

Recent Trends in the Identification of Incidental Pulmonary Nodules

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Abstract

Rationale: Pulmonary nodules are common incidental findings, but information about their incidence in the era of computed tomography (CT) is lacking.

Objectives: To examine recent trends in pulmonary nodule identification.

Methods: We used electronic health records and natural language processing to identify members of an integrated health system who had nodules measuring 4 to 30 mm. We calculated rates of chest CT imaging, nodule identification, and receipt of a new lung cancer diagnosis within 2 years of nodule identification, and standardized rates by age and sex to estimate the frequency of nodule identification in the U.S. population in 2010.

Measurements and Main Results: Between 2006 and 2012, more than 200,000 adult members underwent 415,581 chest CT examinations. The annual frequency of chest CT imaging increased from 1.3 to 1.9% for all adult members, whereas the frequency of nodule identification increased from 24 to 31% for all scans performed. The annual rate of chest CT increased from 15.4 to 20.7 per 1,000 person-years, and the rate of nodule identification increased from 3.9 to 6.6 per 1,000 person-years, whereas the rate of a new lung cancer diagnosis remained stable. By extrapolation, more than 4.8 million Americans underwent at least one chest CT scan and

1.57 million had a nodule identified, including 63,000 who received a new lung cancer diagnosis within 2 years.

Conclusions: Incidental pulmonary nodules are an increasingly common consequence of routine medical care, with an incidence that is much greater than recognized previously. More frequent nodule identification has not been accompanied by increases in the diagnosis of cancerous nodules.

Keywords: coin lesion; lung cancer; computed tomography

At a Glance Commentary

Scientific Knowledge of the Subject: Use of chest computed tomography is increasing over time, but large epidemiological studies of incidental pulmonary nodules and trends in their incidence have not been performed.

What This Study Adds to the Field: Between 2006 and 2012, the annual rate of pulmonary nodule identification in a large, integrated health system increased from 3.9 to 6.6 per 1,000 person-years. By extrapolation, more than 1.5 million adult Americans will have a pulmonary nodule identified each year, a number that is an order of magnitude greater than recognized previously.

Pulmonary nodules are commonly encountered in clinical practice, but basic information about their epidemiology is lacking. Despite the increasing use of

thoracic imaging with chest computed tomography (CT) (1) and the recent adoption of low-dose CT (LDCT) for lung cancer screening (2), there have been no

population-based studies of patients with lung nodules to guide clinical policy in the current era of advanced imaging. To date, most studies of pulmonary nodules have

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been limited by small samples, referral center bias, and a relatively narrow focus on evaluating the accuracy of new or existing diagnostic tests. The lack of a specific *International Classification of Disease, 9th revision* code for pulmonary nodules has also hampered research, although a specific code was introduced in late 2011.

Although most pulmonary nodules are benign, some of them represent a potentially curable form of lung cancer. Widely cited review articles report that approximately 150,000 nodules are identified in Americans each year (3, 4). However, this estimate is based on a projection that grossly overestimated the frequency of cancerous nodules (5). Other estimates of nodule incidence come from studies that were published decades ago. A population-based survey of residents of Cuyahoga County, Ohio, from 1959 reported that a nodule was detected in approximately 0.1% of approximately 675,000 chest radiographs performed (6), and a study of patients referred for chest imaging at the Mayo Clinic (Rochester, Minnesota) from 1958 found that the frequency of nodule detection was approximately 0.2% (7). However, these studies have limited relevance to current practice. Chest imaging is performed with increasing frequency every year (1, 8). Chest CT has essentially replaced radiography as the test of choice for diagnosis, and lung cancer screening with LDCT is poised to disseminate into clinical practice throughout the United States. CT is more sensitive than radiography for detecting pulmonary nodules and lung cancer (9). A systematic review of studies of lung cancer screening with LDCT reported that one or more nodules were identified in approximately 20% of all LDCT screening examinations, a frequency that is two orders of magnitude greater than the one reported historically (10).

