Worldwide Thyroid-Cancer Epidemic? The Increasing Impact of Overdiagnosis

Salvatore Vaccarella, Ph.D., Silvia Franceschi, M.D., Freddie Bray, Ph.D., Christopher P. Wild, Ph.D., Martyn Plummer, Ph.D., and Luigino Dal Maso, Ph.D.

Several reports have described dramatic increases over recent decades in the incidence of thyroid cancer, predominantly small papillary carcinomas, even as thyroid-cancer-related mortality rates have not changed substantially. The largest increase has been observed in South Korea: the incidence among people 15 to 79 years of age (standardized to the world population) increased from 12.2 cases per 100,000 persons in 1993–1997 to 59.9 cases per 100,000 persons in 2003–2007, making thyroid cancer the most commonly diagnosed cancer among women in that country.

The introduction of new diagnostic techniques (ultrasonography, computed tomography, and magnetic resonance imaging), combined with increased medical surveillance and access to health care services, can lead to massive increases in detection of small papillary lesions caused by the

The costing data make it clear that residents contribute to THCs’ finances, as well as to the care of patients — a reality that needs to be taken into account in establishing the true cost of residency training to a sponsoring institution.

As community-based practices that rely largely on ambulatory care reimbursement for financial viability, most THC-sponsoring organizations cannot support residency programs without specific, adequate, and stable funding. Whereas teaching hospitals need residents to assist with clinical coverage for acute and inpatient care, community-based ambulatory care practices don’t have analogous coverage demands. For THCs, initiating residency programs is an elective decision that can’t be considered if it jeopardizes the practice. The decision by the secretary of health and human services to provide $150,000 per resident per year recognized this reality and established a funding level that, absent hard data, met the best estimates available at the time. Our findings suggest that $150,000 per resident per year is reasonably reflective of the true current cost of a resident to a community-based sponsor.

The views expressed in this article are those of the authors and do not necessarily reflect those of the Health Resources and Services Administration, Department of Health and Human Services, or the U.S. government.

Disclosure forms provided by the authors are available at NEJM.org.

From the Department of Health Policy and Management, Milken Institute School of Public Health, George Washington University, Washington, DC (M.R., M.M.J., F.M.); KCN Consulting, Valencia, CA (K.N.); and the Education Health Center Initiative, Seattle (K.N.).

This article was published on June 29, 2016, at NEJM.org.


DOI: 10.1056/NEJMp1607866
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Faculty compensation, 30%
Resident compensation, 26%
Clinical service administration and operational costs, 19%
In-kind costs, 9%
Other educational costs, 17%
large reservoir of asymptomatic, nonlethal disease known to exist in the thyroid gland.\(^1\) Sudden changes in thyroid-cancer incidence have also accompanied large-scale thyroid-gland surveillance in purportedly high-risk populations. In Japan’s Fukushima Prefecture, thyroid-cancer incidence among screened children and adolescents was approximately 30 times as high as the national average only a few months after intensive screening programs for these age groups began in response to the 2011 nuclear accident.\(^4\)

Studies comparing thyroid-cancer incidence during different periods and across countries can help in estimating overdiagnosis — that is, diagnosis of thyroid tumors that would not, if left alone, result in symptoms or death. Here, we provide a measure of thyroid-cancer overdiagnosis over the past two decades in selected high-income countries, based on recently developed methods and high-quality cancer-registry data (Cancer Incidence in Five Continents, International Agency for Research on Cancer, available at http://ci5.iarc.fr/CI5I-X). Using as reference populations those in countries with longstanding cancer registries, we deduced the shape of age-specific trends in thyroid-cancer incidence in the 1960s, before ultrasonography was introduced in the late 1970s.\(^3\) The “historical” age curves were remarkably similar across populations, showing exponential growth of rates with age, a finding consistent with the multistage model of carcinogenesis described by Armitage and Doll and with the behavior of most epithelial cancers. The historical age curve was used to estimate the number of cases that would have been expected if thyroid cancer had continued to be detected primarily through palpation.

The shape of the age-specific curves has changed dramatically since the 1980s, albeit to different extents in various countries (see graphs). Incidence has progressively increased among middle-aged women (and men; see Fig. S1 in the Supplementary Appendix, available at NEJM.org) but has varied to a much lesser extent at older ages, thus altering age curves over the years roughly from an exponential-growth shape to an inverted-U shape.

