RECOMENDACIÓN DG.1

BÚSQUEDA Y SÍNTESIS DE EVIDENCIA DE EFECTOS DESEABLES E INDESEABLES

Guía de Práctica Clínica de Cáncer de Pulmón - 2018

A. PREGUNTA CLÍNICA

En personas mayores de 50 años con Índice Paquete Año (IPA) ≥ 20, ¿Se debe realizar tomografía computarizada de tórax sin contraste de baja dosis" en comparación a "no realizarlo"?

Análisis y definición de los componentes de la pregunta en formato PICO

Población: Personas mayores a 50 años con índice paquete año (IPA) ≥ 20.
Intervención: Tomografía computarizada de tórax sin contraste de baja dosis.
Comparación: No realizar.
Desenlace (outcome): Mortalidad

B. BÚSQUEDA DE EVIDENCIA

Se realizó una búsqueda general de revisiones sistemáticas asociadas al tema de "Lung cancer". Las bases de datos utilizadas fueron: Cochrane database of systematic reviews (CDSR); Database of Abstracts of Reviews of Effectiveness (DARE); HTA Database; PubMed; LILACS; CINAHL; PsyclNFO; EMBASE; EPPI-Centre Evidence Library; 3ie Systematic Reviews and Policy Briefs Campbell Library; Clinical Evidence; SUPPORT Summaries; WHO institutional Repository for information Sharing; NICE public health guidelines and systematic reviews; ACP Journal Club; Evidencias en Pediatría; y The JBI Database of Systematic Reviews and implementation Reports. No se aplicaron restricciones en base al idioma o estado de publicación. Dos revisores de manera independiente realizaron la selección de los títulos y los resúmenes, la evaluación del texto completo y la extracción de datos. Un investigador experimentado resolvió cualquier discrepancia entre los distintos revisores. En caso de considerarse necesario, se integraron estudios primarios.[1]

Seleccionadas las revisiones sistemáticas o estudios primarios asociadas a la temática, se clasificaron en función de las potenciales preguntas a las que daban respuesta. Al momento de definir la pregunta la evidencia ya se encontraba previamente clasificada según intervenciones comparadas. Los resultados se encuentran alojados en la plataforma Living Overview of the Evidence (L·OVE), sistema que permite la actualización periódica de la evidencia.

[1] Para revisar la metodología, las estrategias y los resultados de la búsqueda, favor revisar el informe "*Búsqueda sistemática de evidencia de los efectos deseables e indeseables*" en la sección de método de la Guía de Práctica Clínica respectiva.

C. SÍNTESIS DE EVIDENCIA

Resumen de la evidencia identificada

En las preguntas que comparan diagnósticos, el equipo metodológico consideró necesario distinguir dos enfoques para abordar su respuesta: *impacto diagnóstico* y *exactitud diagnóstica*. Se estableció priorizar estudios que evaluarán el *impacto diagnóstico del test*, es decir aquellos que comparan los resultados en salud de los pacientes diagnosticados/tratados en función a un test versus los resultados de pacientes diagnosticados/tratados en función a otro test. En caso de no encontrar este tipo de estudios, se utilizarían estudios que evaluaran la *exactitud diagnóstica del test*, es decir aquellos que evalúan qué tan bien el test clasifica a los pacientes respecto a si tienen o no una condición.[2]

En este caso, se identificaron 23 revisiones sistemáticas [1-23] que incluyen 76 [24-99] estudios primarios, de los cuales 12 corresponden a ensayos aleatorizados [24-34] que responden a la pregunta de *impacto diagnóstico*, por lo que se decidió omitir la exactitud diagnóstica del test. Para más detalle ver "*Matriz de evidencia*"[3], en el siguiente enlace: Tamizaje con tomografía para cáncer de pulmón

Tabla 1: Resumen de la evidencia seleccionada

Revisión Sistemática	23 [1-23]
Estudios primarios	12 ensayos aleatorizados [24-34], 64 observacionales [35-99]

Estimador del efecto

Se realizó un análisis de la matriz de evidencia, decidiendo excluir dos ensayos ya que comparan tomografía computarizada de baja dosis contra radiografía [27, 31]. Finalmente, se observó que ninguna revisión sistemática presentó los datos suficientes para construir la tabla de resultados, por lo que se decidió extraerlos directamente de los estudios primarios, sin embargo, sólo tres ensayos [26, 32, 34] pudieron entregar datos para el metanálisis.

[2] Schünemann HJ, Schünemann AHJ, Oxman AD, Brozek J, Glasziou P, Jaeschke R, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ [Internet]. 2008 May 17 [cited 2018 Aug 1];336(7653):1106–10.

