IMPORTANCE  We have previously reported on a doubling of thyroid cancer incidence—largely due to the detection of small papillary cancers. Because they are commonly found in people who have died of other causes, and because thyroid cancer mortality had been stable, we argued that the increased incidence represented overdiagnosis.

OBJECTIVE  To determine whether thyroid cancer incidence has stabilized.

DESIGN  Analysis of secular trends in patients diagnosed with thyroid cancer, 1975 to 2009, using the Surveillance, Epidemiology, and End Results (SEER) program and thyroid cancer mortality from the National Vital Statistics System.

SETTING  Nine SEER areas (SEER 9): Atlanta, Georgia; Connecticut; Detroit, Michigan; Hawaii; Iowa; New Mexico; San Francisco–Oakland, California; Seattle–Puget Sound, Washington; and Utah.

PARTICIPANTS  Men and women older than 18 years diagnosed as having a thyroid cancer between 1975 and 2009 who lived in the SEER 9 areas.

INTERVENTIONS  None.

MAIN OUTCOMES AND MEASURES  Thyroid cancer incidence, histologic type, tumor size, and patient mortality.

RESULTS  Since 1975, the incidence of thyroid cancer has now nearly tripled, from 4.9 to 14.3 per 100 000 individuals (absolute increase, 9.4 per 100 000; relative rate [RR], 2.9; 95% CI, 2.7-3.1). Virtually the entire increase was attributable to papillary thyroid cancer: from 3.4 to 12.5 per 100 000 (absolute increase, 9.1 per 100 000; RR, 3.7; 95% CI, 3.4-4.0). The absolute increase in thyroid cancer in women (from 6.5 to 21.4 = 14.9 per 100 000 women) was almost 4 times greater than that of men (from 3.1 to 6.9 = 3.8 per 100 000 men). The mortality rate from thyroid cancer was stable between 1975 and 2009 (approximately 0.5 deaths per 100 000).

CONCLUSIONS AND RELEVANCE  There is an ongoing epidemic of thyroid cancer in the United States. The epidemiology of the increased incidence, however, suggests that it is not an epidemic of disease but rather an epidemic of diagnosis. The problem is particularly acute for women, who have lower autopsy prevalence of thyroid cancer than men but higher cancer detection rates by a 3:1 ratio.
In 2006 we reported on the increasing incidence of thyroid cancer in the United States.6 The report contained a number of epidemiologic observations that led us to express concern that most of the increased incidence represented overdiagnosis: the detection of cancers that are not destined to cause symptoms or death. First, despite a more than 2-fold increase in the rate of thyroid cancer detection, thyroid cancer mortality had remained stable. Second, virtually all of the increase was confined to a type with the least aggressive histologic characteristics: papillary thyroid cancer. Third, the bulk of the increase (87%) was explained by tumors 2 cm or smaller.

We also expressed the fear that the problem of overdiagnosis might get worse. Thyroid cancer has been long recognized to be a common autopsy finding, despite never having caused symptoms during a patient’s life.2,3 Thyroid nodules are extraordinarily common and frequently detected by physical examination of the neck and even more frequently by imaging.4,5 If increased diagnostic scrutiny is added to this mix—more thyroid palpation or more imaging—overdiagnosis will increase. Herein, we examine what has happened since our previous report.

Methods

Data Sources
Incidence data are from Surveillance, Epidemiology and End Results (SEER) 9 program, supported by the National Cancer Institute, spanning the years 1975 to 2009. The SEER 9 areas include approximately 10% of the US population6 and are the longest-contributing sites to the program: Atlanta, Georgia; Connecticut; Detroit, Michigan; Hawaii; Iowa; New Mexico; San Francisco–Oakland, California; Seattle–Puget Sound, Washington; and Utah. SEER is the best source of population-based data available in the United States for cancer incidence, histologic characteristics, and initial treatment.

Mortality data for the same period were obtained from the Center for Disease Control and Prevention’s National Vital Statistics System, which provides information on the underlying cause of death obtained from death certificates filed in each state. Estimates of the total number of new cases of thyroid cancer diagnosed in 2009 are from the North American Association of Central Cancer Registries.

The Dartmouth College institutional review board has deemed studies using deidentified, publicly available data (such as those used herein) to be exempt from institutional review board review.

