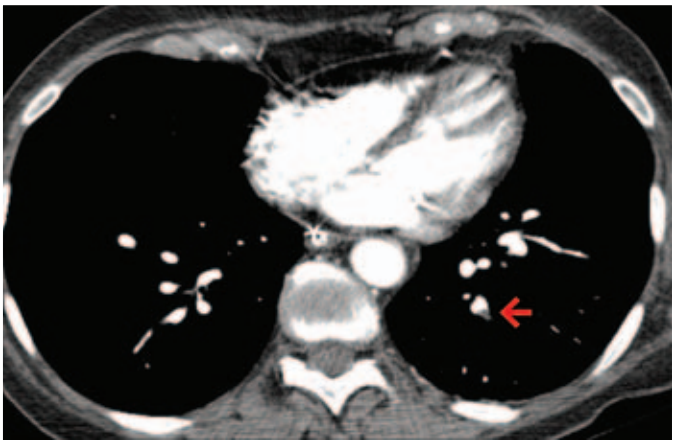
This article is the first of a series on overdiagnosis looking at the risks and harms to patients of expanding definitions of disease and increasing use of new diagnostic technologies.

TOO MUCH MEDICINE

WHEN A TEST IS TOO GOOD

How CT pulmonary angiograms find pulmonary emboli that do not need to be found



Computed tomography pulmonary angiogram showing a small pulmonary embolism (indicated by arrow)

SUMMARY BOX

Clinical context—Pulmonary embolism has been described as one of the most commonly missed deadly diagnoses

Diagnostic change—The introduction and rapid uptake of multidetector computed tomographic pulmonary angiography

Rationale for change—CT pulmonary angiography is much more sensitive than ventilation perfusion scanning so fewer pulmonary emboli will be missed

Leap of faith—Finding "missed" pulmonary emboli saves lives

Increase in disease—US data show 80% rise in incidence of pulmonary embolism between 1998 and 2006 after CT pulmonary angiography was introduced (from 62.1/100 000 to 112.3/100 000)

Evidence of overdiagnosis—Combination of large increase in incidence, reduced case fatality (in-hospital deaths among people with a diagnosis of pulmonary embolism), and a minimal decrease in mortality (deaths from pulmonary embolism in the population) suggests that many of the extra emboli being detected are not clinically important

Harms from overdiagnosis—Substantial increase in complications from anticoagulation. Anxiety and inconvenience for patients following diagnosis and treatment

Limitations—Evidence for overdiagnosis is derived from administrative data or single institution case series. Without prospectively observing untreated patients, it is impossible to be certain which emboli are not clinically important

Conclusion— CT pulmonary angiography has reduced missed pulmonary embolism but seems to result in overdiagnosis. We need to learn which small emboli need treatment

For decades clinicians have been taught that pulmonary embolism—defined by the National Institutes of Health as a "sudden blockage in a lung artery"[1]—always matters and to be vigilant because a missed embolism can be fatal.[2] When a patient presents with shortness of breath, pleuritic chest pain, tachycardia, or signs of right heart strain, clinicians are trained to think "pulmonary embolism." Because these symptoms and signs are neither sensitive nor specific, scoring systems (such as the Wells criteria) have been developed to help clinicians decide which patients to scan,[3] although in practice, many clinicians simply proceed with imaging[4] to confirm or refute the diagnosis.

Explosion in use of CT imaging

Until recently, ventilation-perfusion (VQ) scanning, introduced in the mid-1960s, was the first line test for pulmonary embolism (table) with clinicians maintaining an appropriately high threshold for invasive pulmonary angiography.[5] VQ scanning has the advantage of being non-invasive, but the results are often inconclusive. A new technology introduced in 1998—multidetector computed tomographic (CT) pulmonary angiography—offers higher resolution and more definitive results.