As LDCT screening disseminates into clinical practice, the epidemiology of pulmonary nodules is likely to evolve. To understand future trends in CT use, nodule identification, and cancer detection, it will be helpful to establish their baseline frequencies from a recent time period that is uncontaminated by the adoption of screening with LDCT. We therefore performed this study in a large and sociodemographically diverse population to define the clinical epidemiology of lung nodules that are identified incidentally on chest CT scans performed for indications

other than lung cancer screening. Some of the results have been reported previously in a poster presentation (11).

Methods

We performed a retrospective, observational study of chest CT imaging and lung nodule identification in a large, integrated healthcare system. We used membership data and electronic health records to identify adult members of a prepaid, capitated health plan who underwent chest CT imaging between January 1, 2006 and December 31, 2012. Subsequently, we used a natural language processing (NLP) algorithm to scan the free text of dictated radiology reports of all chest CT scans performed during this time period and to identify reports that noted the presence of one or more pulmonary nodules measuring 4 to 30 mm in widest diameter. We calculated crude annual rates of chest imaging, nodule identification, and the diagnosis of lung cancer within 2 years following nodule detection, and derived rates standardized by age and sex to the U.S. population in 2010. The Institutional Review Board at Kaiser Permanente Southern California (KPSC) approved the study.

Setting

KPSC is an integrated healthcare system that currently provides comprehensive care to approximately 4 million members at 14 hospitals and more than 200 medical offices throughout Southern California. Chest CT scans are performed on 47 scanners at 25 different facilities and are interpreted by general radiologists at each facility. The KPSC member population has a racial, ethnic, and socioeconomic diversity that is representative of the larger population of Southern California from which it is drawn (12). Member retention rates are excellent, with frequencies of 86% at 1 year and 71% at 3 years among active members in 2010. Systematic screening of high-risk smokers and former smokers for lung cancer with LDCT was not implemented before 2013.

Patients

We included all adults (age ≥ 18 yr) who were health plan members at any time between January 1, 2006 and December 31, 2012. For new (incident) lung nodule cases, we required continuous membership for at least 2 years before the date of first nodule detection, allowing for brief gaps in

membership that were no longer than 3 months (92 d) in duration. There were no other exclusions.

Data Sources and Definitions

We identified KPSC members who underwent at least one chest CT scan between January 1, 2006 and December 31, 2012 by searching the KPSC Radiology Information System and Services files for the following Current Procedural Terminology codes for chest CT: 71250, 71260, 71270, and 71275. To identify chest CT scans in which one or more nodules were identified, we refined a NLP algorithm that we developed and validated previously (13). The revised NLP algorithm was expert rule-based and developed iteratively by using a combination of keywords (e.g., nodule, opacity), qualifiers (e.g., nodule size), and exclusionary terms (e.g., lymph, hepatic), as shown in Figure 1. The published version of the algorithm had a sensitivity of 96% and a specificity of 86% for identifying transcripts with a qualifying lung nodule compared with a reference standard of manual review by an experienced pulmonologist (M.K.G.). In a more recent validation, an improved version of the NLP algorithm (which included additional exclusionary terms) had a similar sensitivity (96%) and better specificity (92%). A qualifying (positive) result was defined as the recording of one or more nodules, the largest one of which was noted to measure from 4 to 30 mm in widest diameter. A new (incident) nodule was defined as one that was identified between January 1, 2008 and December 31, 2012 and was not preceded by a previous scan with a qualifying nodule at any time within the previous 2 years.

Statistical Analysis

To describe the frequency of chest CT imaging, nodule detection, and cancer diagnosis, we report counts, percentages, and rates. To account for individuals who had more than one chest CT scan in a given year, we report both scan- and patient-level data. We report annual rates and rates for all years combined, both for the entire sample and for subgroups stratified by age and sex. We expressed all rates in terms of member-years at risk for an event. Confidence intervals (CIs) for rates were calculated based on the Poisson distribution.