Analysis of Incidence and Mortality Trends
We included all incident cases of cancer with “thyroid” as the site of origin (The International Classification of Diseases for Oncology, 3rd Revision7 [ICD-03], code 73.9). Incidence rates were calculated for each year using SEER*Stat software (version 8.0.4; Surveillance Research Program of the National Cancer Institute). All rates are age adjusted to the 2000 standard population.

We also examined incidence trends by histologic type and sex. Histologic type was categorized into 3 groups: papillary (ICD-03 8050, 8052, 8130, 8260, 8340-8344, 8450-8452), follicular (ICD-03 8290, 8330-8332, 8335), or poorly differentiated—a combination of medullary (ICD-03 8345-8346, 8510) and anaplastic (ICD-03 8021). Tests of trend by histologic type and 95% CIs were calculated using Stata software (version 12; StataCorp LP).

Next, we measured changes in overall and papillary thyroid cancer incidence over 2 periods: from baseline to current (1975-2009) and from our prior report to current (2002-2009). We report these changes using measures of absolute change (the subtraction; namely, absolute rate increase) and relative change (the ratio; namely, relative rate [RR]). The 95% CIs for both the absolute and relative changes were calculated with Stata software (version 12), using the count of cases provided by SEER and denominators imputed from the case counts and reported incidence rates.

Size Distribution
We used data from 2 time periods to compare the historical and current size distribution of thyroid cancer: 1988 to 1989 and 2008 to 2009. During that 20-year span, SEER changed the variable used to capture data on tumor size. For 1988 to 1989 the variable was “Extent of Disease 10–Tumor Size”, for 2008 to 2009 it was “Collaborative Stage Tumor Size.” The coding rules for measuring cancer size were the same for both the historical and current variables, so comparisons are expected to be valid.

Because of our interest in calculating the proportion of cancers found in various size categories, we removed cancers with missing size data from both the numerator and the denominator. Similarly, we removed cancers categorized by SEER as “no mass; no tumor found.” Finally, we removed cancers with implausible size (cancers listed as having a size > 200 mm [about 8 in]). In a literature review for the outer limits of thyroid cancer sizes8–11 we found that, while thyroid goiters larger than 200 mm have been reported, there are no reports of thyroid cancers larger than this. From the 1988-1989 cohort, this criterion removed 1 case, listed as measuring 330 mm (about 13 in). From the 2008-2009 cohort, it removed 83 cases: 1 listed as 650 mm, 81 cases listed as 988 mm, and 1 case listed as 989 mm, which is defined as “989 mm or greater” by SEER. The problems with the cases listed as 988 and 989 were likely transcription errors, since they are 1 digit off from codes with distinct meanings: 888 (not applicable) and 999 (size unknown).

Also in the 2008-2009 data, SEER added new size categories based on ranges that we recoded: cancers categorized by SEER as “microscopic” were grouped with those measuring 1 to 5 mm, cancers measuring “less than 1 cm” were grouped with those measuring 5 to 10 mm, cancers measuring “less than 2 cm” were grouped with those measuring 11 to 20 mm, and so on up, through cancers measuring “greater than 5 cm.”

Current Treatment
We categorized current (2009) treatment patterns using the 3 aspects of thyroid cancer treatment: surgery (yes or no) (SEER variable “RX Summary–Surgery Primary Site”), radiation (yes or no) (SEER variable “Radiation”), and neck dissection (yes or no) (SEER variable “RX Summary–Scope Regional Lymph Node Surgery”). Again, given our interest in the distribution...
of treatment, we excluded patients in whom the primary treatment (surgery) was not known (6 women and 1 man).

Surgery and radiation are unambiguously reported in SEER. Total or partial thyroidectomy was categorized as surgery (85% were total thyroidectomy). Any reported source of radiation (radioisotopes, radioactive implants, external beam, or any combination) was categorized as radiation (93% were radioisotopes).

While neck dissection is not unambiguously reported, SEER does have a variable that categorizes the number of lymph nodes removed. Thyroid surgery alone can lead to incidental removal of 1 or 2 nodes; thus, we used the SEER classification of “4 or more regional lymph nodes removed” category as a proxy for lymph node dissection.

To obtain estimates of the total number of Americans undergoing each type of treatment, we multiplied the proportions obtained from SEER by the total number of new cases diagnosed in 2009, as calculated and reported by the North American Association of Central Cancer Registries.12 For example, in 2009, SEER reported that 1524 of 3223 women with thyroid cancer had both surgery and radiation (47%). This was multiplied by 43 210, the total number of estimated thyroid cancer cases in women for that year, to yield an estimate of 20 434 women who had both surgery and radiation.

