JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Thyroid Cancer
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE The incidence of thyroid cancer detection has increased by 4.5% per year over the last 10 years, faster than for any other cancer, but without a corresponding change in the mortality rate. In 2013, the incidence rate of thyroid cancer in the United States was 15.3 cases per 100 000 persons. Most cases of thyroid cancer have a good prognosis; the 5-year survival rate for thyroid cancer overall is 98.1%.

OBJECTIVE To update the US Preventive Services Task Force (USPSTF) recommendation on screening for thyroid cancer.

EVIDENCE REVIEW The USPSTF reviewed the evidence on the benefits and harms of screening for thyroid cancer in asymptomatic adults, the diagnostic accuracy of screening (including neck palpation and ultrasound), and the benefits and harms of treatment of screen-detected thyroid cancer.

FINDINGS The USPSTF found inadequate direct evidence on the benefits of screening but determined that the magnitude of the overall benefits of screening and treatment can be bounded as no greater than small, given the relative rarity of thyroid cancer, the apparent lack of difference in outcomes between patients who are treated vs monitored (for the most common tumor types), and observational evidence showing no change in mortality over time after introduction of a mass screening program. The USPSTF found inadequate direct evidence on the harms of screening but determined that the overall magnitude of the harms of screening and treatment can be bounded as at least moderate, given adequate evidence of harms of treatment and indirect evidence that overdiagnosis and overtreatment are likely to be substantial with population-based screening. The USPSTF therefore determined that the net benefit of screening for thyroid cancer is negative.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends against screening for thyroid cancer in asymptomatic adults. (D recommendation)

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The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendation and Evidence

The USPSTF recommends against screening for thyroid cancer in asymptomatic adults (D recommendation) (**Figure 1**).

Rationale

Importance

In 2013, the incidence rate of thyroid cancer in the United States was 15.3 cases per 100 000 persons, which represents a significant increase from 1975, when the incidence rate was 4.9 cases per 100 000 persons.[1] The increase in thyroid cancer incidence was 6.7%

Figure 1. US Preventive Services Task Force Grades and Levels of Certainty

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

USPSTF indicates US Preventive Services Task Force.

per year from 1997 to 2009, but the rate of increase has slowed to 2.1% per year in recent years (2009-2013).[1] Meanwhile, the change in mortality rate has increased by only about 0.7 deaths per 100 000 persons each year.[1] Most cases of thyroid cancer have a good prognosis.[2] The 5-year survival rate for thyroid cancer overall is 98.1% and varies from 99.9% for localized disease to 55.3% for distant disease.[3]

Detection

The USPSTF found inadequate evidence to estimate the accuracy of neck palpation or ultrasound as a screening test for thyroid cancer in asymptomatic persons.

Benefits of Early Detection and Treatment

The USPSTF found inadequate direct evidence to determine whether screening for thyroid cancer in asymptomatic persons using neck palpation or ultrasound improves health outcomes. However, the USPSTF determined that the magnitude of benefit can be bounded as no greater than small, based on the relative rarity of thyroid cancer, the apparent lack of difference in outcomes between patients who are treated vs only monitored (ie, for the most common tumor types), and the observational evidence demonstrating no change in mortality over time after introduction of a population-based screening program.

Figure 2. Clinical Summary: Screening for Thyroid Cancer

Population	Asymptomatic adults
Recommendation	Do not screen for thyroid cancer. Grade: D

Risk Assessment	Factors that substantially increase the risk for thyroid cancer include a history of radiation exposure to the head and neck as a child, exposure to radioactive fallout, family history of thyroid cancer in a first-degree relative, and certain genetic conditions, such as familial medullary thyroid cancer or multiple endocrine neoplasia syndrome (type 2A or 2B).
Screening Tests	Evidence is inadequate to estimate the accuracy of neck palpation or ultrasound of the thyroid as screening tests for thyroid cancer in asymptomatic persons.
Treatment	Surgery (ie, total or partial thyroidectomy, with or without lymphadenectomy) is the main treatment for thyroid cancer. Additional treatment, including radioactive iodine therapy, may be indicated, depending on postoperative disease status, tumor stage, and type of thyroid cancer. External-beam radiation therapy and chemotherapy are not generally used to treat early-stage, differentiated thyroid cancer.
Balance of Benefits and Harms	The USPSTF concludes with moderate certainty that screening for thyroid cancer in asymptomatic persons results in harms that outweigh the benefits.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

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Harms of Early Detection and Treatment

The USPSTF found inadequate direct evidence to assess the harms of screening for thyroid cancer in asymptomatic persons. The USPSTF found adequate evidence to bound the magnitude of the overall harms of screening and treatment as at least moderate, based on adequate evidence of serious harms of treatment of thyroid cancer and evidence that overdiagnosis and overtreatment are likely consequences of screening.