We attribute the excess cases beyond the number predicted by the multistage model to diagnoses of asymptomatic disease subsequent to improved diagnostic technology and increased surveillance, predominantly in young or middle-aged populations.\(^1\)

Large changes in observed age curves for women emerged in the countries most affected by the thyroid-cancer “epidemic,” including the United States, Italy, and France. A striking increase was observed among South Korean women 50 to 59 years of age, from about 35 cases per 100,000 women in 1998–2002 to more than 120 cases per 100,000 women in 2003–2007. Indeed, since 1999, approximately 13% of South Korean adults had voluntarily undergone thyroid ultrasonography within the framework of organized screening programs for five other types of cancer, and the highest rate of participation (26%) was among women 50 to 59 years of age.\(^1\) Conversely, increases in incidence in the United States, Australia, and Italy began in the 1980s, particularly among women younger than 45 years, around the time of the earliest introduction of ultrasonography in gynecologic and obstetric clinics, which favored opportunistic examinations of the thyroid gland in women of reproductive age.

The estimated number of thyroid-cancer cases attributable to increased thyroid-gland surveillance is also striking and has increased markedly over time. If there had been no changes in the shape of the age curve (estimated on the basis of data from the pre-ultrasonography period), then approximately 228,000 cases diagnosed in women in the United States between 1988 and 2007 would be considered overdiagnosed (see Fig. S2 in the Supplementary Appendix). Corresponding numbers are 65,000 in Italy, 46,000 in France, and 36,000 in Japan. Among South Korean women, overdiagnosis accounted for approximately 77,000 extra cases of thyroid cancer between 1993 and 2007. The number of overdiagnoses was smaller but still substantial in Australia (10,000), England and Scotland (7000), and the Nordic countries (Denmark, Finland, Norway, and Sweden; 6000).

Overdiagnosis increased in many countries between 1988 and 2007 (see graphs and the Supplementary Appendix). We don’t know whether this trend has continued, since post-2007 data were not available. However, if we take the most recent available period, 2003–2007, as typical of current practice, we estimate that overdiagnosis in women accounts for 90% of thyroid-cancer cases in South Korea; 70 to 80% in the United States, Italy, France, and Australia; and 50% in Japan, the Nordic countries, and England and Scotland.

A similar pattern of age curves was observed for men, al-
We added a constraint that sets as equal the expected incidence across periods among people 80 to 84 years of age, to determine whether thyroid-cancer incidence varied only minimally with age or the differences among otherwise similar or geographically close high-income countries. Changes in patterns of somatic mutations in thyroid cancer over time have been reported and may reflect the increasing proportion of papillary carcinomas after the introduction of ultrasonography. In addition, possible changes in exposure to risk factors such as diagnostic radiation, overweight, or diabetes may themselves be correlates of increased medical surveillance. Changes in access to health care, physicians’ practices, and the extent of intentional inspection of the thyroid gland or incidental findings are therefore the most likely explanations of our findings.

It’s important to bear in mind that the vast majority of patients who received a diagnosis of thyroid cancer in the countries we studied underwent total thyroidectomy, and a high proportion also received other harmful treatments (neck lymph-node dissection and radiotherapy) — practices recently discouraged in the guidelines of the American Thyroid Association. Furthermore, studies from Japan have shown that immediate surgery and watchful waiting are equally effective in averting deaths from thyroid cancer: only a small minority (3.5%) of the 1235 patients with papillary microcarcinomas who were followed for an average of 75 months had clinical progression of disease, and none died. The examples of South Korea, the United States, Italy, and France suggest that other countries should exercise caution against systematic screening for thyroid cancer and overtreatment of small nodules (<1 cm) and suggest that watchful-waiting approaches should be considered a research priority and a preferable option for patients with low-risk papillary thyroid cancers.

Finally, the enormous increase in thyroid-cancer incidence in South Korea subsequent to opportunistic ultrasonography-based screening sends a strong warning about data interpretation in the context of large-scale screening of the thyroid gland after radiation exposure from exceptional events like the nuclear accident in Fukushima. Disclosure forms provided by the authors are available at NEJM.org.

From the International Agency for Research on Cancer, Lyon, France (S.V., S.F., F.B., C.P.W., M.P.); and the Cancer Epidemiology Unit, IARC (Centro di Riferimento Oncologico) Aviano National Cancer Institute, Aviano, Italy (L.D.M.).

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DOI: 10.1056/NEJMpa1604142
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