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PROSTATE CANCER AND HEALTH-RELATED QUALITY OF LIFE:

A REVIEW OF THE LITERATURE†

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SUMMARY

With the established effectiveness of diverse treatments for prostate cancer, identification of the physical and psychosocial consequences of the disease and various treatments becomes critical. We review the literature on the effects of prostate cancer and its treatment on health-related quality of life (HRQoL). Studies show that prostate cancer and its treatment affect both disease-specific HRQoL (i.e. urinary, sexual, and bowel function) as well as general HRQoL (i.e. energy/vitality, performance in physical and social roles). Yet, these effects appear to differ across stage of disease and type of treatment. We outline evidence from three sources: (1) studies that compare men with the disease with an age-matched sample of men without the disease, (2) studies that assess men with the disease across time, and (3) cross-sectional studies that highlight predictors of HRQoL. Future research directions are discussed.

INTRODUCTION

Prostate cancer is the most common solid tumor malignancy and the second leading cause of cancer death in American men (American Cancer Society-ACS, 2001). It is also one of the most common malignancies in European men (Borghede *et al*., 1997; Curran *et al*., 1997). While prostate cancer can prove deadly, 93% of men diagnosed with the disease will survive for at least 5 years, and 72.1% will survive for at least 10 years (ACS, 2001). Due to the location of the prostate gland and the delicate nature of treatment, the man with prostate cancer often faces a host of difficulties which can affect health-related quality of life (HRQoL). Thus, concerns about HRQoL are often paramount in the minds of men diagnosed with prostate cancer. This article aims to bring clarity and order to the rapidly growing literature on the effects of prostate cancer and its treatment on men's HRQoL.

While reviews of HRQoL in men with prostate cancer have been done, most have taken a somewhat narrow view of the term. These reviews often emphasize the disease-specific, physical complications while paying less attention to general domains of HRQoL. Certainly, the symptoms of the disease are critically important to understand, but patients and health-care providers also have many questions about the influence of prostate cancer and its treatment on a man's everyday existence. To address this shortcoming in prior reviews, we have chosen to define HRQoL widely, as *both* disease-specific, physical complications and general domains of HRQoL. In the past 5 years, there has been a virtual explosion of research in the HRQoL issues of men with prostate cancer. Thus, there is a pressing need to take stock of this

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accumulating literature. This review synthesizes the findings of recent research from the fields of medicine and psycho-oncology.

Prostate cancer treatment

Since different treatments for prostate cancer have variable effects, it is important to outline the types of therapies that are currently available. Typically, some form of surgery or radiation is used when the cancer is of low grade and confined to the prostate gland (i.e., localized disease). Hormonal and chemotherapeutic options are ordinarily used when the malignancy has spread from the prostate to other areas of the body (i.e., advanced disease). Treatments for localized prostate cancer can result in cure, but those for advanced disease are mainly used to delay disease progression or palliate symptoms.

Therapeutic options for localized disease include surgical and non-surgical approaches. Surgical approaches include radical prostatectomy, transurethral resection of the prostate, and cryosurgery. Radical prostatectomy, including the nerve-sparing approach, involves surgical removal of the entire prostate and is used mainly when it is believed that the cancer has not spread outside of the gland. Transurethral resection of the prostate involves surgical removal of prostate tissue that surrounds the urethra and is mostly used with men who cannot have radical surgery due to other health complications or advanced age. Cryosurgery, which involves freezing malignant areas of the prostate with cooled metal probes, is used by a small proportion of men who are interested in a less aggressive form of surgery.

Non-surgical options for localized disease include external and internal irradiation and ‘watchful waiting’. Radiation therapy is commonly used when prostate cancer is localized to the prostate and the surrounding region. External beam radiotherapy (EBR) makes use of high-energy X-rays or radioactive particles generated outside of the body and focused on the malignancy. EBR can cover the broad area of the pelvis or be stereotaxically conformed to a specified region, thereby reducing the likelihood of damage to surrounding tissue. Internal irradiation, or brachytherapy, utilizes small radioactive pellets that are implanted directly into the prostate. Finally, for some men with localized disease the appropriate course of action after a prostate cancer diagnosis is observation, or ‘watchful waiting’ (Fleming *et al*., 1993). That is, no immediate treatment is administered, rather the cancer is observed and monitored for signs of progression. This is often a reasonable choice for older men with early-stage, low-grade disease and few or no complications, because prostate cancer can be a slow-growing malignancy.

At present, there is no consensus about which therapeutic option is best for men with localized prostate cancer. Existing data from non-randomized studies show similar survival rates (Bonney *et al.*, 1982; Chodak *et al.*, 1994; Gerber *et al.*, 1996; Hanks, 1991; Lu-Yao and Yao, 1997) and the results of randomized clinical trials are still some years away. Hence, the selection of a treatment is based on factors other than survival advantage and may include the effect of therapy on HRQoL.

Hormone therapies and chemotherapy are options for men with advanced prostate cancer. Hormone therapies help to reduce the levels of circulating androgens. Androgen can promote the growth of malignant prostate cancer cells. Surgical and non-surgical hormone therapies exist. Orchiectomy involves the surgical removal of the testicles. It physically eliminates the primary source of androgen in the body. Pharmacological hormone therapies can achieve essentially the same end without surgery. Luteinizing hormone-releasing hormone (LHRH) analogs are used to interrupt testosterone production. Another class of drugs, anti-androgens, are used to block the body’s ability to use androgen. Anti-androgens can be combined with either orchiectomy or LHRH analog to completely block androgen activity. Finally, chemotherapy is an option for a select few men who have prostate cancer that has metastasized

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and for whom hormone therapy has failed. Like hormone therapy, the aim of chemotherapy is to stop the spread of the disease and reduce physical complications such as bone pain.

Prostate cancer and HRQoL

The concept of quality of life has great significance in the health-care arena, because the number of people living with chronic illness is growing rapidly. In weighing options for treating life-threatening diseases, such as cancer, patients and health-care providers are interested in knowing both the number of years a given treatment will add to life and the quality of life in those added years. HRQoL is a multidimensional construct that typically includes four broad categories: physical, functional, social and emotional well-being (Cella and Tulsky, 1993). Cella states that HRQoL refers to the extent to which one's usual or expected physical, social and emotional well-being are affected by a medical condition or its treatment (Cella, 1995). Thus, the minimum criteria for an appropriate measurement of HRQoL include (a) that measurement incorporates the patient's perspective and (b) that it captures physical, social and mental well-being. We adopt this definition for the present review.

