Methodology

Journal of Comparative Effectiveness Research

Design of the North Carolina Prostate Cancer Comparative Effectiveness and Survivorship Study (NC ProCESS)

Ronald C Chen*[1,2,3], William R Carpenter[2,4], Mimi Kim[1], Laura H Hendrix[2,3], Robert P Agans[5], Anne-Marie Meyer[2,6], Anna Hoffmeyer[5], Bryce B Reeve[2,4], Matthew E Nielsen[1,2,7], Deborah S Usinger[1,2], Tara S Strigo[2], Anne M Jackman[1], Mary Anderson[8] & Paul A Godley[1,2,9]

[1]Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, NC, USA
[2]Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, NC, USA
[3]Department of Radiation Oncology, School of Medicine, University of North Carolina at Chapel Hill, NC, USA
[4]Department of Health Policy and Management, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, NC, USA
[5]Carolina Survey Research Laboratory, University of North Carolina at Chapel Hill, NC, USA
[6]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, NC, USA
[7]Department of Urology, School of Medicine, University of North Carolina at Chapel Hill, NC, USA
[8]Prostate Cancer Coalition of North Carolina, NC, USA
[9]Division of Hematology/Oncology, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, NC, USA
*Author for correspondence:
Tel.: +1 919 966 0400
Fax: +1 919 966 7681
ronald_chen@med.unc.edu

The North Carolina Prostate Cancer Comparative Effectiveness & Survivorship Study (NC ProCESS) was designed in collaboration with stakeholders to compare the effectiveness of different treatment options for localized prostate cancer. Using the Rapid Case Ascertainment system of the North Carolina Central Cancer Registry, 1,419 patients (57% of eligible) with newly-diagnosed localized prostate cancer were enrolled from January 2011 to June 2013, on average 5 weeks after diagnosis. All participants were enrolled prior to treatment and this population-based cohort is sociodemographically diverse. Prospective follow-up continues to collect data on treatments received, disease control, survival and patient-reported outcomes. This study highlights several important considerations regarding stakeholder involvement, study design and generalizability regarding comparative effectiveness research in prostate cancer.

Keywords: brachytherapy • comparative effectiveness research • prostate cancer • prostatectomy • radiation

Prostate cancer causes significant burden in the US population and the healthcare system in terms of its prevalence, mortality, suffering and cost. It is the most common cancer in men, diagnosed in more than 240,000 each year in the USA [1]. It is the second leading cause of cancer deaths in men, with mortality >30,000 each year [2]. Over 90% of newly-diagnosed patients have localized disease and are potentially curable [2]. These patients face a wide range of options, including active surveillance (i.e., deferred treatment), radical prostatectomy and radiation therapy. Furthermore, there are different surgical techniques, including the older open prostatectomy and the newer robotic ('minimally invasive') prostatectomy. Within radiation therapy, the options include brachytherapy, intensity-modulated radiation therapy (IMRT), proton therapy and stereotactic body radiation. The comparative patient outcomes of these modern treatment options for localized prostate cancer – in terms of cancer control, morbidity and patient-reported outcomes (PRO, including quality of life) – have not been well studied. While it is well established that surgical and radiation treatments can cause long-term urinary, bowel and sexual dysfunction [3,4], many of the existing studies reported outcomes of patients treated with outdated treatment techniques that no longer reflect the choices patients face today. There is a significant need for comparative effectiveness research (CER) in this disease to provide patients with the necessary data, enabling them to make an informed decision among this large number of current treatment options.

Another major challenge related to localized prostate cancer is the rapid diffusion of newer and more expensive treatments without proven benefit compared with older treatments. A recent study examined the use of an older conformal technique versus the newer IMRT in Medicare prostate cancer patients treated by radiation therapy [5]. IMRT use increased rapidly from 2000 (0.15% of patients) to 2008 (95.9% of patients), essentially replacing the older radiation

Future Medicine part of fsg

technology. However, to date, there are relatively little data demonstrating an incremental benefit from this more expensive radiation technique in patient outcomes [6]. A similar trend of a rapid uptake of the newer robotic prostatectomy versus older open prostatectomy has also been reported [7]. The use of new technologies in prostate cancer led to an increase in healthcare spending in the USA by US$350 million in 2005 alone [8]. Importantly, the rapid diffusion of newer treatments continues currently, with increasing uses of proton therapy and stereotactic body radiation treatments across the USA. CER of patient outcomes from newer versus older treatment technologies is necessary to halt this trend of rapid diffusion without evidence.

