

# ANNOTATED BIBLIOGRAPHY

## PROSTATE CANCER CARE

This annotated bibliography was developed as part of ACCC's "Prostate Cancer Projects: Developing Tools and Measuring Effectiveness" educational project. A literature review of prostate cancer care was conducted of PubMed, CINAH®, Health and Psychosocial Instruments (HaPI), Google Scholar, Cochrane Reviews, and PsycInfo®. Most articles explored early or locally advanced prostate cancer. Key words included *prostate cancer, advanced, metastatic, treatment, quality, measures, metrics, indicators, quality improvement, patient satisfaction, decision aids, decision making, castrate resistant prostate cancer, hormone-refractory prostate cancer, and chemotherapy.*

The bibliography was organized into seven broad categories:

- Quality of care measures
- Quality of life and patient satisfaction
- Physician-client decision support models
- Patient decision-making aids and decision-making
- Treatment options and disease management
- Supportive care services and end-of-life care
- Economics and cost implications.

### I. QUALITY OF CARE MEASURES

Barocas D. A. and D. F. Penson (2010). "Racial variation in the pattern and quality of care for prostate cancer in the USA: mind the gap." *BJU Int* 106(3): 322-328.

**PURPOSE:** To review the literature on racial variation in the pattern of care (PoC) and quality of care (QoC) for prostate cancer, as there are known racial disparities in the incidence and outcomes of prostate cancer. While there are some biological explanations for these differences, they do not completely explain the variation. Differences in the appropriateness and QoC delivered to men of different racial groups may contribute to disparities in outcome.

**METHODS:** We searched the USA National Library of Medicine PubMed system for articles pertaining to quality indicators in prostate cancer and racial disparities in QoC for prostate cancer.

**RESULTS:** While standards for appropriate treatment are not clearly defined, racial variation in the PoC has been reported in several studies, suggesting that African-American men may receive less aggressive treatment. There are validated QoC indicators in prostate cancer, and researchers have begun to evaluate racial variation in adherence to these quality indicators. Further quality comparisons, particularly in structural measures, may need to be performed to fully evaluate differences in QoC.

**CONCLUSIONS:** There is mounting evidence for racial variation in the PoC and QoC for prostate cancer, which may contribute to observed differences in outcome. While some of the sources of racial variation in quality and outcome have been identified through the development of evidence-based guidelines and validated quality indicators, opportunities exist to identify, study and attempt to resolve other components of the quality gap.

Blayney, D. W., K. McNiff, et al. (2009). "Implementation of the Quality Oncology Practice Initiative at a university comprehensive cancer center." *J Clin Oncol* 27(23):3802-3807.

**PURPOSE:** The Quality Oncology Practice Initiative (QOPI) is a voluntary program developed by the American Society of Clinical Oncology (ASCO) to aid oncology practices in quality self-assessment. Few academic cancer centers have been QOPI participants.

**METHODS:** We implemented the QOPI process at the University of Michigan Comprehensive Cancer Center, a large, hospital-based academic cancer center, and report our experience with five rounds of data collection. Patient medical records were selected using QOPI-specified procedures and abstracted locally; results were entered into an ASCO-maintained database and analyzed.

**RESULTS:** Abstractors who were not directly involved with patient care required an average of 62.3 minutes per medical record (4.7 minutes per data element) to abstract data. We found that compliance with quality measures was uniformly high when measures were structured into our electronic medical record. Results from other measures, including those measuring chemotherapy administration in the last 2 weeks of life, were initially markedly different from those reported by other QOPI participants. Our practice changed toward the QOPI national practice norm after a presentation of the results at a faculty research conference. We found that other measures were consistently greater than 90%, including disease-specific diagnosis and treatment measures.

**CONCLUSIONS:** Measuring and showing performance data to physicians was sufficient to change some aspects of physician behavior. Improvement in other measures requires structural practice changes. QOPI, an oncologist-developed system, can be adapted for use in practice improvement at an academic medical center.

Miller, D. C. and C. S. Saigal (2009). "Quality of care indicators for prostate cancer: progress toward consensus." *Urol Oncol* 27(4): 427-434.

**PURPOSE:** Previously-documented variations in patterns of care and patient outcomes suggest differences in the quality of care provided to men with prostate cancer. Herein we describe ongoing efforts to measure the quality of prostate cancer care, including the development and pilot-testing of the RAND prostate cancer quality indicators and the selection of the consensus-based Physician Performance Measurement Set for Prostate Cancer. We also summarize current payer-led initiatives aimed at measuring quality of care for men with prostate cancer.

**CONCLUSIONS:** We conclude that currently-available prostate cancer quality indicators are derived from valid, consensus-based methodologies and capture clinical practices that are necessary for high-quality care in early-stage prostate cancer. Despite this promise, however, the currently available measures have several limitations that should be considered during their implementation in prostate cancer quality assessment and improvement activities.

Owen, J. B., J. R. White, et al. (2009). "Using QRRO survey data to assess compliance with quality indicators for breast and prostate cancer." *J Am CollRadiol* 6(6): 442-447.

**PURPOSE:** Quality Research in Radiation Oncology (QRRO) has embarked on a new national process survey to provide benchmark data that will allow radiation oncologists

to assess the quality of care in their own practices by measuring quality indicators (QIs) and comparing individual with national practice.

**METHODS:** Investigators at QRRO developed QIs on the basis of nationally recognized, evidence-based guidelines such as those of the National Comprehensive Cancer Network, as well as additional emerging QIs for processes involving rapidly emerging technology. They specifically defined the QIs as clinical performance measures. Published results of the national survey database for patients treated in 1998 and 1999 were reviewed and additional analyses conducted to assess data adequacy to measure compliance with these clinical performance measures.

**RESULTS:** Examples of workup QIs for breast cancer patients showed that 97% underwent diagnostic bilateral mammography, 96% underwent pathology reviews, 83% underwent the determination of estrogen receptor status, 81% underwent the determination of progesterone receptor status, and 31% underwent the determination of human epidermal growth factor receptor 2 status. Compliance with treatment QIs for field recommendations on the basis of nodal findings can be measured. Of patients with prostate cancer, 90% underwent digital rectal examinations, 99% underwent prostate-specific antigen tests, and 99% had their Gleason scores determined. Compliance with QIs on the basis of prognostic group can also be measured.

**CONCLUSIONS:** Benchmarking utilization patterns provides a foundation for assessing the appropriateness of cancer care in the future. The QRRO database is a rich data source, and the new survey will provide contemporary benchmark data for these measures.

Penson, D. F. (2008). "Assessing the quality of prostate cancer care." *Curr Opin Urol* 18(3): 297-302.

**PURPOSE:** Until recently, little was known about the quality of prostate cancer care in the United States. This article provides an overview of the methodology of quality of care research, reviews the available quality measures in prostate cancer and presents an overview of the existing literature on the quality of prostate cancer care in the US.

**METHODS:** Researchers have applied methodologies developed in other conditions to construct tools to measure the quality of care in this disease. Initially, researchers from the RAND Corporation developed a preliminary performance measure set. This measure set was tested in a number of settings.

**RESULTS:** Along with a number of clinical guidelines, the RAND measures served as the basis of new prostate cancer measures developed by the American Medical Association's Physician Consortium for Performance Improvement. Recent studies document that patients undergoing radical prostatectomy had worse documented compliance with quality indicators than those undergoing external beam radiotherapy.

**CONCLUSIONS:** There is clearly room for improvement in prostate cancer quality of care in the US. If providers do not take the initiative and address these shortcomings, providers and policymakers will implement changes that may not be in the best interests of patients.

Spencer, B. A., D. C. Miller, et al. (2008). "Variations in quality of care for men with early-stage prostate cancer." *J Clin Oncol* 26(22): 3735-3742.

**PURPOSE:** The commencement of quality-improvement initiatives such as Pay for Performance and the Physician Consortium for Performance Improvement has underscored calls to evaluate the quality of cancer care on a patient level for nationally representative samples.

**METHODS:** We sampled early-stage prostate cancer cases diagnosed in 2000 through 2001 from the American College of Surgeons National Cancer Data Base and explicitly reviewed medical records from 2,775 men (weighted total = 55,160 cases) treated with radical prostatectomy or external-beam radiation therapy. We determined compliance with 29 quality-of-care disease-specific structure and process indicators developed by RAND, stratified by race, geographic region, and hospital type.

**RESULTS:** Overall compliance exceeded 70% for structural and pretherapy disease assessment indicators but was lower for documentation of pretreatment functioning (46.4% to 78.4%), surgical pathology (37.1% to 86.3%), radiation technique (62.6% to 88.3%), and follow-up (55%). Geographic variations were observed as higher compliance in the South Atlantic division than the New England division for having at least one board-certified urologist (odds ratio [OR], 9.2; 95% CI, 1.9 to 45.0), at least one board-certified radiation oncologist (OR, 3.3; 95% CI, 1.2 to 9.0), use of Gleason grading (OR, 4.1; 95% CI, 1.2 to 13.8), and administering total radiation dose  $\geq 70$  Gy (OR, 3.1; 95% CI, 1.6 to 6.1). Teaching/research hospitals and Comprehensive Cancer Centers had higher compliance than Community Cancer Centers, whereas racial differences were not observed for any indicator.

**CONCLUSIONS:** The significant and unwarranted variations observed for these quality indicators by census division and hospital type illustrate the inconsistencies in prostate cancer care and represent potential targets for quality improvement. The lack of racial disparities suggests equity in care once a patient initiates treatment.

Miller, D. C., B. A. Spencer, et al. (2007). "Treatment choice and quality of care for men with localized prostate cancer" *Med Care* 45(5): 401-409.

**PURPOSE:** Variations in patterns of care and treatment outcomes suggest differences in the quality of care for men treated for localized prostate cancer. We sought to compare adherence with quality indicators for prostate cancer care among men treated with radical prostatectomy or external beam radiation therapy.

**METHODS:** We sampled 5230 men diagnosed in 2000 or 2001 with early-stage prostate cancer from 984 facilities reporting to the National Cancer Data Base. Our analytic cohort includes 2604 men (from 770 facilities) treated with radical prostatectomy or external beam radiation.

**RESULTS:** Subject-level compliance with the RAND quality indicators for localized prostate cancer care, stratified by treatment. We applied sampling weights to obtain national estimates of quality indicator adherence. The weighted samples represent 24,547 and 27,125 men treated with radical prostatectomy or external beam radiation therapy, respectively. Compliance with several quality indicators approached 100% in both treatment groups; however treatment-specific variations were noted. Men receiving radiation were less likely than those undergoing surgery to be treated in facilities with a board-certified urologist (odds ratio [OR] = 0.4, 95% confidence interval [95% CI] = 0.2-0.8). Adherence with process of care indicators was appreciably higher among radiation subjects, including documentation of clinical stage (OR = 7.5, 95% CI = 4.8-11.9), pre-therapy assessment of urinary (OR = 2.8,

95% CI = 1.9-4.2) and sexual (OR = 1.6, 95% CI = 1.2-2.2) function, and discussion of treatment options (OR = 1.8, 95% CI = 1.1-2.9).

**CONCLUSIONS:** Documented compliance with process of care quality indicators among men with localized prostate cancer appears superior for those treated with external beam radiation compared with those treated surgically.

Lorenz, K., J. Lynn, et al. (2006). "Cancer care quality measures: symptoms and end-of-life care." *Evid Rep Technol Assess (Full Rep)*(137): 1-77.

**PURPOSE:** To systematically identify quality measures and the evidence for them-to support quality assessment and improvement in the palliative care of patients with cancer in the areas of pain, dyspnea, depression, and advance care planning (ACP), and to identify important gaps in related research.

**METHODS:** Searches of MEDLINE, CINAHL, and PsycINFO in English 1995-2005. We also conducted an extensive Internet search of professional organizations seeking guidelines and other grey literature (i.e., not published in peer-reviewed journals) using similar terms and attempted to contact all measure developers. We searched using terms for each domain for patients (adults and children) with a cancer diagnosis throughout the continuum of care (e.g., diagnosis to death). Pain and depression searches were limited to cancer, but we searched broadly for dyspnea and ACP, because the evidence base for dyspnea is more limited and experts advised that ACP measures would be generalizable to cancer. Measures were included if they expressed a normative relationship to quality and included a measurable numerator and denominator. Citations and articles were each reviewed/abstracted by two of six palliative care researcher/clinicians who described populations, testing, and attributes for each measure.

**RESULTS:** The literature search identified 5,187 titles, of which 4,650 were excluded at abstract review. Of 537 articles, only 25 contained measures: 21 on ACP, 4 on depression, 2 on dyspnea, and 12 on pain. Ten relevant measure sets were identified: ACOVE, QA Tools, Cancer Care Ontario, Cancer Care Nova Scotia, Dana-Farber, Georgia Cancer Coalition, University Health Consortium, NHPCO, VHA, and ASCO. We identified a total of 40 operationalized and 19 non-operationalized measures. The most measures were available for pain (12) and ACP (21), compared with only 4 for depression and 2 for dyspnea. Few of the measures were published, and few had been specifically tested in a cancer population.

**CONCLUSIONS:** A large number of measures are available for addressing palliative cancer care, but testing them in relevant populations is urgently needed. No measures or indicators were available to evaluate the quality of supportive pediatric cancer care. Basic research is urgently needed to address measurement in populations with impaired self-report. Funding field testing of highest quality measures should be an urgent patient and family-centered priority to meet the needs of patients with cancer.

Miller, D. C., J. E. Montie, et al. (2005). "Measuring the quality of care for localized prostate cancer." *J Urol* 174(2): 425-431.

**PURPOSE:** We describe the current status of quality of care measurement for localized prostate cancer and provide a framework for preserving a leadership role for our specialty in this dynamic and controversial field.

**METHODS:** Basic methodological principles of quality of care assessment were reviewed. Several factors that suggest the potential for current variation in the quality of care for patients with localized prostate cancer, particularly those receiving active treatment, were then analyzed. Subsequently contemporary publications and investigations that comprise the current foundation of prostate cancer quality of care research were reviewed.

**RESULTS:** The foundation for much of the emerging research in prostate cancer quality of care assessment is based on the Donabedian structure-process-outcome paradigm. The RAND candidate quality indicators for localized prostate cancer were developed in this framework and they represent the first effort to systematically consider the measurement of quality as it relates to prostate cancer. The feasibility of applying the RAND quality indicators to clinical quality of care assessments has been demonstrated, although further modification and refinement of the indicator set are necessary prior to large-scale, population based implementation of these quality assessment measures. Moreover, future quality of care efforts must make the transition to primarily prospective or concurrent quality assessments, such that measures can be taken to modify the structure and/or process of care at the time of delivery or shortly thereafter.

**CONCLUSIONS:** Prostate cancer quality of care assessment represents a burgeoning domain of urological health services research. To date such initiatives have come from within and outside of our specialty. In the future such efforts are likely to expand and they may have a substantial impact on the clinical and administrative aspects of urological practice. As a result, urologists should maintain a leading role in efforts to further define of quality of care as it relates to prostate cancer and radical prostatectomy.

Miller, D. C., M. S. Litwin, et al. (2003). "Use of quality indicators to evaluate the care of patients with localized prostate carcinoma." *Cancer* 97(6): 1428-1435.

**PURPOSE:** The goal of quality assurance in health care is to preserve and improve patient care. Recently, RAND developed a set of evidence-based candidate indicators for evaluating the quality of care for patients with localized prostate carcinoma; however, the feasibility and sensitivity of these indicators have not been tested in a clinical setting. The objectives of this study were to evaluate the feasibility of measuring these quality indicators and to determine their sensitivity to change in practice patterns over time.

**METHODS:** One hundred sixty-eight men who presented in either 1995 or in 2000 and were treated for localized prostate carcinoma were selected randomly from the University of Michigan tumor registry. A combination of electronic data base review and explicit chart review was used to assess the feasibility of measuring compliance for each indicator. For each indicator in which assessment was feasible, compliance with the RAND indicators was determined for patients in both years. Multivariate regression analysis was used to adjust for potential confounding effects of disease stage, tumor grade, prostate specific antigen (PSA) level, patient age, and therapy.

**RESULTS:** Based on review of available clinical data, measurement of compliance was feasible for 19 of 22 RAND candidate quality indicators (86%). For five indicators, significant differences in documentation (compliance) were detected between 1995 and 2000 ( $P < 0.05$ ). Treatment received and higher PSA levels were associated independently with documentation of compliance for several indicators ( $P < 0.05$ ).

**CONCLUSIONS:** Measurement of the majority of the RAND quality indicators for the treatment of patients with localized prostate carcinoma was feasible, and improvements in several indicators were observed between 1995 and 2000. Demonstration of such variation, even within a single institution, suggests that the indicators are sufficiently sensitive to detect differences in practice patterns.

Spencer, B. A., M. Steinberg, et al. (2003). "Quality-of-care indicators for early-stage prostate cancer." *J Clin Oncol* 21(10): 1928-1936.

**PURPOSE:** Decisions regarding treatment for early-stage prostate cancer are frustrated not only by inadequate evidence favoring one treatment modality but also by the absence of data comparing quality among providers. In fact, the choice of provider may be as important as the choice of treatment. We undertook this study to develop an infrastructure to evaluate variations in quality of care for men with early-stage prostate cancer.

**METHODS:** We enlisted several sources to develop a list of proposed quality-of-care indicators and covariates. After an extensive structured literature review and a series of focus groups with patients and their spouses, we conducted structured interviews with national academic leaders in prostate cancer treatment. We then convened an expert panel using the RAND consensus method to discuss and rate the validity and feasibility of the proposed quality indicators and covariates.

**RESULTS:** The panel endorsed 49 quality-of-care indicators and 14 covariates, which make up our final list of candidate measures. Several domains of quality are represented in the selected indicators, including patient volume, pretreatment referrals, preoperative testing, interpretation of pathology specimens, and 10-year disease-free survival. Covariates include measures of case-mix, such as patient age and comorbidity.

**CONCLUSION:** This study establishes a foundation on which to build quality-of-care assessment tools to evaluate the treatment of early-stage prostate cancer. The next step is to field-test the indicators for feasibility, reliability, validity, and clinical utility in a population-based sample. This work will begin to inform medical decision-making for patients and their physicians.

## II. QUALITY OF LIFE AND PATIENT SATISFACTION

Caffo, O., T. Sava, et al. (2011). "Impact of docetaxel-based chemotherapy on quality of life of patients with castration-resistant prostate cancer: results from a prospective phase II randomized trial." *BJU Int* 108(11): 1825-1832.

**PURPOSE:** To assess quality of life (QoL) outcomes and pain changes in patients affected by castration-resistant prostate cancer enrolled in a phase II randomized trial of 3-week docetaxel (DOC)-based chemotherapy. To provide further data to clarify the conflicting published data concerning the impact of DOC on the patients' QoL.

**METHODS:** QoL outcomes were assessed using the European Organisation for the Research and Treatment of Cancer QLQ-C30 questionnaire. Pain changes were evaluated by means of the Brief Pain Inventory at baseline and after every two DOC courses. The patients completing at least two questionnaires (at baseline and before the third course) were considered evaluable.

**RESULTS:** In all, 59 patients were evaluable. Asymptomatic patients and responders had a better baseline QoL than symptomatic patients and non-responders. There were no statistically significant changes in the QLQ-C30 scales during treatment except in the case of patients receiving DOC and estramustine, who experienced a significant decrease in pain. There was a progressive improvement in the mean intensity and interference scores of the Brief Pain Inventory.

**CONCLUSIONS:** Data on quality of life during docetaxel treatment in castration resistant prostate cancer were mainly provided by SWOG and TAX327 trials. In the TAX327 trial biochemical response and pain predicted survival, whereas quality of life outcomes did not. In the present study, there were no statistically significant changes in the quality of life scales during treatment except in the case of patients receiving docetaxel and estramustine, who experienced a significant decrease in pain. Our data seem to suggest that patients with a better baseline quality of life (and consequently with fewer symptoms) are more likely to achieve a biochemical response. Our data confirm that QoL is generally maintained during chemotherapy. There is a substantial reduction in pain. Our results also suggest that baseline QoL may predict treatment response.

Chamie, K., S. E. Connor, et al. (2011). "Prostate cancer survivorship: Lessons from caring for the uninsured." *Urol Oncol*.

**PURPOSE:** Since 2001, UCLA has operated IMPACT: Improving Access, Counseling, and Treatment for Californians with Prostate Cancer (CaP). Funded by the California Department of Public Health, with a cumulative budget of over \$80 million, the program provides comprehensive care for low-income, uninsured Californian men with biopsy-proven CaP. Health services research conducted with program enrollees, through the UCLA Men's Health Study, yields an opportunity to perform qualitative and quantitative assessments of patient-reported outcomes in these men, all members of historically underserved, primarily minority populations. This review summarizes data from several studies in which validated instruments were administered longitudinally in 727 participants, prospectively measuring health-related quality of life (HRQOL), self-efficacy in interactions with physician interactions, social and emotional health, symptom distress, satisfaction with care, and other patient-reported outcomes.

Chang, P., K. M. Szymanski, et al. (2011). "Expanded prostate cancer index composite for clinical practice: development and validation of a practical health related quality of life instrument for use in the routine clinical care of patients with prostate cancer." *J Urol* 186(3): 865-872.

**PURPOSE:** Measuring the health-related quality of life of patients with prostate cancer in routine clinical practice is hindered by the lack of instruments enabling efficient, real-time, point of care scoring of multiple health related quality of life domains. Thus, we developed an instrument for this purpose.

**METHODS:** The Expanded Prostate Cancer Index Composite for Clinical Practice is a 1-page, 16-item questionnaire that we constructed to measure urinary incontinence, urinary irritation, and the bowel, sexual and hormonal health related quality of life domains. We eliminated conceptually overlapping items from the 3-page Expanded Prostate Cancer Index Composite-26 and revised the questionnaire format to mirror the AUA symptom index, thereby enabling practitioners to calculate health related quality of life scores at the point of care. We administered the Expanded Prostate Cancer Index Composite for Clinical Practice to



a new cohort of patients with prostate cancer in community based and academic oncology, radiation, and urology practices to evaluate instrument validity as well as ease of use in clinical practice.

**RESULTS:** A total of 175 treated and 132 untreated subjects with prostate cancer completed the Expanded Prostate Cancer Index Composite for Clinical Practice. The domain scores of the Expanded Prostate Cancer Index Composite for Clinical Practice correlated highly with the respective domain scores from longer versions of the Expanded Prostate Cancer Index Composite ( $r \geq 0.93$  for all domains). The Expanded Prostate Cancer Index Composite for Clinical Practice showed high internal consistency (Cronbach's alpha 0.64-0.84) and sensitivity to prostate cancer treatment related effects ( $p < 0.05$  in each of 5 health related quality of life domains). Patients completed the Expanded Prostate Cancer Index Composite for Clinical Practice efficiently (96% in less than 10 minutes and with 11% missing items). It was deemed very convenient by clinicians in 87% of routine clinical encounters and clinicians accurately scored completed questionnaires 94% of the time.

**CONCLUSIONS:** The Expanded Prostate Cancer Index Composite for Clinical Practice is a valid instrument that enables patient reported, health related quality of life to be measured efficiently and accurately at the point of care, and thereby facilitates improved emphasis and management of patient reported outcomes.

Maliski, S. L., S. E. Connor, et al. (2011). "Access to health care and quality of life for underserved men with prostate cancer." *Semin Oncol Nurs* 27(4): 267-277.

**PURPOSE:** To explore links between access to care and quality of life for underserved men with prostate cancer through a literature review.

**METHODS:** Data sources included articles published from 2000 to present based on a PubMed search using the key words access, quality of life, health care access, underserved, low income, health literacy, and prostate cancer.

