Assessment, 1995, 62). Impotence among prostatectomy patients has an incidence rate of 66.7% according to the data. Assuming that all patients with impotence opt to receive a penile implant, the average cost to treat impotence would be $11,350 multiplied by .667, which is about $7,500 (ibid.). The cost to treat incontinence with surgery is $8,080 and the incidence rate is 11 percent (ibid.). The average cost to treat incontinence in prostatectomy patients would be, therefore, about $900. The cost to treat urethral stricture is $51, and the incidence rate is 15 percent (ibid.). So, the average cost to treat urethral stricture would be $7. That makes the average investment in treating prostate cancer with a prostatectomy approximately $17,000.

The continuing costs associated with a prostatectomy are only those associated with regular office visits and follow up PSA testing. Assuming an office visit and PSA test every three months, follow up costs are estimated to be $240 per patient per year (ibid.). These follow up costs were discounted using present value techniques and a discount rate of 5 percent per year. Calculating over a five-year span, and adding the initial cost to these figures, the amount computed is about $18,000. This is the average cost for five years of treating a single prostate cancer patient with a prostatectomy.

4.2 Radiotherapy

4.2.1 Effectiveness

Effectiveness data for radiotherapy was researched as a "stand-alone" procedure. Radiotherapy is sometimes used as a follow up treatment after a prostatectomy, but in this project and in the data cited, radiotherapy was used alone to treat prostate cancer. Survival rates for disease specific survival and disease free survival were located. The data show that 36 percent of men who underwent radiotherapy to treat their prostate cancer died from prostate cancer within 10 years after the therapy was completed (Office of Technology Assessment, 1995, 38). Eighty-seven percent of the surviving patients were free of prostate cancer 10 years later (ibid.). It is important to remember that radiotherapy is often a procedure that is performed when the cancer has advanced farther than the cancer typically treated with a prostatectomy.

4.2.2 Quality of Life

Quality of life studies of patients treated with radiotherapy discussed the number of men who had difficulties with impotence, incontinence (that did and did not require surgical treatment), bowel dysfunction, urethral stricture, and death from the procedure.

Table 4-2 shows the percentage of men affected by each of the above complications following a "stand-alone" radiotherapy procedure. Impotence appears to be the complication that affects the largest number of men who receive radiotherapy to treat their prostate cancer. Table 4-2 shows that 44 percent of men are afflicted with some form of impotence after their treatment with radiotherapy (Macdonagh, et al., 1997, 404). The table also shows that 30 percent of men treated by radiotherapy experienced general incontinence problems and 3.1 percent experienced incontinence so severely that surgery was required to treat it (Shrader-Bogen, 1997, 1980). General incontinence and bowel dysfunction affected patients in roughly the same amounts. About 28.4 percent of patients experience some form of bowel dysfunction after radiotherapy, as compared with incontinence's 30 percent (McCammon, 1999, 510). Death from the treatment was minimal. Table 4-2 shows it to be 0.2 percent (Macdonagh, et al., 1997, 406).

Complication Rates For Radiotherapy Procedures							
Complication	**Sexual Dysfunction (Impotence)**	**Incontinence**		**Bowel Dysfunction**	**Urethral Stricture**	**Death During Treatment**
		General	**Surgery Required**			
Mean %	**44%**	**30%**	**3.10%**	**28.4%**	**2.5%**	**0.20%**

Table 4-2 Complication Rates For Radiotherapy Procedures

Source: Macdonagh, R.P. et al. "The Use of Generic Measures of Health-Related Quality of Life In the Assessment of Outcome from Transurethral Resection of the Prostate." British Journal of Urology. 79 (1997): 401-408. McCammon, Kurt A., et al. "Comparative Quality-of-Life Analysis After Radical Prostatectomy or External Beam Radiation For Localized Prostate Cancer." Urology. 53:4 (1999): 509-516. Shrader-Bogen, Cheryl L., et al. "Quality of Life and Treatment Outcomes" Cancer. 79:10 (1997): 1977-1986.

4.2.3 Cost of Treatment

The initial cost of performing a radiotherapy treatment for prostate cancer treatment as obtained from the 1995 Medicare DRG reimbursement rates was about $3,600 (U.S. Congress Office of Technology Assessment, 1995, 61).

As noted before, complication costs depend on both the costs to treat the complication and the incidence rate of the complication. The cost for a penile implant to treat impotence is $11,350. Impotence among radiotherapy patients has an incidence rate of 44 percent according to the data. Therefore, the average cost to treat impotence was $11,350 multiplied by .44, which is about $5,000. The cost to treat incontinence with surgery was $8,080 and the incidence rate is 3.10 percent. The average cost to treat incontinence in radiotherapy patients, therefore, is about $250. The cost to treat urethral stricture was $51, and the incidence rate is 2.5 percent. The average cost to treat stricture was about $1. That makes the investment in treating prostate cancer approximately $8,900.

The continuing costs associated with radiotherapy are only those associated with regular office visits and follow up PSA testing. Using the same assumptions as with prostatectomy, these are estimated to be $240 per patient per year. These follow up costs were discounted using present value techniques and a discount rate of 5 percent per year. Calculating over a five-year span, and adding the initial cost to these figures, the amount computed is about $10,000. This is the average cost of treating a single prostate cancer patient for five years with radiotherapy.

4.3 Hormone Therapy

Hormone therapy can be divided into two different forms, drug treatment and orchiectomy. There are many different combinations of drugs currently being used for hormone therapy. This paper will focus specifically on Bicalutamide. These two treatments are performed in very different ways, but attack the prostate cancer in the same manner. For this reason, they are grouped together in this project. Both approaches have similar effectiveness but different complication profiles.

4.3.1 Effectiveness

There is very little information for survival rates for hormone therapy in general. Studies that indicate effectiveness data for hormone therapy usually indicate effectiveness in terms of general survival two years after the treatment's start. Of patients who had undergone orchiectomy as a form of cancer treatment, the median survival time was 779 days (Kolvenbag, 1999, 50). (The median survival time indicates that half of patients had died by that time and half still survived.)