Results

As shown in Figure 1, the incidence of thyroid cancer was relatively stable until the early 1990s, after which it increased substantially. Thyroid cancer mortality, however, has remained stable over the 35-year period.

Table 1 details the changes in incidence between 1975 and 2009: from 4.9 to 14.3 per 100 000 individuals—a nearly 3-fold increase (RR, 2.9; 95% CI, 2.7-3.1). Over half of the absolute increase (9.4 per 100 000) has occurred in the 7 years since our initial report (5.1 per 100 000). Figure 2 demonstrates that virtually all of the increased diagnosis is attributable to an increase in papillary thyroid cancer, which increased by 9.1 per 100 000 (Table 1).

Figure 3 shows that the increase in thyroid cancer diagnoses has affected women more than men. Although women
have always been found to have more thyroid cancer, the relative increase has been larger in women than men. Table 1 shows that thyroid cancer incidence in women has tripled (RR, 3.3; 95% CI, 3.0-3.6), while the incidence in men has only doubled (RR, 2.2; 95% CI, 1.9-2.6). In absolute terms, the increased incidence in women (from 6.5 to 21.4 = 14.9 per 100 000 women) was almost 4 times greater than that of men (from 3.1 to 6.9 = 3.8 per 100 000 men).

Table 2 shows that the size distribution of detected thyroid cancer has shifted toward smaller lesions. In 1988 to 1989, when SEER first began collecting data on tumor size, 25% of detected thyroid cancers were 1 cm or smaller. In the most recent data (2008-2009), 39% were 1 cm or smaller. Conversely, large tumors now comprise a smaller portion of detected thyroid cancer. In 1988 to 1989, 42% were larger than 2 cm; now, 33% are.

Figure 4 illustrates how the roughly 56 000 Americans diagnosed as having thyroid cancer were treated in 2009. The median age at diagnosis was 49 years for women (mean age, 49 years [range, 9-98 years]), and 53 years for men (mean age, 53 [range, 6-91 years]). The overall patterns were similar for men and women; more than 90% undergo surgery and about half of these also receive radiation therapy. Many also undergo a lymph node dissection. As expected, lymph node dissection is more common in those people who are receiving radiation.

Discussion
We found that there is an ongoing epidemic of thyroid cancer in the United States. It does not seem to be an epidemic of disease, however. Instead, it seem to be substantially an epidemic of diagnosis: thyroid cancer incidence has nearly tripled since 1975, while its mortality has remained stable. Our findings demonstrate that the problem is due to the overdiagnosis of papillary thyroid cancer, an abnormality often present in people who never develop symptoms from it.3,13 We also found that the major burden of overdiagnosis has fallen on women. Over the past 35 years the absolute increase in thyroid cancer in women was almost 4 times greater than that in men. This is particularly notable because thyroid cancer prevalence at autopsy is actually greater in...
men than it is in women.\textsuperscript{3,13-17} This suggests that the problem of overdiagnosis of thyroid cancer in women has probably been present for decades.

Some might argue that—despite stable mortality—the rising incidence of thyroid cancer could still represent a true increase in disease burden because the survival time for thyroid cancer is so long that there has been insufficient time for it to be observed in the mortality trend. However, for this to be true, the lead times would have to be extraordinarily long—more than the 30 years in which mortality has been stable. Others might argue that stable mortality in the face of rising incidence reflects improved treatments for thyroid cancer. For this explanation to be true, the improvements in treatment would have had to exactly offset the rise in incidence. If treatment improved too fast, the mortality line would fall. If treatments improved too slowly, the mortality line would rise. While this explanation is theoretically possible, it is not particularly plausible in explaining 30 years of stable mortality.

Our study has some limitations. The data source, SEER 9, was chosen because of its long history, enabling us to examine long-term trends. However, it includes only about 10% of the population of the United States. To assess how well SEER 9 represents the rest of the country, we examined more recent data sources that are broader in scope (but more limited in time). Between 2005 and 2009, thyroid cancer incidence rose 31% in SEER 9. Concomitant data from SEER 18 showed an increase of 28%, while data from the North American Association of Central Cancer Registries showed an increase of 26%.\textsuperscript{12} These findings suggest that while the precise numbers may change depending on the data source, the general direction and magnitude do not.

