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Active Surveillance for Low-Risk Cancers — A Viable Solution to Overtreatment?

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There is wide variation in the intensity of treatment for low-risk cancers, and many patients are at risk for overtreatment. Despite 5-year survival rates that approach 100% among patients with low-risk differentiated thyroid cancer, prostate cancer, and ductal carcinoma in situ (DCIS), diagnosis of one of these cancers often leads to a cascade of testing and treatment that isn't associated with longer survival but can cause harm (see Supplementary Appendix for a detailed definition of low-risk cancers).[1] For example, many patients with low-risk differentiated thyroid cancer ultimately undergo total thyroidectomy, prophylactic lymph-node resection, and radioactive iodine treatment. Similarly, studies show there has been a rapid increase in the number of patients with DCIS who undergo bilateral mastectomy, and approximately half of patients with low-risk prostate cancer are still treated with radical prostatectomy or radiation. Each of these treatments confers potential risks, including permanent postoperative voice changes and low calcium levels in people with thyroid cancer, surgical complications and lymphedema in those with breast cancer, and long-lasting impotence and incontinence in men with prostate cancer (see table). In addition, intensive treatment is often costly for the patient and the health care system.

The controversy surrounding intensity of treatment for these low-risk cancers has been fueled by the marked increase in thyroid-cancer incidence,[2] stories in the lay press about celebrity experiences with breast cancer, and the baby-boomer generation reaching an age when prostate cancer is common. Treatment decisions are also complicated by reluctance among physicians and patients to adopt less intensive regimens, different reimbursement rates for active surveillance versus definitive local therapies, and patients' fears related to a cancer diagnosis.

In recent years, physicians have increasingly begun to think about active surveillance as a valid way to manage low-risk cancers. But despite benefits such as lower costs and the elimination of surgery- and radiation-related risks, adoption of this approach has been uneven. Active surveillance — which consists of close monitoring of the cancer without initial surgery or other more intensive therapies — differs from watchful waiting, which primarily involves observation and symptom management in patients who are likely to die of

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other causes. Active surveillance has been an option for managing low-risk prostate cancer for many years,[3] but it has only recently been put forth as a viable alternative for other low-risk cancers. Although it isn't considered a mainstream approach for managing thyroid cancer, completed trials from Japan suggest it could be an option for older patients with papillary thyroid cancers 1 cm in diameter or smaller, and ongoing trials in the United States are evaluating active surveillance in a broader cohort of patients with low-risk disease. Meanwhile, there have been discussions about using active surveillance to manage DCIS, but no completed trials or formal plans for widespread adoption.[4]

Successful uptake of active surveillance for low-risk cancers will require overcoming perceived challenges to implementation. Many of these challenges were identified during the adoption of active surveillance for low-risk prostate cancer, but other obstacles specific to breast cancer and thyroid cancer are also likely to arise.

First and most important, for all low-risk cancers, it will be necessary to define what constitutes optimal active surveillance, including the most appropriate type of imaging and other monitoring. Furthermore, determining the ideal duration of active surveillance will be critical; as currently there are no clear guidelines and it may be stopped for clinical reasons, such as tumor progression, or other reasons, including patient anxiety. For thyroid cancer, optimal surveillance probably includes periodic neck ultrasounds and testing of serum thyroglobulin (a tumor marker). However, the reliability of neck-ultrasound findings depends on the skill of the physician performing and reading the ultrasound, and this variability will have implications for moving active surveillance beyond the trial setting and into the community. In addition, it's still not clear how thyroglobulin measurements should be interpreted in patients who have an intact thyroid as thyroglobulin is made by both normal thyroid tissue and by thyroid cancer. Optimal surveillance for DCIS would include regular mammograms, although likely yearly the ideal frequency and whether additional imaging tests or biopsies are necessary remains unknown. And even though active surveillance has become more common for prostate cancer, there is still debate about the most appropriate surveillance strategy.

Second, physician and patient buy-in are critical to the adoption of active surveillance. To some extent, buy-in has already happened for prostate cancer, although rates of uptake suggest there is still room for improvement. Physician buy-in and subsequent implementation of active surveillance may be especially challenging for breast cancer, because whereas in the cases of prostate and thyroid cancers urologists and endocrinologists, respectively, are logically responsible for managing care, it remains to be determined whether surgeons, primary care doctors, or medical oncologists would oversee active surveillance of DCIS.

Third, it's important to identify which patients are appropriate candidates for active surveillance. In the case of prostate cancer, cancer biology as defined by prostate-specific antigen levels, biopsy, and other emerging biomarkers determine candidacy. Patients with thyroid and breast cancers, however, are often much younger than those with prostate cancer. Given the length of follow-up necessary in younger patients and the propensity for some

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younger patients to have more aggressive disease, age could also be an important factor in determining eligibility for active surveillance.[5]

Fourth, a common concern about using active surveillance to manage low-risk cancers is that cancer progression may go unrecognized. During active surveillance of prostate cancer, some patients are lost to follow-up and some don't end up undergoing biopsies or other recommended tests and procedures. Similar challenges are likely to exist for both thyroid and breast cancer.

Finally, although managing cancer with active surveillance eliminates the risk of postoperative and radiation-induced complications, its effect on patients' emotional health hasn't been widely considered. Active surveillance is unlikely to eliminate the worry associated with a cancer diagnosis. Worry tends to lead patients to elect to receive more treatment, so there is reason to believe it may also lead them to undergo more surveillance procedures. Some patients with prostate cancer who initially choose an active-surveillance approach change their minds and opt for more intensive treatment, even when their cancer hasn't progressed. Because patient worry may contribute to changes in the treatment plan, it will be important to create tailored support tools to reduce worry during active surveillance.

The excellent prognosis of most low-risk cancers combined with the potential to reduce treatment side effects make active surveillance a promising alternative to more intensive therapies — and one that may reduce overtreatment. In addition to low-risk prostate cancer, thyroid cancer, and DCIS, other low-risk cancers, including some skin cancers, could potentially be managed with active surveillance. But achieving widespread adoption will require further work. Although active surveillance is currently most accepted for management of low-risk prostate cancer, work is still needed to fine-tune surveillance strategies and reduce the risks associated with incomplete risk assessment, loss to follow-up, inadequate surveillance, and cancer-related worry. For breast and thyroid cancer, the next steps include defining optimal surveillance strategies that can be applied on a large scale, securing physician and patient buy-in, identifying patients who are appropriate candidates for active surveillance, and creating plans to reduce patient harm, including by addressing patient worry. Once active surveillance is established as a valid option for managing each of these cancers, it will be important to evaluate long-term data to ensure that it is leading to improved outcomes.

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Table 1

Low-Risk Cancers for which Active Surveillance Is or Could Be a Treatment Option.

Type of Cancer	Median Age at Diagnosis (yr)	Sex of Affected Patients	Intensive Treatment Option	Risks Associated with Intensive Treatment	Active Surveillance Option	Physician in Charge	Stage of Adoption
Prostate	66	100% male	Radical prostatectomy or radiation	Impotence and incontinence	Prostate exam; prostate-specific antigen testing; biopsy	Urologist	In practice
Thyroid	51	75% female, 25% male	Total thyroidectomy, with or without lymph-node resection and radioactive iodine	Permanent change in voice and permanent low calcium levels	Neck ultrasound and testing of serum thyroglobulin	Endocrinologist	In trials
Breast (DCIS)	62	Nearly 100% female	Mastectomy or lumpectomy with radiation	Surgical complications and lymphedema	Mammography	Unclear	In discussion

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