**CONCLUSIONS:** There is not one reason that adequately explains factors affecting access, health-related quality of life (HRQOL), or the potential relationships between the two for underserved men with prostate cancer. Socioeconomic factors contribute to accessibility and HRQOL, but not consistently, suggesting that there is still much work to be done in identifying factors and relationships that connect access to care and HRQOL for underserved men with prostate cancer. It is particularly important is to develop intervention strategies to address the disparities in access to care and prostate cancer treatment outcomes (including HRQOL) for this vulnerable population. Based on findings from studies, nurses need to be actively involved in the development and implementation of programs that address multiple barriers including socioeconomic status, minority status, health literacy, insurance, and language.

Wadhwa, D., D. Burman, et al. (2011). "Quality of life and mental health in caregivers of outpatients with advanced cancer." *Psychooncology*.

**PURPOSE:** This study evaluates the quality of life (QOL) and mental health (MH) of caregivers of patients with advanced cancer who are receiving ambulatory oncology care and associations with patient, caregiver and care-related characteristics.

**METHODS:** Patients with advanced gastrointestinal, genitourinary, breast, lung or gynaecologic cancer, and their caregivers, were recruited from 24 medical oncology

clinics for a cluster-randomized trial of early palliative care. Caregivers completed the Caregiver QOL-Cancer scale and the Medical Outcomes Study Short Form, version 2, and a questionnaire including care-related factors such as hours/day providing care and change in work situation. Patients completed a demographic questionnaire and measures of their QOL and symptom severity. Associations of these factors with caregiver QOL and MH were examined using linear regression analyses.

**RESULTS:** Of the 191 caregivers, 84% were spouses/partners, 90% cohabited with the patient, half were working and 25% had a change in work situation since the patient's diagnosis. On multiple regression analysis, better caregiver QOL was associated with better caregiver MH and patient physical well-being and with not providing care for other dependents. Worse caregiver MH was associated with female caregiver sex, worse patient emotional well-being, more hours spent caregiving and change in the caregiver's work situation.

**CONCLUSIONS:** Caregivers of ambulatory patients with advanced cancer may have compromised QOL and MH associated with worse patient physical and emotional well-being and with simultaneously caring for others and working outside the home. Early palliative care interventions directed at patient symptoms and caregiver support may improve QOL in this population. Copyright (c) 2011 John Wiley & Sons, Ltd.

Wiechno, P. J., M. Sadowska, et al. (2011). "Does pharmacological castration as adjuvant therapy for prostate cancer after radiotherapy affect anxiety and depression levels, cognitive functions and quality of life?" *Psychooncology*.

**PURPOSE:** Adjuvant hormone therapy for prostate cancer patients after radical radiotherapy has a well-established value. However, the impact of such treatment on the patients' quality of life remains to be elucidated. The objective is to assess the impact of adjuvant hormone therapy with luteinizing hormone-releasing hormone analogue after radical radiotherapy on anxiety and depression levels, cognitive function, sexual function and quality of life of prostate cancer patients.

**METHODS:** Two groups of patients were tested: men treated with adjuvant hormone therapy (88 patients) and men without hormone therapy (61 patients). Anxiety, depression and cognitive functions were evaluated. Patients answered questions addressing problems linked to hormonal equilibrium. The patients rated their mental status, physical status, quality of life and quality of their relationship.

**RESULTS:** There were no statistically significant differences between patients on hormone therapy and without hormone therapy in the level of anxiety and depression ( $p = 0.844$  and  $p = 0.954$ ) as well as in cognitive function ( $p = 0.661$ ). Satisfactory sexual performance was preserved in 9/65 patients (14%) on hormone therapy and the same was applied to 19/49 patients (39%) without hormone therapy. The difference was statistically significant ( $p = 0.003$ ). Hormone therapy was associated with decreased libido ( $p = 0.031$ ), hot flushes ( $p < 0.001$ ) and sweating ( $p < 0.001$ ). No statistically significant differences were found between the groups in the self-rated physical and psychological well-being ( $p = 0.476$  and  $p = 0.597$ ), quality of life ( $p = 0.622$ ) and quality of relationship ( $p = 0.064$ ).

**CONCLUSIONS:** Adjuvant hormone therapy enhances neither anxiety nor depression, does not impair cognitive function but has a negative effect on the

patients' sexual function. It does not worsen self-rated quality of relationship and quality of life. Copyright (c) 2011 John Wiley & Sons, Ltd.

Dalkin, B. L. (2010). "Editorial comment. Comprehensive quality-of-life outcomes in the setting of a multidisciplinary, equal access prostate cancer clinic." *Urology* 76(5): 1238; author reply 1238-1239.

Hacker, E. D. (2010). "Technology and quality of life outcomes." *Semin Oncol Nurs* 26(1): 47-58.

**PURPOSE:** To discuss recent technological advances in quality of life (QOL) data collection and guidance for use in research and clinical practice. The use of telephone-, computer-, and web/internet-based technologies to collect QOL data, reliability and validity issues, and cost will be discussed, along with the potential pitfalls associated with these technologies.

**METHOD:** Data sources included health care literature and web resources.

**CONCLUSIONS:** Technology has provided researchers and clinicians with an opportunity to collect QOL data from patients that were previously not accessible. Most technologies offer a variety of options, such as language choice, formatting options for the delivery of questions, and data management services. Choosing the appropriate technology for use in research and/or clinical practice primarily depends on the purpose for QOL data collection. Technology is changing the way nurses assess QOL in patients with cancer and provide care. As stakeholders in the health care delivery system and patient advocates, nurses must be intimately involved in the evaluation and use of new technologies that impact QOL and/or the delivery of care.

Huang, G. J., N. Sadetsky, et al. (2010). "Health related quality of life for men treated for localized prostate cancer with long-term followup." *J Urol* 183(6): 2206-2212.

**PURPOSE:** Men who undergo primary treatment for prostate cancer can expect changes in health related quality of life. Long-term changes after treatment are not yet fully understood. We characterized health related quality of life evolution from baseline to 4 years after treatment.

**METHODS:** We identified 1,269 men in CaPSURE who underwent primary treatment for clinically localized prostate cancer and completed followup health related quality of life questionnaires for at least 4 years. The men underwent radical prostatectomy, external beam radiotherapy, brachytherapy, combined external beam radiotherapy/brachytherapy or androgen deprivation therapy. Health related quality of life was measured using patient reported questionnaires. Effects of select covariates on quality of life were measured with a multivariate mixed model.

**RESULTS:** Age at diagnosis, time from treatment and primary treatment were significant predictors of health related quality of life in all domains ( $p < 0.05$ ) except primary treatment on sexual bother. Men who underwent radical prostatectomy experienced the most pronounced worsening urinary function but also had the greatest recovery. All treatments worsened urinary bother, and sexual function and bother. All forms of radiotherapy moderately worsened bowel function and bother after treatment but eventual recovery to baseline was noted.

**CONCLUSIONS:** Age at diagnosis, time from treatment and primary treatment type affect health related quality of life. Treatment has a greater impact on disease specific than general health related quality of life. All treatments adversely affect urinary and

sexual function. Most adverse changes develop immediately after treatment. Recovery occurs mostly within 2 years after treatment with little change beyond 3 years.

Rice, K., J. Hudak, et al. (2010). "Comprehensive quality-of-life outcomes in the setting of a multidisciplinary, equal access prostate cancer clinic." *Urology* 76(5):1231-1238.

**PURPOSE:** To identify racial and demographic factors that influence treatment choice and its resulting impact on health-related quality of life (HRQoL) for prostate cancer patients.

**METHODS:** Patients presenting to an equal access, military, multidisciplinary prostate cancer clinic composed the study group. The Expanded Prostate Cancer Index Composite (EPIC), EPIC Demographic, and Medical Outcomes Study Short Form 36 were the instruments used. Evaluation was performed before treatment and every 3 months after treatment.

**RESULTS:** The study group comprised 665 patients. Caucasians were 3-fold more likely to choose surgery (radical prostatectomy [RP]) over external beam radiation therapy (EBRT). Patients who earned more than \$100,000 annually disproportionately chose RP ( $P < .0001$ ). Similarly, those having a graduate school degree disproportionately chose RP ( $P < .0001$ ). Patients undergoing RP had the greatest risk of urinary function decline ( $P < .0001$ ) and sexual bother ( $P = .0003$ ). African Americans (AA) had a greater risk of urinary function decline irrespective of treatment choice. Patients undergoing EBRT had equivalent urinary function to expectant management (EM) at 12 months ( $P < .0001$ ). Brachytherapy was the only treatment that posed an increased risk of urinary bother decline when compared with EM ( $P = .0217$ ). EBRT alone did not show significant decrement in sexual function when compared with EM.

**CONCLUSIONS:** RP was chosen by patients of Caucasian ethnicity and patients with higher income and education level, despite providing the greatest risk of HRQoL decline. EBRT had no significant impact on urinary function, sexual function, or sexual bother scores at 12 months. EBRT may be offered to older patients with minimal HRQoL impact. Pretreatment counseling of HRQoL outcomes is essential to overall prostate cancer management.

Szymanski, K. M., J. T. Wei, et al. (2010). "Development and validation of an abbreviated version of the expanded prostate cancer index composite instrument for measuring health-related quality of life among prostate cancer survivors." *Urology* 76(5): 1245-1250.

**PURPOSE:** Widespread implementation of health-related quality-of-life (HRQOL) measurement in prostate cancer practice and research requires concise instruments. With 50 questions, the full-length Expanded Prostate Cancer Index Composite (EPIC) is cumbersome to administer outside of studies focusing exclusively on HRQOL. To facilitate HRQOL measurement in a broad range of prostate cancer research and practice settings, we developed and validated an abbreviated version of the EPIC. **METHODS:** The 50 questions that constitute the full-length EPIC-50 were evaluated to identify the items suitable for elimination while retaining the ability to measure the 5 prostate cancer-specific HRQOL domains of the EPIC-50. The resulting abbreviated version (EPIC-26) was validated using question responses from 252 subjects who had undergone brachytherapy, external beam radiotherapy, or prostatectomy for prostate cancer. The EPIC-26 internal consistency was measured by Cronbach's alpha coefficient and reliability using test-retest correlation.

**RESULTS:** Using the high item-scale correlations, clinically relevant content, and preservation of domain psychometrics, 26 items were retained in the EPIC-26 from the 50 questions in the full-length EPIC-50. A high correlation was observed between the EPIC-50 and EPIC-26 versions for the urinary incontinence, urinary irritation/obstruction, bowel, sexual, and vitality/hormonal domain scores (all  $r \geq 0.96$ ). The correlations between the different domains were low, confirming that EPIC-26 retained the ability to discern the 5 distinct HRQOL domains. The internal consistency and test-retest reliability for EPIC-26 (Cronbach's alpha  $\geq 0.70$  and  $r \geq 0.69$ , respectively for all 5 HRQOL domains) supported its validity.

**CONCLUSIONS:** EPIC-26 is a brief, valid, and reliable subjective measure of health quality among patients with prostate cancer and is suitable for measuring the HRQOL among patients undergoing treatment of early-stage prostate cancer.

Varricchio, C. G. and C. E. Ferrans (2010). "Quality of life assessments in clinical practice." *Semin Oncol Nurs* 26(1): 12-17.

**PURPOSE:** To provide information about the value of quality of life (QOL) assessments to improve clinical care.

**METHODS:** Data sources included published articles, web resources, clinical practice.

**CONCLUSIONS:** Clinical assessment of QOL can lead to improved patient outcomes and provide a means of evaluating the effectiveness of interventions. QOL assessment provides nurses with a more holistic view of the patient and improves communication between the patient and health care providers.

Waldmann, A., V. Rohde, et al. (2009). "Measuring prostate-specific quality of life in prostate cancer patients scheduled for radiotherapy or radical prostatectomy and reference men in Germany and Canada using the Patient Oriented Prostate Utility Scale-Psychometric (PORPUS-P)." *BMC Cancer* 9: 295.

**PURPOSE:** The PORPUS-P is a short questionnaire for measuring prostate-specific quality of life (QoL), which was designed in Canada for use in prostate cancer (PC) patients. We aimed to generate a German version and compare PORPUS-P scores of German reference men from the general population, and German and Canadian patients with newly diagnosed PC who were scheduled to receive radical prostatectomy (RP) or radiotherapy (RT).

**METHODS:** The study sample consisted of 988 reference men, 121 German and 66 Canadian PC patients scheduled for RT, and 371 German and 68 Canadian PC patients scheduled for RP. All men completed the PORPUS-P (German postal questionnaire, Canada personal interview). Data were gathered from PC patients before the start of therapy. **RESULTS:** Canadian patients were better educated than the German patients, and fewer were retired. Patients scheduled to receive RT were older and more were retired. German RT patients had lower D'Amico risk scores and pre-treatment Gleason scores than RP patients, and Canadian RT patients had higher pre-treatment PSA than RP patients. Urinary and sexual dysfunction were seen in PC patients (especially RT patients), but were also common in the German reference men. Crude mean PORPUS-P scores differed statistically significant between German RT and RP and Canadian RP and RT patients, with RT patients having

higher QoL scores. The differences in age-adjusted mean PORPUS-P scores between reference men and RP patients were not clinically significant, while RT patients had (clinically) significantly lower scores than the reference men.

**CONCLUSIONS:** The German translation of the PORPUS-P appears to be a short and feasible tool for assessing prostate-specific QoL. Although we found a similar response pattern, Canadian and German PC patients scheduled to receive RT or RP rated their pre-treatment quality of life on different levels, which reveals the need for national reference data. Problems in several QoL domains exist before treatment, and differ between PC patients scheduled for RT and RP.

Zavala, M. W., S. L. Maliski, et al. (2009). "Spirituality and quality of life in low income men with metastatic prostate cancer." *Psychooncology* 18(7): 753-761.

**PURPOSE:** To determine how spirituality is associated with health-related quality of life (HRQOL) in an ethnically diverse cohort of low-income men with metastatic prostate cancer.

**METHODS:** Eighty-six participants in a state-funded program that provides free prostate cancer treatment to uninsured, low-income men completed written surveys and telephone interviews containing validated measures of spirituality, and general and disease-specific HRQOL. Assessments were made following diagnosis of metastatic disease. We used multivariate analyses to assess the effect of spirituality and its two subscales, faith and meaning/peace, on HRQOL.

**RESULTS:** African American and Latino men, and men with less than a high-school education had the highest spirituality scores. Spirituality was significantly associated with general and disease-specific HRQOL. We also found a significant interaction between faith and meaning/peace in the physical and pain domains.

**CONCLUSIONS:** Greater spirituality was associated with better HRQOL and psychosocial function. Meaning/peace closely tracks with HRQOL. Higher faith scores, in the absence of high meaning/peace scores, are negatively associated with HRQOL.

Albaugh, J. and E. D. Hacker (2008). "Measurement of quality of life in men with prostate cancer." *Clin J Oncol Nurs* 12(1): 81-86.

**PURPOSE:** Prostate cancer continues to be one of the most common cancers diagnosed in men. In light of the excellent survival rates for prostate cancer, quality of life is a primary concern during and following prostate cancer treatment. Quality of life is defined and determined in multiple ways. This article explores quality of life in men with prostate cancer. Quality-of-life dimensions, measurement tools, and implications of quality of life with prostate cancer on clinical practice for oncology nurses will be presented.

Anger, J. T., S. L. Maliski, et al. (2007). "Outcomes in men denied access to a California public assistance program for prostate cancer." *Public Health Rep* 122(2): 217-223.

**PURPOSE:** To improve access to prostate cancer treatment for low income uninsured men, California initiated a program called IMPACT: Improving Access, Counseling and Treatment for Californians with Prostate Cancer. The program administered free

treatment, case management, counseling, and educational materials to all eligible men until budget cuts led to a state-mandated suspension of enrollment and the establishment of a temporary waitlist in February 2005. To assess the effect of suspension of enrollment on patient outcomes, the authors compared health-related quality of life (HRQOL) in waitlisted and enrolled men.

**METHODS:** Eighty-three men in each group were matched on disease stage, age, and race. HRQOL was captured with the UCLA Prostate Cancer Index short form (PCI-SF), the Medical Outcomes Study Short Form-12 (SF-12), and McCorkle and Young's Symptoms and Degrees of Distress in Patients with Cancer Scale (SDS). Self-efficacy was measured with the Perceived Efficacy in Patient-Physician Interactions (PEPPI) Questionnaire.

**RESULTS:** At intake, waitlisted men demonstrated significantly more symptom-related distress (2.9;  $p=0.04$ ) and less perceived self-efficacy (2.5;  $p=0.005$ ) compared to enrollees. Wait-listed men were significantly less likely to have access to a doctor or nurse case manager, treatment medications, nutrition information, or counseling services ( $p<0.0001$ ).

**CONCLUSIONS:** Men denied enrollment into the IMPACT program exhibited significantly worse symptom distress and self-efficacy compared to enrolled men at initial assessment. The multivariate model suggests that HRQOL in the wait-listed men may be related to their lack of access to medical services. This data illustrates the importance of ongoing public assistance for low income men with prostate cancer.

Bremner, K. E., C. A. Chong, et al. (2007). "A review and meta-analysis of prostate cancer utilities." *Med Decis Making* 27(3): 288-298.

**PURPOSE:** Health-related quality of life is a key issue in prostate cancer (PC) management. The authors summarized published utilities for common health-related quality of life outcomes of PC and determined how methodological factors affect them.

**METHODS:** In their systematic review, the authors identified 23 articles in English, providing 173 unique utilities for PC health states, each obtained from 2 to 422 respondents. Data were pooled using linear mixed-effects modeling with utilities clustered within the study, weighted by the number of respondents divided by the variance of each utility.

**RESULTS:** In the base model, the estimated utility of the reference case (scenario of a metastatic PC patient with severe sexual symptoms, rated by non-PC patients using time tradeoff) was 0.76. Disease stage, symptom type and severity, source of utility, and scaling method were associated with utility differences of 0.10 to 0.32 ( $P<0.05$ ). Utilities from PC patients rating their own health were 0.14 higher than those from the reference case, but utilities from PC patients rating scenarios were lowest. Time tradeoff yielded the highest utilities. Computer administration yielded lower utilities than personal interview ( $P = 0.02$ ). Neither the scale's high anchor nor study purpose had significant effects on utilities.

**CONCLUSIONS:** This study provides pooled utility estimates for common PC health states and describes how clinical and methodological factors can significantly affect these values. When possible, utility estimates for a modeling application should be derived similarly. Formal data synthesis methods might be useful to researchers

integrating utility data from heterogeneous sources. Further exploration of these methods for this purpose is warranted.

Katz, A. (2007). "Quality of life for men with prostate cancer." *Cancer Nurs* 30(4):302-308.

**PURPOSE:** The aim of this article is to selectively review the current research findings related to quality of life and prostate cancer.

**METHOD:** English-language journals indexed in MEDLINE, PubMed, and CINAHL published between 1999 and 2005 were searched for relevant articles using the following keywords: "quality of life and prostate cancer," "prostatectomy," "radiation therapy," "brachytherapy," "cryotherapy," or "androgen deprivation therapy." References in selected articles were reviewed for potentially relevant articles not identified through database searches.

**RESULTS:** All treatment modalities have a significant impact on quality of life for men with local or advanced prostate cancer. Alterations in sexual functioning cause the most significant impact on quality of life for men. Quality of life is decreased in both the short and long term for men with prostate cancer.

**CONCLUSIONS:** Oncology nurses must be cognizant of the challenges that a diagnosis of prostate cancer presents to the man with prostate cancer and his partner. Patients should be fully informed of the potential for impact on quality of life with all treatment modalities, and the oncology nurse can play an important role in both providing this information and supporting the patient when quality of life is impacted.

Matthew, A. G., K. L. Currie, et al. (2007). "Serial personal digital assistant data capture of health-related quality of life: a randomized controlled trial in a prostate cancer clinic." *Health Qual Life Outcomes* 5: 38.

**PURPOSE:** In clinical and research practice linked to prostate cancer treatment, frequent monitoring of patient health-related quality of life (HRQOL) is essential. Practical and analytic limitations of paper questionnaire data capture may be overcome with the use of self-administered personal digital assistant (PDA) data collection. The objective of this study was to assess the reliability, validity, and feasibility of using PDA in place of paper versions of the International Prostate Symptom Score (IPSS), the Patient Oriented Prostate Cancer Utility Survey (PORPUS), and the International Index of Erectile Function-5 (IIEF-5) in a prostate cancer clinic setting.

**METHODS:** 152 participants were randomly assigned to one of three conditions: 1) paper followed by PDA survey; 2) PDA followed by paper survey; or 3) PDA followed by PDA survey. Evaluation included an assessment of data quality (internal consistency, test-retest reliability, response correlation, completeness of data), and feasibility (participation rates, time to completion, preference and difficulty ease of using PDA).

**RESULTS:** Internal consistency was similar for both PDA and paper applications. Test-retest reliability was confirmed for PDA repeated administration. Data from paper and PDA questionnaires were strongly correlated. Lower missed item rates were found in PDA administration. 82.8% of participants preferred using the PDA or



had no preference. Mean difficulty/ease ratings indicated that participants found the PDA easy to use. Age did not significantly correlate with preference or difficulty.

**CONCLUSIONS:** The results confirm the adaptability of the IPSS, IIEF-5, and the PORPUS to PDA administration. Similarly, the findings of this study support the feasibility of using PDA technology for HRQOL serial data capture in the prostate cancer patient population.

Hashine, K., K. Azuma, et al. (2005). "Health-related quality of life and treatment outcomes for men with prostate cancer treated by combined external-beam radiotherapy and hormone therapy." *Int J Clin Oncol* 10(1): 45-50.

**PURPOSE:** Health-related quality of life (HR-QOL) is important when considering the treatment options for prostate cancer.

**METHODS:** From 1992 to 1998, 57 patients were treated by radiotherapy plus hormone therapy (median age, 79 years; median prostate-specific antigen concentration, 15.0 ng/ml; median radiotherapy dosage, 60 Gy). General HR-QOL was measured by the European Organization for Research and Treatment of Cancer Prostate Cancer QOL Questionnaire, and a newly developed disease-specific QOL survey was used to assess urinary and bowel functions. QOL was also measured in a control group of patients admitted for prostate biopsy.

**RESULTS:** The general HR-QOL scores in the radiation group ranged from 70.0 to 91.3, with sexual problems showing the lowest (i.e., worst) score (38.5). Compared with the control group, the scores in the radiation group were worse for physical function and sexual problems. For disease-specific QOL, the radiation group had worse urinary function than controls, but were more satisfied with their urinary function. There was no difference between the radiation group and controls in satisfaction with bowel function. When the control group was subdivided into two groups: age 75 years or less, and age over 75 years, the QOL score in the radiation group was the same as that in the subgroup aged over 75 years. In subgroups of the radiation patients, according to survey period, there was no difference between the first and last surveys in longitudinal HR-QOL evaluations. The 5- and 10-year overall survival rates were 67.6% and 41.6%, respectively, and the 5- and 10-year cause-specific survival rates were 97.9% and 94.7%.

**CONCLUSIONS:** The combination of radiotherapy and hormone therapy has a good outcome and patients do not experience poor HR-QOL, except for sexual problems. Moreover, the disease-specific QOL is good, especially for urinary bother.

Krupski, T. L., G. Sonn, et al. (2005). "Ethnic variation in health-related quality of life among low-income men with prostate cancer." *Ethn Dis* 15(3): 461-468.

**PURPOSE:** To describe and compare health-related quality of life (HRQOL) among Hispanic, African-American, and Caucasian men with localized prostate cancer.