With the increasing availability of CT scanners, there has been an explosion in the use of CT for various indications,[6] including pulmonary embolism. A 2005 US survey of emergency department physicians showed that most considered CT pulmonary angiography to be the first line test for pulmonary embolism.[7] This finding is consistent with observations in health maintenance organisations[8]: use of CT pulmonary angiography rose 14-fold (from 0.3 to 4.0 per 1000 beneficiaries) while VQ scanning decreased by 52% (from 2.3 to 1.1 per 1000 beneficiaries) from 2001 to 2008.

Drivers for greater pulmonary angiography use

Clinicians like CT pulmonary angiography because it allows them to find causes besides pulmonary embolism to explain non-specific symptoms (such as pleural effusion or pneumonia).[7] But the main reason why doctors have embraced the technique is to avoid missing "a silent killer."[9] The widespread availability of CT pulmonary angiography has also encouraged doctors to lower their threshold for looking for pulmonary embolism.[10]

With more testing, more pulmonary emboli are found. These extra diagnoses lead to testing even more patients because of the pervasive belief that finding even a tiny, subsegmental pulmonary embolism means you may have saved a life. Case finding has also increased as a result of the widespread use of non-specific blood tests like D-dimer and troponin, which raise suspicion of pulmonary embolism (and imaging to look for it) in patients in whom it would not otherwise have been considered.[11] Radiologists like CT pulmonary angiography because they can make definitive diagnoses more readily than with VQ scans.[12] Concerns about accusations of malpractice may also increase the use of CT pulmonary angiography.[13]

Commercial interests are also fuelling imaging rates

Purchasing the most advanced multidetector scanners can help a hospital establish a reputation for being on the cutting edge. To recoup the cost of the scanner, though, the machines must be used.[6] In addition, deep vein thrombosis and pulmonary embolism awareness campaigns led by drug companies have encouraged patients to ask about testing. In the US, Sanofi-Aventis, which produces the anticoagulant enoxaparin, ran the direct to consumer advertising campaign "killer legs," sponsored conferences on "economy class

bmj.com

- Read more about the *BMJ*'s Too Much Medicine campaign at bmj.com/too-much-medicine
- Clinical review: Diagnosis and management of pulmonary embolism (*BMJ* 2013;346:f757)

syndrome" (deep vein thrombosis and pulmonary embolism among air travellers) [14]; and created a website featuring scary anecdotes like, "My husband didn't have to die," written by "people just like you" (Preventdvt.org). It also successfully lobbied the US Congress to declare an annual deep vein thrombosis awareness month and a national screening day.[15]

Comparison of imaging tests to diagnose pulmonary embolism

	Pulmonary angiography	Ventilation-perfusion scan	Computed tomography pulmonary angiography
Year introduced	1931	1964	1998
Accuracy relative to gold standard	Gold standard	Sensitivity 98%, specificity 10%	Sensitivity 96-100%, specificity 89-98%
Advantages	Gold standard diagnostic test	Non-invasive No contrast dye (safe for patients with renal impairment) Widely available Less radiation exposure	High sensitivity and specificity Visualises lung parenchyma as well as vasculature Widely available
Disadvantages	Invasive test with potential complication of bleeding Nephrotoxic contrast and moderate radiation exposure More limited availability	Scans hard to interpret Often indeterminate Abnormal chest x ray appearance makes it even harder to interpret	Too much resolution: Finds many subsegmental emboli of unclear importance Incidental findings like pulmonary nodules Higher radiation exposure and nephrotoxic contrast