We reviewed the literature from English-language empirical studies identified from the MEDLINE (coverage from 1965) and PSYCINFO (coverage from 1887) databases and the reference lists of published articles. To capture the full range of HRQoL outcomes, we used the following descriptor terms for our database searches: prostate cancer, quality of life, mental health, adjustment, sexual function, body image, depression, impotence, incontinence, urogenital disorders, fatigue, well-being, anxiety, psychological distress, and mood. In each search, the term 'prostate cancer' was combined with one of the other terms. We used only those articles in which data from subgroups of men with prostate cancer could be clearly identified. Consistent with the operationalization of HRQoL that we have chosen to adopt, this review includes empirical studies that assess *both* disease-specific, physical parameters as well as general HRQoL parameters. For reviews of just the physical symptoms associated with prostate cancer and its treatments, we refer the reader to several excellent articles (see Altwein *et al*., 1997; Middleton *et al*., 1995; Shipley *et al*., 1994; Wasson *et al*., 1993). Furthermore, unlike other reviews (see Herr, 1997; Van Andel *et al*., 1997) we chose to exclude studies that did not use validated measures of HRQoL. Finally, we review here only studies that make inferential statistical comparisons.

We have organized the review into four sections, corresponding to the major HRQoL outcomes related to prostate cancer. We first examine evidence that clarifies the disease-specific sequela of prostate cancer, namely, urinary, sexual, and bowel functioning outcomes. Next, we present the evidence on general HRQoL outcomes. We considered evidence from three types of studies; comparison group (comparisons of men with prostate cancer with an age-matched sample of men without the disease), longitudinal (assessments of men over time), and cross-sectional (assessments of men at one time point). Within each section, we consider the issues of men with localized prostate cancer separately from those of men with advanced prostate cancer, as quality of life concerns are often very different across these two forms of the disease. Whenever possible, we also provide information on the magnitude of HRQoL outcomes.

URINARY FUNCTION

Localized disease

Comparison group studies show that men treated for localized prostate cancer have more problems with urinary function than men of the same age without the disease (Joly *et al*., 1998; Litwin *et al*., 1995). Moreover, treated men seem to have more urinary problems than men who are not treated for the disease (Litwin *et al*., 1995). Thus, urinary dysfunction appears to be a treatment-related complication (see Table 1). Those suffering the most urinary problems are

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those who are treated with radical prostatectomy (RP). Litwin *et al*. (1995) compared three groups of men with localized prostate cancer to a matched comparison group of men without prostate cancer. Those in the diseased group were diagnosed an average of 5–6 years prior to the study and had been treated with either RP (mean time since treatment (TST)=5.3 years) or EBR (mean TST=5.9 years) or were part of an observation-alone group (mean time since diagnosis (TSD)=5.7 years). Across all four groups, men treated with RP had the worst urinary function. Forty percent of men treated with RP reported leaking urine daily (almost twice as often as men treated with EBR). Furthermore, 90% of these men reported using two or fewer absorptive pads per day, while only 30% claimed total urinary control. Men treated with EBR also had worse urinary function than men in the comparison group; however, their problems were not as severe as those of RP-treated men. Among men treated with EBR, 92% claimed total control or occasional leakage, while 23% reported daily mild urinary leakage.

Others have reported elevated rates of urinary problems in men treated with combination radiotherapy. Joly and colleagues (Joly *et al*., 1998) compared men with localized prostate cancer treated with EBR+brachytherapy with a matched sample of men without the disease. Men in the diseased group had been treated an average of 4 years prior to the study. Treated men reported greater urinary incontinence and more burning upon urination than did men in the comparison group. Overall, 40% of men reported urinary incontinence, while 27% reported mild burning upon urination.

A number of cross-sectional studies have directly compared RP with radiation treatments for localized prostate cancer (see Table 1). Men treated with RP have consistently reported more urinary problems (i.e., dripping and leaking urine, lack of urinary control) than men treated with EBR (Fowler *et al*., 1996;Lim *et al*., 1995;Shrader-Bogen *et al*., 1997;Tefilli *et al*., 1998;Yarbro and Ferrans, 1998). For example, Fowler *et al*. (1996) found that 62% of men treated with EBR (TST range=3–5 years) reported no dripping or leaking of urine posttreatment, whereas only 14% of men treated with RP (TST range=2–4 years) reported the same. Similar to comparison group studies, many of these cross-sectional studies assess men several years posttreatment. Overall, the results of comparison group and cross-sectional studies indicate that urinary dysfunction is associated with treatments for localized prostate cancer and that RP leads to the greatest number of problems. Missing from these studies, however, is information about how urinary function changes over time.

Longitudinal studies help to clarify the trajectory of urinary dysfunction in men treated for localized prostate cancer. Recent longitudinal investigations have shown that while declines in urinary function are quite common in the first few months following RP, function improves substantially 1 year after treatment (see Table 1) (Litwin *et al*., 1999;Lubeck *et al*., 1999;Potosky *et al*., 2000;Stanford *et al*., 2000). In the Litwin *et al*. (1999) study, 61% of men treated with RP had reportedly recovered pretreatment urinary function at 1 year posttreatment. This finding contrasts with those of earlier cross-sectional studies (i.e. Litwin *et al*., 1995;Fowler *et al*., 1996;Shrader-Bogen *et al*., 1997) showing high levels of urinary dysfunction 1–5 years post-RP. However, RP-treated men in the Litwin *et al*. (1999) study were younger and had fewer co-morbid conditions than the RP-treated men in the cross-sectional studies. Hence, it may have been easier for them to recover from surgery.

Urinary sequela for men treated non-surgically and those who are observed is quite different. Men treated with EBR, hormone therapy, and those who are observed exhibit few short- or long-term deficits in urinary function (Lubeck *et al*., 1999; Potosky *et al*., 2000). Lubeck and colleagues (Lubeck *et al*., 1999) found few urinary problems in an EBR group, a hormone therapy group or an observation-alone group immediately after treatment or at 1 year and 2 years after treatment. In the large-scale, community-based Prostate Cancer Outcomes Study (PCOS) (Potosky *et al*., 1999), men who had received RP experienced substantial declines in

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urinary function in the months after treatment, men treated with EBR declined only slightly (Potosky *et al*., 2000).

Advanced disease

Treatments for advanced prostate cancer such as combined androgen blockade (CAB) and orchiectomy do not appear to be associated with urinary dysfunction (see Table 2). Litwin and colleagues (Litwin *et al*., 1998) measured urinary function every 3 months after treatment initiation in men with newly diagnosed metastatic prostate cancer who were treated with either CAB (using leuprolide+flutamide) or bilateral orchiectomy. Men had been diagnosed between 0 and 24 months prior to the study period. Both treatment groups had good urinary function prior to treatment. One year after treatment initiation, urinary function had modestly improved from pretreatment levels for both groups. These findings have been replicated in an European sample (Da Silva *et al*., 1996). Importantly, the findings from studies of advanced disease must be cautiously interpreted as many men drop out prior to follow-up. Reasons for dropping out include death and disease progression. Thus, follow-up scores often represent only the healthiest men.