Effectiveness information for the drug Bicalutamide was also given as a median survival time. The median survival under Bicalutamide was 737 days (Kolvenbag, 1999, 50). That is, the survival rate at 737 days would be 50 percent.

The numbers 737 and 779 are both very close to the number 730, which is 365 times two, or two years. That makes 50 percent a good estimate for the two-year survival rate of both procedures.

4.3.2 Quality of Life

Complications associated with hormone therapies are very different than complications associated with radiotherapy and prostatectomy. For example, information on incontinence was discussed in almost every paper that focused on quality of life for patients of a prostatectomy. This information was not included in papers discussing hormone therapy. Since hormone therapy procedures do not involve surgery in the area of the urethra, it can be assumed that incontinence presented itself very rarely, if at all. Impotence, bowel dysfunction, urethral stricture, hot flashes, loss of libido, gynecomastia, and death during treatment, are the aspects of quality of life during hormone therapy with available information. Table 4-3 lists the information for these complications of hormone therapy treatments in terms of percentages. Notice that Bicalutamide results in fewer occurrences for all but one complication.

Table 4-3 shows that 37 percent of men who were treated by orchiectomy experienced some form of impotence, but only 18 percent of men who took Bicalutamide experienced sexual dysfunction (Iversen, 1999, 22). Numbers for bowel dysfunction are similar for both orchiectomy and Bicalutamide, with 6 percent and 5 percent, respectively, of men experiencing bowel difficulties (Iversen 1999, 23). Urethral stricture and death during treatment were examined but found to be non-existent for both

Complication Rates for Hormone Therapy							
Complication	**Sexual Dysfunction (Impotence)**	**Bowel Dysfunction**	**Urethral Stricture**	**Hot Flashes**	**Gynecomastia**	**Loss of Libido**	**Death During Treatment**
Orchiectomy	**37.00%**	**6.00%**	**0.00%**	**50.00%**	**Not available**	**47.00%**	**0.00%**
Bicalutamide	**18.00%**	**5.00%**	**0.00%**	**13.00%**	**50.00%**	**23.00%**	**0.00%**

Table 4-3 Complication Rates for Hormone Therapy

Iversen, P. "Quality of Life Issues Relating to Endocrine Treatment Options." European Urology. 36 (1999) 20-26.

forms of hormone treatment (Iversen, 1999, 23). Table 4-3 shows that hot flashes affected 50 percent of men who were treated with an orchiectomy, but only 13 percent of the men who took Bicalutamide were affected by them (Iversen, 1999, 23). Gynecomastia data were available only for men who took Bicalutamide, and these complications were experienced by half of the men who were so treated. Forty-seven percent of the men who underwent an orchiectomy for treatment of prostate cancer experienced a loss of libido, but only 23 percent of men who took Bicalutamide experienced similar problems (Iversen, 1999, 20-25).

4.3.3 Cost of Treatment

4.3.3.1 Pharmaceutical Approach

The cost of purchasing a one-year supply of Bicalutamide in 1995 is about $3,500 (U.S. Congress Office of Technology Assessment, 1995, 61). This first year of medication serves as the initial cost of treating the cancer.

As before, complication costs of Bicalutamide treatment depend on both the costs to treat the complications and the incidence rate of the various complications. The cost for a penile implant to treat impotence is $11,350. Since impotence among Bicalutamide patients has an incidence rate of 18 percent according to the data, the average cost to treat impotence is $11,350 multiplied by .18, which is about $2,000. That makes the investment in treating prostate cancer approximately $5,500 before follow up costs are added. Other complications may factor into this cost, but this is the basic scenario.

The continuing costs associated with Bicalutamide are those associated with regular office visits and follow up PSA testing, as well as the costs to purchase more medication. These are estimated to be $240 per patient per year for the office visits and PSA tests, and $3,500 per year for the medication. The follow up costs are again discounted using present value techniques and a discount rate of 5 percent per year. Calculating them over a five-year span, and adding the initial cost to these figures, the amount computed is approximately $22,000. This is the average cost of treating a single prostate cancer patient for five years with Bicalutamide. (Note that the average life expectancy of these late prostate cancer stage patients is only about 2 years).

4.3.3.2 Surgical Approach

The initial cost of performing a surgical castration is about $2,000.00 (U.S. Congress Office of Technology Assessment, 1995, 61).

As with the previous treatment alternatives, complication costs depend on both the costs to treat the complications and the incidence rate of the complications. The cost for a penile implant to treat impotence is $11,350. Impotence among castration patients has an incidence rate of 37 percent according to the data. The average cost to treat impotence is, therefore, $11,350 multiplied by .37, which is $4,200. That makes the total initial investment in treating prostate cancer $6,200.

The continuing costs associated with castration are those associated with regular office visits and follow up PSA testing. As above, these are estimated to be $240 per patient per year for the office visits. The follow up costs were discounted using present value techniques and a discount rate of 5 percent per year. Calculating over a five-year span, and adding the initial cost to these figures, the amount computed is approximately $7,300. This is the average cost of treating a single prostate cancer patient for five years with orchiectomy. (Again please note that the average life expectancy of these late prostate cancer stage patients is only about 2 years).

5 Prostate Cancer Management

Health care management, in general, is used to decide the best possible treatment for patients for their particular situation. Cancer care management is used to decide the best possible treatment plan for a patient who has been diagnosed with cancer. This chapter looks at the treatments that have been discussed in previous chapters of this paper and offer a means by which patients may be helped to decide which treatments they feel are right for them.