[3] **Matriz de Evidencia**, tabla dinámica que grafica el conjunto de evidencia existente para una pregunta (en este caso, la pregunta del presente informe). Las filas representan las revisiones sistemáticas y las columnas los estudios primarios que estas revisiones han identificado. Los recuadros en verde corresponden a los estudios incluidos en cada revisión. La matriz se actualiza periódicamente, incorporando nuevas revisiones sistemáticas pertinentes y los respectivos estudios primarios.

Metanálisis

Mortalidad

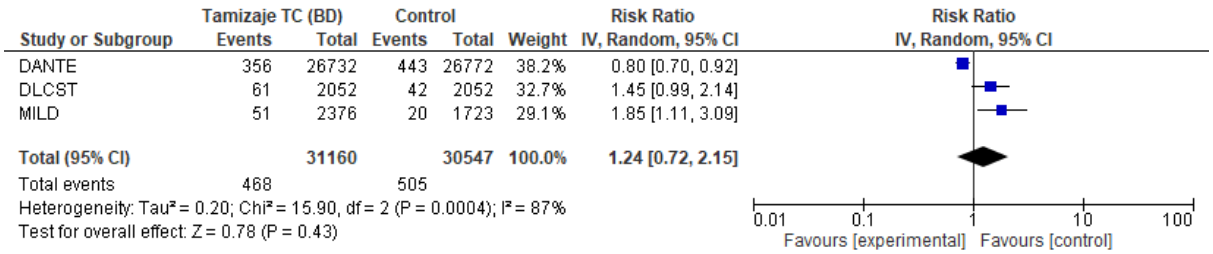

Tabla de Resumen de Resultados (Summary of Findings)

TAMIZAJE CON TOMOGRAFÍA COMPUTARIZADA DE TÓRAX SIN CONTRASTE DE BAJA DOSIS EN PERSONA CON ÍNDICE PAQUETE AÑO (IPA) ≥ 20						
Pacientes	Personas mayores a 50 años con índice paquete año (IPA) ≥ 20.					
Intervención	Tamizaje con tomografía computarizada de tórax sin contraste de baja dosis.					
Comparación	No tamizaje.					
Desenlaces	**Efecto relativo (IC 95%) -- Estudios/ pacientes**	**Efecto absoluto estimado***			**Certeza de la evidencia (GRADE)**	**Mensajes clave en términos sencillos**
		No tamizaje	**Tamizaje con tomografía de baja dosis**	**Diferencia (IC 95%)**		
Mortalidad	RR 1,20 (0,77 a 1,85) -- 3 ensayos / 61.707 pacientes [26, 32, 34]	17 por 1000	20 por 1000	Diferencia: 3 más por 1000 (5 menos a 19 más)	⨁⨁◯◯[1,2,3] Baja	El uso de tamizaje con tomografía computarizada de tórax sin contraste de baja dosis, podría aumentar la mortalidad en cáncer de pulmón. Sin embargo, el efecto podría ser demasiado pequeño para ser considerado importante por los pacientes.

IC 95%: Intervalo de confianza del 95%.
RR: Riesgo relativo.
GRADE: Grados de evidencia Grading of Recommendations Assessment, Development and Evaluation.
* El **riesgo SIN tomografía computarizada de baja dosis** está basado en el riesgo del grupo control en los estudios. El **riesgo CON tomografía computarizada de baja dosis** (y su intervalo de confianza) está calculado a partir del efecto relativo (y su intervalo de confianza).
[1] A pesar que la evidencia identificada proviene de una población que no es directamente la abordada por la pregunta de este informe (no proviene exclusivamente de mayores de 50 años con IPA ≥ 20), se decidió no disminuir la certeza de evidencia por este factor, ya que la mayoría de los pacientes incluidos en los diferentes ensayos eran fumadores activos.
[2] Se disminuyó un nivel de certeza por imprecisión, ya que el intervalo de confianza incluye la posibilidad de beneficio, sin embargo, éste podría ser de baja magnitud.
[3] Se disminuyó un nivel de certeza por inconsistencia entre los resultados (I2 87%).
Fecha de elaboración de la tabla: Agosto, 2018