**METHOD:** Observational study of low-income, ethnically diverse men with non-metastatic prostate cancer. Statewide public assistance program in California. 208 men (51 Caucasian, 115 Hispanic, and 42 African-American men) with non-metastatic disease. Interventions included radical retropubic prostatectomy, radiation therapy, and hormonal therapy. Main outcome measures: Validated instruments

measured general and disease-specific HRQOL, anxiety and fear of recurrence, spirituality, symptom distress, and self-efficacy.

**RESULTS:** Hispanic men with prostate cancer were less educated, more often in significant relationships, and had more variable incomes compared with men of other ethnic/racial backgrounds. In univariate analyses, Caucasian men reported better physical function but less spirituality, while Hispanic men reported worse sexual function. Multivariate analysis revealed that Hispanic men had significantly worse physical function, bowel function, and bowel bother. African-American men experienced greater anxiety over recurrence. African-American and Hispanic men were more spiritual than Caucasian men.

**CONCLUSIONS:** Greater attention to demographic variations in HRQOL may allow physicians to improve outcomes across ethnicities in low-income men with prostate cancer by offering more specialized counseling and providing referral to social support systems.

Ritvo, P., J. Irvine, et al. (2005). "Reliability and validity of the PORPUS, a combined psychometric and utility-based quality-of-life instrument for prostate cancer." *J Clin Epidemiol* 58(5): 466-474.

**PURPOSE:** To assess the measurement properties (reliability and validity) of two newly developed psychometric and utility-based instruments for assessing outcomes associated with prostate cancer. Although utility-based quality-of-life instruments are often used in economic evaluations and psychometric instruments in treatment evaluations, these are complementary approaches to assessing outcomes. In this study we developed and tested these two forms of quality-of-life instruments, both based on a single, validated, health classification system.

**METHODS:** 141 men with cancer of the prostate (CaP), treated with radical prostatectomy, radiation therapy, hormonal therapy, and/or chemotherapy were assessed with both instruments and other standard psychometric and utility-based instruments.

**RESULTS:** Analyses indicate the test instruments are reliable and valid. Full-scale correlations between the instruments and standard instruments indicate validity, as do correlations of key subscales, and an evaluation of linear associations with the UCLA-Prostate Cancer Symptom Scales.

**CONCLUSIONS:** Evidence from this study supports the reliability and construct validity of the tested instruments. Prostate cancer outcomes can now be assessed by a combination of psychometric and utility-based methods, allowing a ready comparison of derived outcomes.

Efficace, F., A. Bottomley, et al. (2003). "Beyond the development of health-related quality-of-life (HRQOL) measures: a checklist for evaluating HRQOL outcomes in cancer clinical trials--does HRQOL evaluation in prostate cancer research inform clinical decision making?" *J Clin Oncol* 21(18): 3502-3511.

**PURPOSE:** The aim of this study was to evaluate whether the inclusion of health-related quality of life (HRQOL), as a part of the trial design in a randomized controlled trial (RCT) setting, has supported clinical decision making for the planning of future medical treatments in prostate cancer.

**METHODS:** A minimum standard checklist for evaluating HRQOL outcomes in cancer clinical trials was devised to assess the quality of the HRQOL reporting and to classify the studies on the grounds of their robustness. It comprises 11 key HRQOL issues grouped into four broader sections: conceptual, measurement, methodology, and interpretation. Relevant studies were identified in a number of databases, including MEDLINE and the Cochrane Controlled Trials Register. Both their HRQOL and traditional clinical reported outcomes were systematically analyzed to evaluate their consistency and their relevance for supporting clinical decision making.

**RESULTS:** Although 54% of the identified studies did not show any differences in traditional clinical end points between treatment arms and 17% showed a difference in overall survival, 74% of the studies showed some difference in terms of HRQOL outcomes. One third of the RCTs provided a comprehensive picture of the whole treatment including HRQOL outcomes to support their conclusions.

**CONCLUSIONS:** A minimum set of criteria for assessing the reported outcomes in cancer clinical trials is necessary to make informed decisions in clinical practice. Using a checklist developed for this study, it was found that HRQOL is a valuable source of information in RCTs of treatment in metastatic prostate cancer.

Turini, M., A. Redaelli, et al. (2003). "Quality of life and economic considerations in the management of prostate cancer." *Pharmacoeconomics* 21(8): 527-541.

**PURPOSE:** The purpose of this article was to provide an overview of the morbidity and mortality of prostate cancer, QOL issues and the economic impact of the disease.

**METHODS:** We searched Medline (from 1990 onwards) for all studies dealing with prostate cancer epidemiology, treatment, screening and staging, and critically reviewed the most relevant articles, focusing on pharmacoeconomic issues.

**RESULTS:** Prostate cancer is the most common cancer in men. In the US, new estimated cases of prostate cancer represented 14.8% of all new cancer cases for 2000, with estimated deaths from prostate cancer comprising 5.8% of all deaths from cancer. Current options for prostate cancer management include radical prostatectomy, cryosurgery, radiotherapy, hormone therapy and watchful waiting. Many of the long-term effects of treatment, such as urinary incontinence, impotence and radiation-induced proctitis, have a large impact on patients' quality of life and, in some patients, may offset the clinical benefits. Regulatory bodies and managed care organisations are assigning increasing importance to the evaluation of QOL benefits as an independent clinical endpoint and a measure of patient satisfaction. Several screening programmes for early detection of prostate cancer, mostly based on prostate-specific antigen (PSA) measurement or digital rectal examination, have been proposed, but their routine implementation in all asymptomatic elderly men has been questioned. There is still no definite proof that patient outcomes are improved by extensive PSA screening. Furthermore, the total cost of a screening programme is difficult to define since it extends well beyond the initial test. Several instruments are used for QOL assessment in prostate cancer, some of which have been specifically developed for, or adapted to, patients with this disease, such as the Functional Assessment Cancer Therapy (FACT) tool, Prostate Cancer Treatment Outcome Questionnaire (PCTO-Q) and Prostate Cancer Specific Quality of Life Instrument (PROSQOLI). More than 50% of treatment costs for prostate cancer are accrued during the patient's last year of life, and total initial care costs decrease with increasing age. In the US, initial average inpatient costs were estimated at \$US 2253,

in 1995, for men aged  $\geq 80$  years, compared with \$US 4540 for men aged 35-64 years.

**CONCLUSIONS:** In recent years, treatments based on combined modalities (i.e., radiotherapy/prostatectomy plus hormonal therapies) have emerged. Although cost-effectiveness analyses of various treatment options have been attempted, the strength of their conclusions appears to be limited by the lack of homogeneous literature data on the effects of such interventions on survival and morbidity.

### III. PHYSICIAN-CLIENT DECISION SUPPORT MODELS

Lin, H. C., H. C. Wu, et al. (2011). "Development of a real-time clinical decision support system upon the Web MVC-based architecture for prostate cancer treatment." *BMC Med Inform Decis Mak* 11: 16.

**PURPOSE:** A real-time clinical decision support system (RTCDSS) with interactive diagrams enables clinicians to instantly and efficiently track patients' clinical records (PCRs) and improve their quality of clinical care. We propose a RTCDSS to process online clinical informatics from multiple databases for clinical decision making in the treatment of prostate cancer based on Web Model-View-Controller (MVC) architecture, by which the system can easily be adapted to different diseases and applications.

**METHODS:** We designed a framework upon the Web MVC-based architecture in which the reusable and extractable models can be conveniently adapted to other hospital information systems and which allows for efficient database integration. Then, we determined the clinical variables of the prostate cancer treatment based on participating clinicians' opinions and developed a computational model to determine the pretreatment parameters. Furthermore, the components of the RTCDSS integrated PCRs and decision factors for real-time analysis to provide evidence-based diagrams upon the clinician-oriented interface for visualization of treatment guidance and health risk assessment.

**RESULTS:** The resulting system can improve quality of clinical treatment by allowing clinicians to concurrently analyze and evaluate the clinical markers of prostate cancer patients with instantaneous clinical data and evidence-based diagrams which can automatically identify pretreatment parameters. Moreover, the proposed RTCDSS can aid interactions between patients and clinicians.

**CONCLUSIONS:** Our proposed framework supports online clinical informatics, evaluates treatment risks, offers interactive guidance, and provides real-time reference for decision making in the treatment of prostate cancer. The developed clinician-oriented interface can assist clinicians in conveniently presenting evidence-based information to patients and can be readily adapted to an existing hospital information system and be easily applied in other chronic diseases.

Armstrong, A. J., E. Garrett-Mayer, et al. (2010). "Prediction of survival following first-line chemotherapy in men with castration-resistant metastatic prostate cancer." *Clin Cancer Res* 16(1): 203-211.

**PURPOSE:** We sought to evaluate predictors of overall survival following progression after systemic chemotherapy in men with metastatic castration-resistant prostate cancer.

**METHODS:** For our study population, we used the TAX327 multicenter randomized phase III trial comparing administration of docetaxel and prednisone every 3 weeks, weekly administration of docetaxel and prednisone, and administration of mitoxantrone and prednisone every 3 weeks. Progression was defined as the earliest of prostate-specific antigen (PSA), tumor, or pain progression. We analyzed predictors of postprogression survival according to both prechemotherapy and postchemotherapy variables with adjustment for potential confounders.

**RESULTS:** Among 1,006 men, 640 had evaluable information on protocol-defined progression leading to further therapy. Median post-progression survival was 14.5 months. In the multivariable analysis, several pretreatment factors were associated with post-progression survival: pain, performance status, alkaline phosphatase, number of sites of metastatic disease, liver metastases, hemoglobin, PSA, and time since diagnosis. In addition, we found that the number of progression factors (PSA, pain, and tumor size), the duration of firstline chemotherapy, and whether progression occurred during chemotherapy independently predicted post-progression survival. We found evidence for the benefit of continuation of chemotherapy beyond progression only for men who had isolated worsening of pain. A nomogram was constructed and internally validated with a concordance index of 0.70.

**CONCLUSIONS:** An internally validated model to predict postchemotherapy survival was developed. Evaluation of men in the postdocetaxel setting should consider the type of progression, duration of therapy, and known pretreatment prognostic factors. Definitions of progression in castration-resistant prostate cancer that include pain should also consider composite measures of tumor or PSA progression. External validation is planned.

Armstrong, A. J., I. F. Tannock, et al. (2010). "The development of risk groups in men with metastatic castration-resistant prostate cancer based on risk factors for PSA decline and survival." *Eur J Cancer* 46(3): 517-525.

**PURPOSE:** There are no known predictive factors of response in men receiving chemotherapy for metastatic castration-resistant prostate cancer (mCRPC). We investigated pre-treatment factors that predicted a 30% PSA decline (30% PSAD) within 3 months of starting chemotherapy, and assessed performance of a risk group classification in predicting PSA declines and overall survival (OS) in men with mCRPC.

**METHODS:** In TAX327, 1006 men with mCRPC were randomized to receive docetaxel (D) in two schedules, or mitoxantrone (M), each with prednisone: 989 provided data on PSA decline within 3 months. Predictive factors for a 30% PSAD were identified using multivariable regression in D-treated men (n=656) and validated in M-treated men (n=333).

**RESULTS:** Four independent risk factors predicted 30% PSAD: pain, visceral metastases, anaemia and bone scan progression. Risk groups (good: 0-1 factors, intermediate: 2 factors and poor: 3-4 factors) were developed with median OS of 25.7, 18.7 and 12.8 months ( $p < 0.0001$ ); 30% PSAD in 78%, 66% and 58% of men ( $p < 0.001$ ); and measurable disease response in 19%, 9% and 5% of men ( $p = 0.018$ ), respectively. In the validation cohort, similar predictive ability was noted for 30% PSAD, tumour response and OS. PCWG2 subtypes were also predictive but resulted in unequal grouping. C-indices were 0.59 and 0.62 for 30% PSAD and OS in the validation dataset, respectively.

**CONCLUSIONS:** Risk groups have been identified and validated that predict PSAD and OS in men with mCRPC and may facilitate evaluation of new systemic regimens warranting definitive testing in comparison with docetaxel and prednisone. Prospective validation of this classification system is needed.

Bellmunt, J., J. Carles, et al. (2009). "Predictive modelling in hormone-refractory prostate cancer (HRPC)." *Clin Transl Oncol* 11(2): 82-85.

Because the evidence is not yet solid enough to strongly recommend whether or not to treat hormone-refractory prostate cancer (HRPC) patients at certain stages of the disease, predictive models might help in decision making. The importance of prognostic models lies in their ability to capture clinically relevant and measurable variables for routine use by clinicians to inform patients, and improve palliation and treatment decisions. Basically this allows for the creation of homogeneous prognostic strata for randomised comparative trials of therapeutic agents. In the last few years different models to predict patient outcome in HRPC have been published in the literature. Recently, based on the phase III randomised trial of docetaxel, a multivariate prognostic model incorporating PSA kinetics has been developed to predict survival at 1, 2 and 5 years in metastatic HRPC men treated with chemotherapy. This novel model includes new independent clinical prognostic factors in addition to PSA-DT such as baseline pain, type of progression at baseline (measurable disease or bone scan compared with PSA only), presence of liver metastases and the number of metastatic disease sites. This nomogram will be a helpful tool to stratify patients for further docetaxel-based trials and could also help us to delineate the potential benefits of chemotherapy at certain points during the natural history of HRPC.

Fitzpatrick, J. M., C. N. Sternberg, et al. (2009). "Treatment Decisions for Advanced Genitourinary Cancers: From Symptoms to Risk Assessment." *European Urol Suppl* 8(9): 738-746.

**PURPOSE:** Current and emerging treatment options for advanced prostate, renal, and bladder cancer were discussed at the annual Interactive Genitourinary Cancer Conference (IGUCC) held in February 2009 in connection with the 2nd World Congress on Controversies in Urology (CURy). To provide practical clinical guidance for physicians and to promote the implementation of recent advances in the management of genitourinary cancers through closer collaboration among urologists, medical oncologists, and radiation oncologists. This article was developed from presentations given at IGUCC 2009. Docetaxel treatment is established as the standard first-line treatment for patients with metastatic castrate-resistant prostate cancer (mCRPC), based on improvements in overall survival regardless of age, performance status, and pain.

**CONCLUSIONS:** Treatment should be introduced according to risk-factor assessment, clinical status, and patient values and preferences. Similarly, management of senior adults with mCRPC should be individually adapted to the patient's health status rather than chronologic age, especially since the benefits and toxicity associated with docetaxel treatment are similar in senior adults and younger patients. Asymptomatic patients with adverse prognostic factors for survival such as visceral metastases, anaemia, and new bone lesions may be candidates for chemotherapy. Prognostic nomograms based on pretreatment parameters aid in

identifying patients for earlier chemotherapy. Second-line treatments for CRPC patients are needed, but currently no agent has demonstrated efficacy in phase 3 clinical trials. For patients with a prior response to docetaxel, retreatment at relapse can be effective and well tolerated. There is a strong rationale for targeting angiogenesis in renal cell carcinoma (RCC), and new targeted therapies have changed treatment paradigms for RCC. In contrast, little progress has been made in the treatment of advanced bladder cancer since the introduction of cisplatin-based chemotherapy; new strategies are needed. Docetaxel (every 3 wk) treatment is a therapeutic option in elderly and asymptomatic mCRPC patients. Docetaxel retreatment is effective in initial responders. Docetaxel (every 3 wk) improves overall survival and palliation in metastatic castrate-resistant prostate cancer patients, regardless of age or pain. Docetaxel retreatment is a therapeutic option in initial responders. Targeted therapies have transformed treatment of renal cell carcinoma, while new treatment strategies are required for bladder cancer.

Nguyen, C. T. and M. W. Kattan (2009). "Development of a prostate cancer metagram: a solution to the dilemma of which prediction tool to use in patient counseling." *Cancer* 115(13 Suppl): 3039-3045.

**PURPOSE:** Many treatment options are available to the human with clinically localized prostate cancer, including surgery, radiation, and even active surveillance. To the authors' knowledge, there is no consensus on the optimal management of this patient population, with most clinicians tending to recommend the treatment with which they are most familiar. Effective patient counseling allowing informed decision making can be best achieved with a formalized system that offers accurate predictions of outcomes for all available treatment approaches.

**METHOD:** The authors organized the currently available prostate cancer prediction tools toward the formation of a metagram that can be used to tailor management to the individual patient. A comprehensive review of the literature was performed to identify published prediction tools intended for use in prostate cancer. Tools were categorized by a combination of treatment modality and the outcome being predicted, and incorporated into a metagram constructed of 16 different treatment options and 10 outcomes related to cancer control, survival, and morbidity.

**RESULTS:** A search of the literature revealed 44 prostate cancer prediction tools that assessed at least 1 of the 160 treatment/outcome combinations that comprise the metagram. Only 31 cells of the metagram were populated with currently available tools.

**CONCLUSIONS:** Prediction tools offer the most accurate estimates of outcomes in prostate cancer, but their current role in patient counseling is complicated by the large number of existing tools, as well as a lack of comparative data. To address this, the authors incorporated the most relevant prediction tools currently available into a prostate cancer metagram that may offer evidence-based and individualized predictions for multiple endpoints after all available treatment options in clinically localized prostate cancer. The metagram also reveals areas of deficiency in the current catalog of prediction tools. Many more prediction tools are needed. *Cancer* 2009;115(13 suppl):3039-45. (c) 2009 American Cancer Society.

Shariat, S. F., P. I. Karakiewicz, et al. (2008). "An updated catalog of prostate cancer predictive tools." *Cancer* 113(11): 3075-3099.

**PURPOSE:** Accurate estimates of risk are essential for physicians if they are to recommend a specific management to patients with prostate cancer. Accurate risk estimates also are required for clinical trial design to ensure that homogeneous, high-risk patient groups are used to investigate new cancer therapeutics. Using the MEDLINE database, a literature search was performed on prostate cancer predictive tools from January 1966 to July 2007.

**METHOD:** The authors recorded input variables, the prediction form, the number of patients used to develop prediction tools, the outcome being predicted, prediction tool-specific features, predictive accuracy, and whether validation was performed. Each prediction tool was classified into patient clinical disease state and the outcome being predicted. First, the authors described the criteria for evaluation (predictive accuracy, calibration, generalizability, head-to-head comparison, and level of complexity) and the limitations of current predictive tools.

**RESULTS:** The literature search generated 109 published prediction tools, including only 68 that had undergone validation. An increasing number of predictive tools addressed important endpoints, such as disease recurrence, metastasis, and survival.

**CONCLUSIONS:** Despite their limitations and the limitations of data, predictive tools are essential for individualized, evidence-based medical decision making. Moreover, the authors recommend wider adoption of risk-prediction models in the design and implementation of clinical trials. Among prediction tools, nomograms provide superior, individualized, disease-related risk estimations that facilitate management-related decisions. Nevertheless, many more predictive tools, comparisons between them, and improvements to existing tools are needed. Cancer 2008. © 2008 American Cancer Society.

Armstrong, A. J., E. S. Garrett-Mayer, et al. (2007). "A contemporary prognostic nomogram for men with hormone-refractory metastatic prostate cancer: a TAX327 study analysis." *Clin Cancer Res* 13(21): 6396-6403.

**PURPOSE:** To develop a prognostic model and nomogram using baseline clinical variables to predict death among men with metastatic hormone-refractory prostate cancer (HRPC).

**METHOD:** TAX327 was a clinical trial that randomized 1,006 men with metastatic HRPC to receive every three week or weekly docetaxel or mitoxantrone, each with prednisone. We developed a multivariate Cox model and nomogram to predict survival at 1, 2, and 5 years.

**RESULTS:** Ten independent prognostic factors other than treatment group were identified in multivariate analysis: (a) presence of liver metastases [hazard ratio (HR), 1.66; P = 0.019], (b) number of metastatic sites (HR, 1.63 if > or =2 sites; P=0.001), (c) clinically significant pain (HR, 1.48; P < 0.0001), (d) Karnofsky performance status (HR, 1.39 if < or =70; P = 0.016), (e) type of progression (HR, 1.37 for measurable disease progression and 1.29 for bone scan progression; P =0.005 and 0.01, respectively), (f) pretreatment prostate-specific antigen (PSA) doubling time (HR, 1.19 if <55 days; P = 0.066), (g) PSA (HR, 1.17 per log rise; P< 0.0001), (h) tumor grade (HR, 1.18 for high grade; P = 0.069), (i) alkaline phosphatase (HR, 1.27 per log rise; P < 0.0001), and (j) hemoglobin (HR, 1.11 per unit decline; P = 0.004). A nomogram was developed based on this multivariate model and validated internally using bootstrap methods, with a concordance index of 0.69.



**CONCLUSIONS:** This multivariate model identified several new independent prognostic factors in men with metastatic HRPC, including PSA doubling time, and led to the successful development of a clinically applicable nomogram. External prospective validation may support the wider use of this prognostic baseline model for men with HRPC treated with chemotherapy.

Richman, M. B., E. H. Forman, et al. (2005). "A novel computer based expert decision making model for prostate cancer disease management." *J Urol* 174(6):2310-2318.

**PURPOSE:** We propose a strategic, computer based, prostate cancer decision making model based on the analytic hierarchy process. We developed a model that improves physician-patient joint decision making and enhances the treatment selection process by making this critical decision rational and evidence based.

**METHODS:** Two groups (patient and physician-expert) completed a clinical study comparing an initial disease management choice with the highest ranked option generated by the computer model. Participants made pairwise comparisons to derive priorities for the objectives and subobjectives related to the disease management decision. The weighted comparisons were then applied to treatment options to yield prioritized rank lists that reflect the likelihood that a given alternative will achieve the participant treatment goal. Aggregate data were evaluated by inconsistency ratio analysis and sensitivity analysis, which assessed the influence of individual objectives and subobjectives on the final rank list of treatment options.

**RESULTS:** Inconsistency ratios less than 0.05 were reliably generated, indicating that judgments made within the model were mathematically rational. The aggregate prioritized list of treatment options was tabulated for the patient and physician groups with similar outcomes for the 2 groups. Analysis of the major defining objectives in the treatment selection decision demonstrated the same rank order for the patient and physician groups with cure, survival and quality of life being more important than controlling cancer, preventing major complications of treatment, preventing blood transfusion complications and limiting treatment cost. Analysis of sub-objectives, including quality of life and sexual dysfunction, produced similar priority rankings for the patient and physician groups. Concordance between initial treatment choice and the highest weighted model option differed between the groups with the patient group having 59% concordance and the physician group having only 42% concordance.

**CONCLUSIONS:** This study successfully validated the usefulness of a computer based prostate cancer management decision making model to produce individualized, rational, clinically appropriate disease management decisions without physician bias.

Terret, C., G. Albrand, et al. (2004). "Geriatric assessment in elderly patients with prostate cancer." *Clin Prostate Cancer* 2(4): 236-240.

**PURPOSE:** As a result of demographic evolution, oncologists will treat more and more elderly patients with prostate cancer. Aging is frequently associated with the coexistence of several medical complications that can increase the complexity of cancer treatment decision-making. Unfortunately, clinical oncologists need to be more familiar with the multidimensional assessment of elderly patients. To acquire

this skill, we implemented a multidimensional geriatric assessment program at our cancer center. This instrument prospectively assessed 60 elderly patients with prostate cancer. We describe geriatric aspects detected in our patient sample and report treatment options proposed to elderly patients with prostate cancer at different disease stages.