Evidence of overdiagnosis

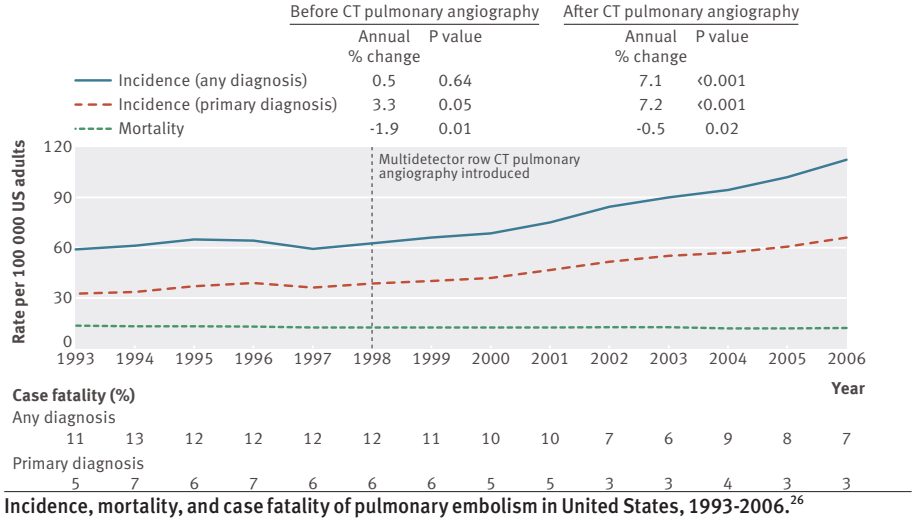
The high resolution of CT pulmonary angiography makes it possible to detect filling defects in subsegmental arteries as small as 2-3 mm in diameter.[16] Only 1% of VQ scans rated as "high probability" correspond to an isolated subsegmental pulmonary embolism,[17] compared with 15% of positive CT pulmonary angiography scans.[18]

If all pulmonary emboli caused important harm or death if untreated, finding more small clots would be an unqualified advance. However, there is evidence that some small clots do not need treatment, and finding them represents overdiagnosis. It has been argued that a normal function of the lungs is to act as a sieve to prevent small emboli formed in leg veins from travelling to the systemic arterial circulation with devastating effect, such as stroke.[19] These emboli are believed to be resorbed by the body without treatment and to have no clinical effect. This idea is supported by the finding that a surprisingly high proportion of consecutive contrast CT scans performed for other indications found incidental pulmonary emboli: in 16% of mechanically ventilated patients,[20] in 17% of inpatients over age 80,[21] and in 20% of trauma patients.[22] In addition, 50-60% of consecutive patients having autopsy were found to have an unsuspected pulmonary embolism when the pulmonary arteries were carefully dissected.[23]

Natural course studies of subsegmental pulmonary embolism also provide evidence that some emboli may not need to be found. Donato and colleagues summarised three month outcomes of 192 patients with isolated subsegmental pulmonary embolism reported in the literature.[24] Among the 65 patients who did not receive anticoagulants (at the clinician's discretion), none had a recurrent pulmonary embolism or death. And only one of the 127 patients who received anticoagulation had a recurrent (non-fatal) pulmonary embolism, a substantially lower rate than the typical recurrence rate with larger pulmonary embolism (6%).[25]

Evidence from population trends and one randomised trial also supports the view that pulmonary embolism is overdiagnosed.[26-30] Using national US administrative data, we showed that age adjusted incidence of pulmonary embolism, which was stable in the five years before the introduction of multidetector CT pulmonary angiography, increased by 80% in the eight years after it was introduced: from 62.1 to 112.3 per 100 000 US adults (figure).[26] Despite this near doubling of diagnoses, age adjusted mortality from pulmonary embolism (deaths in the US population) changed little: from 12.3 to 11.9 per 100 000. Age adjusted case fatality of pulmonary embolism (in-hospital deaths), however, decreased by one third, from 12.1% to 7.8%, P<0.001), suggesting that the extra pulmonary emboli being detected are less lethal (given that treatment has not become more effective). More non-fatal pulmonary emboli dilute case fatality but do not change mortality. Similar patterns have been observed at the state level.[27 28]

The rising incidence of pulmonary embolism and stable mortality is particularly striking given the simultaneous push for venous thromboembolism prophylaxis for hospital patients, most notably through the adoption of a national quality measure (http://qualitymeasures.ahrq.gov). More systematic use of prophylaxis would be expected to decrease both pulmonary embolism incidence and mortality. Nevertheless, incidence has risen. This rise is unlikely to represent a true change in the underlying rate of pulmonary embolism, as the major risk factors for pulmonary embolism have not shown a parallel increase.[27] The more likely explanation is increased use of CT in general[6] resulting in incidental detection of pulmonary embolism on contrast CT scans performed for other reasons[20-22] and CT pulmonary angiography specifically.



