ARTICLE TITLE: Expectant Management for Men With Early Stage Prostate Cancer

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EDUCATIONAL OBJECTIVES:
After reading the article “Expectant Management for Men With Early Stage Prostate Cancer” the learner should be able to:
1. Discuss current and evolving strategies for the expectant management of early stage prostate cancer, and;
2. Identify appropriate candidates for expectant management as well as those men for whom this approach is not recommended.

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Expectant Management for Men With Early Stage Prostate Cancer

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Since the dissemination of prostate-specific antigen screening, most men with prostate cancer are now diagnosed with localized, low-risk prostate cancer that is unlikely to be lethal. Nevertheless, nearly all of these men undergo primary treatment with surgery or radiation, placing them at risk for longstanding side effects, including erectile dysfunction and impaired urinary function. Active surveillance and other observational strategies (ie, expectant management) have produced excellent long-term disease-specific survival and minimal morbidity for men with prostate cancer. Despite this, expectant management remains underused for men with localized prostate cancer. In this review, various approaches to the expectant management of men with prostate cancer are summarized, including watchful waiting and active surveillance strategies. Contemporary cancer-specific and health care quality-of-life outcomes are described for each of these approaches. Finally, contemporary patterns of use, potential disparities in care, and ongoing research and controversies surrounding expectant management of men with localized prostate cancer are discussed. CA Cancer J Clin 2015;65:264-282. © 2015 American Cancer Society.

Keywords: prostate cancer, expectant management, active surveillance, watchful waiting

Introduction

Over the past 2 decades, broad use of prostate-specific antigen (PSA)-based screening has resulted in a marked shift in the clinical stage of men diagnosed with prostate cancer. Many prostate tumors currently being diagnosed are localized, small, early stage, indolent, and of minimal risk to the affected men.1-3 Despite this, a substantial majority of men with low-risk prostate cancer undergo aggressive whole-gland treatment with either surgery or radiation.4

In that context, substantial overdiagnosis and overtreatment of men with prostate cancer in the United States is recognized; as many as 40% of prostate cancer patients may currently be overtreated.5 Autopsy studies have demonstrated that a majority of men who die from other causes are likely to harbor indolent prostate tumors,6,7 and nearly half of men who undergo radical cystoprostatectomy for bladder cancer have previously unsuspected prostate tumors identified upon histologic analysis.8,9 Furthermore, the European Randomized Study of Screening for Prostate Cancer indicated that, to prevent one prostate cancer death at 9 years, the number need to screen was 1254, whereas the number needed to treat was 43.10 Based on models generated from observational data, others have estimated that nearly 100 low-risk patients would have to undergo treatment to save one life.11 In addition, health-related quality of life (HRQOL) may be affected. Even in experienced hands, primary treatment for prostate cancer carries a marked—albeit variable—risk of urinary, sexual, and bowel dysfunction that can persist lifelong.12 Based on these and other results, in 2012, the US Preventive Services Task Force emphasized the “inevitability of...overtreatment” as motivation for its grade D recommendation against PSA-based screening.13

Thus, reducing unnecessary treatment of men with low-risk prostate cancer has become an important priority, because it would decrease treatment-related adverse events and help focus resources on those most likely to benefit.
Surveillance strategies (ie, expectant management) have emerged and are increasingly recommended for patients who are unlikely to benefit from immediate treatment. *Expectant management* is a term that encompasses all approaches that defer or avoid treatment via surveillance after a diagnosis of prostate cancer. Expectant management is separated into *watchful waiting* and *active surveillance* (Fig. 1). Watchful waiting protocols are monitoring programs that do not involve aggressive testing or intervention but, instead, await the symptomatic evidence of progressive disease before further clinical evaluation. These approaches are palliative in nature and focus on managing pain or urinary difficulty (eg, urinary retention or hematuria) in the setting of progressive disease. Watchful waiting is usually used for very elderly individuals or those with multiple comorbidities who are unlikely to benefit from curative treatment, and any treatment offered is only focused on palliation of symptoms. Conversely, active surveillance protocols aim to maintain the opportunity of curing more aggressive disease via structured monitoring (eg, with PSA testing and repeat prostate biopsies), which attempts to identify any change in disease risk (eg, an increase in Gleason score) that would merit definitive treatment. In this review, various approaches to the expectant management of men with prostate cancer are summarized, including contemporary patterns of use, potential disparities in care, and ongoing research and controversies.

**Watchful Waiting: Expectant Management With Palliative Intent**

The inconsistent survival benefit associated with primary treatment of men with low-risk prostate cancer has been long recognized, as has the impact on health-related quality of life associated with radical prostatectomy or pelvic radiation therapy.¹⁴ Even in the pre-PSA era, most expectant management strategies focused on avoiding treatment of older, sicker individuals diagnosed with prostate tumors that were less likely to be lethal than their underlying comorbid illnesses. Watchful waiting strategies traditionally involved deferring intervention until symptomatic progression was evident from signs and symptoms of urinary obstruction or metastatic disease, at which point palliative interventions would be initiated.¹⁵,¹⁶

Men with minimally aggressive prostate cancer who are managed with watchful waiting—particularly those older than age 65 years—have a much greater likelihood of dying from something other than prostate cancer.¹⁷ One of the seminal clinical trials of the pre-PSA screening era was the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) trial, which randomized men to either radical prostatectomy or watchful waiting.¹⁵ Although early results suggested that surgery was associated with improved cancer-specific survival and decreased risk of metastasis,¹⁵,¹⁸ more mature outcomes showed that these benefits were not evident among men older than 65 years; this supported the notion that older patients may best be managed expectantly.¹⁹

The results of the SPCG-4 study were mirrored by the Prostate Cancer Intervention Versus Observation Trial (PIVOT), which randomized Veterans Affairs patients with localized prostate cancer to either radical prostatectomy or watchful waiting.¹⁶ The results of the trial suggested that survival benefits of aggressive treatment for men with prostate cancer were limited to those with a PSA greater than 10 ng/mL and/or those with higher risk prostate tumors. Notably, only 8% of men randomized to observation (and only 6% of low-risk patients) died of prostate cancer after 15 years of follow-up.¹⁶ It is important to acknowledge that the majority of men in PIVOT were diagnosed with nonpalpable tumors through PSA screening.¹⁶ This is in contrast to the SPCG-4 trial, in which 95% of men had clinically palpable tumors.
detected, palpable tumors, which would exclude many of these individuals from contemporary active surveillance protocols. Recent data have demonstrated that Medicare-eligible prostate cancer patients with significant comorbidity are much more likely to die from noncancer-related causes than from prostate cancer.