SEXUAL FUNCTION

Localized disease

Results from comparison group studies show that men with localized prostate cancer report more sexual problems than do similarly aged men without prostate cancer (see Table 1) (Helgason *et al*., 1996,1997;Litwin *et al*., 1995). Unlike urinary problems, however, some sexual problems seem linked to the disease, irrespective of the type of treatment used. For instance, recently diagnosed, treated and untreated men with localized prostate cancer are at a higher risk for developing physiological impotence than men of similar age with no disease (Helgason *et al*., 1996,1997). Litwin *et al*. (1995) also found that sexual function was better in a healthy comparison group of older men than in a group of men with localized disease who were being observed (mean TSD=5.7 years). Thus, certain aspects of sexual function dysfunction may be a result of having localized prostate cancer.

Notwithstanding the possible effects of the disease alone, declines in sexual function appear to be exa-cerbated by certain treatments. Men treated with RP show the most sexual problems (see Table 1). Helgason *et al.* (1997) found that among men recently diagnosed with localized disease (within 1 year), those treated with RP had a higher rate of physiological impotence (86%) then those treated with EBR (57%). Men who were only observed displayed the least impotence (57%). Other cross-sectional comparisons of RP and EBR have replicated this result (Fowler *et al*., 1996;Lim *et al*., 1995;Shrader-Bogen *et al*., 1997;Yarbro and Ferrans, 1998). Once again, conclusions about sexual sequela are difficult to draw from these studies as men are assessed at only one time point, often several years after treatment.

Sexual sequela can be better understood in the context of longitudinal investigations. Results from longitudinal studies reveal that problems in sexual function develop early in men with localized prostate cancer (in both treated and untreated men), and they do not dissipate as rapidly as urinary problems (see Table 1). Men treated with RP develop severe sexual difficulties shortly after treatment (Lubeck *et al*., 1999;Potosky *et al*., 2000;Stanford *et al*., 2000). Furthermore, these men have great difficulty regaining pretreatment levels of sexual function (Litwin *et al*., 1999;Stanford *et al*., 2000). Litwin *et al*. (1999) found that only 31% of the men in their study had recovered pretreatment sexual function by a year after RP. This negative sequela is not unique to those treated with RP. Men treated with radiation and those who are observed only also report experiencing sexual problems (Lubeck *et al*., 1999;Potosky *et al*., 2000). Like those who have had a prostatectomy, sexual function in these other groups

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was poor at baseline and remained poor at one and two year follow-up points (Lubeck *et al*., 1999). Still, negative sexual sequela appears more characteristic of men treated with RP than of those treated with EBR (Potosky *et al*., 2000).

Importantly, some studies have shown that sexual problems are a source of psychosocial distress in men with localized prostate cancer. Helgason *et al*. (1996) have shown that more men with prostate cancer (18%) than without the disease (9%) reported 'severe distress' due to reduced erectile capacity. Also, more men with prostate cancer (16%) than without the disease (6%) reported 'severe distress' due to reduced orgasm pleasure. Others have shown a relation between erectile dysfunction 1 year after treatment and declines in general HRQoL (general health, vitality, and role-emotional function) (Clark *et al*., 1999). Since these studies report data aggregated across several treatments, it is difficult to ascertain the potential impact of any one treatment on distress. The recent longitudinal analysis from the PCOS has begun to clarify differences across treatments. Potosky *et al*. (2000) have shown that sexual 'bother' was greater at 2 years posttreatment for men treated with RP than those treated with EBR, especially in younger men (aged 55–59 years).

Nerve-sparing prostatectomy procedures appear to preserve erectile function in certain men (Catalona and Bigg, 1990; Catalona and Dresner, 1985; Eggleston and Walsh, 1985). Stanford *et al*.'s (2000) recent longitudinal analysis of men from the community-based PCOS seems to support the utility of nerve-sparing prostatectomy over standard prostatectomy in reducing sexual dysfunction. However, definitive conclusions about the nerve-sparing procedure are difficult to draw as men who elect it often constitute a highly selective sample of men. Compared to those who do not elect nerve-sparing RP, those who elect this procedure often have better prognoses, less extensive disease, better pretreatment functional status, and, most importantly, better pretreatment sexual function. Without randomized studies, the superiority of this procedure over standard prostatectomy cannot be definitively determined.

Another promising avenue of coping with reduced sexual function is the use of posttreatment erectile aids (e.g. implants, drugs, and vacuum devices). Perez and colleagues (Perez *et al*., 1997) found that men who used such aids at least 50% of the time after RP (mean TST=2.2 years) reported sexual function that was indistinguishable from a preoperative group. These researchers found similar function across the two groups in several domains of sexuality including arousal, frequency of contact, erectile capacity, and satisfaction with current sexual function. Furthermore, sexual functioning in the men using aids was significantly better than in men who had been treated with either nerve-sparing (mean TST=1.9 years) or standard prostatectomy (mean TST=2.3 years) alone. Conversely, others have shown no benefit of the use of such aids in men with localized disease 1–5 years after treatment (Shrader-Bogen *et al*., 1997).

Advanced disease

With no available studies comparing the sexual function of men with advanced prostate cancer to similarly aged men without prostate cancer, it is difficult to precisely identify the effects of advanced disease on sexual function. The evidence that does exist addressing this question comes from longitudinal studies that include HRQoL assessments prior to treatment (see Table 2). Pretreatment sexual function in men with advanced disease has been found to be quite poor (Da Silva *et al*., 1996;Litwin *et al*., 1998). For example, Litwin *et al*. (1998) found that sexual functioning prior to hormone therapy was extremely low in a sample of newly diagnosed men with metastatic prostate cancer. The level of sexual dysfunction reported is comparable to that reported by men with localized prostate cancer treated with RP (see Litwin *et al*., 1995;Lubeck *et al*., 1999). Such evidence suggests that advanced disease alone may have a substantial impact on sexual function. Nonetheless, while men with metastases report many sexual problems both

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before and while they are on treatment, they report only a moderate level of distress associated with these problems (Litwin *et al*., 1998).

Therapies for advanced disease have also been compared (see Table 2). Both CAB and orchiectomy have resulted in similar levels of sexual dysfunction in the months after treatment initiation (Litwin *et al*., 1998). In a novel study investigating the potential benefit of non-intervention, Herr *et al*. (1993) compared men with metastatic prostate cancer who had received hormonal therapy (either diethylstilbestrol or LHRH analog+flutamide) with a group that deferred treatment. These researchers were interested in ascertaining whether the side effects of hormone therapy (e.g. decreased erectile capacity, loss of interest in sex) outweigh the potential benefits of treatment (e.g., reduction in disease progression). At issue here is whether hormone therapy should be started immediately in men with advanced disease or whether it should be deferred, due to its potential negative effects, until disease progression is clearly evident. At 1–2 months after treatment initiation, the hormone therapy group reported lower interest in and enjoyment of sexuality than the deferred treatment group, though both groups reported at least some problems in these areas. By 6 months, the hormone therapy group reported worse erectile function and less interest in and enjoyment of sex than the untreated group. Although absolute rates of these problems were not provided, mean scores indicate that the sexual problems were most pronounced in the hormone therapy group. On average, this group reported at least a 'moderate' level of problems in this area. Caution must be exercised in interpreting these findings, however, as baseline differences in sexual function were not statistically controlled. In fact, the authors reported that the untreated group included younger, more sexually active men.