Incidence, mortality, and case fatality of pulmonary embolism in United States, 1993-2006.[26]

Limitations of the evidence

Inferring overdiagnosis by observing epidemiological trends has limitations because the evidence is derived from administrative data (coding on discharge records and death certificates) with imperfect accuracy, insufficient clinical detail, and lack of standardisation across institutions. But its strength lies in its representativeness of the population and reflection of actual clinical

practice, in contrast with randomised trials that study a highly selected population under highly controlled conditions.

Case series that identified patients with pulmonary embolism by review of imaging for suspected embolism rather than relying on discharge coding have been able to link outcomes to individual patients. These single institution series show that the rise in incidence is largely due to the increased detection of subsegmental pulmonary embolism.[31-33]

The best evidence of overdiagnosis comes from a trial that randomised 1417 patients with an intermediate to high probability of pulmonary embolism to receive VQ scanning or CT pulmonary angiography.[30] Although CT pulmonary angiography detected more emboli than VQ scans (19.2% *v* 14.2%, P=0.01), there was no difference in death from pulmonary embolism or other unknown causes (0.3% *v* 0.3%) over three months.

Definitive evidence of overdiagnosis would, of course, be the finding that untreated patients never experienced harm from the pulmonary embolism during the rest of their lives and died from another cause, but no such studies exist.

Harms to patients and cost to health systems from overdiagnosis

The main harm from overdiagnosis is unnecessary treatment, which in the case of pulmonary embolism means anticoagulation—a leading cause of medication related death.[34] Because of ongoing controversy about duration of therapy, exposure to unnecessary and dangerous anticoagulation may be lifelong.

In some studies, complications of anticoagulation are more common than the problem treatment is meant to prevent: recurrent venous thromboembolism. Notably, in the largest case series of patients given anticoagulants for isolated subsegmental pulmonary embolism (n=93), the risk of major bleeding was 5.3% but the risk of recurrent venous thromboembolism was only 0.7%.[24] In our study, in parallel with the increased incidence of pulmonary embolism, we found presumed anticoagulation complications for US patients admitted to hospital with pulmonary embolism to have increased from 3.1 to 5.3 per 100 000 (P<0.001) between 1998 and 2006.[26]

Overdiagnosis also causes patients harm from inconvenience and anxiety. The current standard of care (warfarin) requires frequent blood tests, dietary changes, and constant fear of bleeding or clotting if the international normalised ratio is not in the target range. Patients may also be harmed by the fear and anxiety from being unnecessarily told that they have a potentially life threatening disease.[23] In addition, health insurers may charge them higher premiums because they have a "pre-existing condition."

Challenging assumptions in pulmonary embolism

Whenever you think pulmonary embolism, test for it

This remains good advice, but doctors should first use the Wells score (www.mdcalc.com/wells-criteria-for-pulmonary-embolism-pe/) and D-dimer testing to determine the likelihood of pulmonary embolism
Patients with a Wells score <4 do not need any imaging as long as their D-dimer blood concentration is normal

CT pulmonary angiography is always the best test

CT pulmonary angiography is sensitive and easy to get, but for clinically stable patients, alternative tests reduce exposure radiation, cost less, and are less likely to lead to overdiagnosis
VQ scans may make more sense for younger patients (less radiation), patients with normal lungs (a definitive result is more likely), and patients with renal dysfunction (no nephrotoxic contrast)
Detection of deep vein thrombosis by ultrasonography of the legs when pulmonary embolism is suspected makes subsequent lung imaging unnecessary because patients need anticoagulation anyway

All patients need anticoagulants

For patients with an isolated subsegmental pulmonary embolism harms may outweigh benefits. Patients with subsegmental emboli who take anticoagulants have a low chance of having another clot (0.7%) but a 5.3% chance of major bleeding[24]
Patients need to understand these trade-offs and be offered the opportunity to choose whether to take anticoagulants