Our study is also limited because it does not provide insight into the mechanism for how patients get overdiagnosed. There are other data, however, demonstrating that thyroid cancer detection is strongly related to an individual’s exposure to medical care. People with enhanced health care access tend to have not only more small cancers identified but also more thyroid cancers identified overall.\textsuperscript{16,17} In prior work, we sought more detail on the clinical pathways that lead to the detection of thyroid cancers of any size or histologic group.\textsuperscript{20} We identified 3. The first was termed opportunistic screening: physical examinations of the thyroid gland in patients with no symptoms. The second was termed diagnostic cascade, in which multiple tests were ordered to evaluate vague complaints that might have a metabolic origin. In the course of the evaluation a thyroid nodule was uncovered, but it did not plausibly explain the patient’s symptoms (eg, thyroid ultrasonography uncovering a thyroid nodule in a workup to evaluate weight gain). The third was termed serendipitous detection: incidental detection of a thyroid finding during imaging for completely different reasons (eg, carotid artery ultrasonography, or computed tomographic scan of the chest performed for blunt trauma evaluation). In that study, papillary, follicular, and even medullary cancers were uncovered through these pathways, not all of it small. Recent data support this in other centers: not just small cancers are identified through these paths, but also larger cancers.\textsuperscript{21}

Unfortunately, our findings on current treatment patterns suggest that most thyroid cancers are still being treated as though they are destined to cause real problems for the people who have them. Total thyroidectomy is performed for 85% of people diagnosed as having thyroid cancer. All patients who undergo total thyroidectomy are at risk of postoperative complications, such as permanent hypoparathyroidism or vocal cord paralysis, and all will need lifelong thyroid hormone therapy and monitoring. Half of patients receive radiation treatment, most in the form of radioactive iodine—a therapy associated with an increase in the risk of secondary cancers, particularly leukemia.\textsuperscript{22} These aggressive therapies persist despite guidelines suggesting that partial thyroidectomy is a reasonable approach for lower risk cancers\textsuperscript{23} and data indicating that few patients with papillary thyroid cancer derive survival benefit from radioactive thyroid cancer.\textsuperscript{24}

Conclusions

We believe the time has come to address the problem of papillary thyroid cancer overdiagnosis and overtreatment. Providing patients with randomized clinical trial data on an alternative approach—active surveillance of incidentally identified, asymptomatic, small papillary thyroid cancers—is the logical next step. We are pleased to see effort in this direction, both in Japan, where patients have been followed for up to 10 years with favorable results,\textsuperscript{25} and in the United States, where Memorial Sloan-Kettering Cancer Center is successfully recruiting patients into an observational cohort (Michael Tuttle, MD; e-mail communication; April 26, 2013).

A second approach could come from relabeling incidentally identified small thyroid neoplasms, reclassifying them using a term other than cancer. This is the recently suggested approach to resolving the problem of how to lessen aggressive treatment of ductal carcinoma in situ in breast cancer,\textsuperscript{26} a disease in which overdiagnosis is also a recognized problem.

A third approach would be to more closely investigate patient-level patterns of care and thyroid cancer risk factors that result in a thyroid cancer diagnosis. There have been recent reports of increasing thyroid cancer incidence among nonwhite ethnic peoples in the United States, groups, traditionally thought of as being at lower risk of overdiagnosis.\textsuperscript{27,28} If these patterns were understood on the level of the individual, we would be better able to tell which parts of the increasing incidence might be real and which are identification of subclinical disease.

Unfortunately, these approaches take time to implement, and patients and physicians need a way to approach this problem now. A simple way that physicians could begin today would be to openly share with patients the uncertainty surrounding small thyroid cancers—explaining that many will never grow and cause harm to a patient—but it is not possible to know with certainty which ones fall into that category. Many patients are now aware of the problem of prostate cancer overdiagnosis, and the example may be useful in thyroid cancer. In prostate cancer, there has been an explicit shift toward shared decision making: working with the patient to place the
medical evidence in context with that person’s priorities and life circumstance, so that the decision made is in alignment with their values and goals. For some, active surveillance is a desirable option. The same model could be applied to thyroid cancer.

Finally, it is not enough to simply address diagnostic terms and treatments, the upstream step of identification is equally relevant. Physicians’ thresholds to palpate, image, and biopsy the thyroid have likely fallen too far. Clinicians need more than trial results; they also need to be asking themselves whether they are looking too hard for thyroid cancer. Patients—and in the case of thyroid cancer, particularly women—need protection not only from the harms of unnecessary treatment but also the harms of unnecessary diagnosis.

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