This paper has looked at each treatment in terms of three dimensions: effectiveness of the treatment, complications from the treatment, and costs of the treatment. The effectiveness of a treatment refers to its effect on patient survival rates and its ability to cure the cancer. The effectiveness of the treatment is clearly of critical importance. Patient satisfaction, or quality of life, refers to the treatment's impact on the patient's living status in terms of comfort and physical or emotional well being. A treatment must be chosen that allows the patient as comfortable a quality of life as possible. Patients should not have to deal with complications or other problems that they cannot tolerate. Finally, a treatment must be chosen that is reasonable in cost. Unnecessary spending must be avoided in the search for a treatment. By using less expensive treatments, more patients can be treated for the same cost.

This chapter is categorized into sections by cancer stage. For each stage, the relevant treatments are discussed. For example, one would not consider surgery an option if the patient has reached T4 stage where surgery would not be able to remove the extensively metastasized cancer.

The three dimensions of each treatment, as mentioned above, are then discussed. Qualitative information is given about the relative effectiveness of treatments in the various stages. Formally presented effectiveness data are not available categorized by prostate cancer stage. Information on which treatment is generally used for each cancer stage is available, however, and was used to associate treatments with stages in this chapter.

Because certain treatments are generally associated with certain stages, it is assumed in this project that the data collected are accurate for the appropriate cancer stages. This seems to be a reasonable assumption, because a physician will only perform a treatment on a patient with an appropriate cancer stage.

It must be noted that this chapter simply offers one strategy for finding a treatment plan; it is only suggestive. The patient and physician must decide together on the best treatment plan; these suggestions would merely aid in formulating that decision.

5.1 Cancer Stage T1

Most forms of cancer are most easily treated if detected early on. If a patient is diagnosed with a stage T1 tumor, then the tumor is very small and localized.

Normally, an early stage, localized prostate tumor may be treated with either prostatectomy or radiotherapy. Fifty-two percent of surviving patients treated with prostatectomy were prostate cancer free 10 years later and 23 percent of patients died from prostate cancer within that time period, though they had been treated with prostatectomy. Of patients treated with radiotherapy, 87 percent of the survivors were prostate cancer free 10 years after the treatment but 36 percent had died of prostate cancer during that span (see Results chapter).

Watchful waiting is also an option for treatment of prostate cancer depending on the age of the patient. If the patient's age indicates a life expectancy of greater than 10 years, then watchful waiting might not be a preferred treatment option as compared to a more proactive treatment plan, like prostatectomy or radiotherapy (Beemsterboer, P.M.M. et al.,1999, 100). It has been found that prostate cancer tumors in younger men metastasize more quickly, for reasons that are still not entirely clear. The opposite is true for prostate cancer tumors in older men with a life expectancy less than 10 years; their tumors metastasize more slowly (Cassel et al., 1997, 305-315). Because their tumors metastasize more slowly and because their life expectancies are shorter, a man with a life expectancy of less than 10 years diagnosed with stage T1 prostate cancer might opt for watchful waiting. Having a shorter life expectancy and a lower rate of metastasis, he has a lower probability of dying from prostate cancer. Under this same logic, a man with a life expectancy of greater than 10 years who is diagnosed with stage T1 prostate cancer might opt for a more proactive treatment plan.

Complications arise from prostatectomies and radiotherapy. One of the reasons patients often appreciate watchful waiting is that the complications are minimal. The common complications associated with prostatectomy and radiotherapy are bowel dysfunction, sexual dysfunction, incontinence, urethral stricture and death caused by the procedure. Impotence occurs in 44 percent of all patients treated solely with radiotherapy, but occurs in 66.7 percent of patients treated with prostatectomy. The occurrence of incontinence requiring surgery in patients treated with prostatectomy

(11%) is three times that of patients treated with radiotherapy alone (3%). However, the occurrence of bowel dysfunction in patients treated with prostatectomy (10.5%) is only half that of patients treated with radiotherapy (28.4%). The occurrence of urethral stricture is over five times greater in patients treated with prostatectomy (15%) than in patients treated with radiotherapy (2.5%). Death as a result of the treatment is rare in both prostatectomy and radiotherapy. Only 2 percent of patients who undergo prostatectomy die during the actual procedure and only 0.2 percent of patients who undergo radiotherapy die during the actual procedure. (Appendix B summarizes the different treatments and the frequency at which these and other complications occur for each treatment).

Cost should also be considered in these treatments (please refer to the Results chapter for detailed cost data on each treatment). The 5-year cost for a prostatectomy, including the actual procedure, hospital stay, staff and physicians' bills, complications and continuing expenses, is $18,000 (see Results chapter). The 5-year cost for radiotherapy, which includes the regular radiotherapy sessions, complication costs and other continuing expenses, is $10,000 (see Results chapter). Watchful waiting is the least expensive alternative. This approach assumes regular visits to a physician and PSA testing. The 5-year cost for watchful waiting is only $1,100.

When deciding on a treatment plan in stage T1, one must consider the effectiveness of the treatment on this stage of prostate cancer, the patient's life expectancy, the patient's projected quality of life after the treatment and the cost of the treatment. It has been suggested that if the patient has a life expectancy of fewer than 10 years then watchful waiting might be the best option at this stage because the patient would most likely not die of the prostate cancer anyway (Beemsterboer, P.M.M. et al., 1999, 97-104). If the patient has a life expectancy of greater than 10 years, then a more proactive treatment might be chosen.

According to the information used for this chapter, radiotherapy and prostatectomy are the two most effective and most commonly used treatments at stage T1. Prostatectomy has a long list of complications, which occur at great frequency compared to radiotherapy alone. Prostatectomy is also more costly than radiotherapy. Therefore, the treatment suggested for a stage T1 patient with a life expectancy of greater than 10 years may well be radiotherapy.

5.2 Cancer Stage T2

Stage T2 cancer is still considered early stage cancer and is still localized. However, watchful waiting is not used as often for patients with cancer that has progressed to this stage (Lim, Arthur J., et al., 1995, 1421). A stage T2 prostate tumor has a greater chance of metastasizing and breaching the outer prostate gland tissue. Prostatectomy and radiotherapy are the most commonly used treatments at stage T2 (Resnick and Thompson, 1998, 90-93; Margolis, 1997, 38). The complications and costs of the various treatments are the same as mentioned for cancer stage T1.