The need for CER in localized prostate cancer is widely recognized. In the first quartile of the 100 priority CER topics, the Institute of Medicine recommends research to "compare the effectiveness of management strategies for localized prostate cancer on survival, recurrence, side effects, quality of life, and costs" [9]. This topic was also identified as a top priority by the Agency for Healthcare Research and Quality Developing Evidence to Inform Decisions about Effectiveness cancer consortium (canDEcIDE) stakeholder group [10]. In response to these calls, the North Carolina Prostate Cancer Comparative Effectiveness and Survivorship Study (NC ProCESS) was designed. The overall goal of this study was to compare the outcomes of patients treated by different modern treatment options. NC ProCESS is a prospective, population-based cohort of patients with localized prostate cancer. The design of this study and cohort patient characteristics are described in this report.

Patients & methods

Stakeholder engagement

This study benefited from an early involvement of stakeholders. The Agency for Healthcare Research and Quality canDEcIDE stakeholder group was assembled in 2010 to help researchers generate and prioritize cancer-related CER topics [10]. This is one of the first federally funded initiatives to directly involve stakeholders in CER and the importance of stakeholder engagement in this type of research has subsequently become widely recognized. The Agency for Healthcare Research and Quality canDEcIDE stakeholder group consisted of representatives from patient groups (National Coalition for Cancer Survivorship, Patient Advocates in Research), payers and policymakers (Center for Medicare and Medicaid Services, Tricare, Aetna, District of Columbia Department of Health Care Finance/Medicaid, New York State Department of Health, National Cancer Institute, US FDA), physicians and researchers from the American Society of Clinical Oncology, American Cancer Society, American College of Surgeons, Oncology Nursing Society, and American Society for Radiation Oncology. The assembly of this group and process of their engagement and participation has been previously described [10].

Study design & end points

The first stakeholder meeting on 14 January 2010, generated seven high-priority CER topics, including treatment options for localized prostate cancer. Related to this topic, the stakeholders emphasized the importance of community-based research (reflecting patients in 'real world' settings) and generalizability of research findings, a focus on evaluating new technologies, as well as the relevant end points of PRO, treatment-related morbidity, and disease control; the first (PRO) was deemed most important for stakeholders.

NC ProCESS was designed with this stakeholder input and specifically measures the end points and knowledge gaps identified by the Institute of Medicine report and stakeholders: PRO, treatment-related morbidity, cancer control and survival. PRO measures include a validated, prostate cancer-specific instrument – Prostate Cancer Symptom Indices [11] – and the Short-Form 12, a validated measure for health-related quality of life. These measures are assessed at baseline (pretreatment), 3 months, 12 months and yearly after. Starting at the 12 month time point, additional validated measures to assess decisional regret [11] and prostate cancer-specific anxiety [12] are included as well. To address the stakeholder input to provide results generalizable to the community, NC ProCESS was designed as a population-based cohort by partnering with the North Carolina Central Cancer Registry (described below). Furthermore, all PRO assessments are conducted via telephone by trained interviewers. This assessment modality was chosen in an attempt to maximize participation by patients who are traditionally under-represented in clinical research – including those with lower literacy and socioeconomic status. In 2011 and 2012, NC ProCESS updates were presented to the stakeholder group to seek continued feedback.

An additional partnership with the Prostate Cancer Coalition of North Carolina was formed during study design and continues. The Prostate Cancer Coalition of North Carolina is the largest consortium of prostate cancer patient organizations and support groups throughout North Carolina (USA) and maintains an active role in disseminating research findings to patients, their partners and physicians across the state as part of its mission. With the Prostate Cancer Coalition of North Carolina's help, NC ProCESS investigators designed study recruitment materials (including introductory letter and study brochure) and obtained feedback on the PRO instruments in

collaboration with prostate cancer patients in North Carolina.