To estimate rates of chest CT imaging and nodule identification among all adults in the United States, we standardized

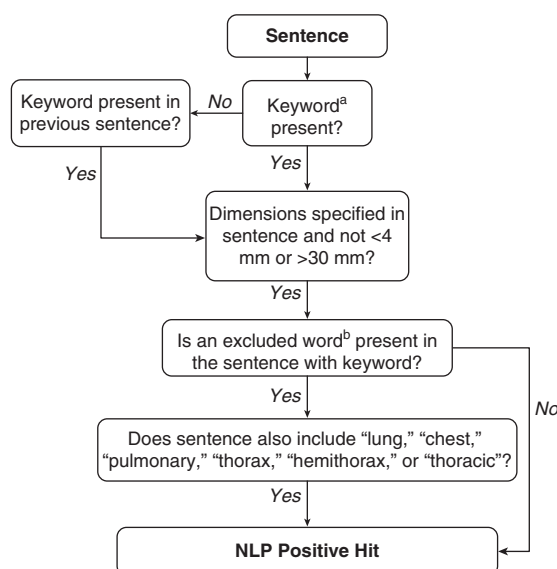


Figure 1. Schematic representation of natural language processing (NLP) algorithm (adapted by permission from Reference 12). ^aSample keywords: nodul*, opacity*, densit*, SPN, mass, tumor, ground glass; ^bsample excluded words: breast, renal, lymph, bladder, hepati*, thyroid, retroperiton*, mediastin*.

observed rates by age and sex, using data from the 2010 U.S. Census (14). We multiplied these rates by the adult population of the United States to estimate how many CT examinations were performed and how many lung nodules were identified in the United States in 2010.

Results

Between January 1, 2006, and December 31, 2012, there were more than 4.6 million unique adult members of KPSC who

collectively accrued more than 16.9 million person-years of membership (Table 1). Adult membership increased from 2.6 million in 2006 to 2.9 million in 2012, an increase of 11.5%. In 2010, most adult members were commercially insured (85%), but some received coverage through Medicare (13%) or Medi-Cal (2%). The mean \pm SD age was 45.6 \pm 17.1 years, and 52% of adult members were women.

Scan-Level Data

The number of chest CT scans performed per year increased from 46,663 in 2006 to

71,206 in 2012, an increase of 53% (Table 1). In total, 415,581 chest CT scans were performed over this 7-year study period, representing an overall rate of 24.5 scans per 1,000 person-years (95% CI, 24.4–24.6). The annual rate of chest CT scanning increased from 20.4 per 1,000 person-years (95% CI, 20.2–20.6) in 2006 to 27.0 per 1,000 person-years (95% CI, 26.8–27.2) in 2012.

The number of positive scans with a qualifying lung nodule increased from 11,172 in 2006 to 21,766 in 2012, an increase of 95% (Table 1). The percentage of scans that were positive increased from 24% in 2006 to 31% in 2012. Overall, 118,770 scans were positive (29%). The annual rate of lung nodule identification increased from 4.9 per 1,000 person-years (95% CI, 4.8–5.0) to 8.3 per 1,000 person-years (95% CI, 8.2–8.4), with an overall rate of 7.0 positive scans per 1,000 person-years (95% CI, 7.0–7.0).

Patient-Level Data

The number of unique patients who underwent at least one chest CT scan increased from 34,915 in 2006 to 53,949 in 2012, an increase of 55% (Table 2). In total, 218,079 unique patients had at least one chest CT scan during the years of the study, representing 4.7% of all adult members. The annual rate of undergoing at least one chest CT scan increased from 15.4 per 1,000 person-years (95% CI, 15.2–15.5) in 2006 to 20.7 per 1,000 person-years (95% CI, 20.5–20.9) in 2012.