Finally, a few studies have compared the use of the anti-androgen, bicalutamide (Casodex) to castration (either surgical or medical) (see Table 2). Chodak *et al*. (1995) found that at 6 months after treatment initiation, sexual function had declined from pretreatment levels in a castrated group, but was maintained at pretreatment levels in a group receiving bicalutamide. Further, two cross-sectional studies have shown that in comparison with castration, treatment with bicalutamide resulted in more interest in sexuality 1 year following the initiation of treatment in both advanced, non-metastatic (Iversen *et al*., 1998) and metastatic men (Tyrrell *et al*., 1998). Unfortunately, the authors of these studies do not provide absolute rates of function. Albeit preliminary, the findings of such studies suggest that for some men with slowly progressing, advanced prostate cancer, 'less' treatment may afford a better HRQoL outcome.

BOWEL FUNCTION

Localized disease

Bowel problems that occur in men with localized prostate cancer are likely the result of treatment. This is supported by evidence from comparison group and cross-sectional studies of treated and untreated men. Bowel function in untreated, observed men with localized disease (mean time since diagnosis=5.7 years) is similar to that of older men without prostate cancer (Litwin *et al*., 1995). Findings from several studies appear to indicate that bowel problems are more likely to occur after treatment, especially after radiotherapy (see Table 1). Problems such as increased frequency, increased urgency, diarrhea, and bleeding with movements are reported more often by men treated with EBR than by men treated with RP (Fowler *et al*., 1996; Lim *et al*., 1995; Shrader-Bogen *et al*., 1997; Yarbro and Ferrans, 1998). Shrader-Bogen *et al*. (1997) observed that 34% of men treated with EBR (mean TSD=3.4 years) reported experiencing bowel urgency at least once per week compared to 15% of men treated with RP (mean TSD=2.6 years). Furthermore, Joly *et al*. found that 21% of men treated with a combination of EBR and brachytherapy (mean TST=4 years) reported digestive complications. Once again, only cross-sectional assessments were made in these studies, limiting conclusions about the sequela of bowel dysfunction.

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Recent longitudinal studies shed light on the trajectory of bowel dysfunction over time (see Table 1). Data from the PCOS show that both men treated with EBR and those treated with RP experienced declines in bowel function at 4 months after the completion of treatment (Potosky *et al*., 2000); however, the declines in the EBR group were greater than those of the RP group. Both groups showed improvements by 10 months posttreatment. This relatively rapid recovery of function within a year of treatment has been observed by others (Litwin *et al*., 1999;Lubeck *et al*., 1999).

Advanced disease

Bowel problems are infrequent in men treated for advanced prostate cancer (see Table 2) (Litwin *et al*., 1998;Moinpour *et al*., 1998). Castrated men in the Litwin *et al*. (1998) study of metastatic disease reported a level of bowel function comparable to that of older men without prostate cancer (see Litwin *et al*., 1995) in the months after treatment initiation. In another study, castrated men with metastases reported ‘none’ to ‘occasional’ bowel problems such as diarrhea in the first 6 months after treatment initiation (Moinpour *et al*., 1998). When problems do arise, treatments have been associated with improvements in function. Bowel function improved in men with metastases treated with either surgical or medical castration (Litwin et al., 1998). Others have observed decreases in constipation over time in men with advanced hormone-resistant prostate cancer who had responded to palliative chemotherapy (time points not specified) (Stockler *et al*., 1998).

GENERAL HRQoL

Localized disease

Although data are sparse, merely having localized prostate cancer does not seem to affect general domains of HRQoL (see Table 1). In the one comparison group study comparing untreated men with localized disease (mean TSD=5.7 years) with an age-matched sample of men without disease, Litwin *et al*. (1995) found no between-group differences in general physical well-being, role-physical well-being (e.g. limitations in work/ home activities due to physical health), body pain, general health, vitality/energy, social well-being, or emotional well-being. Interestingly, data from both comparison group and cross-sectional studies reveal no general HRQoL differences across treatment groups. Men treated with RP appear to have similar general HRQoL to men who have received EBR (Lim *et al*., 1995;Litwin *et al*., 1995;Shrader-Bogen *et al*., 1997;Tefilli *et al*., 1998;Yarbro and Ferrans, 1998). Yet, concluding that treatments for localized prostate cancer have no effect on general HRQoL may be premature. In many of these studies, HRQoL assessments were made years after treatment. A slightly different story emerges when the results of longitudinal investigations are considered.

Longitudinal studies have revealed that men with localized disease treated via RP do show problems in some domains of general HRQoL, but these problems diminish over time (see Table 1). Men treated with RP have reported deficits in role-physical well-being and vitality/ energy shortly after treatment (Lubeck *et al*., 1999). Yet these men also reported substantial and clinically significant improvements in these domains at 1 year posttreatment (Lubeck *et al*., 1999). Others have observed the same recovery trajectory of general HRQoL. Litwin and colleagues (Litwin *et al*., 1999) found that between 86 and 97% of men who opted for RP regained pretreatment levels of physical well-being, role-physical well-being, general health, body pain, vitality/energy, role-emotional well-being, social well-being, and mental health within one year of treatment. In the latter study, race and marital status moderated recovery. Non-whites were less likely than whites to return to pretreatment levels on physical (55% vs 90%), role-physical (64% vs 96%), and social (72% vs 91%) well-being. Unmarried men were

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less likely than married men to regain pretreatment levels of general health (50% vs 83%), and social well-being (70% vs 91%).

Men treated with radiation and those who are observed report even fewer of these complications (see Table 1). Lubeck and colleagues (Lubeck *et al*., 1999) have shown that although men treated with EBR report moderate deficits in role-physical well-being and vitality/energy immediately after treatment, they report no other substantial problems. Men who were observed in this study reported adequate functioning in all domains shortly after diagnosis, providing further evidence that any deficits in general HRQoL are treatment-related. At 1 and 2 years later, baseline levels of general HRQoL were found to persist in both men treated with EBR and those who were observed (Lubeck *et al*., 1999).

Among men treated with EBR, fatigue appears to be the most common complication. EBR has been associated with increases in fatigue from pretreatment to 3 and 12 month follow-up, particularly in those receiving 'whole pelvis' radiation (Beard *et al*., 1997). Yet a few studies have also shown that increases in fatigue are not associated with poor psychological well-being (e.g., mood disturbance, anxiety, depression) (Beard *et al*., 1997; Monga *et al*., 1997). For example, Beard *et al*. (1997) observed decreases in vitality/energy in men receiving 'whole pelvis' radiation from before treatment to 12 months after treatment initiation. However, relatively low levels of depression were indicated at both of these time points. Hence, though fatigue may increase in the year of treatment, it does not appear to be particularly distressing to men with localized disease.