Patient enrollment procedures

Patients were identified and enrolled using the Rapid Case Ascertainment (RCA) mechanism of the North Carolina Central Cancer Registry. RCA is an acceleration of the cancer reporting process, where Registry staff proactively request and obtain information regarding the cancers relevant to the study from local hospitals and facilities. This system has been successfully used to help enroll >12,000 cancer patients in 24 studies spanning eight cancers across North Carolina, with all 100 counties participating. Tumor registrars from larger hospitals send names and pathology/diagnosis information of new cancer patients as well as names/addresses of their physicians to RCA coordinators on a weekly basis. Smaller hospitals (fewer cancer patients/diagnoses) are called on a biweekly basis. This system in North Carolina is unique because, in the significant majority of cases, prostate cancer patients are reported to RCA within 1–2 weeks of diagnosis. This system allowed NC ProCESS staff to gather baseline patient and PRO data prior to initiation of treatment, which is helpful for minimizing potential biases in recruitment and data collection.

Upon identification of a newly-diagnosed prostate cancer patient, NC ProCESS staff mailed a letter to the physician explaining the study; the physician then had 2 weeks to opt-out their patient (Figure 1). Following the physician opt-out period, the patient was mailed an introductory letter and brochure describing the study. Following these procedures, the median time from cancer diagnosis to baseline survey was 5 weeks. Overall, 19% of otherwise eligible patients had received treatment prior to being contacted by study staff and were excluded from participation. The unique RCA system as closely as possible resembles a 'real-time' capture of newly diagnosed prostate cancer patients in North Carolina and allowed this study to enroll all patients prior to treatment initiation.

Results

We received 4,251 cases from the cancer registry. Potential patients were ineligible if they had already started treatment (n = 819), could not be reached by phone (n = 857) or for other reasons (n = 102), including non-English speaking and physician refusal to allow patient contact by study staff. This resulted in 2,473 eligible patients. Of these, 1419 enrolled (57%) from January 2011 to June 2013 and 1,054 (43%) patients declined.

Characteristics of study participants versus non-participants

The comparison of characteristics among participants versus non-participants using data available in the Cancer Registry is summarized in Table 1. Among participants, 70% were Caucasian; of the remainder, almost all were African–American (27 of 30%). Median age of participants was 65 years and the majority had Gleason 6 cancer. Non-participants were modestly different in these characteristics, although the large patient numbers led to small p-values in these comparisons.

Baseline demographic characteristics of participants

Table 2 summarizes self-reported characteristics of the 1,419 participants, demonstrating significant sociodemographic diversity. Approximately one-third of participants had a high school education or less and one-third with family income of US$40,000 per year or less. Almost all had health insurance and 78% were married.

Discussion

The comparative effectiveness of different treatment options in localized prostate cancer is a 'highest priority' research topic [9]. Today, patients with localized prostate cancer face a large number of options ranging from active surveillance to different types of prostatectomy and radiation therapy, but have insufficient data on the comparative outcomes from these modern treatments to make a fully-informed decision. Furthermore, the rapid diffusion of newer and costlier surgical and radiation treatments in the past 10 years [5,7] – without clear evidence that newer technologies improve patient outcomes – is a trend that continues today with even newer treatments and is an

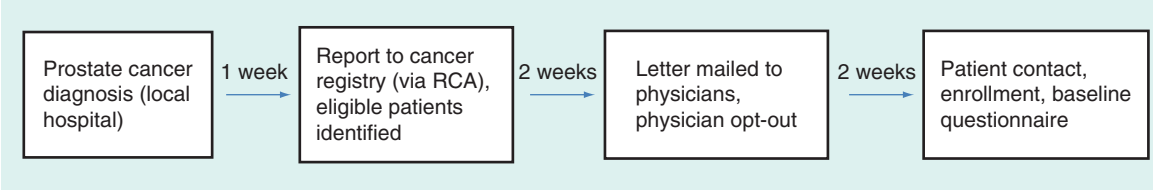

Figure 1. Patient identification and enrollment timeline.
RCA: Rapid case ascertainment.

Table 1. Characteristics of participants and non-participants.

	Participants, n (%)	Non-participants, n (%)	p-value
Race			
Caucasian	999 (70)	785 (74)	0.02
Non-Caucasian	427 (30)	269 (26)	
Age (years)			
Median (range)	65 (41–80)	68 (42–80)	<0.001
Biopsy Gleason Score			
6 or less	821 (58)	541 (51)	<0.001
7	490 (34)	365 (35)	
8	75 (5)	81 (8)	
9	39 (3)	61 (6)	
10	1 (<1)	6 (<1)	

unsustainable practice for the US healthcare system. For patients and physicians, payers and policy makers, CER in this disease is urgently needed. Patients and physicians need to understand the comparative outcomes of different options (e.g., active surveillance, prostatectomy, radiation) to make clinical decisions. Payers and policy makers need data on whether newer treatments improve patient outcomes compared with older treatments to inform their coverage and policy decisions.