**Active Surveillance: Expectant Management With Curative Intent**

In the PSA screening era, it is estimated that as many as 4 in 10 men are overdiagnosed with—and often are over treated for—nonlethal prostate tumors. Although watchful waiting strategies for older men and for those with limited life expectancy appear appropriate, young and healthy patients may require more intense surveillance to ensure accurate risk classification of their disease. On the one hand, men undergoing radical prostatectomy who have low-risk tumors identified pathologically have a less than 1% chance of subsequent prostate cancer-specific mortality. Conversely, up to 33% of men initially classified with low-risk tumors are upstaged or upgraded to intermediate-risk or high-risk disease at radical prostatectomy, exposing them to a considerably higher risk of prostate cancer-specific mortality. These findings suggest the presence of a subset of men who are misclassified with low-risk prostate cancer at the time of their initial prostate biopsy but who will ultimately demonstrate more aggressive disease.

Thus, monitoring strategies (ie, active surveillance) were proposed that would maintain curative intent in patients who subsequently had higher risk disease identified. In contrast to the older, sicker patients who typically are advised to pursue watchful waiting protocols, active surveillance focuses on younger, healthier patients interested in deferring or avoiding the potential negative consequences of primary treatment with surgery or radiation. Active surveillance protocols rely on 4 key principles: 1) patient selection based on cancer risk and life expectancy, 2) confirmation of the initial risk classification, 3) monitoring for the appearance of advancing disease, and 4) treatment reconsideration if an increased cancer risk is identified. Two of the first active surveillance programs were established at the University of Toronto and Johns Hopkins University in the mid-1990s, and the initial results from both studies demonstrated promising cancer-specific survival with minimal morbidity. Recently updated results from the Toronto study (with follow-up as far out as 20 years) indicated that only 1.5% of the cohort of nearly 1000 patients died from prostate cancer, with a 9.2-fold greater hazard from other-cause mortality over that interval. The outcomes from multiple other active surveillance programs have confirmed the feasibility of such strategies for men with low-risk, clinically localized prostate cancer (Table 1).

Recognizing this, researchers in the United Kingdom initiated the Prostate Testing for Cancer and Treatment (ProtecT) study in 2001, which randomized over 1600 prostate cancer patients to either active surveillance or definitive treatment. Initial results, which are due to be reported in 2016, should help clarify the potential benefits of surveillance among a more contemporary cohort of prostate cancer patients.

**Selection of Appropriate Candidates for Active Surveillance**

The selection of appropriate candidates for expectant management of prostate cancer depends on accurate identification of those who will not suffer the negative consequences of their disease (ie, symptomatic local progression, metastatic disease, cancer-specific mortality) before either death from other causes or the timely recognition of higher risk disease that is still amenable to treatment. Thus, the proper use of expectant management hinges upon 2 important variables. First, the metastatic and lethal potential of the prostate tumor must be precisely stratified using extant clinical and pathologic information. Second, an accurate assessment of a patient’s life expectancy must be estimated to calculate the length of time he would be exposed to the risk of metastasis or cancer-specific mortality.

Before the broad adoption of PSA as a screening test, risk stratification for men diagnosed with prostate cancer was based solely on biopsy findings (ie, Gleason score) and clinical staging. The Gleason grading system, initially established in the 1960s and modified in 2005, has been shown to predict biochemical free survival after radical prostatectomy. Clinical staging of prostate cancer—based on digital rectal examination—is less reliable in predicting pathologic stage and risk of biochemical progression after treatment.

A paradigm shift in risk stratification rapidly evolved after the US Food and Drug Administration (FDA) approved PSA testing for the early detection of prostate cancer in 1994. Some have demonstrated an association between higher PSA levels and prostate tumor burden, pathologic stage at radical prostatectomy, and cancer-specific outcomes. However, others have countered that, over time, the preoperative PSA level (as a stand-alone test) has become less predictive of pathologic stage and tumor burden. Addressing other factors, Epstein et al established one of the first sets of criteria to predict pathologically insignificant cancer at radical prostatectomy (defined as Gleason score <7, clinical pathologic tumor [pT] classification <pT3, and tumor volume <0.2 cc). Other predictive nomograms and calculators (eg, Partin tables) incorporate clinical stage, PSA at diagnosis, and pathologic findings at biopsy to estimate cancer-specific outcomes after treatment.
Based on the results of these models, schemes were developed that stratify patients with prostate cancer into discrete risk groups (Table 2). The most broadly adopted system of prostate-cancer risk stratification was developed by D’Amico et al, in which clinical stage, PSA, and Gleason grade are used to classify men at low risk, intermediate risk, or high risk of biochemical failure (ie, rising PSA levels) after treatment.62 In general, classification systems endorsed by other organizations (eg, the American Urological Association and the European Association of Urology) have paralleled the framework described by D’Amico et al.63,64 The National Comprehensive Cancer Network (NCCN) supplemented existing risk-stratification systems by describing a very-low-risk category of prostate cancer patients starting in 2010 (ie, nonpalpable disease, PSA <10 ng/mL, Gleason score <7, and fewer than 3 biopsy cores positive with <50% involvement of any core).65 More recently, researchers at the University of California, San Francisco, leveraged data from the multicenter Cancer of the Prostate Strategic Urologic Research Endeavor registry to create the Cancer of the Prostate Risk Assessment (CAPRA) classification system. The CAPRA system includes patient age at diagnosis and the proportion of positive biopsy cores to assign a score from 1 to 10, in which scores from 0 to 2 indicate low risk, scores from 3 to 5 indicate intermediate risk, and scores from 6 to 10 indicate high risk.66