**RESULTS:** The minimal comprehensive geriatric assessment (mini-CGA) procedure revealed that 66% of our patient population was dependent in one or more of the Katz Activities of Daily Living and 87% were dependent in 1 or more of the Lawton Instrumental Activities of Daily Living; all patients had significant comorbidity according to the Cumulative Illness Rating Scale-Geriatrics, 75% having at least one severe comorbidity. We identified 19 cases of drug interaction. We also observed that half of these patients had a risk of falling and some physical disability; 45% had cognitive disorders requiring more investigation; one third had depressive symptoms. Finally, 65% of the patients were either malnourished or at risk of malnutrition. Many of these problems were unknown before the mini-CGA processing and may interfere with cancer and cancer treatment.

**CONCLUSIONS:** The correct management of elderly patients with cancer requires comprehensive geriatric assessment as well as relevant disease staging at diagnosis. This approach will help us to propose the most appropriate treatment with the main aim of preserving quality of life.

#### IV. PATIENT DECISION AIDS AND DECISION-MAKING

Berry, D. L., B. Halpenny, et al. (2011). "The Personal Patient Profile-Prostate decision support for men localized prostate cancer: A multi-center randomized trial." *Urol Oncol*.

**PURPOSE:** The purpose of this trial was to compare usual patient education plus the Internet-based Personal Patient Profile-Prostate, vs. usual education alone, on conflict associated with decision making, plus explore time-to-treatment, and treatment choice.

**METHODS:** A randomized, multi-center clinical trial was conducted with measures at baseline, 1-, and 6 months. Men with newly diagnosed localized prostate cancer (CaP) who sought consultation at urology, radiation oncology, or multi-disciplinary clinics in 4 geographically distinct American cities were recruited. Intervention group participants used the Personal Patient Profile-Prostate, a decision support system comprised of customized text and video coaching regarding potential outcomes, influential factors, and communication with care providers. The primary outcome, patient-reported decisional conflict, was evaluated over time using generalized estimating equations to fit generalized linear models. Additional outcomes, time-to-treatment, treatment choice, and program acceptability/usefulness, were explored.

**RESULTS:** A total of 494 eligible men were randomized (266 intervention; 228 control). The intervention reduced adjusted decisional conflict over time compared with the control group, for the uncertainty score (estimate -3.61; (confidence interval, -7.01, 0.22), and values clarity (estimate -3.57; confidence interval (-5.85,-1.30). Borderline effect was seen for the total decisional conflict score (estimate -1.75; confidence interval (-3.61,0.11). Time-to-treatment was comparable between groups, while undecided men in the intervention group chose brachytherapy more often than in the control group. Acceptability and usefulness were highly rated.

**CONCLUSIONS:** The Personal Patient Profile-Prostate is the first intervention to significantly reduce decisional conflict in a multi-center trial of American men with newly diagnosed localized CaP. Our findings support efficacy of P3P for addressing decision uncertainty and facilitating patient selection of a CaP treatment that is consistent with the patient values and preferences.

Goh, A. C., M. A. Kowalkowski, et al. (2011). "Perception of cancer and inconsistency in medical information are associated with decisional conflict: a pilot study of men with prostate cancer who undergo active surveillance." *BJU Int.*

**PURPOSE:** Men with prostate cancer who choose active surveillance may experience anxiety and depression. Higher anxiety related to uncertainty surrounding cancer has been shown to increase the likelihood of choosing active treatment in the absence of a clinical indication. Certain characteristics, including physician influence and a neurotic personality, may also increase the risk of psychological distress. Our study identified particular areas that may affect the degree of satisfaction or uncertainty experienced by men choosing active surveillance. We showed that men with a positive outlook who perceived that they were receiving consistent medical information had improved ability to manage uncertainty and felt more in control of their decision-making. Men who were confident in their ability to manage prostate-related symptoms also had less insecurity with their decision. To understand the factors associated with decision-making, we conducted a telephone-based survey as part of a pilot study to develop a psycho-educational intervention for men with prostate cancer who undergo active surveillance.

**METHODS:** From 2007 to 2008, we conducted a cross-sectional study of 34 individuals on active surveillance for prostate cancer. We examined how specific mental health, quality of life and socio-demographic characteristics relate to decision-making. Five validated decision-making scales were used as primary outcomes reflecting the amount of satisfaction, regret and conflict a participant experienced about his decision to undergo active surveillance. A multivariate regression model was developed to identify specific psychosocial factors related to the decision-making outcomes.

**RESULTS:** Primary analyses focused on the decisional satisfaction and conflict measures, as the decisional regret measure showed poor reliability ( $\alpha < 0.70$ ) in this sample. Four psychosocial measures showed strong associations across the decision-making subscales, including the Fife Constructed Meaning Scale (Pearson  $r > 0.26$ ), Mishel Uncertainty in Illness Scale - Inconsistency ( $r > 0.32$ ), Mental Health Index-5 ( $r > 0.33$ ), and Lepore self-efficacy for prostate symptom management scale ( $r > 0.33$ ). Individuals with higher self-efficacy for prostate cancer symptom management ( $P = 0.02$ ) and higher positive meaning for cancer ( $P = 0.03$ ) were less likely to express decision-making conflict as the result of uncertainty. Individuals reporting higher positive meaning for cancer ( $P = 0.01$ ) and less uncertainty in illness attributed to inconsistency ( $P = 0.02$ ) were less likely to exhibit decision-making conflict related to the perceived effectiveness of treatment.

**CONCLUSIONS:** Men choosing active surveillance represent a patient group with unique vulnerabilities that require new psycho-educational interventions to provide information and support that will maintain and improve quality of life. We describe specific characteristics that may put patients at higher risk during the decision-making process and indicate their increased need for such interventions.

Leighl, N. B., H. L. Shepherd, et al. (2011). "Supporting treatment decision making in advanced cancer: a randomized trial of a decision aid for patients with advanced colorectal cancer considering chemotherapy." *J Clin Oncol* 29(15): 2077-2084.

**PURPOSE:** Decision making in advanced cancer is increasingly complex. We developed a decision aid (DA) for patients with advanced colorectal cancer who are considering first-line chemotherapy and reviewing treatment options, prognostic information, and toxicities. We examined its impact on patient understanding, treatment decisions, decisional conflict, decision making, consultation satisfaction, anxiety, and quality of life by using a randomized trial design.

**METHODS:** In all, 207 patients with colorectal cancer who were considering first-line chemotherapy for metastatic disease were randomly assigned to receive a standard medical oncology consultation or a consultation in which the DA (take-home booklet with audio recording, reviewed by an oncologist) was used. Participants completed questionnaires post-consultation, post-decision, and 1 month later.

**RESULTS:** In this study, 100 patients were randomly assigned to the control arm, and 107 received the DA. Median age of the sample was 62 years, 58% were male, 89% had a performance status of 0 or 1, and 36% had received prior adjuvant chemotherapy. Patients receiving the DA demonstrated a greater increase in understanding of prognosis, options, and benefits, with higher overall understanding ( $P < .001$ ). Decisional conflict, treatment decisions, and achievement of involvement preferences were similar between the groups. Anxiety was similar across groups and decreased over time. Most patients were confident in a decision during the first consultation; 74% chose chemotherapy, 7% supportive care alone, and 10% observation.

**CONCLUSIONS:** This randomized trial of a decision aid in advanced cancer showed that its use in advanced colorectal cancer improved patient understanding of prognosis, treatment options, risks, and benefits without increasing anxiety. DAs can improve informed consent and can be tested through randomized trials even in the advanced cancer setting.

Sajid, S., S. G. Mohile, et al. (2011). "Individualized decision-making for older men with prostate cancer: balancing cancer control with treatment consequences across the clinical spectrum." *Semin Oncol* 38(2): 309-325.

Prostate cancer (PCa) is the most prevalent non-skin cancer among men and is the second leading cause of cancer death in men. PCa has an increased incidence and prevalence in older men. Age-associated incidence is on the rise due to increased screening in the older population. This has led to a sharp rise in the detection of early stage PCa. Given the indolent nature of many prostatic malignancies, a large proportion of older men with PCa will ultimately die from other causes. As a result, physicians and patients are faced with the challenge of identifying optimal treatment strategies for localized PCa, biochemically recurrent PCa and later-stage PCa. Age-related changes can impact tolerance of hormonal therapy and chemotherapy in men with metastatic disease and shift the risk-benefit ratio of these treatments. Tools such as the Comprehensive Geriatric Assessment (CGA) can help estimate

remaining life expectancy and can help predict treatment-related morbidity and mortality in older men. Application of CGA in older men with PCa is important to help individualize and optimize treatment strategies. Research that integrates multidisciplinary and multidimensional assessment of PCa and the patient's overall health status is needed.

Soeyonggo, T., P. Warde, et al. (2011). "Information needs of men on androgen deprivation therapy." *BJU Int.*

**PURPOSE:** Although androgen deprivation therapy (ADT) is widely used to treat men with prostate cancer, little is known about the information needs of patients on ADT. We found that patients are generally very satisfied with using ADT and expressed minimal decisional regret with its use up to four years later. For men receiving ADT in the adjuvant setting, their survival estimates with the addition of ADT were quite reasonable when compared to findings in randomized trials. A key area to enhance patient education appears to be side effects, especially around hot flashes and fatigue, which were also the most bothersome treatment sequelae for patients. The objective is to evaluate information needs of men receiving ADT.

**METHODS:** A cross-sectional survey was distributed to English-speaking prostate cancer patients receiving ADT adjuvant to radical therapy or for biochemical relapse. Three cohorts were recruited based on duration of ADT use: <6 months (cohort 1), 6-18 months (cohort 2) and 18 months to 4 years (cohort 3). Several validated questionnaires were used, including the Control Preferences Scale (CPS), Satisfaction with Treatment Decision Scale (SWD) and Decisional Regret Scale (DRS). Patients on adjuvant ADT were asked to estimate their overall survival with and without ADT.

**RESULTS:** Eighty-five men were recruited, of whom 91.8% were receiving a gonadotrophin-releasing hormone agonist, 4.7% were receiving anti-androgen monotherapy and 3.5% were receiving combined androgen blockade. \* Patients preferred the following decision-making roles: 23.5% active, 50.6% collaborative, 27.0% passive. Mean patient satisfaction for ADT use was high at 24.0/30 and decisional regret was low at 7.9/25. There was a perceived overall survival benefit of 3.9-6.9% at 5 years, 3.6-17.8% at 10 years and 5.7-18.1% at 15 years with the addition of adjuvant ADT. Hot flashes and fatigue were reported as the most common theoretical adverse effects as well as those experienced most commonly by patients.

**CONCLUSIONS:** Patients on ADT were generally satisfied with their decisions to start ADT and expressed minimal decisional regret up to 4 years later. A key area to enhance patient education appears to be adverse effects, especially around hot flashes and fatigue.

Berry, D. L., B. Halpenny, et al. (2010). "Development and evaluation of the personal patient profile-prostate (P3P), a Web-based decision support system for men newly diagnosed with localized prostate cancer." *J Med Internet Res* 12(4): e67.

**PURPOSE:** Given that no other disease with the high incidence of localized prostate cancer (LPC) has so many treatments with so few certainties related to outcomes, many men are faced with assuming some responsibility for the treatment decision along with guidance from clinicians. Men strongly consider their own personal characteristics and other personal factors as important and influential to the decision. Clinical researchers have not developed or comprehensively investigated interventions to facilitate the insight and prioritizing of personal factors along with medical factors that are required of a man in preparation for the treatment decision. The purpose of this pilot study was to develop and evaluate the feasibility and usability of a Web-based decision support technology, the Personal Patient Profile-Prostate (P3P), in men newly diagnosed with LPC.

**METHODS:** Use cases were developed followed by infrastructure and content application. The program was provided on a personal desktop computer with a touch screen monitor. Participant responses to the query component of P3P determined the content of the multimedia educational and coaching intervention. The intervention was tailored to race, age, and personal factors reported as influencing the decision. Pre-pilot usability testing was conducted using a "think aloud" interview to identify navigation and content challenges. These issues were addressed prior to deployment in the clinic. A clinical pilot was conducted in an academic medical center where men sought consultation and treatment for LPC. Completion time, missing data, and acceptability were measured.

**RESULTS:** Pre-pilot testing included 4 men with a past diagnosis of LPC who had completed therapy. Technical navigation issues were documented along with confusing content language. A total of 30 additional men with a recent diagnosis of LPC completed the P3P program in clinic prior to consulting with a urologist regarding treatment options. In a mean time of 46 minutes (SD 13 minutes), participants completed the P3P query and intervention components. Of a possible 4560 items for 30 participants, 22 (0.5%) were missing. Acceptability was reported as high overall. The sections of the intervention reported as most useful were the statistics graphs, priority information topics, and annotated external website links.

**CONCLUSIONS:** The P3P intervention is a feasible and usable program to facilitate treatment decision making by men with newly diagnosed LPC. Testing in a multisite randomized trial with a diverse sample is warranted.

Loiselle, C. G., L. Edgar, et al. (2010). "The impact of a multimedia informational intervention on psychosocial adjustment among individuals with newly diagnosed breast or prostate cancer: a feasibility study." *Patient Educ Couns* 80(1): 48-55.

**PURPOSE:** To examine the impact of an 8-week cancer multimedia informational intervention on health-related outcomes among individuals newly diagnosed with cancer.

**METHODS:** Using a pre-/post-quasi-experimental design, participants with breast or prostate cancer (n=250) were conveniently recruited from four oncology ambulatory

clinics and completed questionnaires at three points (enrolment, 1-2 weeks post-intervention, and 3 months later).

**RESULTS:** Repeated-measure analyses showed that, when compared to controls, the intervention significantly improved satisfaction with cancer information over time for women ( $p < .001$ ), prevented deterioration in functional quality of life ( $p = .030$ ) and marginally improved perceived oncologist informational support ( $p = .051$ ). There were no significant differences in psychosocial adjustment among men. Unlike previously suggested, the intervention did not have a differential impact according to levels of personal resources (self-esteem, mastery, and optimism). However, for all outcomes and regardless of group, participants high in personal resources reported better adjustment across time.

**CONCLUSIONS:** Even though the hypotheses were only partially supported, the findings provide preliminary evidence that multimedia interventions can be supportive. With increasing numbers of new cancer diagnoses, cancer survivors and more limited health care resources, further research is needed to evaluate potential benefits of health information technology in providing support to individuals facing cancer.

Taylor, K. L., K. M. Davis, et al. (2010). "Use and evaluation of a CD-ROM-based decision aid for prostate cancer treatment decisions." *Behav Med* 36(4): 130-140.

The survival advantages associated with different treatments for localized prostate cancer (PCa) continue to be uncertain. We evaluated patients' use of an interactive CD-ROM-based decision aid designed to improve informed decision making about PCa treatment. Newly diagnosed, early-stage PCa patients who had not made a treatment decision completed a baseline telephone interview ( $N = 132$ ), were mailed the CD-ROM, and completed a one-month follow-up interview ( $N = 120$ ; 91%). Compared to non-users (21%), CD-users (79%) preferred to make an independent rather than a shared treatment decision (OR = 3.5, CI 1.2, 10.5). The majority of users (63%-90%) responded positively regarding the length and clarity of the information. Further, 76% reported using the CD as much/more than other information sources. A preference for having less decisional control predicted greater satisfaction with the CD ( $F[7,87] = 4.75$ ,  $p < .05$ ). Electronic utilization data revealed that the topics most accessed concerned treatment information and that users spent over an hour using the CD (median = 72 minutes). This electronic educational tool was well-accepted by patients and may be particularly useful for patients who desire less control over their treatment decisions and who are less proactive in seeking information on their own.

Allen, J. D., A. P. Mohllajee, et al. (2009). "A computer-tailored intervention to promote informed decision making for prostate cancer screening among African American men." *Am J Mens Health* 3(4): 340-351.

African American men experience a disproportionate burden of prostate cancer (CaP) morbidity and mortality. National screening guidelines advise men to make individualized screening decisions through a process termed informed decision making (IDM). In this pilot study, a computer-tailored decision-aid designed to promote IDM was evaluated using a pre-/posttest design. African American men aged 40 years and older were recruited from a variety of community settings ( $n = 108$ ). At pretest, 43% of men reported having made a screening decision; at posttest 47% reported this to be the case ( $p = .39$ ). Significant improvements were observed between pre- and posttest on scores of knowledge, decision self-efficacy,

and decisional conflict. Men were also more likely to want an active role in decision making after using the tool. These results suggest that use of a computer-tailored decision aid is a promising strategy to promote IDM for CaP screening among African American men.

Amalraj, S., C. Starkweather, et al. (2009). "Health literacy, communication, and treatment decision-making in older cancer patients." *Oncology* (Williston Park) 23(4):369-375.

Inadequate health literacy and physician-patient communication are associated with poor health outcomes and appear to limit quality of medical decision-making. This review presents and consolidates data concerning health literacy, physician-patient communication, and their impact on medical treatment decisions in elderly cancer patients. This population faces increasingly complex management options, cognitive and sensory deficits, and intergenerational barriers. As a result of these and other factors, older cancer patients have among the lowest health literacy and numeracy rates and often suffer from suboptimal physician-patient communication. These deficiencies impair elderly cancer patients' ability to understand, recall, and act upon information concerning treatment risk and benefit. This situation also makes it difficult for patients to have self-confidence in communicating with their provider and sharing in the decision-making. Moreover, since older cancer patients usually bring a companion to medical appointments, the positive and negative role of a companion in the context of communication and decisionmaking needs to be considered. Future research should center on developing ways to identify and overcome health communication barriers to improve geriatric cancer care.

Halbert, C. H., B. Weathers, et al. (2009). "Racial differences in medical mistrust among men diagnosed with prostate cancer." *Cancer* 115(11): 2553-2561.

**PURPOSE:** Mistrust of healthcare providers and systems is a significant barrier to quality healthcare. However, limited empirical data are available on perceptions of medical mistrust among individuals who are diagnosed with cancer. The objective of this study was to identify socio-demographic, clinical, and cultural determinants of mistrust among men diagnosed with prostate cancer.

**METHODS:** The authors conducted an observational study among 196 African-American men (n = 71) and white men (n = 125) who were newly diagnosed with prostate cancer during 2003 through 2007.

**RESULTS:** Race, education, healthcare experiences, and cultural factors had significant effects on mistrust. African-American men (P = .01) and men who had fewer years of formal education (P = .001) reported significantly greater levels of mistrust compared with white men and men who had more education. Mistrust also was greater among men who had been seeing their healthcare provider for a longer period (P = .01) and among men with lower perceptions of interdependence (P = .01).

**CONCLUSIONS:** The current findings suggested that efforts to enhance trust among men who are diagnosed with prostate cancer should target African-American men, men with fewer socioeconomic resources, and men with lower perceptions of interdependence. Reasons for deterioration in trust associated with greater experience with specialty providers should be explored along with



the effects of interventions that are designed to address the concerns of individuals who have greater mistrust.

Lin, G. A., D. S. Aaronson, et al. (2009). "Patient decision aids for prostate cancer treatment: a systematic review of the literature." *CA Cancer J Clin* 59(6): 379-390.

Treatment decision-making can be difficult and complex for patients with low-risk prostate cancer. To the authors' knowledge, there is no consensus regarding an optimal treatment strategy and the choice of therapy involves tradeoffs between differing harms and benefits that are sensitive to patient values. In such situations, patients are often asked to participate actively in the decision-making process, and high-quality decisions require a well-informed patient whose values and preferences have been taken into consideration. Prior studies have indicated that patients have poor knowledge and unrealistic expectations regarding treatment, and physician judgments concerning patient preferences are often inaccurate. Decision aids (DAs) have been developed to help inform patients with low-risk prostate cancer about treatment options and assist in the decision-making process; however, little is currently known regarding the effects of such programs in this population. Thirteen studies of DAs for patients with prostate cancer were reviewed and it was found that the use of DAs can improve knowledge, encourage more active patient involvement in decision-making, and decrease levels of anxiety and distress. The effect of DAs on treatment choice was less clear, although fewer patients chose surgery compared with historical controls, particularly in Europe. Further studies are needed to determine how best to implement DAs into practice, and whether they improve the consistency between patient preferences and treatment choice.

O'Brien, M. A., T. J. Whelan, et al. (2009). "Are cancer-related decision aids effective? A systematic review and meta-analysis." *J Clin Oncol* 27(6): 974-985.

**PURPOSE:** Decision aids (DAs) have been developed to improve communication between health professionals and patients, and to involve patients in decisions about their health care. Cancer-related decisions can be difficult due to problems in communicating complex information about prognosis and the modest benefits of available treatments. We conducted a systematic review of cancer-related DAs.

**METHODS:** Randomized controlled trials (RCTs) of cancer-related DAs about screening, prevention, and treatment decision making were included. We completed a comprehensive literature search and conducted both qualitative and quantitative analyses. We also conducted a meta regression to explore heterogeneity of effect estimates.

**RESULTS:** We identified 34 RCTs of DAs in a screening (n = 22 trials) or preventive/treatment (n = 12 trials) context. DAs significantly improved knowledge about screening options when compared to usual practice (weighted average effect size, 0.50; 95% CI, 0.27 to 0.73; P < .0001). A similar effect on knowledge was also found for preventive/treatment options (weighted average effect size, 0.50; 95% CI, 0.31 to 0.70; P < .0001). Overall, general anxiety was not increased in most trials and was significantly reduced in a screening context. Decisional conflict was reduced overall but not when screening and preventive/treatment studies were analyzed separately. There were few differences between different types of DAs.

**CONCLUSIONS:** Cancer-related DAs are effective in increasing patient knowledge compared with usual practice without increasing anxiety particularly in the area of cancer screening. Further research is needed to determine the effectiveness of DAs in the prevention and treatment context.

Stalmeier, P. F. and M. S. Roosmalen (2009). "Concise evaluation of decision aids." *Patient Educ Couns* 74(1): 104-109.

**PURPOSE:** Decision aids purport to help patients make treatment related choices. Several instruments exist to evaluate decision aids. Our aim is to compare the responsiveness of several instruments.

**METHODS:** Two different decision aids were randomized in patients at high risk for breast and ovarian cancer. Treatment choices were between prophylactic surgery and screening. Effect sizes were calculated to compare the responsiveness of the measures.

**RESULTS:** One decision aid was randomized in 390 women, the other in 91 ensuing mutation carriers. Three factors were identified related to Information, Well-being and Decision Making. Within each factor, single item measures were as responsive as multi-item measures.

**CONCLUSION:** Four single items: the amount of information received for decision making, strength of preference, I weighed the pros and cons, and general Hhealth, were adequately responsive to the decision aids. These items might be considered for inclusion in questionnaires to evaluate decision aids.

Hu, J. C., L. Kwan, et al. (2008). "Determinants of treatment regret in low-income, uninsured men with prostate cancer." *Urology* 72(6): 1274-1279.

**PURPOSE:** The regret of a prostate cancer treatment choice, a significant dimension of health-related quality of life, has not been well-characterized. Little is known about its association with the fear of cancer recurrence or spirituality.

**METHODS:** We drew subjects from a men's health study composed of a clinically heterogeneous sample of subjects enrolled from a statewide, publicly funded assistance program that provided free prostate cancer treatment for uninsured, low-income men in California. We included men who completed a telephone interviews and self-administered questionnaires at study enrollment and at 6 months of follow-up. Using validated instruments, we measured regret, health-related quality of life, fear of cancer recurrence, and spirituality through telephone interviews and self-administered questionnaires.

**RESULTS:** Of the 195 men, 90 underwent radical prostatectomy (46%), 50 underwent external beam radiotherapy (28%), and 51 underwent hormonal therapy (26%). Of these 195 men, 36 (18%) regretted their treatment choice. Multivariate analyses revealed that nonwhite men were more likely than white men to experience decisional regret (odds ratio [OR] range 7.27 to 12.26). Conversely, men confident of cancer cure (OR 0.19, 95% confidence interval 0.04 to 0.86), men with greater spirituality (OR 0.91, 95% confidence interval 0.87 to 0.96), and men with acute treatment effects (OR 0.34, 95% confidence interval 0.12 to 0.93) were less likely to regret their treatment decisions.