There are several study designs that can be used for CER and none is perfect. Randomized trials are traditionally considered a 'gold standard' study design comparing outcomes from different treatments; however, they have often proven to be impractical in localized prostate cancer. Prior international attempts to randomize patients among treatment modalities (e.g., surgery vs radiation) have been unsuccessful in accruing sufficient patients, while the recently published Prostate Cancer Intervention versus Observation Trial (PIVOT) needed to screen 13,022 patients to randomize 731 over 8 years [13]. This trial began in 1994 and compared radical prostatectomy versus observation for patient with localized prostate cancer; in the most recent report in 2012, no survival benefit was seen from prostatectomy [14]. Randomized trials in general may also have relatively homogeneous patient and institutional participation, with associated concerns related to generalizability of study results to the broader community. Large-scale pragmatic trials can help address important questions, such as the Prostate Testing for Cancer and Treatment (ProtecT) trial (NCT02044172), which randomized 1,643 patients from 2001–2009 to radical prostatectomy, radiation or active monitoring and is awaiting results [15]. This trial achieved a participation rate of 62% of eligible patients.

Observational cohorts, on the other hand, suffer from patient selection biases – which are relevant in localized prostate cancer. Younger and healthier patients are more likely to receive prostatectomy, while older patients are more likely to receive radiation therapy or surveillance [2]. Sophisticated analytic methodologies, such as propensity score and instrumental variables, may be able to partially mitigate this shortcoming [16], but are unlikely to fully account for selection bias. However, population-based cohorts – especially cohorts that are successful in recruiting participants from diverse sociodemographic backgrounds – may improve the generalizability compared with trials and certainly single- or oligo-institutional series. Studies using claims-based datasets, such as the Surveillance, Epidemiology and End Results (SEER)–Medicare-linked database are also valuable in providing population-based outcomes, but are limited by a lack of the granular patient data that can only be obtained by medical record reviews and patient surveys. Ultimately, given the importance of CER in localized prostate cancer and no single perfect study design, multiple studies of different designs are necessary in order to address the current knowledge gaps related to this topic.

NC ProCESS is a prospective, population-based cohort of localized prostate cancer patients. Our participation rate of 57% is significantly higher than most randomized trials (e.g., 5.5% participation in the PIVOT trial) [13], and is similar to a prior population-based cohort [17]. This study benefited tremendously from stakeholder collaboration from initial topic identification/prioritization and throughout study design and conduct. The study end points were chosen to represent outcomes most relevant to stakeholders: patient-reported outcomes including quality of life (which stakeholders indicated were most important),

cancer control and survival. The end points of PRO and treatment-related morbidity are especially relevant in localized prostate cancer because most of the newer treatments (e.g., robotic prostatectomy, proton therapy) purport to reduce treatment-related side effects compared with older surgical and radiation treatments, but do not purport to improve curative efficacy or survival. Stakeholders were also central to several study design decisions, which we believe facilitated the successful recruitment of a sociodemographically diverse cohort, including a high proportion of minority (especially African–American) patients. In fact, the proportion of non-Caucasian patients is higher in participants than non-participants. We believe the intentional use of telephone for PRO data collection minimized obstacles to participation by patients with low literacy and those without ready computer/internet access. However, a small percentage of prostate cancer patients may not have phone access and, therefore, were unable to participate. Furthermore, a consistent use of phone-based data collection for all participants rather than multiple modalities (phone, paper, internet) potentially avoided biases related to differential reporting of data by mode of collection, which can be especially problematic if certain patient subgroups are more likely to use one modality (e.g., more educated patients using internet) than others. Collaboration with patients in creating and revising recruitment materials and assessing comprehensibility of telephone survey scripts were also helpful. Study investigators have continued to seek feedback from stakeholders, who will play a central role in helping disseminate study findings in the future.

Another key aspect of the NC ProCESS cohort is enrollment of all patients and collection of baseline PRO data prior to treatment; thus, all PRO data are collected prospectively without patient recall. This was made possible by the rapidity of the RCA system in North Carolina in obtaining cases from local hospitals within 1–2 weeks of diagnosis. Because PRO

Table 2. Baseline sociodemographic characteristics of the North Carolina Prostate Cancer Comparative Effectiveness and Survivorship Study cohort.