### TABLE 1. Clinical Outcomes Related to Existing Active Surveillance Protocols

| INSTITUTION OR SETTING (REFERENCE) | NO. | MEDIAN FOLLOW-UP, MO | TREATMENT-FREE SURVIVAL RATE: 5-YEAR UNLESS SPECIFIED OTHERWISE, % | DEVELOPMENT OF METASTATIC DISEASE, % | CANCER-SPECIFIC MORTALITY, % | ALL-CAUSE MORTALITY, % |
|----------------------------------|-----|----------------------|-------------------------------------------------|----------------------------------|-----------------------------|-------------------------|
| University of Toronto (Klotz 201527) | 993 | 77 | 76 | 1.3 | 1.5 | 15 |
| Johns Hopkins (Tosoian 201128) | 769 | 32 | 59 | 0 | 0 | 2 |
| ERSPC, Goteborg (Godtman 201329) | 439 | 70 | 61 | 0.4 | <1 | 19 |
| ERSPC, Rotterdam/Helsinki (Bul 201230) | 509 | 89 | Low risk, 50% at 10 y | Low risk, 0.1; Int risk, 2 | Low risk, 1; Int risk, 16 | Low risk, 19; Int risk, 30 |
| Cleveland Clinic (Milocicovic 201131) | 89 | 33 | 87% at 3 y |
| Memorial Sloan-Kettering Cancer Center (Adamy 201132) | 238 | 23 | |
| University of Miami (Soloway 2008, 201033,34) | 230 | 32 | 86 | 0 | 0 | 2 |
| PRIAS (Bul 201335) | 2494 | 19 | 68% at 4 y | <0.1 | 0 | <1 |
| Southern Health (Ischia 201236) | 154 | 23 | 62 |
| University of Copenhagen (Thomsen 201337) | 167 | 41 | 60 |
| UCSF (Dall’Era 2008,38 Welty 201539) | 810 | 60 | 60 | 0.1 | 0 | 2 |
| Royal Marsden Hospital (Selvadurai 201340) | 471 | 68 | 70 | <1 | 4 |
| McGill University (Barayan 201441) | 155 | 65 | 80 | 0 | 0 |
| Hospital Universitario Fundación de Alcorcón (Hernández 201342) | 144 | 38 | 71 | 0 | 0 |
| KSA (Becker 201443) | 387 | 36 | 75% at 2 y |
| Dalhousie University (Matthew Andrews 201444) | 86 | 62 | 62 | 0 | 0 | 5 |
| Keimyung University (Ha 201445) | 35 | 32 | |

Abbreviations: ERSPC, European Randomized Study of Screening for Prostate Cancer; Int risk, intermediate risk; KSA, Canton Hospital Aarau; Int risk, intermediate risk; PRIAS, the Prostate Cancer Research International Active Surveillance registry; UCSF, University of California, San Francisco. aThese were among the patients who were free from progression or reclassification. bThis was the mean follow-up.
divided by prostate volume), rather than PSA level, as a criterion for enrollment.\textsuperscript{28,43,71} It has been demonstrated that PSA density is a particularly important inclusion criterion; results from the Johns Hopkins active surveillance cohort indicated that raising the threshold from 0.15 to 0.175 ng/mL/cc considerably raised the risk for adverse pathology (eg, nonorgan-confined disease and/or Gleason score \textsuperscript{72} \textsuperscript{7} or Gleason score \textsuperscript{7} \textsuperscript{2}–\textsuperscript{10} or \textsuperscript{7} \textsuperscript{10}–20 ng/mL) at radical prostatectomy.\textsuperscript{72} Although some protocols accept certain patients with Gleason 3+4 prostate cancer,\textsuperscript{27,40} most accept men whose tumors are no higher than Gleason 3+3. As a surrogate of tumor volume, the percentage of core involvement (<50%) or the number of positive cores (<2 or 3) is commonly reported; however, the length of involvement in millimeters (cancer core length) appears to be a more discrete surrogate of tumor volume than either the percentage or numbers of cores involved.\textsuperscript{73}

The survival benefits of treatment for men with prostate cancer are not realized for many years.\textsuperscript{19} Thus, life expectancy is an important factor when considering primary treatment, particularly for men diagnosed with low-risk tumors. For instance, both the American Urological Association and the NCCN have issued guidelines for the management of prostate cancer patients that stress the importance of assessing life expectancy during the decision-making process.\textsuperscript{63,74} The NCCN guidelines recommend using the Social Security Administration actuarial life tables (ssa.gov/oact/STATS/table4c6.html; accessed April 6, 2015),\textsuperscript{75} which incorporate age and gender to predict subsequent life expectancy with adjustments for medical comorbidity, based on a physician’s assessment of overall health.\textsuperscript{74} For example, a typical healthy man aged 65 years would have an approximately 18-year life expectancy. If the same individual were thought to be in the bottom quartile of overall health, then that estimate would drop to 9 years. An important caveat to this approach is that these data are from the general population and may not accurately characterize prostate cancer patients.\textsuperscript{26} There are

| TABLE 2. Risk-Stratification Systems for Men Diagnosed With Prostate Cancer |
|----------------------------------|----------------|----------------|----------------|
| **RISK-STRATIFICATION SYSTEM**   | **LOW RISK**   | **INTERMEDIATE RISK** | **HIGH RISK** |
| Epstein criteria                 | Very low risk  | Stage T1c       | Stage ≥3a       |
|                                  |                | Gleason score ≤6 | Stage ≥3a       |
|                                  |                | PSA <10 ng/mL    | Stage ≥3a       |
|                                  |                | ≤2 Positive biopsy cores | Stage ≥3a     |
|                                  |                | ≤50% Cancer in each core | Stage ≥3a     |
|                                  |                | PSA density <0.15 ng/mL/g | Stage ≥3a     |
| D’Amico criteria/EAU guidelines  | Stage T1-T2a   | Stage T2b-T2c or | Stage ≥3a       |
|                                  | Gleason score ≤6 | Gleason score 7 or | Stage ≥3a       |
|                                  | PSA <10 ng/mL  | PSA 10–20 ng/mL  | Stage ≥3a       |
| AUA guidelines                  | Stage T1-T2a   | Stage T2b or     | Stage ≥2c       |
|                                  | Gleason score ≤6 | Gleason score 7 or | Stage ≥2c       |
|                                  | PSA <10 ng/mL  | PSA 10–20 ng/mL  | Stage ≥2c       |
| CAPRA                            | CAPRA score ≤2 | CAPRA score 3–5  | CAPRA score ≥6  |

| **LOW-RISK**                     | **HIGH-RISK**  |
|----------------------------------|----------------|
| **RISK-STRATIFICATION SYSTEM**   | **VERY LOW RISK** | **LOW RISK** | **INTERMEDIATE RISK** | **HIGH RISK** | **VERY HIGH RISK** |
| NCCN guidelines                 | Stage T1c       | Stage T1-T2a   | Stage T2b-T2c or | Stage T3a or | Stage T3b-T4 or |
|                                  | Gleason score ≤6 | Gleason score ≤6 | Stage T3a or | Stage T3b-T4 or |
|                                  | PSA <10 ng/mL  | PSA <10 ng/mL  | Stage T3a or | Stage T3b-T4 or |
|                                  | ≤2 Positive biopsy cores | PSA <10 ng/mL | Stage T3a or | Stage T3b-T4 or |
|                                  | PSA density <0.15 ng/mL/g | PSA >20 ng/mL | Stage ≥3a or | Stage ≥3a or |