Overdiagnosis and overtreatment are also costly to health systems. The mean charge associated with admission for pulmonary embolism in the US increased from roughly $25 000 (£17 000; €19 000) to $44 000 between 1998 and 2006.[35] The mean cost of subsequent warfarin anticoagulation, associated laboratory tests, and clinic visits was $2694.[36] The recent introduction of newer anticoagulants (dabigatran, rivaroxaban) will decrease the need for testing, but the drugs are substantially more expensive than warfarin ($3000 *v* $48 a year[37]).

How to do better

Pulmonary embolism is underdiagnosed as well as overdiagnosed,[38] and ideally, improved tests would make it possible to find all clinically important emboli before patients experience an adverse outcome. Unfortunately, although highly sensitive tests find more emboli, they do so at the cost of overdiagnosis.

Addressing the problem of overdiagnosis is challenging (box). The answer is not simply to do less testing—clinicians should continue to have a low threshold for considering pulmonary embolism—but to test (and subsequently treat) more selectively and to consider alternative tests such as VQ scanning and ultrasonography when appropriate.[39]

Take steps to image less

Clinical practice guidelines[11 40 41] and the Choosing Wisely Campaign[42] suggest clinicians should reserve CT pulmonary angiography for patients at intermediate to high risk of pulmonary embolism based on algorithms that combine clinical probability and D-dimer test results.[43] Large, prospective studies have shown the safety of this approach.[43 44] Use of algorithms could be increased by inserting them into the ordering process for CT pulmonary angiography[45] or empowering radiologists to challenge use of CT pulmonary angiography in patients with a low likelihood of pulmonary embolism.[12]

Avoiding CT pulmonary angiography in patients with a low likelihood of pulmonary embolism would reduce exposure to nephrotoxic contrast and carcinogenic radiation. The average effective radiation dose from a CT pulmonary angiography is 10-15 millisieverts (compared with 2-2.5 mSV for a VQ scan and 5 mSV for invasive pulmonary angiography).[10 46] The radiation exposure is particularly worrisome for young women; for every 1000 20 year old women who have CT pulmonary angiography, about three will develop cancer.[10] Less CT pulmonary angiography would also mean fewer false positive results and "incidentalomas." Roughly a quarter of CT pulmonary angiographs detect an unexpected abnormality such as a pulmonary nodule, thyroid nodule, or adenopathy, resulting in further scans or invasive testing to rule out cancer.[47] Most are false alarms.

Consider less sensitive imaging

An alternative for clinically stable patients is to use other tests for venous thromboembolism, such as VQ scan or Doppler ultrasonography of the legs. Implementing policies to use VQ scans as the first line test for pulmonary embolism in stable patients with a normal x ray appearance can reduce use of CT pulmonary angiography and decrease detection of subsegmental pulmonary embolism without increasing deaths from pulmonary embolism.[29 48]

Consider not treating some subsegmental pulmonary emboli

Although some guidelines recommend anticoagulation for all pulmonary emboli,[41 49] others acknowledge that anticoagulation may not be warranted in all cases because of uncertainty about the balance of benefits and harms for treating isolated subsegmental pulmonary embolism.[11 40] Some authors suggest withholding anticoagulation for stable patients with isolated

subsegmental pulmonary embolism and adequate cardiopulmonary reserve.[50] If a subsegmental pulmonary embolism is not treated, patients should be monitored for new respiratory symptoms and for deep vein thrombosis with serial ultrasonography for three to six months to decide whether anticoagulation can be safely withheld.

Unresolved questions

Many unresolved questions remain which require further research. What is the natural course and prognosis of untreated subsegmental pulmonary embolism? Does asymptomatic, incidentally detected pulmonary embolism have the same outcomes and prognosis as symptomatic pulmonary embolism? What are the benefits and harms of treating subsegmental pulmonary embolism with anticoagulation?