At stage T2, there is a much greater chance that the prostate cancer will prove to be a fatal condition (Lilleby, 1999, 245). Watchful waiting is not the best option at this stage, but still a possibility. Radiotherapy gives good results with fewer side effects than prostatectomy. Similar to stage T1, radiotherapy may well be the better overall treatment plan in terms of cost and quality of life when compared to prostatectomy.

5.3 Cancer Stage T3

There are a variety of treatments that are commonly used for patients diagnosed with stage T3 prostate cancer. Watchful waiting is still an option, although at this cancer stage it is not generally used because the cancer is advanced enough to greatly shorten the patient's life if left untreated (Iversen, P., 1999, 21-22). Radiotherapy is also still an option, but is not so commonly used because cancer stage T3 tumors are no longer localized. Targeting the entire tumor with radiation would produce too much damage to the surrounding tissue (Horwitz, Eric M., M.D. et al., 1999, 1220-1221; Margolis, 1997, 38). Prostatectomy is rarely attempted for patients with this stage of prostate cancer because the tumor has spread beyond the wall of the prostate and simply removing the prostate will not remove the entire tumor (Resnick and Thompson, 1998, 93).

Hormone therapy is a commonly used treatment for stage T3 prostate cancer (Crawford, E.D. et al., 1989, 421). Hormone therapy as a prostate cancer treatment includes either orchiectomy or drug therapy. Of patients treated with orchiectomy, the median survival time was 779 days; of patients treated with Bicalutamide, median survival was 737 days. It is important to note that the effectiveness numbers for radiotherapy versus hormone therapy cannot easily be compared because the data for each are taken from patients at different stages. Since hormone therapy is usually used for patients who have more advanced prostate cancer (cancer stage T3 or T4), the survival rates are much lower than those for prostatectomy or radiotherapy.

Complications that usually accompany hormone therapy include sexual dysfunction, bowel dysfunction, gynecomastia, loss of libido, and hot flashes (see Results chapter). It is important to note that—unlike radiotherapy or prostatectomy—hormone therapy includes virtually no risk of urethral stricture, incontinence or death during treatment.

The two hormone therapy treatments can be compared to each other and to radiotherapy to find a preferred treatment option for patients in this cancer stage. The occurrence of impotence is relatively the same between radiotherapy (44%) and orchiectomy (37%), but much greater than with Bicalutamide (18%). Bowel dysfunction occurs much more often in patients treated with radiotherapy (28%) than patients who receive and orchiectomy (6%) or are treated with Bicalutamide (5%). Gynecomastia, loss of libido and hot flashes are complications that occur with great frequency after hormone therapy. There are no data for gynecomastia in patients having undergone an orchiectomy. Patients treated with Bicalutamide have a 50 percent chance of developing gynecomastia. Hot flashes occur in 50 percent of patients treated with orchiectomy and in 13 percent of patients treated with Bicalutamide. Loss of libido occurs in 47 percent of patients treated with orchiectomy and in 23 percent of patients treated with Bicalutamide. In short, gynecomastia, loss of libido and hot flashes are extremely likely complications for patients undergoing hormone therapy.

Pharmaceutical-based hormone therapy, such as Bicalutamide, is expensive; however, surgical-based hormone therapy, such as orchiectomy, is also expensive (refer to the "Results" chapter for detailed cost data on hormone therapy). Although most patients under hormone therapy treatment only survive about 2 years (again, attributed to the fact that these patients have advanced stage prostate cancer), the costs for hormone therapy have been calculated to 5 years. This allows cost comparisons to be made between these therapies and radiotherapy. The one time cost of an orchiectomy is

$2,000; again all expenses are included, such as hospital stay and staff and physician's services. The 5-year cost for orchiectomy, including regular visits and follow-up treatment, is $7,300 (see Results chapter). The 5-year cost for Bicalutamide, including regular drug treatments and doctor's visits, is $22,000 (see Results chapter).

At stage T3, the prostate cancer has spread so far that only radiotherapy or hormone therapies are reasonable alternatives for treatment (Iversen, P., 1999, 21-22). Radiotherapy and hormone therapies have very different complications associated with them. The patient has to decide with which potential complications he is more comfortable. Hormone therapy usually involves a drug treatment, such as Bicalutamide. The cost turns out to be greater than that of radiotherapy (see Results chapter). At stage T3, not only is radiotherapy less expensive, but it is also considered more effective for this particular stage (Margolis, 1997, 30). However, since at this prostate cancer stage the tumors are no longer localized, a larger area of the body would be irradiated if using radiotherapy. This use of a larger radiation beam damages surrounding tissue and causes greater frequency of complications. So, in spite of the more appealing cost data and seemingly better effectiveness data, hormone therapy is more commonly used than radiotherapy.

At this point we should consider the differences in benefit between radiotherapy and hormonal therapy. This can best be done with a modified cost benefit analysis. The 10-year survival rate under radiotherapy is 64 percent. If we assume that the distribution of patient survival times is linear, the expected survival time would be about six and one half years. The median survival time with an orchiectomy is 779 days, or about 2 years. Radiotherapy will cost $9,900 and an orchiectomy will cost $7,300 (see Results chapter).

The difference in cost between these two therapies is $2,600. The difference in benefit is 4.4 years. If we divide the increased cost of radiotherapy by the increased benefits, we arrive at $590 per year. This is considered by most people to be cost beneficial (Hayman, 1996, 829). This makes radiotherapy the suggested option.

5.4 Cancer Stage T4

At stage T4 of prostate cancer, the tumor is completely undifferentiated, delocalized and has spread beyond the prostate into the surrounding tissue. There is no effective treatment at this stage of prostate cancer to cure the cancer. Normally, watchful waiting is used to monitor the progression of the prostate cancer and hormone therapy is used to try to control the spread of the cancer (Beemsterboer, P.M.M. et al.,1999, 97-104; Seidenfeild, Jerome. et al., 2000, 566-577). At this point the comfort of the patient is the focus of any treatment.