USPSTF Assessment

The USPSTF concludes with moderate certainty that screening for thyroid cancer in asymptomatic persons results in harms that outweigh the benefits.

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to screening in asymptomatic adults (**Figure 2**). It does not apply to persons who experience hoarseness, pain, difficulty swallowing, or other throat symptoms or persons who have lumps, swelling, asymmetry of the neck, or other reasons for a neck examination. It also does not apply to persons at increased risk of thyroid cancer because of a history of exposure to ionizing radiation (eg, medical treatment or radiation fallout), particularly persons with a diet low in iodine, an inherited genetic syndrome associated with thyroid cancer (eg, familial adenomatous polyposis), or a first-degree relative with a history of thyroid cancer.[4,5]

Assessment of Risk

Although the USPSTF recommends against screening in the general asymptomatic adult population, several factors substantially increase the risk for thyroid cancer, including a history of radiation exposure to the head and neck as a child, exposure to radioactive fallout, family history of thyroid cancer in a first-degree relative, and certain genetic conditions, such as familial medullary thyroid cancer or multiple endocrine neoplasia syndrome (type 2A or 2B).[4]

Screening Tests

Although screening for thyroid cancer using neck palpation and ultrasound of the thyroid has been studied, the USPSTF recommends against screening in the general asymptomatic adult population.

Treatment and Interventions

Surgery (ie, total or partial thyroidectomy, with or without lymphadenectomy) is the main treatment of thyroid cancer. Additional treatment, including radioactive iodine therapy, may be indicated, depending on postoperative disease status, tumor stage, and type of thyroid cancer. External-beam radiation therapy and chemotherapy are not generally used to treat early-stage, differentiated thyroid cancer.

Other Considerations

Research Needs and Gaps

The USPSTF found no direct studies that compared screened vs unscreened populations or immediate surgery vs surveillance or

observation and reported health outcomes (ie, morbidity, mortality, quality of life, or harms). Trials or well-designed observational studies that address the benefit of screening in high-risk persons (ie, persons with a history of radiation or family history of differentiated thyroid cancer) are important for understanding how to best advise these patients. Trials or well-designed observational studies of early treatment vs surveillance or observation of patients with small, well-differentiated thyroid cancer are also needed to identify patients at greatest risk for clinical deterioration. Risk prediction tools and molecular markers are needed to help understand the prognosis of differentiated thyroid cancer.

Discussion

Burden of Disease

An estimated 637 115 persons in the United States were living with thyroid cancer in 2013, according to data from the Surveillance, Epidemiology, and End Results Program.[3] In 2017, an estimated 56 870 new cases of thyroid cancer will be diagnosed, representing 3.4% of all new cancer cases in the United States, and 2010 thyroid cancer–related deaths will occur (0.3% of all cancer deaths); the highest percentage of deaths will occur among adults aged 75 to 84 years (27.5%). The incidence of thyroid cancer detection has increased by 4.5% per year over the last 10 years, faster than for any other cancer, but without a corresponding change in the mortality rate, which remained at 0.5 deaths per 100 000 persons in 2013.[6] The estimated 5-year survival rate is 98% but ranges from 99% for localized disease (68% of cancer cases at diagnosis) to 55% for distant disease (4% of cancer cases at diagnosis).[3,6]

Scope of Review

To update its 1996 recommendation, the USPSTF commissioned a systematic evidence review[5,7] to examine the benefits and harms of screening for thyroid cancer in asymptomatic adults. The review also assessed the diagnostic accuracy of screening (including neck palpation and ultrasound) and the benefits and harms of treatment of screen-detected thyroid cancer, which were not part of the previous evidence review.