Conclusion

Pulmonary embolism is unquestionably an important cause of death, and rapid diagnosis and treatment can be life saving. But the diagnostic zeal and technological advances meant to improve outcomes of patients with pulmonary embolism are double edged swords: some patients are helped, but many are harmed through overdiagnosis and overtreatment. The idea that pulmonary embolism can be overdiagnosed will be new and counterintuitive for some clinicians, but the harms are just as real as those of underdiagnosis. To improve outcomes for all patients, we need to learn more about which small emboli need treatment. Importantly, an ongoing prospective cohort study is assessing the safety of withholding treatment for stable patients with isolated subsegmental pulmonary embolism (ClinicalTrials.gov Identifier: NCT01455818).

Renda Soylemez Wiener assistant professor,
Lisa M Schwartz professor,
Steven Woloshin professor,
Correspondence to: R S Wiener **rwiener@bu.edu**

Accepted: 14 April 2013

We thank William C Black for feedback. RSW is supported by a career development award from the National Cancer Institute (K07 CA138772) and the US Department of Veterans Affairs. The funding organisations had no role in the preparation, review, or approval of the manuscript. Data collection on use of CT pulmonary angiography versus VQ scanning in health maintenance organisations was supported by the National Cancer Institute funded by Cancer Research Network Across Health Care Systems (U19CA79689). We thank Rebecca Smith-Bindman, UCSF and the investigators at the contributing data sites for sharing these data: Diana Miglioretti and Eric Johnson (Group Health Cooperative), Sheila Weinmann (Kaiser Permanente Northwest), Robert Greenlee (Marshfield Clinic Research Foundation), Douglas Roblin (Kaiser Permanente Georgia), and Andrew Williams (Kaiser Permanente Hawaii).

Contributors and sources: Research by RSW (a pulmonologist) and LMS and SW (general internists) has focused on understanding overdiagnosis and overtreatment and on how to improve doctor-patient communication around these complex issues. RSW, LMS, and SW contributed equally to the manuscript. All authors drafted the article, critically revised it for important intellectual content, and gave final approval of the manuscript version to be published. RSW is responsible for the overall content as guarantor.