At stage T4, the treatment that most effectively contains the cancer is hormone therapy (Margolis, 1997, 38). Usually the only other approach is watchful waiting, which is used when the patient simply wants to be comfortable and avoid the cost and complications issues. At this point, the patient is most likely going to die of prostate cancer and hormone therapy can only potentially prolong life; it cannot eliminate the problem. Hormone therapy is most commonly used and suggested because it is the only treatment that is effective in slowing the spread of the prostate cancer at this stage.

6 Conclusions and Recommendations

This chapter is divided into three sections, including the topics of overall treatment decisions made in the project (as discussed in Chapter 5), the problems encountered with the prostate cancer studies and possible future research on this project.

The first section is a summary of Chapter 5, highlighting the treatment recommendations depending on patient age and diagnosed prostate cancer stage. The second section discusses the limitations of the available data on prostate cancer treatment. The last section discusses the future research that would improve the ability of men to make informed decisions about prostate cancer treatment.

6.1 Treatment Recommendations

The optimal treatment recommendations for prostate cancer depend on the prostate cancer stage. At each stage, there are certain treatments that are effective in managing the prostate cancer.

Stage T1 tumors are very small and localized in the prostate. These tumors have not penetrated the inner layer of the prostate. Watchful waiting, prostatectomy and radiotherapy are the most commonly used treatments at this stage. Watchful waiting is recommended for patients with a short life expectancy. Prostatectomy and radiotherapy are recommended for patients with a greater life expectancy. If the patient has a short life expectancy, it is less likely that the prostate cancer will be the cause of his death. If the patient has a longer life expectancy, it is more likely that the prostate cancer will be the cause of his death, so a more proactive treatment plan is used.

After cost effectiveness analysis and complications are explored and discussed, it was found that radiotherapy is the suggested choice. Radiotherapy is more cost effective than prostatectomy, because it costs 45 percent less than a prostatectomy and has equivalent or better effectiveness.

Stage T2 tumors are slightly larger than T1 tumors, but are still localized within the prostate. Watchful waiting, prostatectomy and radiotherapy are again the most commonly used treatments at this stage. The threat of the prostate cancer is generally greater at this stage than at T1, so watchful waiting is not as commonly used as the more proactive treatments. And again, given the cost effectiveness analysis and complications of each treatment, radiotherapy is recommended over prostatectomy.

Stage T3 tumors have spread throughout the prostate and some surrounding tissue. Prostatectomy is no longer effective because the cancer is no longer confined to the prostate tissue. Radiotherapy and hormone therapies are usually used to treat a patient at this stage. Radiotherapy is usually more cost effective in treating stage T3 tumors than hormone therapy; radiotherapy costs less than Bicalutamide and is more proactive in treating the cancer. Orchiectomy is cheaper than radiotherapy, but the complications of orchiectomy are more severe. For these reasons, radiotherapy is recommended for stage T3 prostate tumors.

Stage T4 tumors have spread throughout the pelvic area and are no longer effectively treatable by radiotherapy. Hormone therapy is used to control the spread of the cancerous tissue; it is more cost effective and has fewer severe complications than radiotherapy. T4 tumors are so severe that the patient may not desire to undergo any treatment; there are often great complications for a small increase in life expectancy. For this reason watchful waiting may be used at stage T4. However, hormone therapy may be used for a more proactive approach in controlling this stage of the disease.

6.2 Problems with Medical Studies

During the course of this project data had to be gathered and analyzed. While some of the information needed was obtained from books, most of the data came from studies published in medical journals. These studies provided the numerical data needed to evaluate the prostate cancer treatments in terms of cost, complications and effectiveness. Unfortunately, there were some problems in the ways that these studies were conducted. These problems should be discussed to offer an understanding of the limitations that exist in this paper.

Each study records various pieces of medical information about each study participant. Changes in the medical condition of the patients—before and after treatment—are observed. These pieces of information can be called the dimensions of the study. However, there are no standard units for measuring many of the dimensions studied in prostate cancer. For example, multiple studies presented data for the number of patients who experienced incontinence after a procedure. Each study used a different way of defining the difference between no incontinence, mild incontinence, and severe incontinence. This lack of common measurement standards makes comparison between two different studies complicated. (Refer to the Methodology chapter for a more detailed discussion of the important dimensions of a medical study.)

This project examined complications that resulted from various prostate cancer treatments. Many of the studies that explored a certain treatment offered an inadequate amount of data on particular complications. Data were also lacking for other dimensions, especially survival rates. It took much searching to find information on the effectiveness of each treatment, especially hormone therapy. This scarcity of verifying sources made it difficult to assess treatments with confidence in terms of their effectiveness or frequency of complications.

6.3 Future Research

Given more time and resources, this project could be extended in several ways. New experimental treatments received only a brief discussion for background purposes. A full analysis of prostate cancer treatment options should include all available treatments, no matter how new or experimental.

Economic analysis of screening techniques could also be introduced. These screening techniques have some "up-front" cost, but in many cases may remove the need for expensive treatments at a later date. The benefit of diagnosing cancer early should be weighed against the cost of administering tests to patients without any symptoms of prostate cancer. Such analysis of the economics of screening for prostate cancer will have an impact on treatment options, because the recommended treatments depend to some extent on how far the cancer has progressed in a patient.

Each of the treatments should receive a full cost benefit analysis, rather than the simplified version presented in this project. Cost benefit analyses are highly complex and beyond the scope of this particular project. A more in-depth treatment of this topic should include more extensive analysis of all available treatments.

The methods for analyzing complications should also be extended. Each of the procedures that were mentioned for the treating of a complication will also have complications. A complete analysis would take these second, third, or higher subsidiary complications into account.