**CONCLUSIONS:** In our study, a fear of cancer recurrence, less spirituality, a longer interval since treatment, and nonwhite race were associated with treatment regret in low-

income, underserved men with prostate cancer. Attempts to decrease anxiety and enhance spirituality in men treated for prostate cancer might diminish treatment regret. Additional studies in racially diverse cohorts are needed to examine the association of regret with race.

Lis, C. G., D. Gupta, et al. (2008). "Patient satisfaction with health-related quality of life: implications for prognosis in prostate cancer." *Clin Genitourin Cancer* 6(2): 91-96.

**PURPOSE:** The goal of this study was to evaluate the association between patient satisfaction with health-related quality of life (HRQOL), as measured by the Ferrans and Powers Quality of Life Index (QLI), and survival in patients with prostate cancer treated in an integrative cancer treatment setting.

**METHODS:** This is a case series of 230 histologically confirmed stage I-IV prostate cancers treated at Cancer Treatment Centers of America. Quality of Life Index measures overall HRQOL and HRQOL in 4 major subscales: health and physical, social and economic, psychological and spiritual, and family. Study patients were dichotomized into 2 groups based on the median scores for all QLI subscales. Kaplan- Meier and log-rank tests were used to evaluate survival. Multivariate Cox regression analyses were then performed to evaluate the joint prognostic significance of HRQOL and clinical factors.

**RESULTS:** Patient satisfaction with health and physical (P = .0001), psychological and spiritual (P = .03), family (P = .02), and overall HRQOL (P = .0001) were statistically significantly associated with survival upon univariate analysis. Upon multivariate analysis, patient satisfaction with the health and physical subscale was found to be predictive of survival (P = .04), independent of the effects of previous treatment history and Gleason score.

**CONCLUSION:** This study suggests that baseline patient satisfaction with health and physical function, as measured by the QLI, provides useful prognostic information in patients with prostate cancer, independent of previous treatment history and Gleason score. The QLI Index can be used as a stratification variable in the oncology clinic to aid in medical decision-making.

Sanda, M. G., R. L. Dunn, et al. (2008). "Quality of life and satisfaction with outcome among prostate-cancer survivors." *N Engl J Med* 358(12): 1250-1261.

**PURPOSE:** We sought to identify determinants of health-related quality of life after primary treatment of prostate cancer and to measure the effects of such determinants on satisfaction with the outcome of treatment in patients and their spouses or partners.

**METHODS:** We prospectively measured outcomes reported by 1201 patients and 625 spouses or partners at multiple centers before and after radical prostatectomy, brachytherapy, or external-beam radiotherapy. We evaluated factors that were associated with changes in quality of life within study groups and determined the effects on satisfaction with the treatment outcome.

**RESULTS:** Adjuvant hormone therapy was associated with worse outcomes across multiple quality-of-life domains among patients receiving brachytherapy or radiotherapy. Patients in the brachytherapy group reported having long-lasting urinary irritation, bowel and sexual symptoms, and transient problems with vitality or hormonal function. Adverse effects of prostatectomy on

sexual function were mitigated by nerve-sparing procedures. After prostatectomy, urinary incontinence was observed, but urinary irritation and obstruction improved, particularly in patients with large prostates. No treatment-related deaths occurred; serious adverse events were rare. Treatment-related symptoms were exacerbated by obesity, a large prostate size, a high prostate-specific antigen score, and older age. Black patients reported lower satisfaction with the degree of overall treatment outcomes. Changes in quality of life were significantly associated with the degree of outcome satisfaction among patients and their spouses or partners.

**CONCLUSIONS:** Each prostate-cancer treatment was associated with a distinct pattern of change in quality-of-life domains related to urinary, sexual, bowel, and hormonal function. These changes influenced satisfaction with treatment outcomes among patients and their spouses or partners.

Toles, C. A. (2008). "Black men are dying from prostate cancer." *ABNF J* 19(3): 92-95.

Prostate cancer is the most frequently diagnosed cancer in the United States, accounting for 33% of all cancer cases among men (American Cancer Society, 2004). In the United States the number of new cases of prostate cancer was estimated at 230,110 and 29,900 will die (American Cancer Society, 2004). It is anticipated that these numbers will continue to grow despite effective treatment regimens. Black men (African-American) are 2.5 times more likely to die of prostate cancer than White men (Peters, 2005). Recent studies suggest genetics, diet, knowledge, and socioeconomic status as contributory factors, however, there appears to be more to it.

Davison, B. J., S. L. Goldenberg, et al. (2007). "Comparing a generic and individualized information decision support intervention for men newly diagnosed with localized prostate cancer." *Cancer Nurs* 30(5): E7-15.

A randomized study was conducted to compare a generic and individualized approach to providing decisional support to men newly diagnosed with localized prostate cancer. Patients (N = 324) were referred by community urologists to a patient education center where they were randomly assigned to receive either an individualized or generic information intervention. Men assigned to the generic group viewed a video on the various treatments available for localized prostate cancer. Men in the individualized information group used a computer program to identify their information preferences. Computer printouts on top information preferences were individualized according to patient's specific disease characteristics, followed by a discussion of the pros and cons of each recommended treatment option. Both groups received a standardized package of written information. Men completed measures of decision control, satisfaction, and decision conflict at baseline and after a definitive treatment decision was made. Results demonstrated that overall both groups reported increased levels of decision control and lower levels of decision conflict after their treatment decision. All men reported being satisfied with their preparation to make a treatment decision. Compared to the generic information group, men who received the individualized information were more satisfied with the type, amount and method of providing information, and role played in treatment decision making with their physician (P < .002). Both information interventions seem to be similar in providing decisional support to this group of men at the time of diagnosis. Further research is required to determine how to identify men who may benefit from a more individualized approach.

Gaston, C. M. and G. Mitchell (2005). "Information giving and decision-making in patients with advanced cancer: a systematic review." *Soc Sci Med* 61(10): 2252-2264.

Patients with advanced, non-curable cancer face difficult decisions on further treatment, where a small increase in survival time must be balanced against the toxicity of the treatment. If patients want to be involved in these decisions, in keeping with current notions of autonomy and empowerment, they also require to be adequately informed both on the treatments proposed and on their own disease status and prognosis. A systematic review was performed on decision-making and information provision in patients with advanced cancer. Studies of interventions to improve information giving and encourage participation in decision-making were reviewed, including both randomised controlled trials and uncontrolled studies. Almost all patients expressed a desire for full information, but only about two-thirds wished to participate actively in decision-making. Higher educational level, younger age and female sex were predictive of a desire to participate in decision-making. Active decision-making was more common in patients with certain cancers (e.g. breast) than others (e.g. prostate). A number of simple interventions including question prompt sheets, audio-taping of consultations and patient decision aids have been shown to facilitate such involvement.

Holmes-Rovner, M., S. Stableford, et al. (2005). "Evidence-based patient choice: a prostate cancer decision aid in plain language." *BMC Med Inform Decis Mak* 5: 16.

**PURPOSE:** Decision aids (DA) to assist patients in evaluating treatment options and sharing in decision making have proliferated in recent years. Most require high literacy and do not use plain language principles. We describe one of the first attempts to design a decision aid using principles from reading research and document design. The plain language DA prototype addressed treatment decisions for localized prostate cancer. Evaluation assessed impact on knowledge, decisions, and discussions with doctors in men newly diagnosed with prostate cancer.

**METHODS:** Document development steps included preparing an evidence-based DA in standard medical parlance, iteratively translating it to emphasize shared decision making and plain language in three formats (booklet, Internet, and audio-tape). Scientific review of medical content was integrated with expert health literacy review of document structure and design. Formative evaluation methods included focus groups (n = 4) and survey of a new sample of men newly diagnosed with prostate cancer (n = 60), compared with historical controls (n = 184).

**RESULTS:** A transparent description of the development process and design elements is reported. Formative evaluation among newly diagnosed prostate cancer patients found the DA to be clear and useful in reaching a decision. Newly diagnosed patients reported more discussions with doctors about treatment options, and showed increases in knowledge of side effects of radiation therapy.

**CONCLUSIONS:** The plain language DA presenting medical evidence in text and numerical formats appears acceptable and useful in decision-making about localized prostate cancer treatment. Further testing should evaluate the impact of all three media on

decisions made and quality of life in the survivorship period, especially among very low literacy men.

Elkin, E. B., M. E. Cowen, et al. (2004). "Preference assessment method affects decision-analytic recommendations: a prostate cancer treatment example." *Med Decis Making* 24(5): 504-510.

**PURPOSE:** To evaluate the effect of preference assessment method on treatment recommended by an individualized decision-analytic model for early prostate cancer.

**METHODS:** Health state preferences were elicited by time trade-off, rating scale, and a power transformation of the rating scale from 63 men ages 55 to 75. The authors used these values in a Markov model to determine whether radical prostatectomy or watchful waiting yielded the greater quality-adjusted life expectancy.

**RESULTS:** Time tradeoff and transformed rating scale recommendations differed widely. Time tradeoff and transformed rating scale utilities differed in their treatment recommendation for 21% to 52% of men, and the mean difference in quality-adjusted life years varied from less than 0.5 to greater than 1.0.

**CONCLUSIONS:** Treatment recommendations from the prostate cancer decision model were sensitive to the method of preference assessment. If decision analysis is used to counsel individual patients, careful consideration must be given to the method of preference elicitation.

Feldman-Stewart, D. and M. D. Brundage (2004). "Challenges for designing and implementing decision aids." *Patient Educ Couns* 54(3): 265-273.

Decision aids are tools intended to help patients with decisions about their healthcare. We have developed three decision aids to help patients with treatment decisions for: locally advanced non-small cell lung cancer (LA-NSCLC), advanced non-small cell lung cancer (A-NSCLC), and early-stage prostate cancer (ES-PC). In developing the aids, we carried out studies to provide them with an empirical basis, and to evaluate their potential for impact. In this paper we report results that challenge common assumptions and typical practice that currently occurs in the development of decision aids. The challenges relate to: how the content of the aid is defined, how the information is presented, how to incorporate decision aids into the dynamic, complex process of making such decisions, and how to evaluate the aids. We conclude that critical appraisal of issues related to the design and implementation of decision aids is required.

Leighl, N. B., P. N. Butow, et al. (2004). "Treatment decision aids in advanced cancer: when the goal is not cure and the answer is not clear." *J Clin Oncol* 22(9): 1759-1762.

Maliski, S. L., L. Kwan, et al. (2004). "Confidence in the ability to communicate with physicians among low-income patients with prostate cancer." *Urology* 64(2): 329-334.

**PURPOSE:** To describe the confidence of low-income patients with prostate cancer in interacting with physicians. Men with prostate cancer need to communicate easily with their physicians when facing treatment decisions and symptom management; however, little is known about whether low-income men are confident in these interactions.

**METHODS:** We used validated instruments to measure self-efficacy in patient-physician interactions, emotional well-being, symptom distress, satisfaction with care, and health-related quality of life among low-income men receiving prostate cancer treatment through a statewide public assistance program. We abstracted clinical variables from medical records. We dichotomized self-efficacy scores empirically on the basis of the sample distribution and conducted univariate and multivariate analyses.

**RESULTS:** The self-efficacy scores were skewed toward the high scores, with 77% in the high range. Those (23%) with low self-efficacy were more likely to have poor emotional well-being, symptom distress, role limitations--emotional, low social function, and poor urinary, sexual, and bowel outcomes. In multivariate analysis, low-income men were more likely to have low self-efficacy if they were less satisfied with their care, did not have confidence in their provider, or had more symptom distress.

**CONCLUSIONS:** Among low-income patients with prostate cancer, low self-efficacy for interacting with physicians was best predicted by diminished overall satisfaction with care, low confidence in providers, and worse symptom distress. Men with low self-efficacy fared worse over a range of psychosocial outcomes and both general and disease-specific health-related quality of life.

Krahn, M., P. Ritvo, et al. (2003). "Patient and community preferences for outcomes in prostate cancer: implications for clinical policy." *Med Care* 41(1):153-164.

**PURPOSE:** Preferences, or utilities, for health outcomes are central in prostate cancer decision-making. Utilities can be elicited directly from patients using standard techniques, or indirectly, using questionnaires that incorporate preference weights from community members. The objective is to evaluate directly elicited and indirectly elicited (questionnaire-derived, community-weighted) utilities for prostate cancer outcomes and the effects of sexual, urinary, and bowel dysfunction on them.

**METHODS:** Utilities for the current health of 141 prostate cancer patients, recruited from ambulatory clinics, were elicited directly with the Patient Oriented Prostate Utility Scale, rating scale (PORPUS-U(RS)) and standard gamble (PORPUS-U(SG)) subscales. Patients completed the Health Utilities Index (HUI) and Quality of Well Being Scale (QWB), utility instruments incorporating community preferences, and the UCLA Prostate Cancer Index.

**RESULTS:** Patients' treatments included radical prostatectomy (18%), radiation (60%), and hormonal (42%). Mean utility scores for current health were 0.65 (QWB), 0.79 (PORPUS-U(RS)), 0.80 (HUI), 0.86 (PORPUSU(SG)). Utility decrements for dysfunction were small (0.08-0.14 [sexual], 0.06 to 0.13 [urinary], and 0.01 to 0.13 [bowel]), and even smaller when adjusted for concomitant changes in other quality of life (QOL) domains.

**CONCLUSIONS:** Patients' directly elicited utilities for their own health were higher than community-derived utilities obtained from HUI and QWB administration to the same patients. HUI scores of these patients were similar to those of age-matched Canadian men. Sexual, urinary, and bowel problems were common but had less impact on overall QOL than reported in previous utility studies. These results weaken the argument that prostate cancer screening and treatment should be limited because of severe and debilitating side effects.

Lubeck, D. P., G. D. Grossfeld, et al. (2002). "A review of measurement of patient preferences for treatment outcomes after prostate cancer." *Urology* 60(3 Suppl 1):72-77; discussion 77-78.

The diagnosis of early-stage prostate cancer cases creates dilemmas for many men diagnosed with the disease each year. Treatment interventions are all associated with significant treatment morbidity, including impotence and incontinence. The basic concept behind patient preferences, or utilities, is to ask patients to make judgments about the value of particular health outcomes. Several preference-based instruments are available, including the visual analog rating scale, the time trade-off utility assessment, and the standard gamble. These assessments result in scores or weights assigned to different health states. From the perspective of the patient with prostate cancer, the treatment that produces optimal outcomes will depend on the relative importance of several domains, which may include pain, urinary functioning, sexual functioning, and general physical health. Patients with similar diagnoses and overlapping clinical characteristics may have markedly different preferences for treatment outcomes.

Kim, S. P., S. J. Knight, et al. (2001). "Health literacy and shared decision making for prostate cancer patients with low socioeconomic status." *Cancer Invest* 19(7):684-691.

**PURPOSE:** Quality of life (QOL) considerations are important in the treatment decision making process for prostate cancer patients. Although patient involvement in the treatment decision process has been encouraged, low health literacy can limit patient understanding of the complex information about treatments and their probable QOL outcomes and is a barrier to patient participation in the decision-making process. The objectives of the study were to evaluate (i) knowledge, level of satisfaction, and treatment preferences and intentions of men newly diagnosed with prostate cancer after participation in a CD-ROM shared decision making program; and (ii) the relationship between prostate cancer knowledge and health literacy.

**METHODS:** Thirty newly diagnosed prostate cancer patients from two Veteran's Administration (VA) hospitals in Chicago completed a demographic questionnaire and participated in an interactive CD-ROM shared decision making program. Subsequently, knowledge of prostate cancer, satisfaction with the information in the computer CD-ROM program, treatment preferences, and likelihood of following treatment preferences were assessed using interviewer-administered questionnaires. Health literacy was assessed using the Rapid Estimate of Adult Literacy in Medicine (REALM). The Pearson correlation test was used to assess the relationship between health literacy and prostate cancer knowledge. The chi<sup>2</sup> test and the Fischer exact test were used to evaluate relationships between patient demographics and other variables.

**RESULTS:** More than three-quarters of the patients rated the information in the CD-ROM as "very satisfactory" (highest possible rating). Two-thirds of the patients (21 of 30) selected a treatment after participation in the CD-ROM program and 90.5% of these patients stated that they were very or somewhat likely to adhere to their selection. However, prostate cancer knowledge was variable, with one-third of the patients scoring 69.9% or lower. Participants' health literacy was equivalent to a 7th-8th grade reading level (mean = 57.1+/-10.9), and more than one-third of participants (36.7%) had lower than 9th grade literacy levels. Participants' prostate cancer knowledge was correlated with health literacy (Pearson



correlation  $\rho_{or} = 0.65$ ,  $\rho_{op} = 0.0001$ ). Patients were satisfied with the interactive shared decision making CD-ROM program, and two-thirds of patients were able to select a preferred treatment based on the information presented in the program that they intended to follow. However, prostate cancer knowledge scores varied among participants after participation in the CD-ROM program, raising doubts that patients were adequately informed to make appropriate choices regarding their treatment. Lower prostate cancer knowledge scores corresponded to lower literacy scores, indicating that low literacy may have hindered patient understanding of the shared decision making program.

**CONCLUSIONS:** The development of shared decision making tools should include collaborative efforts with the target population to improve the success of shared decision making programs among patients with low health literacy.

Krahn, M., P. Ritvo, et al. (2000). "Construction of the Patient-Oriented Prostate Utility Scale (PORPUS): a multiattribute health state classification system for prostate cancer." *J Clin Epidemiol* 53(9): 920-930.

Health status indexes, such as the EuroQol, consist of a health state classification system and a set of utility weights. Indexes measure quality of life using a 0-1 utility score. Utilities for outcomes in prostate cancer (PC) are of unique importance, but generic indexes do not represent PC outcomes (e.g., sexual, urinary, bowel dysfunction) well, and may not capture their full impact. As a step toward improved utility measurement, we constructed a classification system for PC. We generated items for each of six health domains and rated their importance using interviews with 10 clinical experts and 80 patients. Key concepts were selected for each domain using item importance weightings, and a set of predetermined criteria. Text was developed to express levels of severity within each domain. Experts and two additional groups of patients ( $n = 40$ ,  $n = 96$ ) evaluated textual clarity and endorsed the content validity of the instrument. The final system consists of 10 domains with 4-6 levels each. The content validity of the system was endorsed by patients and experts. In conjunction with a set of utility weights, it may be used to develop a health status index, to improve utility measurement in patients, and to serve as a short psychometric (nonutility) instrument.

Moul, J. W., T. A. Esther, et al. (2000). "Implementation of a web-based prostate cancer decision site." *Semin Urol Oncol* 18(3): 241-244.

Carcinoma of the prostate is the most common form of cancer in males in the United States, second only to skin cancer. Recently, there has been increased public awareness of cancer-related diseases and specifically prostate cancer. As a result, more individuals are routinely screened and diagnosed with prostate cancer. When a man first discovers he has prostate cancer, he is faced with a multitude of questions. Health care providers realize in counseling patients that there is no single treatment choice best suited for every patient. Because of multiple treatment choices for prostate cancer and complex counseling needs due to a varied side effect profiles of the different options, the Internet may be an ideal tool to extend the health care provider. Furthermore, because men may be reluctant to discuss issues with the health care provider directly, the anonymity of the Internet may be of particular value in the disease. The Internet has created a massive body of information with an estimated 320 million Web sites. The provider can use the Internet as a patient educational tool thus affording the patient time to absorb sometimes complicated information. The Internet can help patients focus

on specific aspects of their disease making the patient-provider encounter more productive and allow the patient to take an active role in the treatment decision-making process. More knowledgeable patients can make better decisions about treatment options and have more realistic expectations of their outcomes. We have developed an Internet-based decision for prostate cancer available to both patients and physicians.

## V. TREATMENT OPTIONS AND DISEASE MANAGEMENT

Attard, G. and J. S. de Bono (2011). "Translating scientific advancement into clinical benefit for castration-resistant prostate cancer patients." *Clin Cancer Res* 17(12): 3867-3875.

In the past 12 months, three novel therapeutics-sipuleucel-T, cabazitaxel, and abiraterone acetate-were granted Food and Drug Administration regulatory approval for the treatment of metastatic castration-resistant prostate cancer (CRPC) patients based on phase III studies that showed a survival advantage. Other agents, including the novel antiandrogen MDV3100, are at an advanced stage of clinical phase III evaluation. The treatment paradigm for CRPC has now changed significantly, and this has introduced new challenges for physicians, including selecting patients for specific therapies, developing the best sequencing and combination regimens for the several new effective agents that have recently been approved or are in development, and dissecting mechanisms of resistance that will inform the development of a new generation of therapeutics. This Focus issue reviews the results obtained with immunotherapies, taxane cytotoxics, and androgen receptor targeting therapeutics for CRPC, as well as the postulated mechanisms of resistance to these protocols and proposed strategies for improvement. The use of biomarkers for patient selection, monitoring of treatment activity, and acceleration of drug approval will be critical for achieving further improvements in the treatment for CRPC, and is also discussed in detail.

Garcia, J. A. and B. I. Rini (2011). "Castration-resistant prostate cancer: Many treatments, many options, many challenges ahead." *Cancer*.

Although the long natural history of prostate cancer presents challenges in the development of novel therapeutics, major contributions have been observed recently. A better understanding of the long-term complications of androgen deprivation has changed the initial approach to most patients with advanced disease. Specifically, recognition of the limitations of prostate-specific antigen has driven the pursuit of new tools capable of becoming true surrogates for disease outcome. Understanding the molecular biology of castration-resistant prostate cancer (CRPC) has led to a dramatic paradigm shift in the treatment of patients with metastatic disease where the androgen receptor becomes a central therapeutic target. Specific adrenal inhibitors and engineered super androgen receptor inhibitors have become the most promising agents in the disease. Novel immune therapies have been shown to improve survival in selected patients with castration-resistant disease despite the inability to impact traditional markers of response. Similarly, agents such as cabazitaxel and abiraterone acetate have demonstrated clinical benefit and are now a standard of care in docetaxel-refractory metastatic CRPC patients. All these changes have occurred in a relatively short period and are likely to change the prostate cancer treatment paradigm. This review summarizes the current management of CRPC and discusses potential future directions. *Cancer* 2011. (c) 2011 American Cancer Society.

George, D. and J. W. Moul (2011). “Emerging treatment options for patients with castration-resistant prostate cancer.” *Prostate*.

**PURPOSE:** Most prostate cancer-related deaths occur in patients with castration-resistant prostate cancer (CRPC). Recent preclinical and clinical studies have identified intracellular signaling pathways and changes in the tumor and bone microenvironment as potential key drivers of CRPC. This increased understanding of mechanisms associated with CRPC has driven the development of numerous new agents, many of which are poised to alter the current CRPC treatment landscape.

**METHODS:** A review of literature was conducted to identify ongoing and planned phase III studies of novel agents to treat CRPC.

**RESULTS:** Multiple studies were identified, including novel androgen biosynthesis inhibitors (abiraterone, TAK-700), androgen-receptor inhibitors (MDV3100), angiogenesis inhibitors (aflibercept, tasquinimod), endothelin antagonists (zibotentan, atrasentan), a Src tyrosine kinase inhibitor (dasatinib), a novel radiotherapy (radium-223), and new immunotherapies (ipilimumab and ProstVac). In addition, both sipuleucel-T (an immunotherapy) and cabazitaxel (third-generation taxane) and the RANK-L inhibitor, denosumab, have recently been approved by the US Food and Drug Administration.