Selected cross-sectional studies of men with localized prostate cancer have revealed correlates of general HRQoL (see Table 1). These studies point to potential predictors of general HRQoL beyond treatment. Schag and colleagues (Schag *et al*., 1994) have found that the presence of psychiatric co-morbidities is related to poorer quality of life in men with prostate cancer (mean TSD=3.5 years). Having more psychiatric comorbidities (i.e., previous psychiatric history, alcohol abuse, drug abuse) was found to be associated with worse global quality of life. Furthermore, when compared to men with co-morbid heart conditions, those with co-morbid psychiatric conditions show worse physical, role, social, cognitive, and emotional well-being (TSD range=1.5–3.5 years) (Borghede *et al*., 1997). Others have found that pain is predictive of depression and anxiety in men with non-metastatic cancer (mean TSD=2.1 years) (Heim and Oei, 1993). Finally, Fossa and colleagues (Fossa *et al*., 1997) have found an association between fatigue and global quality of life. Fatigue was strongly related to lower global quality of life across three treatment groups (EBR, RP, and hormone therapy) and even among diseased men in an observation group. These findings contrast with those mentioned above, showing no relation between fatigue and psychosocial well-being in men treated with EBR. Note, however, that men in the aforementioned studies were assessed within a year of treatment, whereas those in the Fossa study had all been diagnosed at least one year prior to the study period. Perhaps increases in fatigue are expected in the months immediately following treatment and therefore more likely to be tolerated.

Advanced disease

Few studies have been undertaken that clarify whether advanced prostate cancer affects general HRQoL independent of treatment. Currently, only one comparison group study on general HRQoL outcomes has been conducted in men with advanced prostate cancer (see Table 2). Albertsen *et al*. (1997) compared men in remission and those with progressing disease to age-matched norms on the SF-36. At the time of the study, all men were being treated with CAB for at least 1 month. Men with progressive disease showed significantly more bodily pain, less vitality/energy, and poorer social and emotional well-being than men in remission. Men in remission were no different than the normative group in general domains of HRQoL. This

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study suggests that progressing, advancedstage disease may negatively impact general HRQoL.

Most studies of general HRQoL in men with advanced prostate cancer are longitudinal and focus on how general HRQoL fluctuates across time and treatment. Studies of castration (both surgical and medical) have shown only minor deficits in general HRQoL after treatment initiation (see Table 2). Most problems seem limited to emotional and social domains. Some have found declines in emotional well-being at 3 and 6 months after castration therapy (Cassileth *et al*., 1992;Moinpour *et al*., 1998). Litwin and colleagues found that the biggest improvements in general HRQoL in the year after CAB or orchiectomy were in emotional, role-emotional, and social well-being. What is unclear is which type of castration results in more problems. Moinpour *et al*. (1998) found that emotional function was worse in a CAB group than a group that was orchiectomized at 3 and 6 months after treatment initiation. However, Cassileth *et al*. (1992) found that at 6 months after treatment initiation, a group receiving LHRH analog continued to show improvements in mood, whereas an orchiectomized group had fallen back to pretreatment levels. Collectively, these studies do not clarify which treatment is associated with better general HRQoL; however, these mixed results do illustrate the importance of allowing men at least some autonomy in selecting a therapeutic course.

A few studies have compared castration with the use of anti-androgen, a less aggressive form of therapy in men with advanced prostate cancer (see Table 2). Men treated with the anti-androgen bicalutamide have shown greater improvements in overall health, emotional and social well-being 1 month after treatment than men treated with either surgical or medical castration (Chodak *et al*., 1995). These improvements are not limited to the short term. In both men with advanced, metastatic (Tyrrell *et al*., 1998) and advanced, nonmetastatic disease (Iversen *et al*., 1998), those treated with bicalutamide showed better general physical well-being after 1 year than men who were either surgically or medically castrated. These studies support the conclusion that ‘less’ treatment may result in a better general HRQoL outcome. Of course, less aggressive treatment may not be an option for all men, especially those with rapidly progressing disease.

Finally, some studies have examined the effects of palliative treatments on the general HRQoL of men with hormone-resistant disease (see Table 2). In these studies, palliation was achieved through the use of chemotherapy and/or low doses of prednisone. Moore and colleagues (Moore *et al*., 1994) found improvements in pain, social and emotional well-being after treatment with mitoxantrone (up to 8 cycles) and prednisone. Improvements were observed at 6, 12, and 18 weeks after treatment initiation. Others have demonstrated similar improvements in pain and overall well-being in the months following the initiation of this treatment regimen (Stockler *et al*., 1998;Tannock *et al*., 1989). Noteworthy in these and all studies of advanced disease is the potential biasing influence of participant attrition. Sizeable percentages of men are lost over the course of these studies due to death or disease progression. Hence findings may not be easily generalized to all men with advanced disease, as those with poorest functional status are less likely to be represented.

DISCUSSION

The HRQoL of men with prostate cancer encompasses both disease-specific and general aspects. The disease and its treatments can affect both of these areas; however, effects differ across stage of disease, time, and type of treatment. In men treated for localized prostate cancer, disease-specific domains like urinary, sexual, and bowel function are the most profoundly affected, whereas with some exceptions, general HRQoL is spared. All men with advanced prostate cancer, whether treated or not treated, experience sexual dysfunction, yet it does not appear to be particularly distressing to many men. What may bother these men more are the

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numerous deficits in general domains of HRQoL. We summarize the evidence for these conclusions below.

Urinary and sexual function are the most common disease-specific domains of HRQoL affected by localized prostate cancer and its treatments. Comparison group (e.g., Litwin *et al*., 1995), longitudinal (e.g., Stanford *et al*., 2000), and cross-sectional (e.g., Shrader-Bogen *et al*., 1997) studies all illustrate that urinary and sexual problems are prevalent in men treated for localized disease. Comparison group studies (e.g., Helgason *et al*., 1996) show that sexual problems can also occur in untreated men with localized disease. However, urinary and sexual problems are the worst in treated men, especially those treated via a surgical removal of the prostate gland. Longitudinal studies (e.g., Lubeck *et al*., 1999) show that while urinary problems like incontinence and urgency dissipate over time, sexual problems like poor erection quality and low desire tend to persist. Bowel problems are less frequently reported in men treated for localized disease, although several longitudinal (e.g., Potosky *et al*., 2000) and cross-sectional (e.g., Shrader-Bogen *et al*., 1997) studies have shown that they are more prevalent in men treated with EBR than in men treated with RP. These problems dissipate within a year of treatment.

Only longitudinal studies (e.g., Lubeck *et al*., 1999) have uncovered any problems in general HRQoL in men with localized disease. These problems, restricted to men treated with either RP or EBR, are limited to a loss of energy and some inability to perform daily activities. However, these problems appear to be temporary, lasting less than one year after treatment.