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Appendix A – Prostate Cancer Studies

This appendix gives the information and nature of the medical studies used to obtain information for this paper. The purpose of showing this information is to give the reader an idea of how the studies relate to each other and to understand the source of the project's data. The following is the format by which the studies' information is given:

Article Title

- Treatments used in study
- Symptoms studied in relation to treatments
- Clinical stages of cancer with which patients were diagnosed
- Number of patients in study
- Data collection method
- Patient ages
- Duration of follow up period
- Geographical location of where the study took place
- Ethnicity of the patients
- Results and conclusions of the study

Shrader-Bogen, Cheryl L. et al. "Quality of Life and Treatment Outcomes" Cancer. 79:10 (1997): 1977-1986.

- Prostatectomy or Radiation Therapy treatments used

- Examined effects on bowel symptoms (diarrhea, bleeding and urgency), incontinence and sexual dysfunction (erection, need for corrective treatment)
- Patients diagnosed with clinically localized prostate carcinoma (stage T1 or T2)
- 132 patients had prostatectomy; 142 patients had radiation therapy
- Data collected by mailed out questionnaires (demographic survey, Functional Therapy Assessment of Cancer Therapy-General, FACT-G, and Prostate Cancer Treatment Outcome Questionnaire, PCTO-Q)
- Mean age of patients for prostatectomy was 66.2 years; 75.3 years for radiation therapy patients
- Follow up period was 1-5 years
- Study took place in Minnesota
- 94% of patients were Caucasian, 2.2% Native American, 1.5% Hispanic, 0.8% African American, 0.8% other
- prostatectomy group reported more urinary problems and more sexual dysfunction; radiotherapy group reported more bowel problems

Jonler, Morten, Neilsen, Ole Steen, Wolf, Hans. "Urinary Symptoms, Potency and Quality of Life in Patients with Localized Prostate Cancer Followed Up with Deferred Treatment." Urology. 52 (1998): 1055-1063.

- TURP, hormone deprivation or radiation therapy were used
- Examined effects on incontinence, impotence and satisfaction with treatment plan
- No specific stage of cancer was studied

- 16 patients had TURP; 4 patients had hormone deprivation; 23 patients had radiation therapy
- data collected by self-administered questionnaire
- patients were age 79 years or less (mean at questionnaire was 83 years)
- median follow up period was 3 years
- study took place in Denmark
- 21% of patients reported problem with incontinence; 12% of patients reported problem with impotence; 85% of patients were satisfied with the treatment plan

Lim, Arthur J. et al. "Quality of Life: Radical Prostatectomy versus Radiation Therapy For Prostate Cancer." The Journal of Urology. 154 (1995): 1420-1425.

- Prostatectomy or Radiation Therapy treatments used
- Examined effects on bowel, urinary and sexual function
- Patients diagnosed with stage T1c, T2a, T2b or T3 prostate cancer
- 136 patients underwent radical prostatectomy; 60 patients underwent external beam radiotherapy
- data collected by patient questionnaire
- mean age for prostatectomy patients was 65 years; mean age for radiotherapy patients was 70 years
- the follow up period ranged from 3 months to more than 18 months
- study took place in Miami, Florida
- 77% patients were Caucasian, 4% were African American, 8% were Hispanic, 11% were categorized as other

- the radical prostatectomy group had worse sexual function and urinary incontinence, while the external beam radiotherapy group had worse bowel function

McCammon, Kurt A. et al. "Comparative Quality-of-Life Analysis After Radical Prostatectomy or External Beam Radiation for Localized Prostate Cancer." Urology. 53:4 (1999): 509-516.

- Prostatectomy or Radiation Therapy treatments used
- Examined effects on bowel, urinary and sexual function; also reported on patient satisfaction of treatment
- Patients diagnosed with clinically localized prostate carcinoma (stage T1 or T2)
- 203 patients treated by radical prostatectomy; 257 patients treated by external beam irradiation
- data collected by patient questionnaire and by physician observation
- prostatectomy patients ranged in age from 44 to 74 years (median of 64 years); radiotherapy patients ranged in age from 45 years to 86 years (median of 64 years)
- follow up period was 1 year
- study took place in Virginia
- no patient ethnicity specified
- prostatectomy patients had worse urinary incontinence; radiotherapy patients had worse bowel function; it was reported that while both groups had similar sexual function results, the prostatectomy patients experienced a greater impact on sexual relationships; patient satisfaction with treatment varied

Macdonagh, R.P. et al. "The Use of Generic Measures of Health-Related Quality of Life In the Assessment of Outcome from Transurethral Resection of the Prostate." British Journal of Urology. 79 (1997): 401-408.

- TURP used
- Examined effects on quality of life (social interaction, pain, energy, emotional reactions) and morbidity
- Patients diagnosed with benign prostatic obstruction (BPO), similar if not identical to BPH
- Patients split into 2 groups: group 1 consisted of 314 patients who received TURP immediately; group 2 consisted of 51 patients who were followed for 6months before having the TURP
- Data collected by 2 questionnaires: the EuroQol (EQ) and the Nottingham Health Profile (NHP)
- Mean age of group 1 was 72 years; mean age of group 2 was 69 years
- Follow up period for group 1 was in intervals including 6 weeks, 6 months and 1 year; the follow up period for group 2 was 6 months
- Study took place at University of York in England
- Patients experienced significant improvement of quality of life (such as incontinence) symptoms after TURP, especially the younger, fitter, more symptomatic patients

Beemsterboer, P.M.M., et al. "Advanced Prostate Cancer: Course, Care, and Cost Implications." The Prostate. 40 (1999) 97-104.

- Patients who had died from the years 1994-1998 were studied for their total prostate cancer healthcare received

- Studied symptoms, complaints, costs and treatments used
- 70 patients studied
- data collected by looking in patient files
- mean age at prostate cancer diagnosis was 70 years
- study took place at the University of Rotterdam, The Netherlands
- much data was taken, including most frequently experienced symptoms, treatment and hospital costs, treatments used and cause of death

Iversen, P. "Quality of Life Issues Relating to Endocrine Treatment Options." European Urology. 36 (1999) 20-26.