The number of unique patients who had at least one positive CT scan with a qualifying lung nodule increased from 8,973

Table 1. Frequency of Chest CT Imaging and Positive Chest CT Scans, Scan-Level Data 2006 to 2012

Year	Total Members (N)	Chest CT Scans Performed (n)	Positive Chest CT Scans [n (% of Scans)]	Time at Risk for Scanning* (Person-Years)	Chest CT Scans Performed† [Rate per 1,000 Person-Years (95% CI)]	Positive CT Scans† [Rate per 1,000 Person-Years (95% CI)]
2006	2,623,719	46,663	11,172 (23.9)	2,288,046	20.4 (20.2–20.6)	4.9 (4.8–5.0)
2007	2,673,078	50,571	13,645 (27.0)	2,342,118	21.6 (21.4–21.8)	5.8 (5.7–5.9)
2008	2,672,351	55,264	15,171 (27.5)	2,369,685	23.3 (23.1–23.5)	6.4 (6.3–6.5)
2009	2,663,055	60,430	17,250 (28.5)	2,375,472	25.4 (25.2, 25.6)	7.3 (7.2–7.4)
2010	2,698,679	63,036	19,420 (30.8)	2,412,059	26.1 (25.9–26.3)	8.1 (7.9–8.2)
2011	2,822,145	68,411	20,346 (29.7)	2,540,580	26.9 (26.7–27.1)	8.0 (7.9–8.1)
2012	2,916,094	71,206	21,766 (30.6)	2,635,220	27.0 (26.8–27.2)	8.3 (8.2–8.4)
2006–2012 Total‡	19,069,121	415,581	118,770 (28.6)	16,963,179	24.5 (24.4–24.6)	7.0 (7.0–7.0)

Definition of abbreviations: CI = confidence interval; CT = computed tomography.

*Follow-up endpoints were defined as disenrollment, death or the end of each year, whichever occurred first.

†Ninety-five percent CIs were determined based on a Poisson model for a rare event.

‡Members with more than 1 year of membership were counted more than once.

Table 2. Frequency of Chest CT Imaging and Positive Chest CT Scans, Adult Member-Level Data 2006 to 2012

Year	Total Members (N)	Members with ≥ 1 Chest CT Scan [n (% of Members)]	Members with ≥ 1 Positive Chest CT Scan [n (% of Members Scanned)]	Time at Risk for Scanning* (Person-Years)	Time at Risk for Having Positive Scan [†] (Person-Years)	≥ 1 Chest CT Scan Performed [‡] [Rate per 1,000 Person-Years (95% CI)]	≥ 1 Positive CT Scan [‡] [Rate per 1,000 Person-Years (95% CI)]
2006	2,623,719	34,915 (1.3)	8,973 (25.7)	2,270,315	2,283,728	15.4 (15.2–15.5)	3.9 (3.8–4.0)
2007	2,673,078	37,294 (1.4)	10,860 (29.1)	2,323,514	2,336,821	16.1 (15.9–16.2)	4.6 (4.6–4.7)
2008	2,672,351	41,073 (1.5)	12,132 (29.5)	2,349,300	2,363,762	17.5 (17.3–17.7)	5.1 (5.0–5.2)
2009	2,663,055	45,411 (1.7)	13,794 (30.4)	2,352,838	2,368,731	19.3 (19.1–19.5)	5.8 (5.7–5.9)
2010	2,698,679	47,773 (1.8)	15,592 (32.6)	2,388,202	2,404,342	20.0 (19.8–20.2)	6.5 (6.4–6.6)
2011	2,822,145	51,499 (1.8)	16,289 (31.6)	2,514,851	2,532,401	20.5 (20.3–20.7)	6.4 (6.3–6.5)
2012	2,916,094	53,949 (1.9)	17,368 (32.2)	2,607,705	2,626,455	20.7 (20.5–20.9)	6.6 (6.5–6.7)
2006–2012 Total	19,069,121	311,914 (1.6)	95,008 (30.5)	16,806,725	16,916,239	18.6 (18.5–18.6)	5.6 (5.6–5.7)
2006–2012 Unique members [§]	4,613,081	218,079 (4.7)	68,998 (31.6)				

Definition of abbreviations: CI = confidence interval; CT = computed tomography.

*Follow-up endpoints were defined as yearly first chest CT scan, disenrollment, death, or the end of each year, whichever occurred first.

[†]Follow-up endpoints were defined as yearly first positive chest CT scan, disenrollment, death, or the end of each year, whichever occurred first.

[‡]Ninety-five percent CIs were determined based on a Poisson model for a rare event.