**CONCLUSIONS:** Various combinations of these agents could theoretically be used to treat future patients with CRPC by targeting multiple signaling pathways as well as aspects of the tumor and bone microenvironments. Additional research will be needed to understand how to best use these agents and individualize care to optimize CRPC patient outcomes. *Prostate* (c) 2011 Wiley-Liss, Inc.

George, D. J., P. W. Kantoff, et al. (2011). “Clinical roundtable monograph: new and emerging treatments for advanced prostate cancer.” *Clin Adv Hematol Oncol* 9(6):1-11; discussion 11-15.

Historically, the treatment of metastatic castration-resistant prostate cancer (CRPC) has been limited to chemotherapeutic regimens that did not improve patient survival. In 2004, clinical studies began to demonstrate significant improvements in patient outcomes, including overall survival, with docetaxel versus mitoxantrone chemotherapy. Since these pivotal trials, the combination of docetaxel plus prednisone has become a standard of care for patients with metastatic CRPC. However, the limited survival benefit achieved with this regimen prompted several investigations into the development of alternative therapeutic options. Recent advances have now led to an unprecedented number of new drug approvals within the past year, providing many new treatment options for patients with metastatic CRPC. Sipuleucel-T, considered a new paradigm in cancer treatment, is the first such immunotherapeutic agent approved by the US Food and Drug Administration. Other successes include abiraterone acetate, the first androgen biosynthesis inhibitor, and cabazitaxel, a novel microtubule inhibitor, both of which have demonstrated improved survival following docetaxel failure. The bone-targeting agent denosumab, also recently approved in this setting, offers these patients significant improvement in the prevention of skeletal-related events. The data supporting the approval of each of these agents are described in this monograph, as are current approaches in the treatment of metastatic CRPC and ongoing clinical trials of novel treatments and strategies. The experts also discuss several of the issues regarding the introduction of these novel agents into clinical practice for metastatic CRPC patients.

Goetz, D. (2011). "New options for the management of castration-resistant prostate cancer: a case perspective." *J Natl Compr Canc Netw* 9 Suppl 3: S13-23; quiz S24.

Prostate cancer is the leading cause of cancer and second leading cause of death among men. Management of localized disease is fairly straight-forward, but treatment for locally advanced or metastatic disease is much less so. Androgen-deprivation therapy serves as the foundation of treatment for patients with locally advanced or metastatic disease. Although most patients with prostate cancer show a response to medical or surgical castration, many eventually experience a hormone-refractory, incurable state. Until recently, therapeutic options for CRPC have been limited and focused on systemic chemotherapeutic options. Unfortunately, however, this provides a minimal increase in overall survival, at the cost of significant additional toxicities. Therefore, much research has gone into developing other suitable therapies with potentially less toxicity. This article uses a case study approach to discuss new options for the treatment of castration-resistant prostate cancer.

Higano, C. S. and E. D. Crawford (2011). "New and emerging agents for the treatment of castration-resistant prostate cancer." *Urol Oncol* 29(6 Suppl): 1-8.

Most men with recurrent prostate cancer (CaP) initially respond to androgen deprivation therapy but eventually develop metastatic castration-resistant prostate cancer (CRPC). Over the last decade, new therapeutic targets have been identified in CRPC and several new drugs have reached advanced stages of clinical development. In 2010, the Food and Drug Administration (FDA) approved sipuleucel-T and cabazitaxel, and in 2011, abiraterone for patients with metastatic CRPC based on phase 3 trials showing improved survival. Although not yet available for clinical use, a press release in June 2011 announced that radium 223 also demonstrated a survival advantage in men with metastatic CRPC. Emerging therapies in advanced stages of clinical development in CRPC include the hormonal therapies MDV3100 and TAK 700, and the immunotherapy ipilimumab. Results are also pending on phase 3 studies comparing docetaxel plus prednisone with docetaxel given with the novel agents aflibercept, dasatinib, lenalidomide, and custirsen. In addition to these new and emerging therapeutic agents, denosumab was approved for the prevention of skeletal complications in patients with bone metastases due to solid tumor malignancies, providing an alternative to zoledronic acid. While the addition of these new treatment options is a great advance for men with metastatic CRPC, there are many new questions arising regarding sequencing of these treatments with each other, with previously existing therapies, and with the emerging agents now in clinical trials. Furthermore, there are concerns that on-going phase 3 trials may be contaminated if patients go off study treatment to start 1 of the newly approved agents or take the agent subsequently. These realities make clinical trial design more challenging than ever.

Joniau, S., P. A. Abrahamsson, et al. (2011). "Current Vaccination Strategies for Prostate Cancer." *Eur Urol*.

**PURPOSE:** The first therapeutic cancer vaccine demonstrating effectiveness in a phase 3 study was approved by the US Food and Drug Administration on 29 April 2010. The pivotal trial demonstrated overall survival (OS) benefit in patients treated with antigen-loaded leukapheresis cells compared with a control infusion. Results of other prostate cancer (PCa) vaccination strategies are awaited, as this approach may herald a new era in the care for patients with advanced PCa. The objective is to consider effectiveness and safety of

vaccination strategies in the treatment of PCa.

**METHODS:** We searched three bibliographic databases (January 1995 through October 2010) for randomised phase 2 and 3 studies of vaccination strategies for PCa based on predetermined relevant Medical Subject Heading terms and free text terms. Data from 3 randomised phase 3 and 10 randomised phase 2 vaccination trials are discussed with respect to clinical outcome in terms of progression-free survival and OS, toxicity, prostate-specific antigen (PSA) response, and immunologic response.

**RESULTS:** Three phase 3 trials (D9901, D9902A, and D9902B) that enrolled a total of 737 patients, all controlled and double-blinded, tested the efficacy of sipuleucel-T. The largest of these three trials, called Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT), has demonstrated safety and effectiveness of sipuleucel-T (now marketed as Provenge) as measured by prolonged survival of 512 asymptomatic patients with metastatic castration-resistant PCa (mCRPC). The study showed a 4.1-mo median survival benefit in the sipuleucel-T vaccine-treated group compared with the control group (25.8 vs 21.7 mo; hazard ratio [HR]: 0.78; 95% confidence interval [CI], 0.62-0.98; p=0.032) and extended 3-yr survival (31.7% vs 23.0%). In contrast, two phase 3 vaccination trials with a whole-tumour-cell mixture of two PCa cell lines (GVAX) and testing GVAX either alone or in combination with chemotherapy versus chemotherapy alone (VITAL1 and 2) were terminated prematurely based on futility and increased deaths. Other phase 2 vaccination trials testing different types of vaccines in castration-resistant PCa patients have been reported with variable outcomes. Notably, a controlled, double-blind, randomised phase 2 vaccine trial of PROSTVAC-VF, a recombinant viral vector containing complementary DNA encoding PSA, in 125 patients with chemotherapy-naïve, minimally symptomatic mCRPC also demonstrated safety but no significant effect on the time to disease progression. In comparison with controls (n=40), PROSTVAC-VF-treated patients (n=82) experienced longer median survival of 8.5 mo (25.1 vs 16.6 mo; HR: 0.56; 95% CI, 0.37-0.85; p=0.0061) and extended 3-yr survival (30% vs 17%). In general, PCa vaccines are perceived to have less toxicity compared with current cytotoxic or targeted therapies. Evaluation of clinical efficacy of different vaccination strategies (eg, protein-, peptide- and DNA-based vaccines) in the context of properly designed and controlled phase 3 studies is warranted.

**CONCLUSIONS:** Cancer vaccines represent a new paradigm in the treatment of PCa. The IMPACT trial showed improved survival but no difference in time to disease progression in mCRPC patients with minimal tumour burden. Observations in phase 2 and 3 trials pave the way for other vaccination approaches for this disease, raise questions regarding the most appropriate clinical trial designs, and underscore the importance of identifying biomarkers for antitumour effect to better implement such therapies.

Kirby, M., C. Hirst, et al. (2011). "Characterising the castration-resistant prostate cancer population: a systematic review." *Int J Clin Pract* 65(11): 1180-1192.

**PURPOSE:** Castration-resistant prostate cancer (CRPC) is an advanced form of prostate cancer associated with poor survival rates. However, characterisation of the disease epidemiology is hampered by use of varying terminology, definition and disease management. The aim of this review was to conduct a systematic review to provide greater clarity on the sum of the available epidemiologic evidence and to guide future research into the disease prevalence, progression, characteristics and outcome.

**METHODS:** Systematic searches of PubMed and Embase were performed in March 2010 to identify relevant observational studies relating to the epidemiology, progression and outcomes of CRPC. Further studies were identified for inclusion in our review through manual searches of the authors' bibliographical databases and the reference lists of the included articles.

**RESULTS:** We identified 12 articles (10 full papers and 2 abstracts) reporting studies that included a total of 71,179 patients observed for up to 12 years for evaluation in our review. Five studies looked at the prevalence of CRPC in patients with prostate cancer. Together, the data indicate that 10-20% of prostate cancer patients develop CRPC within approximately 5 years of follow-up. Two studies reported the prevalence of bone metastases present at diagnosis of CRPC. Together,  $\geq 84\%$  were shown to have metastases at diagnosis. Of those patients with no metastases present at diagnosis of CRPC, 33% could expect to develop them within 2 years. The median survival of patients with CRPC was reported in five studies, with values varying from 9 to 30 months. A pooled, sample-weighted survival estimate calculated from the survival data included in this review is 14 months. Very few studies that met our inclusion criteria evaluated treatment patterns in CRPC. One study reported that only 37% of patients with CRPC received chemotherapy, with the remainder receiving only steroids and supportive care. The most common palliative therapies administered to patients with skeletal symptoms were radiotherapy, radionuclide therapy, bisphosphonates and opioids.

**CONCLUSIONS:** This review highlights the poor prognosis of patients with CRPC, and demonstrates a survival of 9-13 months in those patients with metastatic CRPC. Furthermore, progression to CRPC is associated with deterioration in quality of life, and few therapeutic options are currently available to patients with CRPC. However, epidemiologic study of these patients is hampered by differing terminology, definitions and treatment paradigms. Our review highlights the need for further well-designed, epidemiological studies of CRPC, using standardised definitions and methods.

Larsson, R., N. P. Mongan, et al. (2011). "Clinical trial update and novel therapeutic approaches for metastatic prostate cancer." *Curr Med Chem* 18(29): 4440-4453.

Recurrent prostate cancer (PCa) remains a major clinical challenge. Invasive and metastatic PCa lesions often exhibit a partial and time-limited response to therapy before the cancer progresses and the patient succumbs to the disease. Despite recent advances in early diagnosis and treatment, approximately one-third of treated patients will relapse and become resistant to currently available treatments. In this review we evaluate current treatment practices and recent advances in therapy for localized prostate malignancy and advanced, metastatic prostate cancer. Some of the promising new drugs for PCa treatment include MDV3100, an androgen receptor (AR) antagonist that prevents androgens from binding to the AR and nuclear translocation and co-activator recruitment of the ligand-receptor complex; abiraterone, an orally administered drug that irreversibly inhibits a rate-limiting enzyme in androgen biosynthesis, CYP17; and several newer cytotoxic drugs (epothilones, satraplatin). Key new insights are that cancer stem cells play a role in PCa and that PCa cells are dependent on the AR for proliferation, even in the hormone refractory state of the disease. We also discuss potential molecular targets for new drug candidates for the treatment of metastatic PCa.

Lee, J. L., J. Eun Kim, et al. (2011). "Role of androgen deprivation treatment in patients with castration-resistant prostate cancer, receiving docetaxel-based chemotherapy." *Am J Clin Oncol* 34(2): 140-144.

**PURPOSE:** To assess the impact of continued androgen deprivation therapy (ADT) in patients with castration-resistant prostate cancer (CRPC) receiving firstline docetaxel-based chemotherapy.

**METHODS:** A retrospective review was performed on 78 patients fulfilling the criteria for CRPC who were treated with docetaxel-based chemotherapy over 5 years.

**RESULTS:** Thirty-nine patients received concurrent ADT (ADT group), whereas 39 patients discontinued ADT (No-ADT group). PSA response rates were 66.7% for ADT patients and 48.7% for No-ADT patients ( $P = 0.27$ ). The median progression-free survival and overall survival were 5.0 months and 24.8 months for ADT patients and 4.9 months and 22.1 months for No-ADT patients, respectively ( $P = 0.57$ ,  $P = 0.94$ ). Follow-up testosterone levels were available in 13 patients of the No-ADT group and none of them recovered a normal serum testosterone level over a median follow-up duration of 8.3 months from ADT discontinuation. ADT was recommenced in 21 of 39 patients in the No-ADT group and, of these, 6 (29%) achieved a PSA response.

**CONCLUSION:** Clinical outcomes were not significantly different when patients with CRPC received concurrent ADT, or were not so treated, when receiving first-line docetaxel-based chemotherapy. Despite ADT withdrawal, serum testosterone level did not recover to the noncastrated level during the period of chemotherapy, and reinduction of hormone sensitivity occurred in about one-quarter of patients.

Madan, R. A., J. B. Aragon-Ching, et al. (2011). "From clinical trials to clinical practice: therapeutic cancer vaccines for the treatment of prostate cancer." *Expert Rev Vaccines* 10(6): 743-753.

Therapeutic options for patients with metastatic castration-resistant prostate cancer are increasing, spurring an urgent need to better understand which treatments are best for individual patients. The recent approval of a first-in-class agent, sipuleucel-T, has intensified this need. This therapeutic cancer vaccine has demonstrated a survival advantage in two Phase III trials, but does not alter progression in the short term. Therefore, a new therapeutic approach for patients with metastatic castration-resistant prostate cancer is taking shape, based on broader understanding of available therapies. This new clinical approach seeks to maximize patient benefit from treatment, minimize associated toxicities, and may have far-reaching implications for other therapeutic cancer vaccines currently in clinical development.

Myklak, K. and S. Wilson (2011). "An update on the changing indications for androgen deprivation therapy for prostate cancer." *Prostate Cancer* 2011: 419174.

Quality of life has become increasingly more important for men diagnosed with prostate cancer. In light of this and the recognized risks of androgen deprivation therapy (ADT), the guidelines and use of ADT have changed significantly over the last few years. This paper reviews the current recommendations and the future perspectives regarding ADT. The benefits of ADT are evident

neoadjuvantly and adjuvantly in patients treated with external beam radiation therapy for intermediate- and high-risk disease, in patients who have undergone prostatectomy with lymph node involvement, in high-risk patients after definitive therapy, and in patients who have developed progression or metastasis. Finally, this paper reviews the risks and benefits of each of these scenarios and the risks of androgen deprivation in general, and it delineates the areas where ADT was previously recommended, but where evidence is lacking for its additional benefit.

Seruga, B. and I. F. Tannock (2011). "Chemotherapy-based treatment for castration-resistant prostate cancer." *J Clin Oncol* 29(27): 3686 -3694.

Most men with metastatic prostate cancer respond to various types of androgen ablation but progress to castration-resistant disease. The TAX 327 and Southwest Oncology Group (SWOG) 99-16 clinical trials established docetaxel-based chemotherapy as preferred first-line treatment for most men with symptomatic metastatic castration-resistant prostate cancer (mCRPC). However, only about half receive benefit from docetaxel, and those who respond initially progress and eventually die of (or with) mCRPC. Both cellular mechanisms and the tumor microenvironment are implicated in the development of resistance to docetaxel. New agents are being evaluated for men with mCRPC, either as firstline treatment in combination with docetaxel, or in men progressing during or after treatment with docetaxel. Thus far, agents evaluated in phase III trials in combination with docetaxel have not improved outcome, including the vaccine GVAX, high-dose vitamin D (DN-101), and the antiangiogenic agent bevacizumab. In contrast, cabazitaxel, a taxane that is not cross-resistant to docetaxel, substantially improved the outcome of men progressing during or after treatment with docetaxel-based chemotherapy when compared with mitoxantrone and prednisone. However, translation of benefit of cabazitaxel demonstrated in the TROPIC (Treatment of Hormone-Refractory Metastatic Prostate Cancer) trial into general oncologic practice will be challenging because this agent may cause serious toxicity. With the approval of less toxic hormonal agents (eg, abiraterone acetate) in the setting of docetaxel-resistant mCRPC, clinicians will have an opportunity to balance benefits and harms of new agents in an individual patient and may be able to use different agents in sequence.

Elliott, S., D. M. Latini, et al. (2010). "Androgen deprivation therapy for prostate cancer: recommendations to improve patient and partner quality of life." *J Sex Med* 7(9): 2996-3010.

**PURPOSE:** Use of improved prostate cancer detection, more patients begin androgen deprivation therapy (ADT) earlier and remain on it longer than before. Patients now may be androgen deprived for over a decade, even when they are otherwise free of cancer symptoms.

**METHODS:** An ADT Survivorship Working Group was formed to develop and evaluate interventions to limit the physiological and emotional trauma patients and their partners experience from this treatment. The multidisciplinary Working Group met for 2 days to define the challenges couples face when patients commence ADT. A writing sub-group was formed. It compiled the meeting's proceedings, reviewed the literature and, in consultation with the other members of the working group, wrote the manuscript. Expert opinion of the side effects of ADT that affect the quality of life (QOL) of patients and their partners and the recommendations for managing ADT to optimize QOL were based on the best available



literature, clinical experience, and widespread internal discussions among Working Group members.

**RESULTS:** Side effects identified as particularly challenging include: (i) body feminization; (ii) changes in sexual performance; (iii) relationship changes; (iv) cognitive and affective symptoms; and (v) fatigue, sleep disturbance, and depression. Recommendations for managing ADT include providing information about ADT side effects before administration of ADT, and, where appropriate, providing referrals for psychosocial support. Sexual rehabilitation principles for persons with chronic illness may prove useful. Psychological interventions for sexual sequelae need to be offered and individualized to patients, regardless of their age or partnership. Support should also be offered to partners.

**CONCLUSIONS:** Our hope is that this plan will serve as a guide for optimizing how ADT is carried out and improve the lives of androgen-deprived men and their intimate partners.

Pal, S. K., P. Twardowski, et al. (2010). "Critical appraisal of cabazitaxel in the management of advanced prostate cancer." *Clin Interv Aging* 5: 395-402.

Docetaxel remains a cornerstone of therapy for the patient with metastatic castration-resistant prostate cancer (CRPC). However, the landscape of CRPC therapy is changing rapidly - recently, data from the phase III TROPIC study revealed a survival advantage with the novel taxane cabazitaxel/prednisone (compared with mitoxantrone/prednisone) in a cohort of 755 men with docetaxel-refractory metastatic CRPC. Interestingly, cabazitaxel bears substantial structural similarity to docetaxel but appears to be mechanistically distinct. In preclinical studies, the agent has antitumor activity in a variety of docetaxel-refractory in vitro and in vivo models. Subsequent to phase I testing in advanced solid tumors (where neutropenia was identified as a dose-limiting toxicity), the agent was assessed in a phase II trial in advanced, taxanerefractory breast cancer and in the aforementioned phase III TROPIC study. This review describes in detail the preclinical and clinical development of cabazitaxel.

Mulders, P. F. and J. A. Schalken (2009). "Measuring therapeutic efficacy in the changing paradigm of castrate-resistant prostate cancer." *Prostate Cancer Prostatic Dis* 12(3): 241-246.

One of the current challenges in the evaluation of novel agents for the treatment of advanced prostate cancer is the identification of a surrogate end point for overall survival (OS). Prostate-specific antigen (PSA) levels have been used as a screening tool and a biomarker of response to both hormonal and cytotoxic agents. However, PSA levels do not seem to be a suitable surrogate end point for OS in trials of targeted agents for castrate-resistant prostate cancer (CRPC). These findings suggest the need for adopting measures of efficacy that more accurately reflect the mechanisms of action of these agents in phase II trials, in order to realize improvements in OS in the phase III setting. The Prostate Cancer Clinical Trials Working Group (PCWG2) have recently made recommendations for the design of future trials and advised that PSA levels should not be the sole criterion on which to base clinical decisions. Here, we appraise the end points that have been used in phase II and III trials in patients with CRPC, and highlight the need for the adoption of the PCWG2 guidelines, the recommendations of which include radiographic imaging, in addition to bone scintigraphy, and

symptomatic or radiographic disease progression criteria.

Oudard, S., E. Banu, et al. (2009). "What is the real impact of bone pain on survival in patients with metastatic hormone-refractory prostate cancer treated with docetaxel?" *BJU Int* 103(12): 1641-1646.

**PURPOSE:** To determine the benefit of starting early chemotherapy with docetaxel (the recommended first-line treatment) for patients with asymptomatic metastatic hormone-refractory prostate cancer (HRPC).

**METHODS:** Data were analysed from 145 patients with HRPC treated with chemotherapy between February 2000 and June 2002 in one French centre. Eligible patients were categorized into three groups according to the bone pain at baseline, i.e. minimal/no pain, mild, and moderate/severe pain. The primary endpoint was the effect of bone pain on overall survival (OS).

**RESULTS:** Docetaxel was administered to 67% of patients. The risk of death was 1.56 and 2.11 times higher for patients with mild or moderate/severe pain than for those with minimal/no pain ( $P = 0.027$ ). The median (95% confidence interval (CI)) OS was 23.1 (18.5-27.6) and 14.1 (8.9-19.2) months ( $P = 0.001$ , log-rank-test) for patients with minimal pain or no pain treated with docetaxel-based chemotherapy compared with mitoxantrone, respectively. The prostate-specific antigen doubling time (PSA-DT) had a significant effect on OS in patients with minimal/no pain, with a median of 32.4 and 16.5 months for a PSA-DT of  $\geq 45$  and  $< 45$  days, respectively ( $P < 0.001$ ).

**CONCLUSIONS:** Our results suggest that patients with HRPC and minimal or no bone pain could have better survival than those with mild pain or moderate to severe pain, independent of the treatment administered. In addition, patients with HRPC and minimal or no bone pain treated with docetaxel-based chemotherapy have a significantly better OS than those treated with mitoxantrone. The PSA-DT can be useful to identify asymptomatic patients who are candidates for early treatment.

Zafeirakis, A. and G. S. Limouris (2009). "Predictive value of the clinically and scintigraphically important bone lesions in hormone-refractory prostate cancer (HRPC)." *Clin Transl Oncol* 11(11): 773-774.

Droz, J. P. and A. Chaladaj (2008). "Management of metastatic prostate cancer: the crucial role of geriatric assessment." *BJU Int* 101 Suppl 2: 23-29.

Prostate cancer predominantly affects older men, with a median age at diagnosis of 68 years. Due to the increased life expectancy, management of prostate cancer in senior adults (aged  $> 70$  years) represents a major public health problem. This patient population may not receive optimal therapy for their disease, if decisions are made based on their chronological age alone. More so than age alone, health status is a major factor affecting individual life expectancy. Comorbidity is the key predictor of health status and should weigh more heavily on the treatment decision than age alone. Other important parameters to consider in senior adults are the degree of dependence in activities of daily living, the nutritional status and the presence or not of a geriatric syndrome. Although clinical trials are rarely designed specifically for senior adults, evidence suggests that healthy senior adults have similar treatment outcomes to their younger counterparts. The urological approach in senior adults with advanced prostate cancer should be fundamentally the same as in younger patients. In hormone-sensitive metastatic prostate cancer,

androgen deprivation represents the first-line treatment. In senior adults, care should be given to the increased risk of metabolic syndrome, cardiovascular mortality and bone fracture. In hormone-refractory metastatic prostate cancer, chemotherapy with docetaxel (75 mg/m<sup>2</sup>) every 3 weeks plus low-dose prednisone is the standard and shows the same efficacy in healthy senior adults as in younger patients. The tolerance of docetaxel (3-weekly schedule) has not been specifically studied in vulnerable and frail senior adults. The place of weekly docetaxel in this setting should be further evaluated. Palliative treatments (palliative surgery, radiopharmaceuticals, radiotherapy, medical treatments for pain and symptoms, pharmacological palliative therapies) should also be integrated in the global management of these patients. In conclusion, treatment decisions in senior adults should be adapted to health status. Healthy senior adults should be treated the same as younger patients. The development of guidelines for the management of localized and advanced prostate cancer in senior adults is underway.