Characteristics	Participants, n (%)
Educational attainment	
Eighth grade or less	55 (4)
Some high school	119 (8)
High school graduate	309 (22)
Some college	396 (28)
College graduate	540 (38)
Household income (US$)	
Less than 10,000	77 (5)
10,001–20,000	144 (10)
20,001–40,000	307 (22)
40,001–70,000	365 (26)
70,001–90,000	178 (13)
>90,000	286 (20)
Unknown	62 (4)
Employment status	
Full-time	478 (34)
Part-time	114 (8)
Unemployed	49 (3)
Retired	651 (46)
Disabled, not working	127 (9)
Medical insurance	
Yes	1359 (97)
Marital status	
Married	1110 (78)

is an important end point of this study, we feel that an accurate assessment of pretreatment PRO status is necessary to calculate PRO changes attributable to different treatments. In addition, multiple prior observational studies have demonstrated that patients who undergo radical prostatectomy versus radiation therapy have significantly better pretreatment bowel, urinary and sexual function [3,18]. Thus, an accurate pretreatment PRO assessment without using patient recall will best allow the analytic ability to account for this patient selection bias. Furthermore, enrolling all patients before treatment begins avoids potential biases related to participation based on immediate post-treatment outcomes (i.e., severe treatment morbidity may selectively decrease enrollment). The tradeoff in this analytic design is the exclusion of patients who have started treatment prior to being contacted by study staff. In a recent analysis of Medicare prostate cancer patients, the median time from diagnosis to starting treatment was approximately 3 months [19]. In the NC ProCESS, our ability to contact patients by a median of 5 weeks after diagnosis led to an exclusion of a modest number (19%) of otherwise eligible patients from participation – which was mostly due to initiation of androgen-deprivation therapy. We are not aware of other population-based systems that allow such rapid reporting of cancer cases to enable all patients to enroll before treatment.

The ability of NC ProCESS to accrue a large patient cohort within a short 2.5 years allows this study to provide timely data to inform decision-making in localized prostate cancer. With the continued rapid diffusion of newer treatments in this disease, researchers have a limited window of time to study patient outcomes of newer versus older treatments. In a recent example, IMRT completely replaced the older radiation technology for prostate cancer treatment in just 8 years [5]. Once a new technology achieves wide adoption, it is no longer possible to conduct meaningful CER of this technology. Furthermore, as surgical and radiation treatments continue to evolve, studies that require many years to complete may lose relevance by the time data are reported. In this regard, NC ProCESS and other population-based observational cohorts offer an advantage over randomized trials in examining CER questions. With accrual completed, the investigators expect that NC ProCESS will be able to report PRO data by 2015, providing timely data that can help inform decision-making and policy. Cancer control and survival data are expected after 2018.

Conclusion & future perspective

In summary, there is an urgent need for studies to examine the comparative effectiveness of modern treatment options in localized prostate cancer. This disease impacts a large number of men in the USA; the disease and its treatments can cause significant morbidity, mortality and cost to the patients and the healthcare system. NC ProCESS is a study designed to compare among treatment options the patient outcomes most relevant to stakeholders: PRO, cancer control and survival. This study has important strengths and limitations, but represents a serious attempt at answering the call for CER in localized prostate cancer and addressing current knowledge gaps. Given the importance of this topic and short window of time for research – against a background of rapid diffusion of new technologies – multiple studies of different designs are needed simultaneously in order to provide the necessary data to inform patients, physicians, payers and policy makers regarding the comparative effectiveness of different options for this disease.

Acknowledgements

The authors would like to thank Jane Darter for assistance with this study. They would also like to thank the stakeholders and colleagues at AHRQ (including William Lawrence and Scott Smith) for their input and guidance throughout this study.

Financial & competing interests disclosure

The authors thank the Agency for Healthcare Research & Quality (AHRQ) for funding this study, and the AHRQ Developing Evidence to Inform Decisions about Effectiveness (DEcIDE)

Executive summary

- Comparative effectiveness of modern treatment options for localized prostate cancer is a high-priority research topic.
- The North Carolina Prostate Cancer Comparative Effectiveness and Survivorship Study (NC ProCESS) is a population-based cohort of prostate cancer patients enrolled from throughout North Carolina, USA, before treatment, and followed prospectively.
- Potentially eligible patients were identified using Rapid Case Ascertainment of the North Carolina Central Cancer Registry, and enrolled on average 5 weeks after diagnosis.
- Investigators and stakeholders collaborated to design this study and select outcomes most relevant to stakeholders, including patient-reported outcomes, cancer control and survival.
- Patients enrolled between January 2011 and June 2013 and represent diverse sociodemographic backgrounds.

network. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

References

1 Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J. Clin.* 62, 10–29 (2012).