[§]Members with more than 1 year of membership were counted once.

in 2006 to 17,368 in 2012, an increase of 94% (Table 2). During all years, 68,998 unique patients had at least one positive CT scan with a qualifying lung nodule (1.5% of all unique members). The mean age of patients with a nodule was 63.4 ± 14.4 years, and this group included 44% never smokers, 36% former smokers, 10% current smokers, and 1% passive smokers; the remaining patients had missing information on smoking status. The size distribution of the largest nodule was 4 to 5 mm (24%), 6 to

8 mm (21%), 9 to 12 mm (18%), 13 to 20 mm (22%), and >20 mm (15%). The annual rate of having at least one positive scan increased from 3.9 per 1,000 person-years (95% CI, 3.8–4.0) in 2006 to 6.6 per 1,000 person-years (95% CI, 6.5–6.7) in 2012.

Overall, 45,435 patients (1.7% of all unique members with 2 years of near-continuous membership) had a scan that met our definition for a new (incident) nodule between 2008 and 2012 (Table 3). The incidence increased from 4.7 per 1,000

person-years (95% CI, 4.6–4.8) in 2008 to 5.4 per 1,000 person-years (95% CI, 5.3–5.5) in 2012. In 2010, the incidence increased with increasing age from 0.4 per 1,000 person-years (95% CI, 0.3–0.5) among 18 to 24 year olds to 20.3 per 1,000 person-years (95% CI, 18.5–22.2) among 85 to 89 year olds. The incidence was slightly higher overall for adult women (5.8 per 1,000 person-years, 95% CI, 5.6–5.9) than for adult men (5.2 per 1,000 person-years, 95% CI, 5.0–5.3). However, among

Table 3. Incidence of New Positive Chest CT Scans, Adult Member-Level Data 2008 to 2012*

Year	Total Members [†] (N)	Members with New Positive CT Scan [†] [n (% of Members)]	Time at Risk for Having a New Positive CT Scan ^{†‡} (Person-Years)	New Positive CT Scan [§] [Rate Per 1,000 Person-Years (95% CI)]
2008	1,790,173	7,947 (0.4)	1,707,826	4.7 (4.6–4.8)
2009	1,850,370	8,829 (0.5)	1,758,735	5.0 (4.9–5.1)
2010	1,885,287	9,868 (0.5)	1,799,880	5.5 (5.4–5.6)
2011	1,936,767	9,738 (0.5)	1,859,358	5.2 (5.1–5.3)
2012	1,999,830	10,297 (0.5)	1,925,423	5.4 (5.3–5.5)
2008–2012 Total	9,462,427	46,679 (0.5)	9,051,223	5.2 (5.1–5.2)
2008–2012 Unique members	2,722,053	45,435 (1.7)		

Definition of abbreviations: CI = confidence interval; CT = computed tomography.

*Members with continuous membership for at least 2 years, except for brief enrollment gaps ≤ 92 days.

[†]Members with positive chest CT scans in previous 2 years were excluded from the denominator.

[‡]Excludes enrollment gaps, and follow-up endpoints were defined as yearly first positive chest CT scan within 2 years, disenrollment, death, or the end of each year, whichever occurred first.

[§]Ninety-five percent CIs were determined based on a Poisson model for a rare event.

^{||}Members with more than 1 year of membership were counted once.

those aged 70 years or older, the rate was higher for men than for women (Figure 2).

Among patients who had at least one positive CT scan for a qualifying lung nodule between 2006 and 2012, 3,557 of them received a lung cancer diagnosis within 2 years of the date of a positive transcript (Table 4). This represented 5.2% of all patients with a qualifying lung nodule, and 0.11% of all adult members. The rate of lung cancer diagnosis within 2 years did not appear to increase over time, with an overall rate of 2.9 per 10,000 person-years (95% CI, 2.8–3.0). The median time between the date of the positive scan and the date of the lung cancer diagnosis was 55 days (interquartile range, 21–200 d). Cancer diagnoses increased nonlinearly from 0.1 per 10,000 person-years (95% CI, 0.0–0.5) among 35 to 39 year olds to 16.4 per 10,000 person-years (95% CI, 13.0–20.8) among 80 to 84 year olds.