Abbreviations: AUA, American Urological Society; CAPRA, Cancer of the Prostate Risk Assessment; EAU, European Association of Urology; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen.
Expectant Management of Men With Prostate Cancer

As of the 2015 National Comprehensive Cancer Network (NCCN) guidelines, overall expectations of patients with advanced-stage prostate cancer have improved, largely due to lower treatment side effects. However, for those with localized prostate cancer, the NCCN guidelines incorporate overall survival (OS) and prostate-specific antigen (PSA) treatment-free survival (TFS) to determine the most appropriate treatment. 

PSA screening in men older than 50 years is recommended by the American Cancer Society (ACS), and screening is increasingly being used in men younger than 50 years of age. However, PSA screening is associated with several limitations, including time bias associated with PSA screening.80

PSA-era mortality rates from patients who were diagnosed in the pre-PSA era and, hence, may not accurately adjust for the leadtime bias associated with PSA screening.80

Expectancy: only 66% of physicians are able to accurately predict which patients live more or less than 10 years.81

Thus, 5-year and 10-year estimates of the competing risk from other-cause mortality, specific to prostate cancer patients, have been generated.20,82 For instance, Albertsen et al demonstrated that men who were 1) younger than 75 years of age, 2) diagnosed with one comorbid condition, and 3) diagnosed with a low-risk prostate cancer had a 25-fold higher rate of overall mortality compared with their rate of cancer-specific death.82 Furthermore, Daskivich et al also demonstrated that the risk of cancer-specific mortality for prostate cancer patients with 2 or more comorbid conditions was significantly exceeded by other-cause mortality.20

Monitoring Strategies to Identify Increased Cancer Risk and Criteria for Discontinuing Active Surveillance

Although the NCCN guidelines incorporate overall health status into assessments of life expectancy, the recommendation relies on a subjective assessment by the physician at the time of diagnosis. Providers who care for prostate cancer patients are typically poor assessors of life expectancy: only 66% of physicians are able to accurately predict which patients live more or less than 10 years.81

### TABLE 3. Inclusion Criteria for Existing Active Surveillance Protocols

| INSTITUTION OR SETTING (REFERENCE) | CLINICAL STAGE | PSA, ng/mL | PSA DENSITY, ng/mL/cc | GLEASON SCORE | NO. OR % POSITIVE CORES | % INVOLVEMENT OF SINGLE CORE |
|-----------------------------------|----------------|------------|------------------------|---------------|------------------------|-----------------------------|
| University of Toronto (Klotz 201527) | Age <70 y, ≤10; age ≥70 y, ≤15 | Age <70 y, ≤3 + 3 = 6; age ≥70 y, ≤3 + 4 = 7 | ≤0.2 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| Johns Hopkins (Tosoian 201158) | T1c | ≤0.15 | ≤3 + 3 = 6 | ≤2 Cores | 50% |
| ERSPC, Goteborg (Godman 201359) | T1c-T2 | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| ERSPC, Rotterdam/Helsinki (Bul 201260) | T1c-T2 | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| Cleveland Clinic (Mocinovic 201161) | T1-T2 | ≤3 + 3 = 6 | "Limited cancer burden" | "Limited cancer burden" | ≤50 |
| Memorial Sloan-Kettering Cancer Center (Adamy 201162) | T1-T2a | ≤10 | ≤3 + 3 = 6 | ≤3 Cores | ≤50 |
| University of Miami (Soloway 2008, 201063,64) | T1-T2a | ≤10 | ≤3 + 3 = 6 | ≤3 Cores | ≤50 |
| PRIAS (Bul 201365) | T1c-T2 | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| University of Copenhagen (Thomsen 201366) | T1-T2a | ≤10 | ≤3 + 3 = 6 | ≤3 Cores | ≤50 |
| UCSF (Dall’Era 2008, Welty 201567) | T1-T2a | ≤10 | ≤3 + 3 = 6 | ≤3 Cores | ≤50 |
| Royal Marsden Hospital (Selvidurai 201368) | T1-T2 | ≤15 | Age <65 y, ≤3 + 3 = 6; age ≥65 y, ≤3 + 4 = 7 | ≤50% |
| McGill University (Barayan 201469) | T1-T2 | ≤3 + 4 = 7 | ≤2 Cores | ≤50 |
| Hospital Universitario Fundación de Alcorcón (Hernández 201370) | T1c-T2a | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| KSA (Becker 201471) | T1c | ≤0.15 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| Dalhousie University (Matthew Andrews 201472) | T1-T2a | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |
| Keimyung University (Ha 201473) | T1 | ≤10 | ≤3 + 3 = 6 | ≤2 Cores | ≤50 |

Abbreviations: ERSPC, European Randomized Study of Screening for Prostate Cancer; GS, Gleason score; KSA, Canton Hospital Aarau; PRIAS, the Prostate Cancer Research International Active Surveillance registry; PSA, prostate-specific antigen; UCSF, University of California, San Francisco.
examinations to identify disease that is more aggressive than originally observed (Table 4). All of the published protocols use various combinations of pathologic and clinical changes as triggers for treatment of patients enrolled in active surveillance (Table 5).

Arguably, the most important aspect of any active surveillance protocol is a timely repeat biopsy after diagnosis. Findings on repeat prostate biopsy that would merit consideration of primary treatment of a man on active surveillance include upgrading of Gleason score, increase in the number of positive cores, and changes in tumor involvement of the cores. In general, most protocols recommend a repeat prostate biopsy within 12 months of diagnosis to confirm that an active surveillance candidate does not harbor more aggressive disease than initially diagnosed. Some have argued that the repeat biopsy should be within 3 to 6 months of diagnosis, because nearly 25% of patients who undergo an immediate repeat biopsy are upgraded/upstaged to more aggressive disease, usually based on an increase in Gleason score. Results from the existing active surveillance protocols also report similar proportions of patients who had a higher Gleason score or larger tumor burden at the time of the first repeated biopsy after diagnosis. Importantly, of the components typically included in active surveillance, findings at repeat biopsy may be the strongest indicator of adverse findings at radical prostatectomy.