2 Siegel R, Desantis C, Virgo K *et al.* Cancer treatment and survivorship statistics, 2012. *CA Cancer J. Clin.* 62, 220–241 (2012).

3 Chen RC, Clark JA, Talcott JA. Individualizing quality-of-life outcomes reporting: how localized prostate cancer treatments affect patients with different levels of baseline urinary, bowel, and sexual function. *J. Clin. Oncol.* 27, 3916–3922 (2009).

4 Resnick MJ, Koyama T, Fan KH *et al.* Long-term functional outcomes after treatment for localized prostate cancer. *N. Engl. J. Med.* 368, 436–445 (2013).

5 Sheets NC, Goldin GH, Meyer AM *et al.* Intensity-modulated radiation therapy, proton therapy, or conformal radiation therapy and morbidity and disease control in localized prostate cancer. *JAMA* 307, 1611–1620 (2012).

6 Pearlstein KA, Chen RC. Comparing dosimetric, morbidity, quality of life, and cancer control outcomes after 3D conformal, intensity-modulated, and proton radiation therapy for prostate cancer. *Semin. Radiat. Oncol.* 23, 182–190 (2013).

7 Hu JC, Gu X, Lipsitz SR *et al.* Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA* 302, 1557–1564 (2009).

8 Nguyen PL, Gu X, Lipsitz SR *et al.* Cost implications of the rapid adoption of newer technologies for treating prostate cancer. *J. Clin. Oncol.* 29, 1517–1524 (2011).

9 Institute of Medicine. *Initial National Priorities for Comparative Effectiveness Research.* The National Academies Press, Washington, DC, USA (2009).

10 Greenberg C, Wind J, Chang G *et al.* Stakeholder engagement for comparative effectiveness research in cancer care: experience of the DEcIDE Cancer Consortium. *J. Comp. Eff. Res.* 2(2), 117–125 (2013).

11 Clark JA, Talcott JA. Symptom indexes to assess outcomes of treatment for early prostate cancer. *Med. Care* 39, 1118–1130 (2001).

12 Roth AJ, Rosenfeld B, Kornblith AB *et al.* The memorial anxiety scale for prostate cancer: validation of a new scale to measure anxiety in men with prostate cancer. *Cancer* 97, 2910–2918 (2003).

13 Wilt TJ. The Prostate Cancer Intervention Versus Observation Trial: VA/NCI/AHRQ Cooperative Studies Program #407 (PIVOT): design and baseline results of a randomized controlled trial comparing radical prostatectomy with watchful waiting for men with clinically localized prostate cancer. *J. Natl Cancer Inst. Monogr.* 2012(45), 184–190 (2012).

14 Wilt TJ, Brawer MK, Jones KM *et al.* Radical prostatectomy versus observation for localized prostate cancer. *N. Engl. J. Med.* 367, 203–213 (2012).

15 Lane JA, Donovan JL, Davis M *et al.* Active monitoring, radical prostatectomy, or radiotherapy for localized prostate cancer: study design and diagnostic and baseline results of the ProtecT randomised Phase 3 trial. *Lancet Oncol.* 15(10), 1109–1118 (2014).

16 Concato J. Is it time for medicine-based evidence? *JAMA* 307, 1641–1643 (2012).

17 Potosky AL, Harlan LC, Stanford JL *et al.* Prostate cancer practice patterns and quality of life: the Prostate Cancer Outcomes Study. *J. Natl Cancer Inst.* 91, 1719–1724 (1999).

18 Sanda MG, Dunn RL, Michalski J *et al.* Quality of life and satisfaction with outcome among prostate-cancer survivors. *N. Engl. J. Med.* 358, 1250–1261 (2008).

19 Stokes WA, Hendrix LH, Royce TJ *et al.* Racial differences in time from prostate cancer diagnosis to treatment initiation: a population-based study. *Cancer* 119, 2486–2493 (2013).