Health-related quality of life issues in men with more advanced stage disease are quite different. Longitudinal studies (e.g., Litwin *et al*., 1998) have indicated that few urinary and bowel problems occur for these men either before or after treatment. Furthermore, results of longitudinal studies (e.g., Da Silva *et al*., 1996) indicate that men treated for advanced disease have heightened sexual dysfunction both before and after treatment, indicating that some sexual problems are disease-related. These problems are reported to be only moderately distressing, however (e.g., Litwin *et al*., 1998). Since men with more advanced disease are faced with the possibility that death could occur within a year of diagnosis, sexual function may be less of a priority. Finally, evidence from both longitudinal (e.g., Chodak *et al*., 1995) and cross-sectional (e.g., Iversen *et al*., 1998) studies indicates that less aggressive forms of treatment (i.e., anti-androgen therapy) are associated with better sexual function than more aggressive therapies (i.e., surgical or medical castration). However, it is important to recognize that less aggressive treatment may not be an option for all men, especially those with rapidly progressing disease.

In contrast to men with localized disease, general HRQoL deficits are observed in men with advanced disease. One comparison group study (e.g., Albertsen *et al*., 1997) suggests that irrespective of treatment, progressing disease is related to more bodily pain, less vitality/energy, and poorer social and emotional well-being than disease in remission. Longitudinal studies (e.g., Litwin *et al*., 1998) show that deficits in social and emotional well-being occur in men treated with either surgical or medical castration in the first 6 months after treatment. Yet substantial improvements occur in these domains after 1 year. Notably, this may be an artifact of survival. Those advanced patients still alive at 1 year follow-up are most likely those with the best functional status. In comparison, anti-androgen therapy seems to result in fewer immediate declines in general HRQoL (e.g., Chodak *et al*., 1995). Finally, for advanced patients with hormone-resistant disease, palliative chemotherapy is associated with improvements in pain, social, and emotional well-being (e.g., Stockler *et al*., 1998).

Clearly, additional studies of prostate cancer and HRQoL are needed. There is a particularly pressing need for more research of men with advanced disease. Advanced prostate cancer seems to affect numerous areas of HRQoL. Studies of medical treatments like hormone therapy

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often target response to treatment and time to disease progression as a primary endpoint. While unargu-ably important, these are not the only indicators of treatment efficacy. It is also important to determine the varied effects of treatment on HRQoL. Thus, future research should address not only what treatments result in a clinical response or delay time to progression, but also which ones have the best chance of maximizing HRQoL. Also, an understanding of the interrelations among HRQoL domains will be critical. For example, are pain and fatigue equally associated with mental health?

Related to issues of treatment impact on HRQoL is the issue of decision-making about treatment. Since all treatments for prostate cancer involve a risk/benefit tradeoff it will be important to clarify how patients make treatment decisions. Does quality of life information enter into this decision? If so, how heavily is it weighted? Do men with prostate cancer feel they have adequate information about HRQoL prior to choosing a treatment? Is this information presented to them clearly? Are there useful methodologies for determining treatment preferences? A relatively recent addition to HRQoL measurement, the preference-based utilities approach, may provide an avenue for understanding decisions about treatment. Utility-based approaches like the Quality of Well-Being Scale (Kaplan and Anderson, 1996) and time-tradeoff (Albertsen *et al.*, 1998; Bennett *et al.*, 1997; Chapman *et al.*, 1998) have been used to assess the cost-effectiveness of various medical technologies. These methods are often used to determine quality-adjusted life years, which presumably provide a measure of survival time adjusting for declines in HRQoL. Albeit promising, the usefulness of such approaches in the area of prostate cancer has yet to be fully determined.

Finally, interest has grown recently in the identification and treatment of psychological distress in men with prostate cancer. A study by Roth and colleagues (Roth *et al.*, 1998) suggests that many distressed prostate cancer patients go untreated because there are no suitable means available for identifying their distress. They piloted a rapid screening procedure that uses two pencil-and-paper self-report measures to detect distress: the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) and a ‘Distress Thermometer’. The approach was successful in identifying patients in need of psychological intervention. Others (see Lepore and Helgeson, 1999) have piloted a psychoeducational support group intervention that has successfully reduced psychological distress in men treated for localized prostate cancer. At present, these novel approaches to psychological screening and treatment have the potential of reducing some of the quality of life burden of this disease; however, they await larger-scale empirical tests.

As the number of new cases of prostate cancer grows, it will be important for clinical investigators and health-care professionals to work collaboratively to educate men and their families about the consequences of the disease and its treatments for HRQoL. This is particularly important given that several options for treatment exist. Knowledge of the potential risks and benefits of therapeutic choices will help men and their families make informed decisions about their illness. Ultimately, any course of therapy must meet both the physical and psychosocial needs of both the man with prostate cancer and his family.

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Table 1

Summary of studies of localized prostate cancer

Study	Design	Characteristics of population[a]	Summary of major findings[b]
Litwin *et al.* (1995)	Comparison group	214 men with localized PC 98 RP (23 NS); TST mean=5.3 years 56 EBR; TST mean=5.9 years 60 OB; TSD mean=5.7 years 273 age-matched men without PC (CG)	RP group had the worst UrF of all groups. EBR group had worse UrF than OB group CG had the best SxF of all groups All groups had good BwF No differences between NS and standard RP in UrF, SxF, or BwF No differences between groups in general HRQoL
Joly *et al.* (1998)	Comparison group	71 men with localized PC treated with EBR+BT; TST mean =4 years 71 age-matched men without PC (CG)	EBR+BT group had worse UrF than CG EBR+BT group had worse SxF than CG No differences between groups in BwF No differences between groups in general HRQoL
Helgason *et al*. (1996,1997)	Comparison group	342 men with localized or advanced PC 109 HT 22 RP 37 EBR 35 MX 139 OB TSD for all groups =within 1 year 314 age-matched men without PC (CG)	HT, RP, EBR, MX, & OB groups had worse SxF and more distress over poor SxF than CG HT group had the worst SxF followed by the RP and EBR groups. Of men with PC, the OB group had the best SxF
Lubeck *et al*. (1999)	Longitudinal Assessment points Time 1 (T1): Baseline or immediately after treatment Time 2 (T2): 1 year Time 3 (T3): 2 years	692 men with localized or advanced PC 351 RP 75 EBR 179 HT 87 OB TSD unavailable (Note: 18% of HT group had advanced disease)	UrF was poor in RP group at T1, but improved by T2 UrF in EBR, HT and OB groups was good at T1 and remained good at T2 and T3 SxF was poor in all groups at T1, T2, and T3 BwF was poor in RP and EBR groups at T1, but improved by T2 BwF was good in HT and OB groups at T1, T2, and T3 General HRQoL substantially declined in RP group at T1, but improved by T2 General HRQoL slightly declined in EBR group at T1, but improved by T2 General HRQoL was good in HT and OB groups at T1, T2, and T3
Litwin *et al.* (1999)	Longitudinal Assessment points Time 1 (T1): Pretreatment	90 men with localized PC treated with RP NS used with	61% recovered T1 UrF by T2 31% recovered T1 SxF by T2 96% recovered T1 BwF by T2