- Hormone therapy used
- Examined effects on bowel and sexual function and physical activity
- No specific cancer stage given; patients generally had advanced stage prostate cancer
- Approximately 1200 patients were studied
- Data collected using a questionnaire
- No patient age data given
- No follow up period specified
- Study took place at University of Copenhagen, Denmark
- There was some bowel dysfunction among patients with hormone therapy, but a reduced chance of sexual dysfunction; the study concluded that hormone therapy is preferred for patients with metastatic disease who are being treated for longer periods of time.

Clark, Jack A. et al. "Changes in Quality of Life Following Treatment For Early Prostate Cancer." Urology. 53:1 (1999): 161-167.

- Radical prostatectomy or external beam radiotherapy used
- Examined effects on urinary, bowel and sexual symptoms
- Patients diagnosed with early non-metastatic prostate cancer (stage T1 or T2)
- 125 men studied
- data collected by patient questionnaire
- mean patient age was 68 years
- follow up periods of 3 and 12 months used
- study took place in Massachusetts
- prostatectomy patients had worse urinary incontinence and sexual dysfunction; radiotherapy patients had worse bowel function

Crawford, E.D. et al. "A Controlled Trial of Leuprolide With and Without Flutamide in Prostate Carcinoma." New England Journal of Medicine. 321 (1989): 419-424.

- hormone therapy used (Leuprolide with and without Flutamide)
- examined effects on survival rate
- patients diagnosed with mid stage prostate cancer (stage T2 or T3)
- 303 men treated with Leuprolide and Flutamide; 300 men treated with Leuprolide with placebo
- data collected by physician observation
- no mean patient age given
- follow up period was to patient death

- data for study taken from Colorado, Maryland, Washington, California, Washington D.C. and Minnesota
- a significant improvement was found for patient survival in patients using both Leuprolide and Flutamide with no significant difference in side effects

Gray, Mikel, Petroni, Gina R., Theodorescu, Dan. "Urinary Function after Radical Prostatectomy: A Comparison of the Retropubic and Perineal Approaches." Urology. 53:5 (1999): 881-891.

- retropubic and perineal approaches to radical prostatectomy used
- examined effects on urinary incontinence
- patients diagnosed with clinically localized prostate cancer (stage T1 or T2)
- 72 men had the perineal approach; 95 men had the retropubic approach
- data collected by patient questionnaire
- patient age ranged from 43 to 80 years, with a mean of 68 years
- follow up period was about 2 years
- study took place in Virginia
- this study concludes that there is little difference between the retropubic approach and the perineal approach on post-operative urinary continence

Koprowski, C.D., Berkenstock, K.G., Borofski, A.M. "External Beam Radiation Versus 125 Iodine Implant in the Definitive Treatment of Prostate Carcinoma." International Journal of Radiation Oncology Biology Physics. 21 (1991): 955-960.

- external beam irradiation and 125 iodine implant were used
- examined the comparative effectiveness of the two procedures

- patients ranged in stage of prostate cancer from T1 to T3
- 101 patients were irradiated with Iodine-125 implant; 175 patients treated with external beam radiotherapy
- data collected by physician observation
- mean age of external beam radiotherapy patients was 65 years; mean age of iodine-125 implant patients was 64 years
- mean follow up period for external beam radiotherapy patients was 67 months; mean follow up period for iodine-125 implant patients was 57 months
- Data for this study came from New Jersey, Wisconsin, Pennsylvania and Washington D.C.
- the study concludes that the iodine-125 implant is only appropriate for a minority of early stage prostate cancer patients (T1) because of its poor ability to control local carcinomas; most patients in early stages should be treated with either external beam radiotherapy or radical prostatectomy

Lilleby, Wolfgang M.D. et al. "Long Term Morbidity and Quality of Life in Patients With Localized Prostate Cancer Undergoing Definitive therapy or Radical Prostatectomy." International Journal of Radiation Oncology Biology Physics. 43:4 (1999): 735-743.

- Radical prostatectomy or external beam radiotherapy used, with a control group on watchful waiting
- Examined effects on urinary symptoms and general quality of life

- Most of the radiotherapy patients were diagnosed with stage T2 or T3; most of the prostatectomy patients were diagnosed with stage T2 and most of the watchful waiting patients were diagnosed with stage T1 and T2.
- 154 patients underwent radiotherapy, 108 underwent prostatectomy, 38 patients followed watchful waiting
- data collected by mailed out questionnaire
- median age of radiotherapy patients was 66 years, median age of prostatectomy patients was 63 years and median age of watchful waiting patients was 66 years
- questionnaires about symptoms were administered at least 12 months after the procedure
- this study took place in Norway
- this study concluded that the prostatectomy group suffered more severe incontinence and other urinary symptoms while the radiotherapy group suffered more severe quality of life impairments in terms of fatigue and sexuality

Kolvenbag, Geert J.C.M., et al. "Bicalutamide Dosages in the Treatment of Prostate Cancer." The Prostate. 39 (1999): 47-53

- Bicalutamide or Flutamide are used in hormone treatment
- examined effectiveness of each drug
- cancer stage of patients not given
- number of patients not given
- data collected by physician observation
- patient ages not given