Referencias

1. Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, Byers T, Colditz GA, Gould MK, Jett JR, Sabichi AL, Smith-Bindman R, Wood DE, Qaseem A, Detterbeck FC. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA : the journal of the American Medical Association. 2012;307(22):2418-29.
2. Bepler G, Goodridge Carney D, Djulbegovic B, Clark RA, Tockman M. A systematic review and lessons learned from early lung cancer detection trials using low-dose computed tomography of the chest. Cancer control : journal of the Moffitt Cancer Center. 2003;10(4):306-14.
3. Black C, Bagust A, Boland A, Walker S, McLeod C, De Verteuil R, Ayres J, Bain L, Thomas S, Godden D, Waugh N. The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews. Health technology assessment (Winchester, England). 2006;10(3):iii-iv, ix-x, 1-90.
4. Coureau G, Salmi LR, Etard C, Sancho-Garnier H, Sauvaget C, Mathoulin-Pélissier S. Low-dose computed tomography screening for lung cancer in populations highly exposed to tobacco: A systematic methodological appraisal of published randomised controlled trials. European journal of cancer (Oxford, England : 1990). 2016;61:146-56.
5. Fu C, Liu Z, Zhu F, Li S, Jiang L. A meta-analysis: is low-dose computed tomography a superior method for risky lung cancers screening population?. The clinical respiratory journal. 2016;10(3):333-41.
6. Gopal M, Abdullah SE, Grady JJ, Goodwin JS. Screening for lung cancer with low-dose computed tomography: a systematic review and meta-analysis of the baseline findings of randomized controlled trials. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2010;5(8):1233-9.
7. Humphrey L, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, Zakher B, Fu R, Slatore C. Screening for Lung Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. 2013;
8. Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, Zakher B, Fu R, Slatore CG. Screening for lung cancer with low-dose computed tomography: a systematic review to update the U.S. Preventive Services Task Force recommendation. Annals of internal medicine. 2013;159(6):411-20.
9. Humphrey LL. Lung cancer screening: an update for the U.S. Preventive Services Task Force [Systematic evidence review no 31]. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. 2007;
10. Manser R, Lethaby A, Irving LB, Stone C, Byrnes G, Abramson MJ, Campbell D. Screening for lung cancer. Cochrane database of systematic reviews (Online). 2013;6(6):CD001991.
11. Mazzone PJ, Silvestri GA, Patel S, Kanne JP, Kinsinger LS, Wiener RS, Soo Hoo G, Detterbeck FC. Screening for Lung Cancer: CHEST Guideline and Expert Panel Report. Chest. 2018;153(4):954-985.
12. Ollier M, Chamoux A, Naughton G, Pereira B, Dutheil F. Chest CT Scan Screening for Lung Cancer in Asbestos Occupational Exposure: A Systematic Review and Meta-analysis. Chest. 2014;145(6):1339-46.

13. Poghosyan H, Kennedy Sheldon L, Cooley ME. The impact of computed tomography screening for lung cancer on smoking behaviors: a teachable moment?. Cancer nursing. 2012;35(6):446-75.
14. Puggina A, Broumas A, Ricciardi W, Boccia S. Cost-effectiveness of screening for lung cancer with low-dose computed tomography: a systematic literature review. European journal of public health. 2016;26(1):168-75.
15. Seigneurin A, Field JK, Gachet A, Duffy SW. A systematic review of the characteristics associated with recall rates, detection rates and positive predictive values of computed tomography screening for lung cancer. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(4):781-91.
16. Selva A, Puig T, López Alcalde J, Bonfill X. [Efficacy of screening for lung cancer. Systematic review]. Medicina clínica. 2011;137(12):565-71.
17. Slatore CG, Baumann C, Pappas M, Humphrey LL. Smoking behaviors among patients receiving computed tomography for lung cancer screening. Systematic review in support of the U.S. preventive services task force. Annals of the American Thoracic Society. 2014;11(4):619-27.
18. Slatore CG, Sullivan DR, Pappas M, Humphrey LL. Patient-centered outcomes among lung cancer screening recipients with computed tomography: a systematic review. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2014;9(7):927-34.
19. Usman Ali M, Miller J, Peirson L, Fitzpatrick-Lewis D, Kenny M, Sherifali D, Raina P. Screening for lung cancer: A systematic review and meta-analysis. Preventive medicine. 2016;89:301-14.
20. Vidal Serrano S, Llanos Méndez A. [CT screening for lung cancer; sistematic review]. Medicina clínica. 2007;129(15):582-7.
21. Wu GX, Raz DJ, Brown L, Sun V. Psychological Burden Associated With Lung Cancer Screening: A Systematic Review. Clinical lung cancer. 2016;17(5):315-324.
22. Yau G, Lock M, Rodrigues G. Systematic review of baseline low-dose CT lung cancer screening. Lung cancer (Amsterdam, Netherlands). 2007;58(2):161-70.
23. Raymakers AJ, Mayo J, Lam S, FitzGerald JM, Whitehurst DG, Lynd LD. Cost-Effectiveness Analyses of Lung Cancer Screening Strategies Using Low-Dose Computed Tomography: a Systematic Review. Applied health economics and health policy. 2016;14(4):409-18.
24. Veterans Affairs Medical Centre. Garg K, Keith RL, Byers T, Kelly K, Kerzner AL, Lynch DA, Miller YE. Randomized controlled trial with low-dose spiral CT for lung cancer screening: feasibility study and preliminary results. Radiology. 2002;225(2):506-10.
25. LUSI. Becker N, Motsch E, Gross ML, Eigentopf A, Heussel CP, Dienemann H, Schnabel PA, Pilz L, Eichinger M, Optazaite DE, Puderbach M, Tremper J, Delorme S. Randomized study on early detection of lung cancer with MSCT in Germany: study design and results of the first screening round. Journal of cancer research and clinical oncology. 2012;138(9):1475-86.
26. DLCST (Danish Lung Cancer Screening Trial). Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, Døssing M, Hansen H, Kofoed KF, Larsen KR, Mortensen J, Rasmussen JF, Seersholm N, Skov BG, Thorsen H, Tønnesen P, Pedersen JH. CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. Thorax. 2012;67(4):296-301.