Various active surveillance strategies incorporate PSA kinetics (changes in PSA over time) as a benchmark for reclassification while on active surveillance to signal a recommendation for treatment or repeat biopsy. These include a PSA doubling time (ie, the time required for PSA to increase 2-fold) of 3 years and a PSA velocity (ie, the rate of PSA increase over time) from 0.75 to 1.00 ng/mL per year. The evidence for a strong association between PSA kinetics and adverse outcomes for men on active surveillance is limited. Prostate cancer patients historically managed with watchful waiting had a higher risk of cancer-specific mortality when their PSA doubling time was less than 3 years. Furthermore, for men on active surveillance, data from the European Randomized Study of Screening for Prostate Cancer suggest that those with a PSA doubling time less than 4 years have a higher risk of biochemical recurrence after delayed treatment. Conversely, the PSA doubling time has not been associated with the likelihood of reclassification while on surveillance nor with upstaging after radical prostatectomy. In addition, PSA velocity only marginally improves the ability to predict adverse outcomes for patients on active surveillance over simply using the PSA level at entry.

**TABLE 4. Monitoring Protocols**

| INSTITUTION OR SETTING (REFERENCE) | INTERVAL BETWEEN DRE/PSA, MO | TIMING OF CONFIRMATORY BIOPSY AFTER DIAGNOSTIC BIOPSY, MO | INTERVAL BETWEEN SUBSEQUENT BIOPSIES, Y |
|-----------------------------------|-----------------------------|----------------------------------------------------------|---------------------------------------|
| University of Toronto (Klotz 201527) | 3 (Years 1–2) then 6 | 6–12 | 3–4 |
| Johns Hopkins (Tosoian 201128) | 6 | 12 | 1 |
| ERSPC, Goteborg (Godtman 201329) | Discretionary | Discretionary | Discretionary |
| ERSPC, Rotterdam/Helsinki (Bul 201230) | Discretionary | Discretionary | Discretionary |
| Cleveland Clinic (Micocovic 201131) | 6–12 | 12 | 1–2 |
| Memorial Sloan-Kettering Cancer Center (Adamy 201132) | 6 | 6 | 1–3 |
| University of Miami (Soloway 2008, 201033,34) | 3–4 (Year 1–2), then 6 | 9–12 | 1 |
| PRIAS (Bul 201335) | 3 (Year 1–2), then 6 | 12 | 3 |
| Southern Health (Ischia 201236) | 3–6 | 12–18 | 3 |
| University of Copenhagen (Thomsen 201337) | 3 | 15 |
| UCSF (Dall’Era 2008, Welty 201538) | 3 | 12 | 1–2 |
| Royal Marsden Hospital (Selvadurai 201339) | 3–4 (Year 1–2), then 6 | 18–24 | 2 |
| McGill University (Barayan 201440) | 3–6 | 12–18 | 1–3 |
| Hospital Universitario Fundación de Alcorcón (Hernández 201341) | 6 | Immediatea | 1–3 |
| KSA (Becker 201442) | 6 | 12 | 1 |
| Dalhousie University (Matthew Andrews 201443) | 3–6 | 12–18 | 1–4 |
| Keimyung University (Ha 201444) | 3–6 | 12 | 3 |

Abbreviations: DRE, digital rectal examination; ERSPC, European Randomized Study of Screening for Prostate Cancer; KSA, Canton Hospital Aarau; PRIAS, the Prostate Cancer Research International Active Surveillance registry; PSA, prostate-specific antigen; UCSF, University of California, San Francisco. aPatients with PSA doubling times of 3 to 10 years underwent annual biopsy. bConfirmatory biopsy was immediate if a patient had <12 cores on diagnostic biopsy.
Changes in clinical stage noted on digital rectal examination are also used in some active surveillance protocols as a sign of disease progression. However, few published reports describe rates of progression noted on prostate palpation, and an increase in clinical stage has not been correlated with findings at delayed radical prostatectomy.90

Clinical Outcomes of Active Surveillance Protocols

In order for active surveillance to be considered a reasonable alternative to immediate treatment for men with localized prostate cancer, the benefits of such an approach (eg, avoiding side effects of primary treatment) must outweigh the risks from the surveillance itself. Key outcomes of interest related to active surveillance include treatment-free survival, cancer-specific mortality, overall mortality, and HRQOL.91

Treatment-free survival

Table 1 summarizes outcomes related to treatment-free survival across the major published active surveillance series. Although criteria for progression or reclassification varied between individual protocols, approximately 25% to 33% of men enrolled in active surveillance went on to receive delayed treatment of their prostate cancer at a median time to treatment of 1.3 to 3.5 years.92 In general, across most available studies, the 5-year treatment-free survival rate was 60% to 80%, and it dropped to about 50% after 10 years (Table 1). In general, treatment was initiated for clinical progression or pathologic reclassification for about 3 of every 4 patients on active surveillance who received delayed prostatectomy or radiation. The other men on active surveillance who received delayed treatment did so under their own volition, usually because of reasons like anxiety related to surveillance or concerns related to repeat biopsies.27,28,39

Clinical outcomes of delayed intervention with radiation or surgery

Data from the population-based Health Professionals Follow-Up Study showed similar prostate cancer-specific mortality and incidence of metastatic disease among patients undergoing deferred prostate cancer treatment (median, 3.9 years) compared with those undergoing...
immediate treatment. 93 Multiple cohort studies have not demonstrated a higher risk of Gleason score upgrading, extraprostatic disease, or positive margins for men on active surveillance compared with men undergoing immediate radical prostatectomy. 90,94 Prostate cancer patients who qualify for active surveillance assume little, if any, risk of missing an opportunity for cancer control after undergoing delayed treatment.

Metastatic disease and mortality
Across all of the studies of interest, metastatic disease was exceedingly rare among active surveillance protocols that reported this outcome. Furthermore, all-cause and other-cause mortality either were comparable to or far exceeded cancer-specific mortality among low-risk patients on active surveillance. Table 1 summarizes these outcomes across studies.