Nelius, T., T. Klatte, et al. (2008). "Impact of PSA flare-up in patients with hormonerefractory prostate cancer undergoing chemotherapy." *Int Urol Nephrol* 40(1): 97-104.

**PURPOSE:** The intention of this study is to describe the impact and underlying potential basis of the prostate-specific antigen (PSA) flare-up phenomenon in patients with hormone-refractory prostate cancer (HRPC) treated with docetaxel-based chemotherapy.

**METHODS:** We retrospectively identified 74 consecutive patients who received docetaxel/estrामustinebased chemotherapy at our institution. Patients were evaluated based on modified criteria from the Prostate-Specific Antigen Working Group regarding survival and toxicity. Additionally, two androgen receptor mutations derived from patients with advanced disease were analyzed for promiscuous transactivation activity.

**RESULTS:** The 74 patients were stratified into four groups: response, partial response, flare-up-initial PSA elevation, and progression. Median survival in the flare-up group (n=8) was 20 months and did not differ from the response group (p=0.564). The flare-up group showed a maximum PSA elevation from baseline between 3.4 and 28.3% (between three and six weeks) followed by PSA decline  $\geq$ 50% from the baseline level in seven of the eight patients. The androgen receptor mutations AR(877) and AR(715) displayed a 37.5- and 5.2-fold increase in transactivation activity by progesterone and a 12.6- and 5.4-fold increase by estrogen compared to the AR(WT), respectively.

**CONCLUSIONS:** A considerable portion of HRPC patients experience an initial PSA flare-up under systemic chemotherapy. In this study, occurrence of flare-up phenomenon did not impact survival. Chemotherapy should be continued a minimum of six weeks before removing patients from a docetaxel-based regimen. We showed evidence that co-medication with dexamethasone/prednisolone and/or estrामustine itself can induce an initial PSA flare-up via androgen receptor mutations.

Scher, H. I., S. Halabi, et al. (2008). "Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group." *J Clin Oncol* 26(7): 1148-1159.

**PURPOSE:** To update eligibility and outcome measures in trials that evaluate systemic treatment for patients with progressive prostate cancer and castrate levels of testosterone.

**METHODS:** A committee of investigators experienced in conducting trials for prostate cancer defined new consensus criteria by reviewing previous criteria, Response Evaluation Criteria in Solid Tumors (RECIST), and emerging trial data.

**RESULTS:** The Prostate Cancer Clinical Trials Working Group (PCWG2) recommends a two-objective paradigm: (1) controlling, relieving, or eliminating disease manifestations that are present when treatment is initiated and (2) preventing or delaying disease manifestations expected to occur. Prostate cancers progressing despite castrate levels of testosterone are considered castration resistant and not hormone refractory. Eligibility is defined using standard disease assessments to authenticate disease progression, prior treatment, distinct clinical subtypes, and predictive models. Outcomes are reported independently for prostate-specific antigen (PSA), imaging, and clinical measures, avoiding grouped categorizations such as complete or partial response. In most trials, early changes in PSA and/or pain are not acted on without other evidence of disease progression, and treatment should be continued for at least 12 weeks to ensure adequate drug exposure. Bone scans are reported as "new lesions" or "no new lesions," changes in soft-tissue disease assessed by RECIST, and pain using validated scales. Defining eligibility for prevent/delay end points requires attention to estimated event frequency and/or random assignment to a control group.

**CONCLUSIONS:** PCWG2 recommends increasing emphasis on time-to-event end points (ie, failure to progress) as decision aids in proceeding from phase II to phase III trials. Recommendations will evolve as data are generated on the utility of intermediate end points to predict clinical benefit.

Armstrong, A. J., E. Garrett-Mayer, et al. (2007). "Prostate-specific antigen and pain surrogacy analysis in metastatic hormone-refractory prostate cancer." *J Clin Oncol* 25(25): 3965-3970.

**PURPOSE:** It is currently unclear if early prostate-specific antigen (PSA) or pain improvements are adequate surrogates for overall survival in men with metastatic hormone-refractory prostate cancer (HRPC). Here we examined various degrees of PSA decline and pain response as surrogates for the survival benefit observed in the TAX327 trial.

**METHODS:** In the TAX327 trial, 1,006 men with HRPC were randomly assigned to receive docetaxel in two schedules, or mitoxantrone, each with prednisone: 989 men provided data on 3-month PSA decline. Surrogacy was examined for post-treatment changes in PSA and pain response using Cox proportional hazards models to calculate the proportion of treatment effect (PTE) explained by each potential surrogate.

**RESULTS:** A  $\geq 30\%$  PSA decline within 3 months of treatment initiation provides the highest degree of surrogacy, with a PTE of 0.66 (95% CI, 0.23 to 1.0), and was associated with a hazard ratio (HR) of 0.50 (95%

CI, 0.43 to 0.58) for overall survival after adjusting for treatment effect. Introduction of a  $\geq 30\%$  PSA decline is predictive of survival regardless of treatment arm. Other changes in PSA or PSA kinetics, PSA normalization, and pain responses were highly prognostic but weaker surrogates for survival.

**CONCLUSIONS:** In the TAX327 trial, a PSA decline of  $\geq 30\%$  within 3 months of chemotherapy initiation had the highest degree of surrogacy for overall survival, confirming data from the Southwest Oncology Group 9916 trial. However, given the wide CIs around the estimate of this moderate surrogate effect, overall survival should remain the preferred end point for phase III trials of cytotoxic agents in HRPC.

Calabro, F. and C. N. Sternberg (2007). "Current indications for chemotherapy in prostate cancer patients." *Eur Urol* 51(1): 17-26.

Recently, data from two randomized studies, TAX327 and SWOG 9916, which compared docetaxel-based chemotherapy to mitoxantrone-based therapy, have demonstrated that treatment with docetaxel can prolong life in a statistically significant way in patients with hormone refractory prostate cancer (HRPC). In the TAX237 trial the median overall survival rates for patients treated with docetaxel every 3 wk was 18.9 mo, compared with 16.4 mo for the patients in the control arm ( $p=0.009$ ). Patients treated with the combination of docetaxel and estramustine in the SWOG trial had a significant improvement in median survival (18 mo vs 16 mo,  $p=0.01$ ), longer progression-free survival (6 mo compared with 3 mo,  $p<0.0001$ ), and a 20% reduction in the risk of death. The optimal timing of docetaxel-based chemotherapy is still unknown because there are no prospective clinical trials indicating whether earlier treatment is more effective than delayed treatment. There are now increasing options also for second-line therapies in the palliative treatment of HRPC, and ongoing studies on new drugs such as satraplatin and ixabepilone will define the role of these agents in this setting. Preliminary neoadjuvant and adjuvant chemotherapy studies in high-risk prostate cancer patients have demonstrated that these approaches are feasible and do not add morbidity to surgery or radiotherapy, but their impact on survival still needs to be proven in randomized studies.

Gomella, L. G. (2007). "Contemporary use of hormonal therapy in prostate cancer: managing complications and addressing quality-of-life issues." *BJU Int* 99 Suppl 1: 25-29; discussion 30.

While both short- and long-term androgen deprivation therapy (ADT) are effective for treating prostate cancer, with the clinical benefits patients can often have significant side-effects. It is important that these complications are recognized and managed appropriately so that adverse effects on the patient's quality of life (QoL) are minimized. The incidence of deaths from prostate cancer has decreased over the last decade, probably as a result of various factors including improved screening and diagnosis, improved treatments, and better risk assessment to help guide therapy. A meta-analysis of prostate cancer trials comparing the use of early vs late hormonal therapy found that 10-year overall survival increased by up to 20% between 1990 and 2000, and this was attributed to the earlier use of hormone therapy (HT) in these patients. Data from the USA Cancer of the Prostate Strategic Urological Research Endeavor database also suggest a significant decrease in risk in the last two decades in the USA, with more patients being identified with low-risk disease at diagnosis. In addition, there has been an increase in recent years in the use of HT at all stages of prostate cancer. The extensive use of ADT has raised concerns about

potential adverse effects. ADT might be associated with a range of adverse effects that vary in their degree of morbidity and effect on the patient's QoL. They include hot flashes, osteoporosis, loss of libido or impotence, and psychological effects, e.g. depression, memory difficulties or emotional lability. Effective strategies are available for managing the major side-effects of HT, but to many patients these unwanted effects are often less important than the benefits of treatment. An investigation of health-related QoL found that men with prostate cancer receiving ADT had a poorer QoL than those not receiving ADT, but the difference was less pronounced after controlling for comorbidities. Many new therapies are currently under investigation which aim to maximize the clinical effects of ADT while reducing the adverse effects.

Jones, R. A., S. M. Underwood, et al. (2007). "Reducing prostate cancer morbidity and mortality in African American men: issues and challenges." *Clin J Oncol Nurs* 11(6): 865-872.

Prostate cancer is the most commonly diagnosed cancer in men in the United States. It disproportionately affects African American men when compared to other ethnic groups. African American men are two to three times more likely to die of prostate cancer than white men. The reasons for the disparity remain unclear, but several factors may be involved, such as age, race, nationality, nutrition, exercise, and family history of cancer. Detection of prostate cancer in high-risk African Americans is important but continues to be controversial. This article reviews the current issues and challenges regarding prostate cancer in African American men. Nurses play a vital role in the health care and education of patients; therefore, they must be aware of the issues.

Oudard, S., E. Banu, et al. (2007). "Prostate-specific antigen doubling time before onset of chemotherapy as a predictor of survival for hormone-refractory prostate cancer patients." *Ann Oncol* 18(11): 1828-1833.

**PURPOSE:** We evaluated the possible use of prostate-specific antigen doubling time (PSA-DT) before chemotherapy initiation as a surrogate marker of survival in hormone-refractory prostate cancer (HRPC) patients.

**METHODS:** Data from 250 consecutive metastatic HRPC patients treated with chemotherapy between February 2000 and November 2006 were retrospectively analysed. At least three PSA assays were required within 3 months before chemotherapy. PSA-DT was calculated as  $\ln 2$  divided by the slope of the log PSA line, and the difference between two log PSA levels was divided by the time interval. The primary endpoint was overall survival (OS). Survival rates according to PSA-DT were stratified on chemotherapy regimen. Multivariate Cox regression analysis was performed to isolate the impact of PSA-DT on OS, controlling for associate prognostic covariates.

**RESULTS:** Patients received docetaxel- (82%) or mitoxantrone-based chemotherapy. The median PSA-DT was 45 days (range 4.7-1108 days). There were 174 deaths (70%). The median survival was 16.5 months (95% confidence interval [CI] =12.5-20.5) and 26.4 months (95% CI =20.3-32.4) for patients with a PSA-DT <45 and  $\geq$ 45 days, respectively. In the multivariate setting, the adjusted hazard ratio (HR) was 1.39 (95% CI = 1.03-1.89; P = 0.04), stratified by chemotherapy regimen.

**CONCLUSIONS:** A short PSA-DT before onset of chemotherapy in HRPC patients was associated with an increased risk of death. This could be useful as a stratification parameter in trials with new drugs in a metastatic setting.

Sowery, R. D., A. I. So, et al. (2007). "Therapeutic options in advanced prostate cancer: present and future." *Curr Urol Rep* 8(1): 53-59.

Patients with advanced prostate cancer now have many treatment options available including first- and second-line hormonal therapy, radiotherapy, bisphosphonate therapy with zoledronic acid, and taxane-based chemotherapy. These options now give clinicians an opportunity to offer their patients symptomatic relief and most importantly improve overall survival. This article reviews the current treatment options available for men with advanced prostate cancer. In addition, novel treatment options under development, including calcitriol, immunotherapies, small molecule inhibitors, and nucleotide-based targeted therapy, are discussed.

Mike, S., C. Harrison, et al. (2006). "Chemotherapy for hormone-refractory prostate cancer." *Cochrane Database Syst Rev* (4): CD005247.

**PURPOSE:** Prostate cancer mainly affects elderly men, and its incidence has steadily increased over the last decade. The management of this disease is replete with controversy. In men with advanced, metastatic prostate cancer, hormone therapy is almost universally accepted as the initial treatment of choice and produces good responses in most patients. However, many patients will relapse and become resistant to further hormone manipulation; the outlook for these patients is poor. Many have disease extending to the skeleton, which is associated with severe pain. Therapies for these men include chemotherapy, bisphosphonates, palliative radiotherapy, and radioisotopes. Systemic chemotherapy has been evaluated in men with hormone-refractory prostate cancer (HRPC) for many years, with disappointing results. However, more recent studies with newer agents have shown encouraging results. There is therefore a need to explore the value of chemotherapy in this disease. The present review aims to assess the role of chemotherapy in men with metastatic HRPC. The major outcome was overall survival. Secondary objectives include the effect of chemotherapy on pain relief, prostate-specific antigen (PSA) response, quality of life, and treatment-related toxicity.

**METHODS:** Trials were identified by searching electronic databases, such as MEDLINE, and handsearching of relevant journals and conference proceedings. There was no restriction of language or location. Only published randomised trials of chemotherapy in HRPC patients were eligible for inclusion in this review. Randomised comparisons of different chemotherapeutic regimens, chemotherapy versus best standard of care or placebo, were relevant to this review. Randomised, dose-escalation studies were not included in this review. Data extraction tables were designed specifically for this review to aid data collection. Data from relevant studies were extracted and included information on trial design, participants, and outcomes. Trial quality was also assessed using a scoring system for randomisation, blinding, and description of patient withdrawal.

**RESULTS:** Out of 107 randomised trials of chemotherapy in advanced prostate cancer identified by the search strategy, 47 were included in this review and represented 6929 patients with HRPC. Only two trials compared the same chemotherapeutic interventions and therefore a meta-analysis was considered inappropriate. The quality of some trials was poor because of poor reporting, low-patient recruitment, or poor trial design. For clarity, trials were categorised according to the major drug used, but this was not a

definitive grouping, since many trials used several agents and would be eligible for inclusion in a number of categories. Drug categories included estramustine, 5-fluorouracil, cyclophosphamide, doxorubicin, mitoxantrone, and docetaxel. Only studies using docetaxel reported a significant improvement in overall survival compared to best standard of care, although the increase was small (< 2.5 months). The mean percentage of patients achieving at least a 50% reduction in PSA compared to baseline was as follows: estramustine 48%; 5-fluorouracil 20%; doxorubicin 50% (one study only); mitoxantrone 33%; and docetaxel 52%. Pain relief was reported in 35% to 76% of patients receiving either single agents or combination regimens. A three weekly regime of docetaxel significantly improved pain relief compared to mitoxantrone plus prednisone (the latter regimen approved as standard therapy for HRPC in the USA). All chemotherapeutics, either as single agents or in combination, were associated with toxicity; the major ones being myelosuppression, gastrointestinal toxicity, cardiac toxicity, neuropathy, and alopecia. Quality of life was significantly improved with docetaxel compared to mitoxantrone plus prednisone.

**CONCLUSIONS:** Patients with HRPC have not traditionally been offered chemotherapy as a routine treatment because of treatment-related toxicity and poor responses. Recent data from randomised studies, in particular those using docetaxel, have provided encouraging improvements in overall survival, palliation of symptoms, and improvements in quality of life. Chemotherapy should be considered as a treatment option for patients with HRPC. However, patients should make an informed decision based on the risks and benefits of chemotherapy.

Rayford, W. (2006). "Managing the low-socioeconomic-status prostate cancer patient." *J Natl Med Assoc* 98(4): 521-530.

Management of patients with low socioeconomic status and/or low literacy who have prostate cancer presents a challenge to healthcare professionals. Improving treatment outcomes for these men requires specific educational programs to provide a better understanding of prostate cancer including careful post-treatment follow-up to ensure they have recovered well, that the cancer is not progressing and that complications are not proving troublesome. Practice nurses and health educators/navigators can play an important role in achieving these objectives. Education and knowledgeable advice can lead to earlier diagnosis of prostate cancer, improved patient participation in the treatment decision-making process and effective management of post-treatment complications.

Thompson, I. M., Jr., C. M. Tangen, et al. (2006). "Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial." *JAMA* 296(19): 2329-2335.

**PURPOSE:** Despite a stage-shift to earlier cancer stages and lower tumor volumes for prostate cancer, pathologically advanced disease is detected at radical prostatectomy in 38% to 52% of patients. However, the optimal management of these patients after radical prostatectomy is unknown. The objective is to determine whether adjuvant radiotherapy improves metastasis-free survival in patients with stage pT3 N0 M0 prostate cancer.

**METHODS:** Randomized, prospective, multi-institutional, US clinical trial with enrollment between August 15, 1988, and January 1, 1997 (with database frozen for statistical analysis on September 21, 2005). Patients were 425 men with pathologically advanced prostate cancer who had undergone radical prostatectomy. Men were randomly assigned to receive 60 to 64 Gy of external beam



radiotherapy delivered to the prostatic fossa (n = 214) or usual care plus observation (n = 211). Primary outcome was metastasis-free survival, defined as time to first occurrence of metastatic disease or death due to any cause. Secondary outcomes included prostate-specific antigen (PSA) relapse, recurrence-free survival, overall survival, freedom from hormonal therapy, and postoperative complications.

**RESULTS:** Among the 425 men, median follow-up was 10.6 years (interquartile range, 9.2-12.7 years). For metastasis-free survival, 76 (35.5%) of 214 men in the adjuvant radiotherapy group were diagnosed with metastatic disease or died (median metastasis-free estimate, 14.7 years), compared with 91 (43.1%) of 211 (median metastasis-free estimate, 13.2 years) of those in the observation group (hazard ratio [HR], 0.75; 95% CI, 0.55-1.02; P = .06). There were no significant between-group differences for overall survival (71 deaths, median survival of 14.7 years for radiotherapy vs 83 deaths, median survival of 13.8 years for observation; HR, 0.80; 95% CI, 0.58-1.09; P = .16). PSA relapse (median PSA relapse-free survival, 10.3 years for radiotherapy vs 3.1 years for observation; HR, 0.43; 95% CI, 0.31-0.58; P<.001) and disease recurrence (median recurrence-free survival, 13.8 years for radiotherapy vs 9.9 years for observation; HR, 0.62; 95% CI, 0.46-0.82; P = .001) were both significantly reduced with radiotherapy. Adverse effects were more common with radiotherapy vs observation (23.8% vs 11.9%), including rectal complications (3.3% vs 0%), urethral strictures (17.8% vs 9.5%), and total urinary incontinence (6.5% vs 2.8%).

**CONCLUSIONS:** In men who had undergone radical prostatectomy for pathologically advanced prostate cancer, adjuvant radiotherapy resulted in significantly reduced risk of PSA relapse and disease recurrence, although the improvements in metastasis-free survival and overall survival were not statistically significant. Trial Registration [clinicaltrials.gov](https://clinicaltrials.gov) Identifier: NCT00394511.

Jones, R. A. and J. Wenzel (2005). "Prostate cancer among African-American males: understanding the current issues." *J Natl Black Nurses Assoc* 16(1): 55-62.

Prostate cancer affects African-American males within the United States in a disproportionate number compared to White males. African-American males are 1.7 times more likely to develop and 2-3 times more likely to die from prostate cancer than White males. Numerous reasons for this disparity exist, including low socioeconomic status, distrust, conflicting cultural beliefs, and past healthcare experiences. Controversies surrounding this topic and perhaps contributing to the disparity include cancer-screening recommendations, cancer-related myths, and potential prevention modalities. Nursing research must focus on cancer-related issues among African-Americans to increase the awareness and knowledge of health-care professionals and the public to help decrease morbidity and mortality within African-Americans and other minority populations, and particularly among more vulnerable sections of at-risk minority populations. This article focuses on current issues related to African-American men and prostate health.

Konstantinos, H. (2005). "Prostate cancer in the elderly." *Int Urol Nephrol* 37(4):797-806.

Prostate cancer is the second leading cause of cancer deaths among men. Despite earlier diagnosis due to prostate specific antigen (PSA) screening, it is still a disease of the elderly. Diagnosis is based on digital rectal examination (DRE) and PSA assessment. Refinements in PSA testing (age-specific

reference ranges, free PSA, PSA density and velocity) increased specificity and limited unnecessary prostate biopsies. Diagnosis in earlier stages (T1 and T2) commonly leads to cure with current treatment modalities. These include radical prostatectomy, external beam radiotherapy and brachytherapy. Other treatment options under development include cryotherapy and high-intensity focused ultrasound. Metastatic prostate cancer is incurable and treatment is based on hormonal therapy. Cytotoxic chemotherapy has only limited role in hormone-independent prostate cancer. Radioisotopes and biphosphonates may alleviate bone pain and prevent osteoporosis and pathological fractures. Follow-up is based on PSA. Prognostic factors for recurrence include stage, Gleason score, pre- and posttreatment PSA. Quality of life issues play an important role in selecting treatment, especially in the elderly due to comorbidities that may negatively affect the overall quality of life. A holistic approach is recommended addressing all quality of life issues without focus only in cancer control.

## VI. SUPPORTIVE CARE SERVICES AND END-OF-LIFE CARE

Chambers, S. K., R. U. Newton, et al. (2011). "Living with prostate cancer: randomised controlled trial of a multimodal supportive care intervention for men with prostate cancer." *BMC Cancer* 11: 317.

**PURPOSE:** Prostate cancer is the most common male cancer in developed countries and diagnosis and treatment carries with it substantial morbidity and related unmet supportive care needs. These difficulties may be amplified by physical inactivity and obesity. We propose to apply a multimodal intervention approach that targets both unmet supportive care needs and physical activity.

**METHODS:** A two arm randomised controlled trial will compare usual care to a multimodal supportive care intervention "Living with Prostate Cancer" that will combine self-management with tele-based group peer support. A series of previously validated and reliable self-report measures will be administered to men at four time points: baseline/recruitment (when men are approximately 3-6 months post-diagnosis) and at 3, 6, and 12 months after recruitment and intervention commencement. Social constraints, social support, self-efficacy, group cohesion and therapeutic alliance will be included as potential moderators/mediators of intervention effect. Primary outcomes are unmet supportive care needs and physical activity levels. Secondary outcomes are domain-specific and health-related quality of life (QoL); psychological distress; benefit finding; body mass index and waist circumference. Disease variables (e.g., cancer grade, stage) will be assessed through medical and cancer registry records. An economic evaluation will be conducted alongside the randomized trial. This study will address a critical but as yet unanswered research question: to identify a population-based way to reduce unmet supportive care needs; promote regular physical activity; and improve disease-specific and health-related QoL for prostate cancer survivors. The study will also determine the cost-effectiveness of the intervention. **TRIAL REGISTRATION:** ACTRN12611000392965.

Dy, S. M., S. M. Asch, et al. (2011). "Quality of end-of-life care for patients with advanced cancer in an academic medical center." *J Palliat Med* 14(4): 451-457.

**PURPOSE:** We assessed key aspects of the quality of end-of-life care using validated explicit process quality measures in an academic medical center (hospital and cancer center) before expanding to a broader palliative care initiative.

**METHODS:** We evaluated 21 indicators most relevant to end-of-life care from the Cancer Quality-ASSIST supportive oncology indicator set for 238 patients with advanced/metastatic solid tumors who died between 2-15 months after diagnosis. These included outpatient and hospital indicators for cancer symptoms and information and care planning that met criteria for feasibility, reliability, and validity. We abstracted detailed information from medical records to specify the necessary data elements.