27. NLST (National Lung Screening Trial). National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD. Reduced lung-cancer mortality with low-dose computed tomographic screening. The New England journal of medicine. 2011;365(5):395-409.
28. DEPISCAN. Blanchon T, Bréchot JM, Grenier PA, Ferretti GR, Lemarié E, Milleron B, Chagué D, Laurent F, Martinet Y, Beigelman-Aubry C, Blanchon F, Revel MP, Friard S, Rémy-Jardin M, Vasile M, Santelmo N, Lecalier A, Lefébure P, Moro-Sibilot D, Breton JL, Carette MF, Brambilla C, Fournel F, Kieffer A, Frija G, Flahault A, Dépiscan Group. Baseline results of the Depiscan study: a French randomized pilot trial of lung cancer screening comparing low dose CT scan (LDCT) and chest X-ray (CXR). Lung cancer (Amsterdam, Netherlands). 2007;58(1):50-8. b6098a6ad7b253451198e66e948729f9eeca647b
29. ITALUNG. Lopes Pegna A, Picozzi G, Mascalchi M, Maria Carozzi F, Carrozzi L, Comin C, Spinelli C, Falaschi F, Grazzini M, Innocenti F, Ronchi C, Paci E, ITALUNG Study Research Group. Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT. Lung cancer (Amsterdam, Netherlands). 2009;64(1):34-40. documents/88a61f752a77e1b87393d953765bf63014893547
30. UKLS (UK Lung Screen). Baldwin DR, Duffy SW, Wald NJ, Page R, Hansell DM, Field JK. UK Lung Screen (UKLS) nodule management protocol: modelling of a single screen randomised controlled trial of low-dose CT screening for lung cancer. Thorax. 2011;66(4):308-13.
31. LSS (Lung Screening Study). Gohagan JK, Marcus PM, Fagerstrom RM, Pinsky PF, Kramer BS, Prorok PC, Ascher S, Bailey W, Brewer B, Church T, Engelhard D, Ford M, Fouad M, Freedman M, Gelmann E, Gierada D, Hocking W, Inampudi S, Irons B, Johnson CC, Jones A, Kucera G, Kvale P, Lappe K, Manor W, Moore A, Nath H, Neff S, Oken M, Plunkett M, Price H, Reding D, Riley T, Schwartz M, Spizarny D, Yoffie R, Zylak C. Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest X-ray screening for lung cancer. Lung cancer (Amsterdam, Netherlands). 2005;47(1):9-15.
32. MILD. Pastorino U, Rossi M, Rosato V, Marchianò A, Sverzellati N, Morosi C, Fabbri A, Galeone C, Negri E, Sozzi G, Pelosi G, La Vecchia C. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2012;21(3):308-15.
33. NELSON (Dutch-Belgian Randomised Lung Cancer Screening Trial). van Iersel CA, de Koning HJ, Draisma G, Mali WP, Scholten ET, Nackaerts K, Prokop M, Habbema JD, Oudkerk M, van Klaveren RJ. Risk-based selection from the general population in a screening trial: selection criteria, recruitment and power for the Dutch-Belgian randomised lung cancer multi-slice CT screening trial (NELSON). International journal of cancer. Journal international du cancer. 2007;120(4):868-74.
34. DANTE. Infante M, Cavuto S, Lutman FR, Brambilla G, Chiesa G, Ceresoli G, Passera E, Angeli E, Chiarenza M, Aranzulla G, Cariboni U, Errico V, Inzirillo F, Bottoni E, Voulaz E, Alloisio M, Destro A, Roncalli M, Santoro A, Ravasi G, DANTE Study Group. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. American journal of respiratory and critical care medicine. 2009;180(5):445-53. f0305b47e86178d1be258b3fe9e16550e97c7d44