HRQOL and anxiety
A concern for HRQOL is a major force supporting active surveillance. The potentially deleterious impact of radical prostatectomy and radiation therapy on HRQOL has been documented both in prospective observational studies and in large, multi-institutional registries of prostate cancer patients. 12,95

Compared with those who undergo radical prostatectomy, prostate cancer patients managed with watchful waiting have superior erectile function and urinary control in the initial 2 to 5 years after diagnosis. 16,96 However, bowel function, depression/anxiety, and overall HRQOL do not differ at 5 years. 96 Furthermore, men managed with observation tend to have increased anxiety and depression over time. 96 After longer follow-up, urinary incontinence outcomes still were inferior among patients in a radical prostatectomy group (41%) compared with a watchful waiting group (11%) and a population-based control group (3%). However, the differences between radical prostatectomy and watchful waiting patients in erectile dysfunction (84% vs 80%) were attenuated, and both groups had substantially worse sexual function than men in the general population (46%) (which is likely related to the prevalent use of androgen-deprivation therapy and its associated impact on sexual function among the cohort of men with prostate cancer). 97

Thus, even in the absence of surgery or radiation, watchful waiting is associated with detrimental effects on HRQOL beyond the effects of advancing age. Similar findings were noted in a cohort of US veterans who deferred treatment for clinically localized prostate cancer; men reported significant decreases in urinary control and symptoms and sleep patterns for at least a year after diagnosis. 98 What remains unclear is the degree to which these changes were because of psychosocial effects related to the threat of progressive disease or direct physiologic effects from the disease itself.

Also unclear is whether active surveillance and watchful waiting have a similar impact on the mental and physical health of men with prostate cancer. HRQOL may be worse for men who are managed with intense surveillance strategies, in part because of the additional and frequent reevaluations with PSA testing and prostate biopsies that are central to active surveillance. Two subsets of men in the Prostate Cancer Research International Active Surveillance study reported no significant worsening in HRQOL, erectile function, or urinary control over the first 9 to 12 months on active surveillance. 99,100 Furthermore, it is unclear whether repeat prostate biopsies induce erectile dysfunction over time. One cross-sectional study of active surveillance patients reported a significant association between erectile dysfunction and the number of biopsies performed. 101

However, a more recent longitudinal study that accounted for changes over time demonstrated that men experience marginal decreases in International Index of Erectile Function scores and increases in phosphodiesterase-5 inhibitor use for up to 4 years on active surveillance, changes that were independent of the number of biopsies performed. 102 There is also some concern that repeated prostate biopsies can impact erectile function in active surveillance patients who undergo delayed radical prostatectomy. One small retrospective cohort study demonstrated a greater prevalence of erectile dysfunction at 6 months after radical prostatectomy among men who had undergone multiple prior prostate biopsies. 103 Ultimately, population-based data across longer intervals will help clarify concerns regarding changes in erectile function among patients with prostate cancer who are managed with active surveillance.

Few studies have examined the long-term impact of active surveillance on the HRQOL and mental health of men with prostate cancer. However, other studies assessed the short-term impact of active surveillance on HRQOL and demonstrated improved HRQOL scores among patients on active surveillance compared with population-based control groups and patients who underwent radical prostatectomy; some ascribe this to baseline differences in the type of men who pursue expectant management of their cancer. 100,104-107 Furthermore, based on the mental health index of the Medical Outcomes Study 36-item Short-Form Health Survey, active surveillance patients appear to enjoy generally good mental health 106,108 and do not suffer major, short-term, negative effects. 100,109 Less than 10% of active surveillance patients elect to pursue deferred treatment because of anxiety (in the absence of risk reclassification). 110,111

Concerns have been raised that depression and anxiety may have a negative impact on HRQOL for men on active surveillance. Men with a claims-based diagnosis of depression are more likely to pursue expectant management over primary treatment of their prostate cancer. 112
However, overall, depression is uncommon among patients on active surveillance, and the development of worsening depressive symptoms is rare in this group. Others have confirmed the observation that general and disease-specific anxiety measurements are comparable to those observed in men who undergo radical prostatectomy. Burnet et al reported that baseline anxiety scores were inversely related to age at enrollment. They also reported higher anxiety scores among men who had been followed for a longer interval.  

### Contemporary Use of Active Surveillance

For the most part, reports of active surveillance have been limited to individual institutions and small multi-institutional cohorts. Population-based studies of expectant management use for men with prostate cancer do not differentiate between watchful waiting and active surveillance. The Cancer of the Prostate Strategic Urologic Research Endeavor registry indicated that 9 in 10 men diagnosed with low-risk prostate cancer from 1990 through 2007 underwent primary treatment, with no notable increases in the use of expectant management over time. However, more recent reports examining data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and the American College of Surgeons' National Cancer Database indicate that the proportion of men receiving noncurative initial management of low-risk prostate cancer increased 20% to 30% during 2008 to 2010. Indeed, medical record abstraction of nearly 700 men with low-risk prostate cancer who were treated in Michigan showed that nearly half were initially managed with active surveillance. Nevertheless, it remains unclear what proportion of those on active surveillance actually receive guideline-based monitoring (ie, serial PSA testing and repeat prostate biopsy). Among the Michigan cohort, only 33% underwent a repeat prostate biopsy after diagnosis. Furthermore, a population-based study used linked Surveillance, Epidemiology, and End Results-Medicare data to demonstrate that the use of repeated prostate biopsy among patients with prostate cancer ranged from 2% to 30% across health care markets. Thus, active surveillance, which was not used often in the past, now appears to be increasingly selected as a management strategy.

### Factors Related to Adoption and Potential Disparities in Use

In general, cancer control is the most important priority for patients with prostate cancer who are making a decision regarding treatment, particularly among younger men. Fear of erectile dysfunction and impaired urination also plays a major role for those choosing active surveillance. However, the physician recommendation may represent the most critical aspect of the decision-making process. Emblematic of this are multiple studies that have described how the patient’s final decision relies principally on what the physician advises. Although urologists and radiation oncologists acknowledge that active surveillance is beneficial and underused for men with low-risk prostate cancer, nearly 4 of 5 physicians prefer primary treatment for a typical man with low-risk prostate cancer. Furthermore, urologists who provide a second opinion are less likely to recommend active surveillance as a management strategy for men with localized prostate cancer. Some have argued that another barrier preventing physicians from recommending active surveillance is the financial disincentive related to not providing specialty care (eg, proton beam therapy).  