Competing interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

1 National Heart Lung and Blood Institute. What is pulmonary embolism? www.nhlbi.nih.gov/health/health-topics/topics/pe/.
2 Handler JA, Feied CF. Acute pulmonary embolism. Aggressive therapy with anticoagulants and thrombolytics. *Postgrad Med* 1995;97:61-2, 65-8, 71-2.
3 Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med* 2001;17;135:98-107.
4 Adams DM, Stevens SM, Woller SC, Evans RS, Lloyd JF, Snow GL, et al. Adherence to PIOPED II investigators' recommendations for computed tomography pulmonary angiography. *Am J Med* 2013;126:36-42.
5 Stein PD, Hull RD, Ghali WA, Patel KC, Olson RE, Meyers FA, et al. Tracking the uptake of evidence: two decades of hospital practice trends for diagnosing deep vein thrombosis and pulmonary embolism. *Arch Intern Med* 2003;163:1213-9.
6 Smith-Bindman R, Miglioretti DL, Larson EB. Rising use of diagnostic medical imaging in a large integrated health system. *Health Aff (Millwood)* 2008;27:1491-502.
7 Weiss CR, Scatarige JC, Diette GB, Haponik EF, Merriman B, Fishman EK. CT pulmonary angiography is the first-line imaging test for acute pulmonary embolism: a survey of US clinicians. *Acad Radiol* 2006;13:434-46.
8 Smith-Bindman R, Miglioretti DL, Johnson E, Lee C, Feigelson HS, Flynn M, et al. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. *JAMA* 2012;307:2400-9.
9 Calder KK, Herbert M, Henderson SO. The mortality of untreated pulmonary embolism in emergency department patients. *Ann Emerg Med* 2005;45:302-10.
10 Smith-Bindman R, Lipson J, Marcus R, Kim KP, Mahesh M, Gould R, et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med* 2009;169:2078-86.
11 Remy-Jardin M, Pistolesi M, Goodman LR, Gefter WB, Gottschalk A, Mayo JR, et al. Management of suspected acute pulmonary embolism in the era of CT angiography: a statement from the Fleischner Society. *Radiology* 2007;245:315-29.
12 Gottlieb RH. Imaging for whom: patient or physician? *AJR Am J Roentgenol* 2005;185:1399-403.
13 Rohacek M, Buatsi J, Szucs-Farkas Z, Kleim B, Zimmermann H, Exadaktylos A, et al. Ordering CT pulmonary angiography to exclude pulmonary embolism: defense versus evidence in the emergency room. *Intensive Care Med* 2012;38:1345-51.
14 Duff Wilson A. Many new drugs have strong dose of media hype. *Seattle Times* 2010 Mar 16. http://seattletimes.com/html/health/sick4.html.
15 PreventDVT.org. About the Coalition to Prevent Deep-Vein Thrombosis. www.preventdvt.org/coalition/about.aspx.
16 Ghaye B. Peripheral pulmonary embolism on multidetector CT pulmonary angiography. *JBR-BTR* 2007;90:100-8.
17 Stein PD, Henry JW. Prevalence of acute pulmonary embolism in central and subsegmental pulmonary arteries and relation to probability interpretation of ventilation/perfusion lung scans. *Chest* 1997;111:1246-8.
18 Carrier M, Righini M, Wells PS, Perrier A, Anderson DR, Rodger MA, et al. Subsegmental pulmonary embolism diagnosed by computed tomography: incidence and clinical implications. A systematic review and meta-analysis of the management outcome studies. *J Thromb Haemost* 2010;8:1716-22.
19 Goodman LR. Small pulmonary emboli: what do we know? *Radiology* 2005;23:654-8.
20 Minet C, Lugosi M, Savoye PY, Menez C, Ruckly S, Bonadona A, et al. Pulmonary embolism in mechanically ventilated patients requiring computed tomography: prevalence, risk factors, and outcome. *Crit Care Med* 2012;40:3202-8.
21 Ritchie G, McGurk S, McCreath C, Graham C, Murchison JT. Prospective evaluation of unsuspected pulmonary embolism on contrast enhanced multidetector CT (MDCT) scanning. *Thorax* 2007;62:536-40.
22 Schultz DJ, Brasel KJ, Washington L, Goodman LR, Quickel RR, Lipchik RJ, et al. Incidence of asymptomatic pulmonary embolism in moderately to severely injured trauma patients. *J Trauma* 2004;56:727-31; discussion 731-3.
23 Robin ED. Overdiagnosis and overtreatment of pulmonary embolism: the emperor may have no clothes. *Ann Intern Med* 1977;87:775-81.
24 Donato AA, Khoche S, Santora J, Wagner B. Clinical outcomes in patients with isolated subsegmental pulmonary emboli diagnosed by multidetector CT pulmonary angiography. *Thromb Res* 2010;126:e266-70.
25 Heit JA, Lahr BD, Petterson TM, Bailey KR, Ashrani AA, Melton LJ 3rd. Heparin and warfarin anticoagulation intensity as predictors of recurrence after deep vein thrombosis or pulmonary embolism: a population-based cohort study. *Blood* 2011;118:4992-9.