35. Mazzone PJ, Obuchowski N, Fu AZ, Phillips M, Meziane M. Quality of life and healthcare use in a randomized controlled lung cancer screening study. Annals of the American Thoracic Society. 2013;10(4):324-9. documents/8e9ef87d63030a02df9a59c916472fb63491ac71
36. Nahorecki A, Chabowski M, Kuźniar T, Kędzierski B, Jaźwiec P, Szuba A, Janczak D. Low-dose computer tomography as a screening tool for lung cancer in a high risk population. Advances in experimental medicine and biology. 2015;852:31-7.
37. Crestanello JA, Allen MS, Jett JR, Cassivi SD, Nichols FC, Swensen SJ, Deschamps C, Pairolero PC. Thoracic surgical operations in patients enrolled in a computed tomographic screening trial. The Journal of thoracic and cardiovascular surgery. 2004;128(2):254-9.
38. Pastorino U, Bellomi M, Landoni C, De Fiori E, Arnaldi P, Picchio M, Pelosi G, Boyle P, Fazio F. Early lung-cancer detection with spiral CT and positron emission tomography in heavy smokers: 2-year results. Lancet. 2003;362(9384):593-7.
39. Sobue T, Moriyama N, Kaneko M, Kusumoto M, Kobayashi T, Tsuchiya R, Kakinuma R, Ohmatsu H, Nagai K, Nishiyama H, Matsui E, Eguchi K. Screening for lung cancer with low-dose helical computed tomography: anti-lung cancer association project. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2002;20(4):911-20.
40. MAYO. Swensen SJ, Jett JR, Sloan JA, Midthun DE, Hartman TE, Sykes AM, Aughenbaugh GL, Zink FE, Hillman SL, Noetzel GR, Marks RS, Clayton AC, Pairolero PC. Screening for lung cancer with low-dose spiral computed tomography. American journal of respiratory and critical care medicine. 2002;165(4):508-13.
41. Veronesi G, Bellomi M, Mulshine JL, Pelosi G, Scanagatta P, Paganelli G, Maisonneuve P, Preda L, Leo F, Bertolotti R, Solli P, Spaggiari L. Lung cancer screening with low-dose computed tomography: a non-invasive diagnostic protocol for baseline lung nodules. Lung cancer (Amsterdam, Netherlands). 2008;61(3):340-9.
42. Chong S, Lee KS, Chung MJ, Kim TS, Kim H, Kwon OJ, Choi YH, Rhee CH. Lung cancer screening with low-dose helical CT in Korea: experiences at the Samsung Medical Center. Journal of Korean medical science. 2005;20(3):402-8.
43. Rzyman W, Jelitto-Gorska M, Dziedzic R, Biadacz I, Ksiazek J, Chwirot P, Marjanski T. Diagnostic work-up and surgery in participants of the Gdansk lung cancer screening programme: the incidence of surgery for non-malignant conditions. Interactive cardiovascular and thoracic surgery. 2013;17(6):969-73.
44. Wagnetz U, Menezes RJ, Boerner S, Paul NS, Wagnetz D, Keshavjee S, Roberts HC. CT screening for lung cancer: implication of lung biopsy recommendations. AJR. American journal of roentgenology. 2012;198(2):351-8.
45. Henschke CI, International Early Lung Cancer Action Program Investigators. Survival of patients with clinical stage I lung cancer diagnosed by computed tomography screening for lung cancer. Clinical cancer research : an official journal of the American Association for Cancer Research. 2007;13(17):4949-50.
46. Sone S, Li F, Yang ZG, Honda T, Maruyama Y, Takashima S, Hasegawa M, Kawakami S, Kubo K, Haniuda M, Yamanda T. Results of three-year mass screening programme for lung cancer using mobile low-dose spiral computed tomography scanner. British journal of cancer. 2001;84(1):25-32.
47. Dominioni L, Rotolo N, Mantovani W, Poli A, Pisani S, Conti V, Paolucci M, Sessa F, Paddeu A, D'Ambrosio V, Imperatori A. A population-based cohort study of chest x-ray screening in smokers: lung cancer detection findings and follow-up. BMC cancer. 2012;12:18.