Age- and Sex-standardized Rates

Standardized by age and sex to the adult population of United States in 2010, the rate of undergoing at least one chest CT scan in 2010 was 20.7 per 1,000 person-years (95%

CI, 20.5–20.8). The standardized annual rate of having at least one positive CT scan with a qualifying nodule was 6.7 per 1,000 person-years (95% CI, 6.6–6.8), the standardized rate of having a new nodule identified was 5.0 per 1,000 person-years (95% CI, 4.9–5.1), and the standardized rate of receiving a lung cancer diagnosis within 2 years of a having a scan with a qualifying nodule was 2.7 per 10,000 person-years (95% CI, 2.5–3.0). Extrapolating to the U.S. population of more than 234.5 million adults in 2010, we estimated that more than 4.8 million Americans underwent at least one chest CT scan, 1.57 million had at a lung nodule identified on at least one chest CT scan, approximately 1.2 million had a new nodule identified, and more than 63,000 received a new lung cancer diagnosis within 2 years.

Discussion

In this retrospective cohort study from a large, integrated healthcare system, we found that incidental pulmonary nodules were identified much more frequently than

previously reported, and that their incidence increased steadily from 2006 to 2012. Over this 7-year period, adult membership in the health plan increased by 11.5%, whereas the annual number of chest CT scans increased by 53%, the annual number of scans with a lung nodule increased by 95%, and the frequency of nodule detection on a given scan increased from 24 to 31%. As a result, the annual rate of lung nodule identification increased substantially, from 4.9 to 8.3 per 1,000 patient-years of exposure time.

Our results indicate that both increased use of chest CT scanning and more frequent detection of a nodule on any given scan are jointly responsible for the rise in nodule identification. Increased use appears to be the more important factor, especially since 2010 when the detection frequency seems to have reached a plateau at approximately 32% of all scans performed. However, it seems plausible that greater proficiency in detection could at least be partly explained by greater awareness among general radiologists, which has been spurred by advances in lung cancer screening over the last 15 years and publication of the Fleischner Society recommendations for pulmonary nodule evaluation in 2005 (15). Improvements in CT technology also may have contributed to the initial increase, but only partly, because of the limited turnover in scanners during the study years. Only 10 of 47 scanners were removed from service and replaced during the study period, including 3 in the first year and 2 in the last year of the study. Protocols for image acquisition and reconstruction were updated sporadically, employing thinner sections, and coronal and sagittal reconstructions that probably facilitated nodule detection.

Although nodule identification increased over time, the incidence of receiving a lung cancer diagnosis within 2 years of nodule detection did not increase, suggesting that increases in imaging and detection produced more false positive results and did not identify additional cases of lung cancer. Importantly, this should not be interpreted to mean that the increased use of chest CT was not warranted, because the scans in this study were performed for indications other than lung cancer screening. However, it does suggest that the benefits of increased vigilance for detecting an incidental nodule on any given scan may have reached or surpassed their limits.