**RESULTS:** Overall adherence was 53% (95% confidence interval [CI], 50%-56%); this varied widely among indicators. Adherence was highest for pain indicators; in particular, 97% of eligible subjects' hospitalizations had documented screening for pain, and, after an outpatient pain medication was changed, 97% of patients had a pain assessment at the subsequent visit. For other symptoms, adherence ranged from 0% for documentation of life expectancy for patients starting parenteral or enteral nutrition to 87% for assessment of nausea or vomiting on hospital admission. For information and care planning, results ranged from 6% for documentation of ventilation preferences prior to intubation to 68% for documented communication of risks and benefits or prognosis prior to starting chemotherapy.

**CONCLUSIONS:** Cancer Quality-ASSIST indicators are useful for practical quality assessment of cancer end-of-life care in an academic medical center. These results will serve as useful data for targeting areas for quality improvement and measuring progress.

Lindqvist, O. (2011). "Living with bodily changes in hormone-refractory prostate cancer." *Semin Oncol Nurs* 27(4): 309-316.

**PURPOSE:** To review the current knowledge on living with bodily changes in hormone refractory prostate cancer (HRPC), treatment options, and common symptoms, and suggestions for improving our understanding of the experience of HRPC.

**METHODS:** Data sources were existing literature, research, and clinical experience.

**CONCLUSIONS:** Alleviation of bodily problems and providing care for men with HRPC is of utmost importance. It is important to talk about their situation and everyday life before asking about expected changes and problems related to the disease and its treatments. A preliminary framework is suggested for understanding the experience of HRPC from a nursing perspective. These results support an existing body of knowledge emphasizing the paramount importance of symptom alleviation, but indicate another motivation, that of freeing time, when time is so limited. The importance of dialogue between patients and health care providers is highlighted.

Yennurajalingam, S., B. Atkinson, et al. (2011). "The Impact of an Outpatient Palliative Care Consultation on Symptom Burden in Advanced Prostate Cancer Patients." *J Palliat Med*.

**PURPOSE:** There are limited studies characterizing cancer-related symptoms in outpatient advanced prostate cancer patients. The aim of this retrospective study was to describe the impact of an outpatient palliative care (PC) consultation on symptoms in patients with advanced prostate cancer.

**METHODS:** We retrospectively reviewed the medical records of 55 consecutive patients with advanced prostate cancer seen in our institution's outpatient PC center. Information regarding demographics, disease status, Edmonton Symptom Assessment System (ESAS) scores, Eastern Cooperative Oncology

Group (ECOG) Performance Status, laboratory data, and pharmacological interventions were analyzed.

**RESULTS:** The median age of the study's patients was 66 years old, with 73% Caucasian ethnicity. All patients had metastatic disease and 96% had received prior cytotoxic chemotherapy. The most frequently occurring symptoms upon presentation were pain, fatigue, and drowsiness (>50%). Pain and fatigue were also the most severe symptoms, each having median ESAS scores of 7 (on a 0-10 scale). We instituted a median of 3 pharmacological interventions per patient, with a median of 15 days to follow-up assessment. At follow-up, patients reported significant symptom improvements in pain, drowsiness, fatigue, depression, sleep, sense of well-being, and anxiety.

**CONCLUSIONS:** Based on our preliminary data, we conclude that patients with advanced prostate cancer referred to PC experience severe and clinically significant symptoms. An outpatient PC consultation is associated with significant symptom improvement in this subset of a distressed population. Future prospective studies are warranted to further describe symptom burden and the role for outpatient PC for advanced prostate cancer patients.

Dy, S. M., K. A. Lorenz, et al. (2010). "Cancer Quality-ASSIST supportive oncology quality indicator set: feasibility, reliability, and validity testing." *Cancer* 116(13):3267-3275.

**PURPOSE:** Although measuring the quality of symptom management and end-of-life care could help provide a basis for improving supportive care for advanced cancer, few quality indicators in this area have been rigorously developed or evaluated.

**METHODS:** The authors conducted a pilot evaluation of a comprehensive set of 92 supportive oncology quality indicators, Cancer Quality-ASSIST, including outpatient and hospital indicators for symptoms commonly related to cancer and its treatment and information and care planning. They operationalized the indicators and developed an electronic abstraction tool and extensive guidelines and training materials. Quality assurance nurses abstracted the medical records for 356 advanced cancer patients in 2 settings: a Veterans Administration hospital and an academic hospital and cancer center. The authors evaluated the indicators' feasibility, inter-rater reliability, and validity.

**RESULTS:** The authors successfully evaluated 78 indicators across the domains; results were similar in the 2 settings. They could not feasibly evaluate 3 indicators because of low prevalence; 22 indicators had significant inter-rater reliability issues, 9 had significant validity issues, and 3 had both reliability and validity issues, leaving a set of 41 indicators most promising for further testing and use in this population, with an overall kappa score of 0.85 for specified care.

**CONCLUSIONS:** Of 92 Cancer Quality-ASSIST quality indicators for symptoms, treatment toxicity, and information and care planning, 41 were sufficiently feasible, reliable, and valid to be used for patients with advanced cancer in these settings. This set of indicators shows promise for describing key supportive care processes in advanced cancer.

Grant, M. and V. Sun (2010). "Advances in quality of life at the end of life." *Semin Oncol Nurs* 26(1): 26-35.

**PURPOSE:** To provide an overview of the developments in promoting quality of life (QOL) at the end of life (EOL) in oncology settings, to describe implications for clinical care for cancer patients at the EOL, and to address the continuing challenges for assessing QOL at the EOL.

**METHODS:** Review of published articles, clinical guidelines, and web resources.

**CONCLUSIONS:** QOL continues to be an important aspect of patient care at the EOL. Nursing has made substantial contributions to the literature on QOL at the EOL through instrument development, clinical care priorities, and research. Oncology nurses practicing in clinical and research settings must be aware of the importance of QOL assessment for terminally ill cancer patients, be informed about the process of selecting relevant QOL measures for the EOL, and apply current knowledge to quality cancer care.

Lebret, T., P. Coloby, et al. (2010). "Educational tool-kit on diet and exercise: survey of prostate cancer patients about to receive androgen deprivation therapy." *Urology* 76(6): 1434-1439.

**PURPOSE:** To test a tool-kit designed to improve well-being in patients with prostate cancer. Lifestyle changes might lessen the metabolic, cardiovascular, and osseous side effects of androgen deprivation therapy (ADT) in prostate cancer patients.

**METHODS:** Urologists supplied 10 consecutive patients initiating ADT with a tool-kit (information brochure, practical guidance on diet and exercise, recipe booklet, and lifestyle diary). The urologists completed a total 4 questionnaires, at study initiation, one at the patients' first and second visits, and one at study completion.

**RESULTS:** Overall, 91 urologists completed all questionnaires; 585 patients (median age, 75 years) were seen at the first visit, and 511 patients at the second. Patient response rate to the first questionnaire was 62% and 56% to the second. After the first visit, 82% of respondents reported being very glad or glad to receive the kit; among those having read the practical guidance (301/362), 57% had started implementation and 36% intended to do so. After the second visit, 76% were satisfied with the tool-kit and 84% were implementing guidance. Clinician satisfaction rate was 82%: benefits were improved patient dialogue (62%), follow-up (55%), and better explanation of side effects (51%). Only 14 clinicians were not pleased by the tool kit. Their main criticisms (too long, tedious, not tailored to individual needs) matched those of patients.

**CONCLUSIONS:** Written detailed guidance on diet and physical exercise for patients about to receive ADT met a genuine need and was well perceived by both clinicians and patients. Implementation rate was high. However, content should be adapted to patient age and disease stage.

McNiff, K. K., M. N. Neuss, et al. (2008). "Measuring supportive care in medical oncology practice: lessons learned from the quality oncology practice initiative." *J Clin Oncol* 26(23): 3832-3837.

We provide a brief review of the use of quality measures to assess supportive care in the medical oncology office. Specifically, we discuss the development and implementation of supportive care measures in the Quality Oncology Practice Initiative (QOPI), a voluntary quality measurement and improvement program of the American Society of Clinical Oncology. QOPI has demonstrated that medical oncologists voluntarily engage in self-assessment and often select measures related to supportive care for measurement and improvement. Results to date have demonstrated that there is room for improvement in this domain. Because supportive care measures appropriate for use through structured

chart review in the outpatient oncology setting are not generally available in the published literature, measures have been developed and tested through the program. Additional measures are in development for implementation in QOPI in 2008.

Lindqvist, O., A. Widmark, et al. (2006). "Reclaiming wellness--living with bodily problems, as narrated by men with advanced prostate cancer." *Cancer Nurs* 29(4): 327-337.

Having advanced prostate cancer means living with considerable bodily problems, a living we know little about. Thus, the aim of this study was to illuminate meanings of living with bodily problems, as narrated by men with advanced metastasized hormone refractory prostate cancer. Eighteen participants were interviewed, and the text was analyzed using a phenomenological-hermeneutic approach. Findings show that meanings of living with bodily problems are to live in cyclical movements between experiencing wellness and experiencing illness. New, or changed, bodily problems mean losing wellness and experiences of being ill. Understanding and, to some extent, being in control of bodily problems, make it possible to reclaim wellness and to experience oneself as being well. Findings also show that pain and fatigue are the most prominent problems and that they have different meanings. Pain being a threat of dying in agony, whereas fatigue is more of an emissary of death. Reclaiming wellness versus adaptation and enduring versus suffering deriving from 2 different perspectives, the inside or life world perspective and the outside or professional perspective, are questions discussed in the article. One clinical implication for nursing is the risk of obstructing the patients' possibility of reclaiming wellness by focusing on symptoms and disease.

Gore, J. L., T. Krupski, et al. (2005). "Mental health of low income uninsured men with prostate cancer." *J Urol* 173(4): 1323-1326.

**PURPOSE:** We evaluated mental health outcomes in a cohort of low income, uninsured men with prostate cancer and identified factors that influence mental health.

**METHODS:** We performed a retrospective cohort study of 277 subjects enrolled in a program that provides free care to men with prostate cancer who have an annual income of no more than 200% of the federal poverty level. We compared scores on the 5-item RAND Mental Health Inventory (MHI-5) to those in individuals with other chronic diseases. We also examined the relationship between MHI-5 scores and validated measures of general and disease specific health related quality of life. Disease specific quality of life included measures of distress related to urinary, sexual and bowel habits. Multivariate analyses were performed to evaluate factors associated with mental health score.

**RESULTS:** Most men studied were Hispanic (51.6%) and had at most a high school education (85.9%). Mean MHI-5 score +/- SD was 68 +/- 23 on a 100-point scale, significantly worse than cohorts of men with diabetes, congestive heart failure and chronic pulmonary disease. Hispanic ethnicity, urinary bother and bowel bother were negatively associated with mental health. Spirituality and physical functioning were positively associated with mental health.

**CONCLUSIONS:** Economically disadvantaged men with prostate cancer report worse mental health than people with other chronic diseases. Patients especially at risk are those with significant urinary or bowel distress, poor physical health, low spirituality and Hispanic ethnicity.

Katz, D., T. M. Koppie, et al. (2002). "Sociodemographic characteristics and health-related quality of life in men attending prostate cancer support groups." *J Urol* 168(5): 2092-2096.

**PURPOSE:** Prostate cancer can be associated with anxiety, depression and fears of recurrence and side effects of treatment. Support groups may help meet the needs of patients with cancer by providing treatment information and emotional support. We describe men in prostate cancer support groups and compare them to a national registry.

**METHODS:** Men attending prostate cancer support groups in the San Francisco Bay area completed a questionnaire including sociodemographic and clinical characteristics, health related quality of life items, satisfaction with treatment, relief of prostate cancer symptoms and bother from perceived side effects of treatment. Patients in support groups were compared to men enrolled in a national prostate cancer registry (Cancer of the Prostate Strategic Urological Research Endeavor).

**RESULTS:** Men attending support groups had higher annual income and education levels, lower median serum prostate specific antigen and higher cancer grades than men in Cancer of the Prostate Strategic Urological Research Endeavor. Clinical stage was comparable for the 2 groups. Men in support groups were satisfied with treatment and alleviation from symptoms. Adjusting for ethnicity, marital status, age and type of treatment, sexual function scores were higher in men who attended support groups ( $p = 0.001$ ). There was no statistically significant difference in bowel and urinary function between groups, although urinary function approached statistical significance at  $p = 0.05$ . Sexual and bowel bother scores indicated less bother for men in support groups ( $p < \text{or} = 0.025$ ).

**CONCLUSIONS:** Men enrolled in support groups have unique socio-demographic characteristics. Their health related quality of life appears to be better than that of other men with prostate cancer. Whether this is related to support group participation is not known. Additional studies are required to determine whether routine support group participation improves outcomes in men with prostate cancer.

## VII. ECONOMICS AND COST IMPLICATIONS

Ferrusi, I. L., N. B. Leighl, et al. (2011). “Do economic evaluations of targeted therapy provide support for decision makers?” *J Oncol Pract* 7(3 Suppl): 36s-45s.

**PURPOSE:** Decision makers must make decisions without complete information. That uncertainty can be decreased when economic evaluations use local data and can be quantified by considering the variability of all model inputs concurrently per international evaluation guidelines. It is unclear how these recommendations have been implemented in evaluations of targeted cancer therapy. By using economic evaluations of adjuvant trastuzumab, we have assessed the extent to which decision support recommendations were adopted.

**METHODS:** Systematic review. Published economic evaluations of adjuvant trastuzumab treatment in early-stage breast cancer were examined as an established example of targeted therapy. Canadian, United Kingdom, and US economic evaluation guidelines were reviewed to establish extraction criteria. Extraction characterized the use of effectiveness evidence and local data sources for model parameters, sensitivity analysis methods (scenario, univariate, multivariate, and probabilistic) and uncertainty representation (ie, cost-effectiveness plane, scatterplot, confidence ellipses, tornado diagrams, cost-effectiveness acceptability curve).

**RESULTS:** Fifteen economic evaluations of adjuvant trastuzumab were identified in the literature. Local data were used to estimate costs (15 of 15) and utilities rarely (two of 15) but not trastuzumab efficacy. Univariate sensitivity analysis was most common (12 of 15), whereas probabilistic analysis was less frequent (10 of 15). Two thirds of all studies provided visual representation of results and decision uncertainty.

**CONCLUSION:** Authors of adjuvant trastuzumab economic evaluations rarely use local data beyond costs. Quantification of uncertainty and its representation also fell short of guideline recommendations. This review demonstrates that economic evaluations of adjuvant trastuzumab, as an example of targeted cancer therapy, can be improved for decision-making support.

Nguyen, P. L., X. Gu, et al. (2011). “Cost implications of the rapid adoption of newer technologies for treating prostate cancer.” 29(12): 1517-1524. *J Clin Oncol*

**PURPOSE:** Intensity-modulated radiation therapy (IMRT) and laparoscopic or robotic minimally invasive radical prostatectomy (MIRP) are costlier alternatives to three-dimensional conformal radiation therapy (3D-CRT) and open radical prostatectomy for treating prostate cancer. We assessed temporal trends in their utilization and their impact on national health care spending.

**METHODS:** Using Surveillance, Epidemiology, and End Results-Medicare linked data, we determined treatment patterns for 45,636 men age  $\geq 65$  years who received definitive surgery or radiation for localized prostate cancer diagnosed from 2002 to 2005. Costs attributable to prostate cancer care were the difference in Medicare payments in the year after versus the year before diagnosis.

**RESULTS:** Patients received surgery (26%), external RT (38%), or brachytherapy with or without RT (36%). Among surgical patients, MIRP utilization increased substantially (1.5% among 2002 diagnoses v 28.7% among 2005 diagnoses,  $P < .001$ ). For RT, IMRT utilization increased substantially (28.7% v 81.7%;  $P < .001$ ) and for men receiving



brachytherapy, supplemental IMRT increased significantly (8.5% v 31.1%;  $P < .001$ ). The mean incremental cost of IMRT versus 3D-CRT was \$10,986 (in 2008 dollars); of brachytherapy plus IMRT versus brachytherapy plus 3D-CRT was 10,789; of MIRP versus open RP was \$293. Extrapolating these figures to the total US population results in excess spending of \$282 million for IMRT, \$59 million for brachytherapy plus IMRT, and \$4 million for MIRP, compared to less costly alternatives for men diagnosed in 2005.

**CONCLUSIONS** Costlier prostate cancer therapies were rapidly and widely adopted, resulting in additional national spending of more than \$350 million among men diagnosed in 2005 and suggesting the need for comparative effectiveness research to weigh their costs against their benefit.

McKeage, K. and G. L. Plosker (2008). "Zoledronic acid: a pharmaco-economic review of its use in the management of bone metastases." *Pharmacoeconomics* 26(3): 251-268.

Zoledronic acid (Zometa) is a third-generation nitrogen-containing parenteral bisphosphonate indicated for the treatment of bone metastases due to solid tumours or multiple myeloma and for hypercalcaemia of malignancy (HCM). In patients with advanced breast or prostate cancer, zoledronic acid 4 mg every 3-4 weeks for up to 15 months significantly reduced the proportion of patients with  $\geq 1$  skeletal-related event (SRE), excluding HCM, compared with placebo. In patients with advanced breast cancer or multiple myeloma, the incidence of SREs was similar in patients treated with zoledronic acid 4 mg or pamidronic acid 90 mg every 3-4 weeks for up to 25 months but, in breast cancer patients, zoledronic acid reduced the risk of SREs, including HCM, by an additional 20% compared with pamidronic acid. In modelled cost-utility studies comparing direct costs based on efficacy and resource-use data from these and other trials, results have varied. In the most recent study performed from the perspective of the UK NHS and modelled over a 10-year treatment period in women with advanced breast cancer, intravenous zoledronic acid and oral ibandronic acid were dominant over no treatment. Intravenous zoledronic acid was the most cost effective, in terms of incremental costs per QALY gained, followed by oral ibandronic acid, intravenous pamidronic acid and intravenous ibandronic acid. Two other modelled analyses in patients with advanced breast cancer, also conducted from the perspective of the NHS, evaluated the cost utility of three bisphosphonate therapies in patients receiving hormonal therapy or intravenous chemotherapy. Analyses were modelled over 14.3 months (i.e. expected survival) and assumptions varied markedly from results in clinical breast cancer trials. Also, efficacy assumptions for zoledronic acid were not based on clinical trials with the drug. The results of these analyses suggest that oral ibandronic acid is more cost effective than intravenous zoledronic acid and intravenous pamidronic acid in terms of incremental cost per QALY gained. In a global, 15-month modelled cost-effectiveness analysis of patients with advanced prostate cancer, conducted from a third-party perspective, the incremental cost per QALY gained for zoledronic acid versus no treatment was \$US159 200 (year 2000 value), which is about 3-fold greater than commonly accepted thresholds for cost effectiveness. In conclusion, a recent modelled economic analysis suggests that intravenous zoledronic acid 4 mg is dominant relative to no treatment in the management of bone metastases in patients with advanced breast cancer. In contrast, in patients with advanced prostate cancer, the incremental cost per QALY gained for zoledronic acid 4 mg versus no treatment was predicted to be higher than commonly accepted thresholds. Compared with other bisphosphonates in the setting of advanced breast cancer, intravenous zoledronic acid was more cost effective than oral or intravenous ibandronic acid and intravenous pamidronic acid in one study, but less cost effective than oral ibandronic acid in another. Further efficacy and economic data comparing intravenous zoledronic acid with oral ibandronic

acid are needed. Meanwhile, zoledronic acid appears to be the most cost effective intravenous bisphosphonate for the management of bone metastases in patients with advanced breast cancer and possibly in patients with different types of advanced solid tumours.

Zeliadt, S. B. and D. F. Penson (2007). "Pharmacoeconomics of available treatment options for metastatic prostate cancer." *Pharmacoeconomics* 25(4): 309-327.

The resources devoted to managing metastatic prostate cancer are enormous, yet little attention has been given to directly measuring the economic consequences of treatment alternatives. The purpose of this article was to evaluate the pharmacoeconomics of available treatments for metastatic prostate cancer, including hormone-sensitive disease, androgen-independent prostate cancer and locally advanced/progressive disease. We identified 58 articles addressing economic issues related to metastatic prostate cancer. Treatment alternatives with considerably different costs are available in many areas of disease management, most notably, medical androgen deprivation therapy (ADT) versus surgical castration; combined androgen blockage (CAB) versus monotherapy for initial treatment of hormone-sensitive disease; as well as bisphosphonates and bonetargeted radioisotopes for palliation. The few available pharmacoeconomic studies indicate that the additional costs are not supported by clear and compelling evidence of differences in survival or quality-of-life (QOL) outcomes. Our review revealed that authors often use considerably different assumptions about efficacy and survival outcomes in their analyses, which may be due to the inconsistency of available clinical evidence. Although there have been many clinical trials comparing various therapies, we identified only three trials that included economic assessments. Thus, few sources of economic data are available and most pharmacoeconomic studies rely on information mined from indirect sources. We note that, while there has been considerable enthusiasm about the role of docetaxel regimens in the past 2 years, no study has yet examined the costs of these therapies. Survival remains poor for metastatic disease, thus QOL is the primary consideration for many therapies. However, QOL for treatment of metastatic disease is poorly measured and, in most analyses, the impact of therapy on QOL was inferred based on speculation by the authors. Given the large cost burdens of these treatments, it is essential that we more fully understand the true QOL gains potentially offered by more expensive therapies. The economic studies of advanced prostate cancer highlight several aspects of clinical care that are filled with considerable uncertainty and remain guided by forces other than optimal resource allocation. It is essential that we address the weaknesses in our understanding of the economic consequences of therapies for prostate cancer, and find ways to include economic information into the process of determining optimal therapy.

Matchar, D. B., D. C. McCrory, et al. (1997). "Treatment considerations for persons with metastatic prostate cancer: survival versus out-of-pocket costs." *Urology* 49(2): 218-224.

**PURPOSE:** Treatment decisions for metastatic prostate cancer require the consideration of factors such as survival, quality of life, costs of care, and toxicities. In this study, we queried physicians who had extensive experience with prostate cancer about features of metastatic prostate cancer, patients' quality of life, and factors influencing their decision to prescribe flutamide.

**METHODS:** Data were gathered through physician surveys and focus group discussions. Demographic information on the physicians and their patients was collected. Physicians made assessments of five health states related to metastatic prostate cancer, based on the

time trade-off technique, and on the desirability of flutamide, based on average expected improvement in survival free of progressive disease, side effects, and drug cost.

**RESULTS:** Physicians were internally consistent in their judgments of the factors most important to quality of life for individuals with metastatic prostate cancer. Physicians considered bone pain and weight loss/anorexia the most important factors. Physicians who cared for a higher proportion of older persons or Medicare recipients rated each scenario as less undesirable than did physicians with a lower proportion of these patients. Out-of-pocket cost was the major factor predicting whether a physician would prescribe flutamide. Physicians working for health maintenance organizations were more likely to prescribe flutamide but were more sensitive to out-of-pocket costs than were other physicians.

**CONCLUSIONS:** Physicians varied in their perceptions of quality of life for persons with metastatic prostate cancer and in their willingness to prescribe flutamide. These perceptions and prescribing preferences are strongly influenced by factors other than health status or specific health benefits. In deciding to prescribe flutamide, concerns over out-of-pocket expenditures loom large for most clinicians. It would be important to know the degree to which these concerns are shared by patients and whether prescribing preferences differ for Medicare managed-care patients who have pharmaceutical benefits.