48. Callol L, Roig F, Cuevas A, de Granda JI, Villegas F, Jareño J, Arias E, Albiach JM. Low-dose CT: a useful and accessible tool for the early diagnosis of lung cancer in selected populations. Lung cancer (Amsterdam, Netherlands). 2007;56(2):217-21.
49. Townsend CO, Clark MM, Jett JR, Patten CA, Schroeder DR, Nirelli LM, Swensen SJ, Hurt RD. Relation between smoking cessation and receiving results from three annual spiral chest computed tomography scans for lung carcinoma screening. Cancer. 2005;103(10):2154-62.
50. Kaerlev L, Iachina M, Pedersen JH, Green A, Nørgård BM. CT-Screening for lung cancer does not increase the use of anxiolytic or antidepressant medication. BMC cancer. 2012;12:188.
51. International Early Lung Cancer Action Program Investigators, Henschke CI, Yip R, Miettinen OS. Women's susceptibility to tobacco carcinogens and survival after diagnosis of lung cancer. JAMA. 2006;296(2):180-4.
52. Gietema HA, Wang Y, Xu D, van Klaveren RJ, de Koning H, Scholten E, Verschakelen J, Kohl G, Oudkerk M, Prokop M. Pulmonary nodules detected at lung cancer screening: interobserver variability of semiautomated volume measurements. Radiology. 2006;241(1):251-7.
53. Toyoda Y, Nakayama T, Kusunoki Y, Iso H, Suzuki T. Sensitivity and specificity of lung cancer screening using chest low-dose computed tomography. British journal of cancer. 2008;98(10):1602-7.
54. Menezes RJ, Roberts HC, Paul NS, McGregor M, Chung TB, Patsios D, Weisbrod G, Herman S, Pereira A, McGregor A, Dong Z, Sitartchouk I, Boerner S, Tsao MS, Keshavjee S, Shepherd FA. Lung cancer screening using low-dose computed tomography in at-risk individuals: the Toronto experience. Lung cancer (Amsterdam, Netherlands). 2010;67(2):177-83.
55. Henschke CI, Yip R, Yankelevitz DF, Smith JP, International Early Lung Cancer Action Program Investigators*. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. Annals of internal medicine. 2013;158(4):246-52.
56. Sinicrope PS, Rabe KG, Brockman TA, Patten CA, Petersen WO, Slusser J, Yang P, Swensen SJ, Edell ES, de Andrade M, Petersen GM. Perceptions of lung cancer risk and beliefs in screening accuracy of spiral computed tomography among high-risk lung cancer family members. Academic radiology. 2010;17(8):1012-25.
57. Van't Westeinde SC, van Klaveren RJ. Screening and early detection of lung cancer. Cancer journal (Sudbury, Mass.). 2011;17(1):3-10.
58. Nawa T, Nakagawa T, Kusano S, Kawasaki Y, Sugawara Y, Nakata H. Lung cancer screening using low-dose spiral CT: results of baseline and 1-year follow-up studies. Chest. 2002;122(1):15-20.
59. Sone S, Takashima S, Li F, Yang Z, Honda T, Maruyama Y, Hasegawa M, Yamanda T, Kubo K, Hanamura K, Asakura K. Mass screening for lung cancer with mobile spiral computed tomography scanner. Lancet. 1998;351(9111):1242-5.
60. International Early Lung Cancer Action Program Investigators, Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW, Smith JP, Miettinen OS. Survival of patients with stage I lung cancer detected on CT screening. The New England journal of medicine. 2006;355(17):1763-71.
61. Bastarrika G, García-Velloso MJ, Lozano MD, Montes U, Torre W, Spiteri N, Campo A, Seijo L, Alcaide AB, Pueyo J, Cano D, Vivas I, Cosín O, Domínguez P, Serra P, Richter JA, Montuenga L, Zulueta JJ. Early lung cancer detection using spiral computed tomography and positron emission tomography. American journal of respiratory and critical care medicine. 2005;171(12):1378-83.