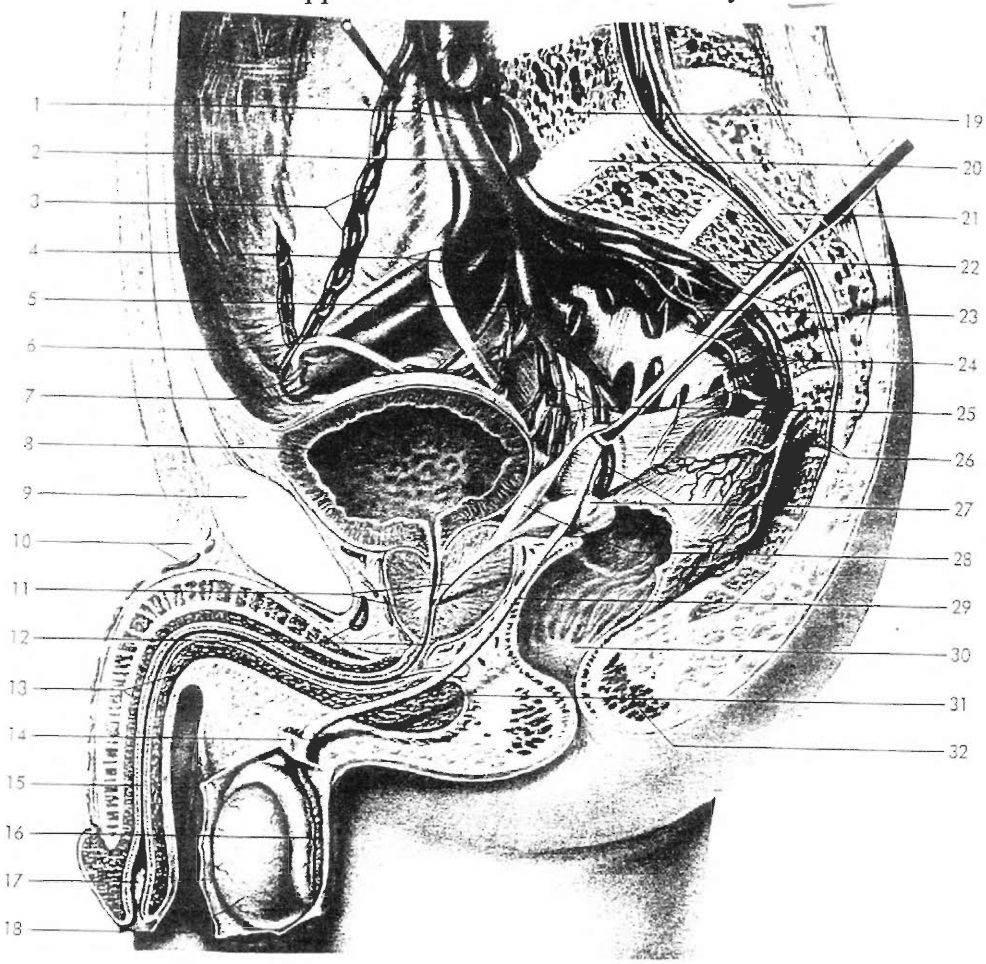
- follow up period was at least 160 weeks
- this study took place jointly in Delaware and the United Kingdom
- this study concludes that Bicalutamide is more effective than Flutamide and that a dose of 50 mg is considered an effective dose

Appendix B – Comparison of Treatments and Complications

Complication	Watchful Waiting	Prostatectomy	Radiation Therapy	Hormone Therapy	
				Bicalutamide	Castration
Sexual Dysfunction	0.00%	66.70%	44.00%	18.00%	37.00%
Incontinence					
General	0.00%	31.00%	30.00%	Not available	Not available
Surgery Required	0.00%	11.00%	3.10%	Not available	Not available
Bowel	0.00%	10.50%	28.40%	5.00%	6.00%
Urethral Stricture	0.00%	15.00%	2.50%	0.00%	0.00%
Death during Treatment	0.00%	2.00%	0.20%	0.00%	0.00%
Peripheral Edema	0.00%	0.00%	0.00%	Not available	Not available
Hot flashes	0.00%	0.00%	0.00%	13.00%	50.00%
Gynecomastia	0.00%	0.00%	0.00%	50.00%	Not available
Loss of libido	0.00%	0.00%	0.00%	23.00%	47.00%
Nausea Vomiting	0.00%	0.00%	0.00%	Not available	Not available

Source: Macdonagh, R.P. et al. "The Use of Generic Measures of Health-Related Quality of Life In the Assessment of Outcome from Transurethral Resection of the Prostate." British Journal of Urology. 79 (1997): 401-408. McCammon, Kurt A. et al. "Comparative Quality-of-Life Analysis After Radical Prostatectomy or External Beam Radiation For Localized Prostate Cancer." Urology. 53:4 (1999): 509-516. Shrader-Bogen, Cheryl L. et al. "Quality of Life and Treatment Outcomes" Cancer. 79:10 (1997): 1977-1986. Iversen, P. "Quality of Life Issues Relating to Endocrine Treatment Options." European Urology. 36 (1999) 20-26.

Appendix C – Male Pelvic Anatomy



Atlas of the Normal Anatomy. Pearl River: Lederle Laboratories Division, American Cynamid Company, 1956.

1. Common Iliac artery and vein
2. Internal Iliac (hypogastric) artery
3. Spermatic artery and vein
4. Ureter, external iliac artery and vein
5. Superior vesicle artery and vein
6. Deep iliac circumflex artery and vein: right ductus deferens
7. Inferior epigastric artery and vein
8. Urinary bladder
9. Symphysis pubus
10. Fundiform ligament of penis; superficial dorsal vein
11. Prostate gland; ejaculatory duct
12. Deep dorsal vein of penis; prostatic urethra
13. Corpus cavernosum
14. Spermatic chord (cut)
15. Cavernous urethra
16. Epididymis
17. Navicular fossa
18. Testis
19. Fifth lumbar vertebra
20. Middle sacral artery; intervertebral fibrocartilage
21. Vertebral Canal
22. Lumbosacral trunk; superior gluteal artery
23. Lateral sacral artery; sympathetic trunk ganglion
24. Sacral nerves; coccygeous muscle
25. Inferior vesical artery and vein
26. Superior hemorrhoidal artery and vein
27. Seminal vesicles; middle hemorrhoidal artery and vein
28. Ampulla of ductus deferens
29. Left ductus deferens
30. Rectum
31. Bulb of urethral
32. Sphincter ani extermus muscl