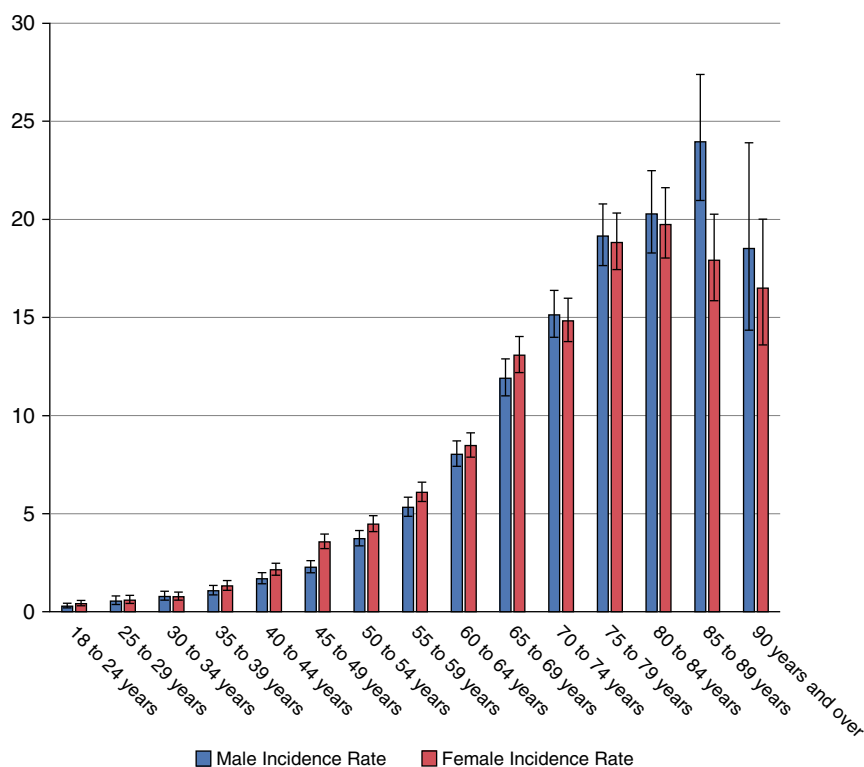


Figure 2. Age-specific rates of new pulmonary nodules identified by chest computed tomography scan (per 1,000 person-years). Error bars represent the 95% confidence interval.

Table 4. Incidence of New Lung Cancer Diagnosis within 2 Years of a Positive Chest CT Scan, Adult Member–Level Data 2006–2012*

Year	Total Members [†] (N)	Members with Positive CT Scan and Subsequent Diagnosis of Lung Cancer [‡] [n (% of Members)]	Time at Risk for Having Positive CT Scan ^{‡§} (Person-Years)	Positive CT Scan and Subsequent Diagnosis of Lung Cancer ≤ 2 yr [Rate Per 10,000 Person-Years (95% CI)]
2006	1,731,137	575 (0.03%)	1,648,956	3.5 (3.2–3.8)
2007	1,755,595	483 (0.03%)	1,669,778	2.9 (2.7–3.2)
2008	1,797,679	452 (0.03%)	1,717,467	2.6 (2.4–2.9)
2009	1,858,690	512 (0.03%)	1,769,463	2.9 (2.7–3.2)
2010	1,894,978	555 (0.03%)	1,812,514	3.1 (2.8–3.3)
2011	1,948,496	507 (0.03%)	1,873,990	2.7 (2.5–3.0)
2012	2,012,440	475 (0.02%)	1,941,342	2.5 (2.2–2.7)
2006–2012 Total	12,999,015	3,559 (0.03%)	12,433,510	2.9 (2.8–3.0)
2006–2012 Member level total [¶]	3,118,169	3,557 (0.11%)		

Definition of abbreviations: CI = confidence interval; CT = computed tomography.

*Members with continuous membership for at least 2 years, except for brief enrollment gaps ≤92 days.

[†]Members with a nodule identified within previous 2 years or lung cancer diagnoses within previous 5 years were excluded.

[‡]Cancerous lung nodule diagnoses were within 2 years of positive chest CT scans.

[§]Excludes enrollment gaps, and follow-up endpoints were defined as first cancerous lung nodule diagnosis, disenrollment, death, or the end of each year, whichever occurred first.

^{||}Ninety-five percent CIs were calculated based on a Poisson model for a rare event.

[¶]Members with more than 1 year of membership were counted once.

We also found that nodule identification was slightly more common among women than men, and that rates increased dramatically with increasing age, at least until the age of 89 years. The age-related increase in nodule identification was not matched by proportional increases in new cancer diagnoses, so it probably resulted from the accumulation over time of indolent infections, granuloma and scar formation, and reactive lymph node enlargement.