62. Novello S, Fava C, Borasio P, Dogliotti L, Cortese G, Crida B, Selvaggi G, Lausi P, Brizzi MP, Sperone P, Cardinale L, Ferraris F, Perotto F, Priola A, Scagliotti GV. Three-year findings of an early lung cancer detection feasibility study with low-dose spiral computed tomography in heavy smokers. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2005;16(10):1662-6.
63. Sone S, Nakayama T, Honda T, Tsushima K, Li F, Haniuda M, Takahashi Y, Suzuki T, Yamanda T, Kondo R, Hanaoka T, Takayama F, Kubo K, Fushimi H. Long-term follow-up study of a population-based 1996-1998 mass screening programme for lung cancer using mobile low-dose spiral computed tomography. Lung cancer (Amsterdam, Netherlands). 2007;58(3):329-41.
64. Tsushima K, Sone S, Hanaoka T, Kubo K. Radiological diagnosis of small pulmonary nodules detected on low-dose screening computed tomography. Respirology (Carlton, Vic.). 2008;13(6):817-24.
65. Cox LS, Clark MM, Jett JR, Patten CA, Schroeder DR, Nirelli LM, Swensen SJ, Hurt RD. Change in smoking status after spiral chest computed tomography scan screening. Cancer. 2003;98(11):2495-501.
66. Schnoll RA, Miller SM, Unger M, McAleer C, Halbherr T, Bradley P. Characteristics of female smokers attending a lung cancer screening program: a pilot study with implications for program development. Lung cancer (Amsterdam, Netherlands). 2002;37(3):257-65.
67. Tiitola, Mia, Kivisaari, Leena, Huuskonen, Matti S., Mattson, Karin, Koskinen, Heikki, Lehtola, Hannu, Zitting, Anders, Vehmas, Tapio. Computed tomography screening for lung cancer in asbestos-exposed workers. Lung Cancer. 2002;35(1):17-22.
68. Miller A, Markowitz S, Manowitz A, Miller JA. Lung cancer screening using low-dose high-resolution CT scanning in a high-risk workforce: 3500 nuclear fuel workers in three US states. Chest. 2004;125(5 Suppl):152S-3S.
69. Roberts HC, Patsios DA, Paul NS, DePerrot M, Teel W, Bayanati H, Shepherd F, Johnston MR. Screening for malignant pleural mesothelioma and lung cancer in individuals with a history of asbestos exposure. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2009;4(5):620-8.
70. Mastrangelo G, Ballarin MN, Bellini E, Bizzotto R, Zannol F, Gioffrè F, Gobbi M, Tessadri G, Marchiori L, Marangi G, Bozzolan S, Lange JH, Valentini F, Spolaore P. Feasibility of a screening programme for lung cancer in former asbestos workers. Occupational medicine (Oxford, England). 2008;58(3):175-80.
71. Das M, Mühlenbruch G, Mahnken AH, Hering KG, Sirbu H, Zschiesche W, Knoll L, Felten MK, Kraus T, Günther RW, Wildberger JE. Asbestos Surveillance Program Aachen (ASPA): initial results from baseline screening for lung cancer in asbestos-exposed high-risk individuals using low-dose multidetector-row CT. European radiology. 2007;17(5):1193-9.
72. Vierikko T, Järvenpää R, Autti T, Oksa P, Huuskonen M, Kaleva S, Laurikka J, Kajander S, Paakkola K, Saarelainen S, Salomaa ER, Tossavainen A, Tukiainen P, Uitti J, Vehmas T. Chest CT screening of asbestos-exposed workers: lung lesions and incidental findings. The European respiratory journal. 2007;29(1):78-84.
73. Fasola G, Belvedere O, Aita M, Zanin T, Follador A, Cassetti P, Meduri S, De Pangher V, Pignata G, Rosolen V, Barbone F, Grossi F. Low-dose computed tomography screening for lung cancer and pleural mesothelioma in an asbestos-exposed population: baseline results of

a prospective, nonrandomized feasibility trial--an Alpe-adria Thoracic Oncology Multidisciplinary Group Study (ATOM 002). The oncologist. 2007;12(10):1215-24.
74. Clin B, Morlais F, Guittet L, Gislard A, Marquignon MF, Paris C, Caillard JF, Launoy G, Letourneux M. Performance of chest radiograph and CT scan for lung cancer screening in asbestos-exposed workers. Occupational and environmental medicine. 2009;66(8):529-34.
75. Veronesi G, Maisonneuve P, Bellomi M, Rampinelli C, Durli I, Bertolotti R, Spaggiari L. Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. Annals of internal medicine. 2012;157(11):776-784.
76. Fujikawa A, Takiguchi Y, Mizuno S, Uruma T, Suzuki K, Nagao K, Niijima M, Edo H, Hino M, Kuriyama T. Lung cancer screening--comparison of computed tomography and X-ray. Lung cancer (Amsterdam, Netherlands). 2008;61(2):195-201.
77. Bach PB, Jett JR, Pastorino U, Tockman MS, Swensen SJ, Begg CB. Computed tomography screening and lung cancer outcomes. JAMA. 2007;297(9):953-61.
78. Matsumoto M, Horikoshi H, Moteki T, Hatori N, Tateno Y, Iinuma T, Matsumoto T, Yamamoto S, Baba T. [A pilot study with lung-cancer screening CT (LSCT) at the secondary screening for lung cancer detection]. Nihon Igaku Hoshasen Gakkai zasshi. Nippon acta radiologica. 1995;55(3):172-9.
79. Vierikko T, Kivistö S, Järvenpää R, Uitti J, Oksa P, Virtema P, Vehmas T. Psychological impact of computed tomography screening for lung cancer and occupational pulmonary disease among asbestos-exposed workers. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2009;18(3):203-6.
80. Anderson CM, Yip R, Henschke CI, Yankelevitz DF, Ostroff JS, Burns DM. Smoking cessation and relapse during a lung cancer screening program. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2009;18(12):3476-83.
81. Shemesh J, Henschke CI, Farooqi A, Yip R, Yankelevitz DF, Shaham D, Miettinen OS. Frequency of coronary artery calcification on low-dose computed tomography screening for lung cancer. Clinical imaging. 2006;30(3):181-5.
82. Pastorino, U., Marchiano, A., Sverzellati, N. et al. A less intensive screening modality, such as CT every 2 years instead of annual CT, is not harmful for heavy smokers. JOURNAL OF THORACIC ONCOLOGY. 2011;6.
83. Beinfeld MT, Wittenberg E, Gazelle GS. Cost-effectiveness of whole-body CT screening. Radiology. 2005;234(2):415-22.
84. Chirikos TN, Hazelton T, Tockman M, Clark R. Cost-effectiveness of screening for lung cancer. JAMA. 2003;289(18):2358; author reply 2358-9.
85. Marshall D, Simpson KN, Earle CC, Chu C. Potential cost-effectiveness of one-time screening for lung cancer (LC) in a high risk cohort. Lung cancer (Amsterdam, Netherlands). 2001;32(3):227-36.
86. Pyenson BS, Sander MS, Jiang Y, Kahn H, Mulshine JL. An actuarial analysis shows that offering lung cancer screening as an insurance benefit would save lives at relatively low cost. Health affairs (Project Hope). 2012;31(4):770-9.
87. Pyenson BS, Henschke CI, Yankelevitz DF, Yip R, Dec E. Offering lung cancer screening to high-risk medicare beneficiaries saves lives and is cost-effective: an actuarial analysis. American health & drug benefits. 2014;7(5):272-82.