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Study	Design	Characteristics of population[a]	Summary of major findings[b]
	Time 2 (T2): 1 year	some men (numbers unspecified) TSD unavailable	86–97% recovered T1 function in domains of general HRQoL by T2
Beard *et al*. (1997)	Longitudinal Assessment points Time 1 (T1): Pretreatment Time 2 (T2): 3 months Time 3 (T3): 1 year	121 men with localized PC treated with EBR 25 whole-pelvis EBR 60 small-field, non-conformal EBR 36 3-D conformal EBR TSD unavailable	All showed increased fatigue from T1 to T2 and from T1 to T3 Whole-pelvis EBR group showed the greatest increases in fatigue from T1
Monga *et al*. (1997)	Longitudinal Assessment points Time 1 (T1): Pretreatment Time 2 (T2): 7–8 weeks after treatment initiation Time 3 (T3): 5–6 months posttreatment	13 men with localized PC treated with EBR TSD mean=111.1 days	All showed increased fatigue from T1 to T2 All showed recovery of T1 fatigue levels at T3 Changes in fatigue over time were not associated with depression
Clark *et al.* (1999)	Longitudinal Assessment points Time 1 (T1): Pretreatment Time 2 (T2): 3 months Time 3 (T3): 12 months	125 men with localized PC treated with either RP or EBR (*n*'s per treatment unavailable) TSD unavailable	Declines in SxF after treatment were associated with declines in general HRQoL General HRQoL declined from T1 to T2 General HRQoL at T3 recovered to T1 level
Stanford *et al*. (2000)	Longitudinal Assessment points Retrospective Time 1 (RT1): Prediagnosis, assessed retrospectively at 6 months postdiagnosis Time 2 (T2): 6 months postdiagnosis Time 3 (T3): 1 year postdiagnosis Time 4 (T4): 2 years postdiagnois (Note: Intervals from diagnosis to assessment closely approximate the intervals from treatment to assessment)	1291 men with localized PC treated with RP TSD (see assessment points)	UrF declined substantially from RT1 to T2, but improved at T3 and T4 Age and marital status were associated with posttreatment UrF. Older (75–79 years) men had greater difficulty reco vering UrF than younger (<60 years) men. Married men had better post treatment UrF than unmarried men SxF declined substantially from RT1 to T2 and remained poor at T3 and T4 Posttreatment SxF was poorest in men who reported poor pretreatment SxF Men treated with NS RP had better SxF at T4 than those treated with standard RP Age and ethnicity were associated with posttreatment SxF. Older (≥60 years) men had greater difficulty recovering SxF than younger men (<60 years) Posttreatment SxF was better in Afri can—American men than in white and Hispanic men
Potosky *et al.* (2000)	Longitudinal Assessment points Retrospective Time 1 (RT1): Prediagnosis, assessed retrospectively at 6 months postdiagnosis Time 2 (T2): 6 months postdiagnosis Time 3 (T3): 1 year	1591 men with localized PC 1156 RP 435 EBR TSD (see assessment points) TST medians between date of RP or date of EBR completion and T2, T3, and T4 were 17 weeks (≈4 months), 43 weeks (≈10 months),	UrF declines were greater in the RP group than in the EBR group at 4 and 10 months after completion of treatment SxF declines were greater in the RP group than in the EBR group at 4 and 10 months after treatment completion. During the second year after treatment completion, SxF improved slightly in the RP group, but declined

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Study	Design	Characteristics of population[a]	Summary of major findings[b]
	postdiagnosis Time 4 (T4): 2 years postdiagnois	and 95 weeks (≈22 months), respectively. Note: median interval from diagnosis to completion of EBR was 8 weeks longer than that between diagnosis and date of RP.	slightly in the EBR group. RP group reported greater bother due to poor SxF BwF declines were greater in the EBR group than the RP group at 4 months after treatment completion. BwF improved slightly in both the EBR and RP groups at later time points No differences between groups in general HRQoL at 22 months after treatment (note: cross-sectional comparison only)
Fowler *et al*. (1996)	Cross-sectional	994 men with localized PC 621 EBR: TST unavailable, but probable range 3–5 years 373 RP: TST unavailable, but probable range 2–4 years	RP group had worse UrF than EBR group RP group had worse SxF than EBR group EBR group had worse BwF than RP group
Lim *et al.* (1995)	Cross-sectional	135 men with localized PC 89 RP: TST 20%–6 months or less 20%–6–12 months 31%–12–18 months 28%—more than 18 months 46 EBR TST 22%–6 months or less 13%–6–12 months 30%–12–18 months 35%—more than 18 months	RP group had worse UrF than EBR group RP group had worse SxF than EBR group EBR group had worse BwF than RP group General HRQoL did not differ between groups
Shrader-Bogen *et al.* (1998)	Cross-sectional	274 men with localized PC 132 RP; TSD mean= 2.6 years 142 EBR; TSD mean= 3.4 years TST range=1–5 years for all men	RP group had worse UrF than EBR group RP group had worse SxF than EBR group EBR group had worse BwF than RP group General HRQoL did not differ between groups
Tefilli *et al*. (1998)	Cross-sectional	63 men with locally recurrent PC undergoing salvage procedures after primary treatment 39 salvage EBR (RP was primary treatment); TST median=3.1 years 24 salvage RP (EBR was primary treatment); TST median=3.0 years	Salvage RP groups had worse UrF than salvage EBR group Both groups had poor SxF General HRQoL did not differ between groups
Yarbro and Ferrans (1998)	Cross-sectional	121 men with localized or advanced PC	RP group had worse UrF than EBR group

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Study	Design	Characteristics of population[a]	Summary of major findings[b]
		(Note: Only 3 patients had metastases) 68 RP; TST mean=2.5 years 53 EBR; TST mean=2.1 years	Both groups had poor SxF. RP group had worse SxF than EBR group EBR group had worse BwF than RP group General HRQoL did not differ between groups
Perez et al. (1997)	Cross-sectional	294 men with localized PC treated with RP 86 NS; TST mean= 1.9 years 89 standard RP; TST mean=2.3 years 74 NS or standard RP using erectile aids at least 50% of time; TST mean=2.2 years 45 pre-RP; TSD unavailable	Erectile aid group had better SxF than both the NS and standard RP groups SxF was similar in the erectile aid and pre-RP groups
Schag *et al*. (1994)	Cross-sectional	104 men with localized PC No disaggregation by treatment; TSD mean=3.5 years	Higher psychiatric co-morbidity (incl. previous psychiatric history, alcohol abuse, and drug abuse) was associated with worse general HRQoL
Borghede *et al*. (1997)	Cross-sectional	1138 men with localized or advanced PC Treatments included RP, EBR, and HT. OB patients also included. No disaggregation by group; TSD range=1.5 to 3.5 years.	Patients with psychiatric co-morbidities (anxiety or depression) had worse general HRQoL than patients with medical co-morbidities and those with no co-morbidities
Heim and *et al* (1993)	Cross-sectional	47 men with localized or advanced PC 41 non-metastatic 6 metastatic TSD mean=2.1 years	Patients experiencing pain were more depressed and anxious than patients not experiencing pain All metastatic patients reported experiencing pain, while only 30% of non-metastatic patients reported experiencing pain
Fossa *et al*. (1997)	Cross-sectional	379 men with localized or advanced PC Localized 114 EBR 96 RP 57 OB Advanced 112 HT TSD for all groups was 1 year or later.	Fatigue was associated with poor general HRQoL