However, the use of active surveillance has been promoted in certain instances. Men with low-risk prostate cancer who underwent consultation in a multidisciplinary setting were twice as likely to select active surveillance as men who were not offered such consultation. Media reports touting the benefits of active surveillance may also influence men toward that choice. In addition, patients and family members appear to exert considerable influence in the decision-making process, and patients have ranked family support as one of the top three reasons to pursue active surveillance.

### Evolving Strategies and Current Controversies

#### Imaging With Multiparametric Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of men diagnosed with localized prostate cancer may be of great importance in helping to determine cancer risk. In fact, in the United Kingdom, the most recent treatment guidelines from the National Institute for Health and Care Excellence recommend using MRI to evaluate all men who are considering active surveillance for their prostate cancer. Furthermore, the most recent NCCN guidelines state that multiparametric MRI should be considered when risk-stratifying potential candidates for active surveillance. These recommendations are based on reports that multiparametric MRI (with and without targeted biopsy) is quite robust in identifying high-grade disease and extraprostatic extension in men initially characterized with low-risk disease. A recent systematic review acknowledged the difficulty in synthesizing the current literature due to various definitions of a “positive MRI” and reclassification thresholds. In one large series, abnormal MRI findings before radical prostatectomy were predictive of Gleason upgrading above the score identified at the time of biopsy. In another study, men with the most striking MRI abnormalities were associated with a 45% to 100% likelihood of finding...
Gleason score upgrading at radical prostatectomy, whereas those with less concerning MRI lesions had upgrading rates comparable to those of patients with negative MRIs. Moving forward, the maturation of existing data, combined with adoption of consensus-based guidelines for reporting MRI findings, will help clarify the role of multiparametric MRI in the management of men who are considering active surveillance.

MRI-Guided Prostate Biopsies

The active surveillance protocols described herein all used transrectal-ultrasound (TRUS)-guided prostate biopsies that sampled at least 10 cores in a standard template fashion. Alternative biopsy strategies that could help to improve risk-stratification for men considering active surveillance are of great interest. Using MRI to guide biopsies is the most compelling approach as of this writing. MRI can identify prostate cancer, especially high-grade lesions. Targeting these lesions can then be accomplished using a cognitive approach with direct in-bore methods or with image-fusion devices, which allow the fusion of real-time TRUS images with stored MRIs.

Figure 2 illustrates how MRI-ultrasound fusion biopsy has the potential to improve the selection of patients for active surveillance, in the example case, by revealing a high-grade cancer that was not observed on conventional biopsy. Among men undergoing their first diagnostic prostate biopsy, MRI-ultrasound–targeted biopsy identifies more high-grade cancers than conventional biopsy, particularly if the tumors are anterior. When men have one or more prior negative biopsies, the cancer detection rate is 34% to 56%, and the majority of tumors identified are considered important. The most convincing predictor of clinically significant prostate cancer is a highly suspicious lesion on MRI. Among men who underwent a confirmatory MRI-ultrasound fusion or in-bore, MRI-guided prostate biopsy after an initial TRUS-guided diagnostic biopsy, reclassification to aggressive disease was observed in 38%
to 79% if the MRI revealed a region of interest for targeting.\textsuperscript{138,147,148} Overall, interest has increased in incorporating MRI-ultrasound fusion prostate biopsies as an integral component of active surveillance programs.

**Saturation Biopsy**

Another technique to improve the accuracy of biopsy is transperineal extended sampling, typically performed under general anesthesia, which allows the sampling of up to 90 cores using a brachytherapy template (including anterior and transitional zones of the prostate not typically sampled by standard TRUS-guided biopsies).\textsuperscript{149} For men undergoing their initial biopsy, cancer detection rates with the extended perineal method are comparable to rates with the TRUS-guided approach.\textsuperscript{150} However, among men who have had one or more negative prostate biopsies, transperineal saturation prostate biopsies revealed more cancers than repeat TRUS-guided biopsies, particularly when tumors were located in the transition zone or anterior region of the gland.\textsuperscript{151,152} However, transperineal prostate biopsies carry a 6% to 11% risk of urinary retention, requiring the placement of a urethral catheter.\textsuperscript{153,154}

**Use of Biomarkers for Inclusion and Monitoring**

In addition to PSA, other prostate cancer biomarkers have been identified and evaluated over the past decade to help guide decision making for men who are considering prostate biopsy or treatment for prostate cancer. For example, a urine-based test for prostate cancer-associated 3 (PCA-3), a gene overexpressed in prostate cancer tissue,\textsuperscript{155} was developed and approved by the FDA to help identify men who are most likely to have cancer on repeat biopsy.\textsuperscript{156} Despite this ability to improve prostate cancer detection, the relationship between PCA-3 levels and treatment outcomes is less clear. Although some studies showed a relationship between higher PCA-3 levels and adverse features at prostatectomy,\textsuperscript{157} others were unable to replicate this finding.\textsuperscript{158,159} Among active surveillance patients, PCA-3 levels were not associated with an increased risk of reclassification on repeat biopsy.\textsuperscript{160}

Other novel assays, such as the Prostate Health Index\textsuperscript{161} and the 4KScore (OPKO Health, Miami, Fla),\textsuperscript{162} show promising preliminary results in their ability to predict high-grade disease at the time of prostate biopsy, but their role in decision making regarding prostate cancer treatment remains unclear. Studies have suggested that the Prostate Health Index,\textsuperscript{163} the pro-PSA: free-PSA ratio,\textsuperscript{164} and free-PSA\textsuperscript{165} are all associated with adverse findings at repeat biopsy for patients on active surveillance. Unfortunately, these tests do not have the discriminatory ability to replace interval prostate biopsy for men on active surveillance. Novel, tissue-based RNA expression profiles (ie, the Oncotype DX Genomic Prostate Score [Genomic Health, Redwood City, Calif]\textsuperscript{166} and the Prolaris cell cycle progression score [Myriad Genetics, Salt Lake City, Utah\textsuperscript{167}]) have been developed to help predict prostate-cancer specific outcomes after prostatectomy. Although they have been shown to help risk-stratify patients who are considering active surveillance, long-term outcomes have not been assessed.\textsuperscript{168}