26 Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. *Arch Intern Med* 2011;171:831-7.
27 Burge AJ, Freeman KD, Klapper PJ, Haramati LB. Increased diagnosis of pulmonary embolism without a corresponding decline in mortality during the CT era. *Clin Radiol* 2008;63:381-6.
28 DeMonaco NA, Dang Q, Kapoor WN, Ragni MV. Pulmonary embolism incidence is increasing with use of spiral computed tomography. *Am J Med* 2008;121:611-7.
29 Sheh SH, Bellin E, Freeman KD, Haramati LB. Pulmonary embolism diagnosis and mortality with pulmonary CT angiography versus ventilation-perfusion scintigraphy: evidence of overdiagnosis with CT? *AJR Am J Roentgenol* 2012;198:1340-5.
30 Anderson DR, Kahn SR, Rodger MA, Kovacs MJ, Morris T, Hirsch A, et al. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. *JAMA* 2007;298:2743-53.
31 Auer RC, Schulman AR, Tuorto S, Gonen M, Gonsalves J, Schwartz L, et al. Use of helical CT is associated with an increased incidence of postoperative pulmonary emboli in cancer patients with no change in the number of fatal pulmonary emboli. *J Am Coll Surg* 2009;208:871-8; discussion 878-80.
32 Parvizi J, Smith EB, Pulido L, Mamelak J, Morrison WB, Purtill JJ, et al. The rise in the incidence of pulmonary embolus after joint arthroplasty: is modern imaging to blame? *Clin Orthop Relat Res* 2007;463:107-13.
33 Prologo JD, Gilkeson RC, Diaz M, Asaad J. CT pulmonary angiography: a comparative analysis of the utilization patterns in emergency department and hospitalized patients between 1998 and 2003. *AJR Am J Roentgenol* 2004;183:1093-6.
34 Wysowski DK, Nourjah P, Swartz L. Bleeding complications with warfarin use: a prevalent adverse effect resulting in regulatory action. *Arch Intern Med* 2007;167:1414-9.
35 Park B, Messina L, Dargon P, Huang W, Ciocca R, Anderson FA. Recent trends in clinical outcomes and resource utilization for pulmonary embolism in the United States: findings from the nationwide inpatient sample. *Chest* 2009;136:983-90.
36 Bullano MF, Willey V, Hauch O, Wygant G, Spyropoulos AC, Hoffman L. Longitudinal evaluation of health plan cost per venous thromboembolism or bleed event in patients with a prior venous thromboembolism event during hospitalization. *J Manag Care Pharm* 2005;11:663-73.
37 Gage BF. Cost of dabigatran for atrial fibrillation. *BMJ* 2011;343:d6980.
38 Tapson VF. Acute pulmonary embolism: comment on "time trends in pulmonary embolism in the United States." *Arch Intern Med* 2011;171:837-9.
39 Lapner ST, Kaeron C. Diagnosis and management of pulmonary embolism. *BMJ* 2013;346:f757.
40 Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galie N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *Eur Heart J* 2008;29:2276-315.
41 British Thoracic Society Standards of Care Committee Pulmonary Embolism Guideline Development Group. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax* 2003;58:470-83.
42 Choosing wisely: an initiative of the American Board of Internal Medicine. Lists. http://choosingwisely.org/?page_id=13.
43 Van Belle A, Buller HR, Huisman MV, Huisman PM, Kaasjager K, Kamphuisen PW, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 2006;295:172-9.
44 Perrier A, Roy PM, Sanchez O, Le Gal G, Meyer G, Gourdier AL, et al. Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med* 2005;352:1760-8.
45 Raja AS, Ip IK, Prevedello LM, Sodickson AD, Farkas C, Zane RD, et al. Effect of computerized clinical decision support on the use and yield of CT pulmonary angiography in the emergency department. *Radiology* 2012;262:468-74.
46 Mettler FA Jr, Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology* 2008;248:254-63.
47 Hall WB, Truitt SG, Scheunemann LP, Shah SA, Rivera MP, Parker LA, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Arch Intern Med* 2009;169:1961-5.
48 Stein EG, Haramati LB, Chamarthy M, Sprayregen S, Davitt MM, Freeman LM. Success of a safe and simple algorithm to reduce use of CT pulmonary angiography in the emergency department. *AJR Am J Roentgenol* 2010;194:392-7.
49 Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis. 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141(suppl 2):e419-94S.
50 Stein PD, Goodman LR, Hull RD, Dalen JE, Matta F. Diagnosis and management of isolated subsegmental pulmonary embolism: review and assessment of the options. *Clin Appl Thromb Hemost* 2012;18:20-6.

Cite this as: *BMJ* 2013;347:f3368