Extrapolating our findings to the U.S. population in 2010, we estimated that more than 1.5 million Americans would be expected to have a nodule identified each year. This estimate is an order of magnitude greater than the conventionally reported statistic of 150,000 cases per year. This surprising finding has important implications for clinical policy and research prioritization. Resources for nodule evaluation are already limited and will be further stretched by the uptake of lung cancer screening, with an estimated 8 million Americans currently meeting eligibility criteria (16). Furthermore, practices for lung nodule evaluation have not been standardized, and existing guidelines are dominated by weak recommendations based on low-quality evidence (17). Studies to compare the effectiveness of strategies for nodule

evaluation should be prioritized. As lung cancer screening diffuses into routine clinical practice, the frequency of nodule identification may increase substantially, although it seems likely that incidental nodules will continue to outnumber screening-detected nodules, at least over the short run.

The validity of our findings is supported by comparison with benchmarks from previous studies of CT imaging, studies of lung cancer screening, and data from the Surveillance Epidemiology and End Results tumor registry. A study of CT imaging performed in six other integrated health systems reported use rates for chest CT of 23 per 1,000 in 2008 (1), which matches our estimate of chest CT use in that year. The strikingly higher rate of chest CT use among the elderly that we observed has also been reported previously (8). A unique and important contribution of our study is that we were able to report imaging test results and use. Our finding that a (likely) incidental lung nodule was identified on 29% of all chest CT examinations demonstrates that incidental nodules are detected at least as frequently as screening-detected nodules, as documented in a systematic review of 8 randomized trials and 13 cohort studies of screening with LDCT, which reported a frequency range of 3 to 51% (mean 20%)

(10). Our projected number of cancerous nodules is supported by a previous analysis of Surveillance Epidemiology and End Results registry data for 84,152 cases of non-small cell lung cancer, with complete information for tumor size and stage, which found that 23,180 cases (28%) had a tumor size ≤25 mm and 39,574 cases (47%) had a tumor size ≤35 mm (18). By extrapolation, approximately 72,000 of the 224,210 cases of lung cancer in the United States in 2014 were ≤30 mm in size, a figure that is actually slightly greater than the 63,000 malignant pulmonary nodules per year that we estimated based on our data.

One limitation of our study is the imperfect accuracy of the NLP algorithm for nodule identification. In our sample, the net balance of false positive minus false negative cases (as defined by the NLP algorithm) was approximately 15%, and this should be taken into account when interpreting our estimates. In addition, we included nodules as small as 4 mm in diameter. Although this is consistent with the definition used in previous studies of nodules found on chest CT, recent data suggest that screening-detected nodules that measure less than 6 to 7 mm in diameter are unlikely to be cancerous and do not require further evaluation other than repeat annual screening (19, 20).

Another limitation is that we standardized population-based estimates by age and sex but not by race/ethnicity. However, no published evidence exists that nodules are more or less common among patients from particular racial or ethnic subgroups. More important factors affecting nodule prevalence are believed to include smoking history, geographic location, and CT scanner settings, although a systematic review of LDCT screening found no association between any of these variables and nodule identification rates (10).

We believe our results are broadly generalizable to the overall U.S. population, but rates of imaging and nodule detection may differ in other clinical settings. Although the age distribution of the KPSC membership is similar to that of the Southern California region overall, rates of nodule detection will be higher in settings

that serve a larger percentage of older persons. Likewise, rates of nodule detection may be higher in geographic regions characterized by higher rates of infection with endemic mycoses, and detection rates may also be higher at academic centers where scans are typically reviewed and interpreted by specialist chest radiologists. Finally, economic incentives may favor greater use of imaging at the margin in fee-for-service environments compared with what we observed in our capitated setting.

We conclude that incidental pulmonary nodules are identified in clinical practice much more frequently than previously recognized. Increased identification over time appears to be due to more frequent use of CT imaging as a diagnostic tool, and to a lesser extent, more vigilant detection of nodules on any given CT scan. Rates increased dramatically with

increasing age, and were slightly greater for women than men. The stable incidence of cancerous nodules in the face of greater use of imaging and higher rates of nodule identification suggests that more frequent diagnostic imaging does not identify more cases of lung cancer. This does not imply that screening of high-risk asymptomatic individuals will not improve early detection of lung cancer or lung cancer-specific mortality, but it does establish that incidental pulmonary nodules are an increasingly common consequence of routine medical care. ■

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