**Use of 5α-Reductase Inhibitors**

Two large, randomized trials demonstrated that the 5α-reductase inhibitors (5-ARIs) finasteride and dutasteride were effective in decreasing the incidence of prostate cancer.\textsuperscript{169,170} However, because of a slightly increased risk of high-grade prostate cancers among healthy men enrolled in one of the trials, the FDA ruled against their use as chemopreventive agents for prostate cancer. Nonetheless, these findings stimulated interest in 5-ARIs as potential tools to halt the progression of disease among men undergoing active surveillance. A retrospective cohort trial demonstrated that men treated with 5-ARIs had significantly lower rates of pathologic reclassification (19% with 5-AIR vs 37% without) and opting for delayed treatment (20% vs 38%), even after adjusting for potential confounders.\textsuperscript{171} Furthermore, the randomized REDEEM (Reduction by Dutasteride of Clinical Progression Events in Expectant Management) trial demonstrated that men who received dutasteride (vs placebo) had lower rates of clinical reclassification, higher rates of negative prostate biopsies, and improved cancer-related anxiety.\textsuperscript{172} Nonetheless, 5-ARI administration for men on active surveillance should be considered an off-label use of the product.

**Inclusion of Intermediate-Risk Patients**

Although active surveillance protocols were originally directed toward patients with very-low-risk and low-risk prostate tumors, men with intermediate-risk disease are now being considered as candidates for such an approach. This is reflected in the expansion of enrollment criteria by select programs to include either older patients (ie, age >70 years) with Gleason score 3 + 4 tumors\textsuperscript{27} or other men with intermediate-risk tumors to defer treatment.\textsuperscript{29,30,36,39} Although they did not meet traditional criteria for active surveillance, men with intermediate-risk disease (based on CAPRA scores of 3–5) at the University of California, San Francisco had progression-free survival and rates of deferred treatment comparable to those observed in men with lower-risk tumors.\textsuperscript{173} However, the University of Toronto cohort of 993 active surveillance patients had 15 deaths from prostate cancer after follow-up as long as 20 years, and many of those patients had Gleason 7 disease noted on repeat biopsy.\textsuperscript{27} The short interval between enrollment and death for this group of patients suggests that Gleason 7 disease was present at enrollment into active surveillance; this should introduce caution for providers who are considering expectant
management for patients with higher grade prostate tumors.\textsuperscript{27} Nevertheless, among intermediate-risk patients, other-cause mortality still exceeds cancer-specific mortality, but the risk of death from prostate cancer (approximately 15% after a median follow-up of nearly 7.5 years) becomes considerably more significant.\textsuperscript{30} Along these lines, another population-based study of US veterans using data from the Shared Equal Access Regional Cancer Hospital (SEARCH) database\textsuperscript{174} demonstrated the increased prevalence of biochemical recurrence and prostate-cancer specific mortality among patients with intermediate-risk disease who underwent radical prostatectomy more than 9 months after diagnosis.\textsuperscript{175} Nevertheless, the liberalization of enrollment to include some men with Gleason 3 + 4 tumors, based on increasingly sophisticated biopsy methods, appears to be gaining acceptance.

**Active Surveillance of Black Prostate Cancer Patients**

Results from recent studies have caused some concern over the appropriateness of active surveillance for black men. At Johns Hopkins, black men who met clinical criteria for very-low-risk prostate cancer had a significantly higher risk of pathologic upgrading, upstaging, and positive surgical margins at the time of radical prostatectomy.\textsuperscript{176,177} However, this may be related to differences in the distribution of tumors among black men. Pathologic examination of prostate specimens from radical prostatectomy indicted that black men were more likely than white men to have anterior tumors that were probably under sampled at diagnostic biopsy.\textsuperscript{178} Incorporating imaging studies, such as multiparametric MRI, and/or anterior prostate sampling may abrogate the racial disparities noted in these studies.

**Informed Decision Making: Role of Decision Aids and Other Decision-Support Strategies**

In the setting of multiple treatment options with highly variable outcomes, the decision-making process for men with prostate cancer is complex and challenging. In particular, among economically disadvantaged patients with prostate cancer, men who had lower baseline knowledge related to prostate cancer treatments exhibited increased decisional conflict and uncertainty, suggesting that certain patient populations may benefit from the use of educational decision aids.\textsuperscript{179} Decision aids (eg, pamphlets, videos, Web-based modules) contain disease-specific and treatment-specific information and attempt to help patients more clearly understand the risks and benefits of all available treatment options.\textsuperscript{180} However, patient education materials often do not address all available treatment options and can leave out important details related to radical prostatectomy and radiation therapy.\textsuperscript{181} Nevertheless, patients with prostate cancer who used a “decision navigation intervention” to help guide decision making related to treatment had lower decisional regret and conflict scores compared with controls.\textsuperscript{182} However, the impact of decision aids on treatment choice is less clear, and most studies indicate that physicians have the strongest influence on that decision.\textsuperscript{183,184} More research is needed to clarify the role and potential benefits of decision aids in the informed decision-making process for patients who are considering active surveillance.

**Conclusion**

Expectant management of men with prostate cancer is a useful approach for a large proportion of those with localized prostate cancer, whether it is watchful waiting or active surveillance with curative intent. Using strict inclusion criteria for very-low-risk or low-risk disease can select a group of prostate cancer patients for active surveillance who would avoid the side effects of therapy while experiencing comparable survival and quality of life (through at least 5-10 years of follow-up). A summary and recommendations regarding expectant management and active surveillance are detailed in Table 6.

Considerable questions remain regarding both the identification of optimal candidates for surveillance as well as understanding the ideal monitoring strategy after the initiation of observational protocols. Further work will be required to more clearly define the roles of multiparametric MRI, genomic markers (eg, Oncotype DX), and chemoprevention for men who are considering active surveillance of their prostate tumors. Furthermore, despite increased adoption of expectant management, active surveillance still remains underused, and more data will be needed to clarify factors contributing to this finding at a population level.
Future studies should also help identify disparities based on race or socioeconomic factors.

Ultimately, the decision-making process surrounding treatment for a man with localized prostate cancer must take an individualized approach. The risks and benefits of treatment for a man with localized prostate cancer must be reviewed with the patient in light of existing knowledge, potentially with the use of decision aids to help enable a truly shared decision-making process. Active surveillance is a viable approach for most men with low-risk prostate cancer, and its broader adoption has the potential to stop the overtreatment of men with indolent lesions and redirect resources to men with more serious cancers.

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