88. Mahadevia PJ, Fleisher LA, Frick KD, Eng J, Goodman SN, Powe NR. Lung cancer screening with helical computed tomography in older adult smokers: a decision and cost-effectiveness analysis. JAMA. 2003;289(3):313-22.
89. Black WC, Gareen IF, Soneji SS, Sicks JD, Keeler EB, Aberle DR, Naeim A, Church TR, Silvestri GA, Gorelick J, Gatsonis C, National Lung Screening Trial Research Team. Cost-effectiveness of CT screening in the National Lung Screening Trial. The New England journal of medicine. 2014;371(19):1793-802.
90. McMahon PM, Kong CY, Bouzan C, Weinstein MC, Cipriano LE, Tramontano AC, Johnson BE, Weeks JC, Gazelle GS. Cost-effectiveness of computed tomography screening for lung cancer in the United States. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2011;6(11):1841-8.
91. Okamoto N. Cost-effectiveness of lung cancer screening in Japan. Cancer. 2000;89(11 Suppl):2489-93.
92. Manser R, Dalton A, Carter R, Byrnes G, Elwood M, Campbell DA. Cost-effectiveness analysis of screening for lung cancer with low dose spiral CT (computed tomography) in the Australian setting. Lung cancer (Amsterdam, Netherlands). 2005;48(2):171-85.
93. Villanti AC, Jiang Y, Abrams DB, Pyenson BS. A cost-utility analysis of lung cancer screening and the additional benefits of incorporating smoking cessation interventions. PloS one. 2013;8(8):e71379.
94. Shmueli A, Fraifeld S, Peretz T, Gutfeld O, Gips M, Sosna J, Shaham D. Cost-effectiveness of baseline low-dose computed tomography screening for lung cancer: the Israeli experience. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2013;16(6):922-31.
95. Marshall D, Simpson KN, Earle CC, Chu CW. Economic decision analysis model of screening for lung cancer. European journal of cancer (Oxford, England : 1990). 2001;37(14):1759-67.
96. Shaham D, Breuer R, Copel L, Agid R, Makori A, Kisselgoff D, Goitein O, Izhar U, Berkman N, Heching N, Sosna J, Bar-Ziv J, Libson E. Computed tomography screening for lung cancer: applicability of an international protocol in a single-institution environment. Clinical lung cancer. 2006;7(4):262-7.
97. ELCAP (Early Lung Cancer Action Project). Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, Libby D, Pasmantier M, Koizumi J, Altorki N, Smith JP. Early lung cancer action project: a summary of the findings on baseline screening. The oncologist. 2001;6(2):147-52.
98. PLuSS (Pittsburgh Lung Screening Study). Byrne MM, Weissfeld J, Roberts MS. Anxiety, fear of cancer, and perceived risk of cancer following lung cancer screening. Medical decision making : an international journal of the Society for Medical Decision Making. 2008;28(6):917-25.
99. PALCAD (ProActive Lung Cancer Detection). MacRedmond R, McVey G, Lee M, Costello RW, Kenny D, Foley C, Logan PM. Screening for lung cancer using low dose CT scanning: results of 2 year follow up. Thorax. 2006;61(1):54-6.