Accuracy of Screening Tests

Evidence on the accuracy of screening for thyroid cancer using neck palpation or ultrasound is limited, with only 2 applicable studies for each screening method, all of which compared the screening method with a reference standard in a screening population. Two fair-quality prospective studies from Finland by the same investigator reported low sensitivity for neck palpation to detect thyroid nodules.[8,9] In a study of randomly selected adults (n = 253), 5.1% had abnormal findings on neck examination (thyroid nodule or diffuse enlargement), and sensitivity and specificity to detect thyroid nodules were 11.6% (95% CI, 5.1%-21.6%) and 97.3% (95% CI, 93.8%-99.1%), respectively.[7,8] One study of women presenting for mammography (n = 101) reported sensitivity of 27.8% for neck palpation to detect thyroid nodules in women with an abnormal ultrasound finding (women with negative neck palpation findings were not followed up, so the false-positive rate could not be estimated).[7,9]

Two fair-quality population-based studies, both conducted in South Korea by the same investigator, reported on diagnostic accuracy of screening using ultrasound only.[10,11] The prospective study (n = 2079 screened; 113 referred for biopsy with fine-needle aspiration) found that the sensitivity and specificity of having 1 or more malignant features (ie, microcalcification or irregular shape) detected on screening ultrasound were 94.3% (95% CI, 84.3%-98.8%) and 55.0% (95% CI, 41.6%-67.9%), respectively. A retrospective analysis of 130 asymptomatic adults selected from 1009 patients who had biopsy with fine-needle aspiration, based on ultrasound findings (ie, having ≥2 high-risk sonographic characteristics), reported sensitivity and specificity of 94.8% and 86.6%, respectively (calculated per thyroid nodule rather than per patient; CIs not provided). However, this study did not follow up patients with negative ultrasound findings and therefore may have overestimated the sensitivity of this screening method.

Effectiveness of Early Detection and Treatment

No studies directly compared patient health outcomes for screened vs unscreened populations. No randomized trials evaluated whether earlier treatment or treatment of screen-detected, well-differentiated thyroid cancer results in better patient outcomes compared with observation (ie, delayed or no treatment).[5] Two observational studies (reported in 5 articles[12-16]) met the inclusion criteria for benefit of early treatment. One fair-quality, retrospective, observational study using Surveillance, Epidemiology, and End Results data from 1973 to 2005 compared survival rates of persons treated (n = 35 663) vs not treated (n = 440) for papillary thyroid cancer.[12] Overall, untreated persons had a slightly worse 20-year survival rate compared with treated persons (97% vs 99%; $P < .001$). However, there were statistically significant baseline differences between the 2 groups, and the study did not adjust for potential confounding.

Another fair-quality prospective study conducted in Japan reported the recurrence and survival rates for 2 separate cohorts (1993-2004 and 2005-2013) with papillary microcarcinoma.[13-16] In the first cohort, 1055 persons chose treatment with immediate surgery and 340 opted for surveillance. After approximately 6 years of follow-up, 32.1% of patients who opted for surveillance had surgery, and 2 patients in the immediate surgery group and none in the observation group had died. In the second cohort, 974 persons opted for treatment with immediate surgery, and 1179 opted for active surveillance. After approximately 4 years of follow-up, 8% of patients who opted for active surveillance had surgery, and no patients in either group developed distant metastases or died of thyroid cancer. Because of major limitations in the design of both studies (eg, lack of adjustment for confounding), it is uncertain whether earlier or immediate treatment vs delayed or no surgical treatment improves patient outcomes for papillary carcinoma or microcarcinoma.

Potential Harms of Screening and Treatment

No studies directly examined the harms of screening for thyroid cancer using neck palpation or ultrasound. Overall, evidence on the harms of screening for thyroid cancer is very limited, including harms of diagnostic biopsy with fine-needle aspiration (eg, hospitalization, postprocedural hematoma, and needle tract implementation).[5,17,18] The USPSTF found 36 fair-quality studies reporting on surgical harms, 32 studies on permanent hypoparathyroidism (hypocalcemia), 28 studies on permanent recurrent laryngeal nerve palsy (vocal cord paralysis), 2 studies on surgical mortality, and 15 studies on other major surgical harms.[7] The majority of studies

were retrospective observational studies, although 3 randomized trials were included. Cohort size ranged from 76 to 13 854 persons. Only 7 studies were conducted in the United States.