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[a] PC=prostate cancer, RP=radical prostatectomy, NS=nerve-sparing procedure, EBR=external beam radiotherapy, OB=observation-alone, BT=brachytherapy, TST=time since treatment, TSD=time since diagnosis, CG=comparison group, HT=hormone treatment, MX=mixed treatment (HT+RP or HT+EBR), Pre-RP=awaiting radical prostatectomy.

[b] UrF=urinary function, SxF=sexual function, BwF=bowel function, HRQoL=health-related quality of life.

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Table 2

Summary of studies of advanced prostate cancer

Study	Design	Characteristics of population[a]	Summary of major findings[b]
Albertsen *et al*. (1997)	Comparison group	113 men with advanced, metastatic PC 60 in remission receiving CAB for at least 3 months 53 with progressing disease receiving CAB for at least 1 month TSD unavailable	Remission group had less pain, more vitality/energy, better social well-being, and better mental health than the progressing disease group No differences in general HRQoL between the remission group and a normative group from the general population
Litwin *et al.* (1998)	Longitudinal Assessment points Pretreatment baseline Every 3 months in the first year after treatment initiation Every 6 months in the second year after treatment initiation	63 men with newly diagnosed, advanced PC 47 CAB 16 ORC TSD coincides with assessment points	No treatment group differences in any HRQoL domain Both CAB and ORC groups had good UrF and good BwF at baseline. UrF and BwF improved modestly in both groups during the first year after treatment initiation Both CAB and ORC groups had poor SxF at baseline. SxF remained poor in both groups after treatment initiation General HRQoL improved in both groups by 1 year after treatment initiation. Greatest improvements were seen in emotional, role-emotional, and social well-being
Da Silva *et al.* (1996)	Longitudinal Assessment points Pretreatment baseline 1, 3, and 6 months following study entry and every 6 months thereafter.	49 men with newly diagnosed, advanced PC treated with either CAB or ORC. TSD mean=4 months (Note: No disaggregation by treatment)	UrF was good at baseline and improved at an average follow-up of 1 year SxF was poor at baseline and remained poor at an average follow-up of 1 year Pain was mild at baseline and improved at an average follow-up of 1 year
Chodak *et al.* (1995)	Longitudinal Assessment points Pretreatment baseline 1, 3, 6, and 12 months after treatment initiation	486 men with advanced PC 243 AA 243 ORC or MC TSD unavailable	Baseline SxF was maintained in AA group at 6 months, but declined in ORC/MC group Overall health, emotional and social well-being showed greater improvements at 1 month in the AA group than the ORC/MC group

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Study	Design	Characteristics of population[a]	Summary of major findings[b]
Herr *et al*. (1993)	Longitudinal Assessment points 1, 2 and 6 months after selection of therapeutic course	35 men with newly diagnosed, advanced PC 16 hormonally treated (7 diethylstilbestrol; 9 CAB) 19 OB TSD unavailable	Hormonally treated group had worse SxF than the OB group at 1–2 months Hormonally treated group had worse SxF, greater fatigue, and worse physical well-being than did the OB group at 6 months
Moinpour *et al*. (1998)	Longitudinal Assessment points Pretreatment baseline 1, 3, 6 months after randomization to treatments	737 men with advanced, metastatic PC 370 CAB (ORC+flutamide) ORC+placebo TSD unavailable	BwF (sp. diarrhea) was worse in the CAB group than the ORC+placebo group at 3 months after treatment initiation Emotional well-being was worse in the CAB group than in the ORC+placebo group at 3 and 6 months after treatment initiation
Stockler *et al*. (1998)	Longitudinal Assessment points Pretreatment baseline Every 3 weeks while on treatment	161 men with advanced, hormone-resistant PC treated with either mitoxantrone+ prednisone or prednisone alone TSD median=3 years (Note: No disaggregation by treatment)	Pain, constipation, overall well-being, appetite, and fatigue improved in responders to palliative treatments at follow-up (time points not specified)
Tannock *et al*. (1989)	Longitudinal Assessment points Pretreatment baseline Every month while on treatment	37 men with advanced, metastatic PC previously treated with ORC or estrogen All treated with low-dose prednisone TSD median=2.3 years TST median=1.5 years (from initial hormone therapy)	Pain improved from baseline to 1 month after prednisone initiation. Reductions in pain were strongly associated with an overall sense of well-being
Cassileth *et al*. (1992)	Longitudinal Assessment points Pretreatment baseline 3 and 6 months after treatment initiation	147 men with advanced, metastatic PC 115 MC 32 ORC TSD unavailable	General HRQoL and mood improved at 3 months in both the MC and ORC groups General HRQoL and mood improvements are maintained at 6 months in the MC group General HRQoL and mood decline to baseline levels in the ORC group
Moore *et al*. (1994)	Longitudinal Assessment points Pretreatment baseline Every 6 weeks while on treatment (every 2 cycles of treatment)	27 men with advanced, hormone-resistant PC All treated with mitoxantrone (maximum 8 cycles) and low-dose prednisone; TSD median=3 years	Pain, social and emotional well-being improved from baseline to 6, 12, and 18 weeks for those who remained on study
Iversen *et al*. (1998)	Cross-sectional	480 men with advanced, non-metastatic PC 320 AA 160 ORC or MC TSD unavailable TST=1 year from the HRQoL assessment	AA group had greater sexual interest and physical well being than did ORC/MC group
Tyrrell *et al*. (1998)	Cross-sectional	808 men with advanced, metastatic PC	AA group had greater sexual interest and physical well-being

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Study	Design	Characteristics of population[a]	Summary of major findings[b]
		544 AA 264 ORC/MC TSD unavailable TST=1 year from the HRQoL assessment	than did ORC/MC group

[a] PC=prostate cancer, CAB=complete androgen blockade, ORC=orchiectomy, AA=anti-androgens, MC=medical castration, OB=observation-alone, TSD=time since diagnosis, TST=time since treatment.

[b] UrF=urinary function, BwF=bowel function, SxF=sexual function, HRQoL=health-related quality of life.