Considerable evidence has documented the harms of treatment with surgery and radioactive iodine therapy. The rate of permanent hypoparathyroidism varied widely (15 study groups); best estimates were 2 to 6 events per 100 total thyroidectomies, and estimates varied more with lymph node dissection. The rate of permanent recurrent laryngeal nerve palsy varied less (14 study groups), at an estimated 1 to 2 events per 100 operations (with or without lymph node dissection). Sixteen fair-quality studies (n = 94 823) provided evidence for potential harms of radioactive iodine remnant ablation or therapy.[7] Estimates of a secondary malignancy ranged from approximately 12 to 13 excess cancers per 10 000 person-years,[7,19,20] and salivary gland harms (eg, dry mouth) ranged from 2.3 to 21 events per 100 persons.[7,21-26]

Although no direct studies of whether screening causes overdiagnosis exist, ecological and cross-sectional data suggest that screening for thyroid cancer leads to an increase in incidence of disease without any resulting change in mortality.[5] Multiple studies in the United States show a rising incidence in thyroid cancer detection over time, with no corresponding change in the mortality rate.[7] The best ecological evidence on the overdiagnosis of thyroid cancer comes from South Korea, which has had an organized cancer screening program since 1999.[27] Although the program did not officially include screening for thyroid cancer, clinicians frequently offered thyroid screening using ultrasound for a small additional cost. In 2011, the rate of thyroid cancer diagnosis was 15 times the rate in 1993, while the thyroid cancer–specific mortality rate remained stable.[27]

Autopsy studies provide additional evidence on overdiagnosis of thyroid cancer. A 2014 review by Lee et al[28] summarizes 15 studies published between 1969 and 2005 on latent thyroid cancer discovered at autopsy. Of the 8619 thyroid glands incidentally obtained at autopsy, 989 (11.5%) tested positive for papillary thyroid carcinoma. The majority of the tumors were tiny (diameter <1 to 3 mm).

Estimate of Magnitude of Net Benefit

The USPSTF found inadequate direct evidence on the benefits of screening but determined that the magnitude of the overall benefits of screening and treatment can be bounded as no greater than small, given the relative rarity of thyroid cancer, the apparent lack of difference in outcomes between treatment and surveillance (for the most common tumor types), and observational evidence showing no change in mortality over time after introduction of a mass screening program. Similarly, the USPSTF found inadequate direct evidence on the harms of screening but determined that the magnitude of the overall harms of screening and treatment can be bounded as at least moderate, given adequate evidence of harms of treatment and indirect evidence that overdiagnosis and overtreatment are likely to be substantial with population-based screening. Therefore, the USPSTF determined with moderate certainty that the net benefit of screening for thyroid cancer is negative.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from November 22 to December 26, 2016. Many respondents shared personal stories of how their clinician noticed a lump during physical examination, often prompted by symptoms such as hoarseness or throat pain, and expressed concern that the recommendation would prevent diagnosis of such cancer cases. Clinicians who interpreted the recommendation as discouraging them from performing neck examination also expressed concern. In response, the USPSTF expanded the Clinical Considerations section to clarify that this recommendation does not apply to persons who experience hoarseness, pain, difficulty swallowing, or other throat symptoms or persons who have lumps, swelling, asymmetry of the neck, or to other reasons for a neck examination.

Update of Previous USPSTF Recommendation

This is an update of the 1996 USPSTF recommendation.[29] In 1996, the USPSTF recommended against screening for thyroid cancer in asymptomatic adults using either neck palpation or ultrasound (D recommendation). In addition, using older methodology, the USPSTF issued a C recommendation for screening in asymptomatic adults with a history of radiation of the external upper body (primarily the head and neck) in infancy or childhood; in 1996, a C recommendation was defined as "insufficient evidence to recommend for or against." The USPSTF focused its current recommendation on the general asymptomatic adult population.

Recommendations of Others

The American Cancer Society does not specifically recommend screening for thyroid cancer using neck palpation or any other method.[30] In 1996, the American Academy of Family Physicians recommended against screening for thyroid cancer using neck palpation or ultrasound in asymptomatic persons.[31] The Canadian Task Force on the Periodic Health Examination does not include examination of the thyroid in its 2015 Preventive Care Checklist Form.[32] The American Thyroid Association[33] and the American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi[34] issued guidelines for the diagnosis and management of thyroid nodules in 2016; these guidelines included no recommendation on screening for thyroid cancer in asymptomatic persons.

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