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de São Paulo

Programa *Team Up* da Oncologia BP



Parceria: AstraZeneca

Rastreamento para Câncer de Pulmão

José Rodrigues Pereira

Coordenador do Serviço de Pneumologia do Hospital BP

Objetivos

- Apresentação dos dois maiores estudos de rastreamento para câncer de pulmão
- Identificação do paciente de risco
- Evidências de benefícios adicionais além do câncer de pulmão
- Pontos importantes para a implementação
- Importância da cessação do tabaco

Pauta

- Estudos randomizados
- Intervalo entre as tomografias
- Benefício adicionais
- Implementação
- Cessação do tabaco

Estudos randomizados

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

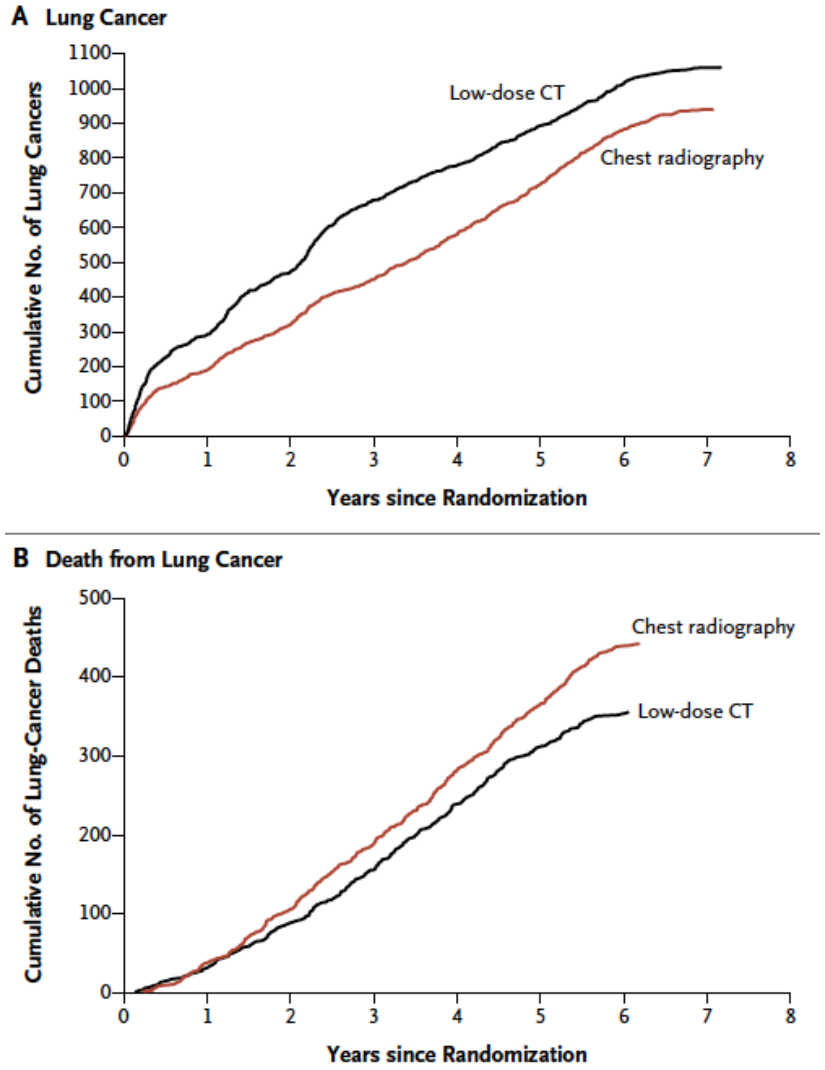
The National Lung Screening Trial Research Team*

Alto risco
Carga tabágica: ≥ 30 maços/ano
Tabagista atual/ex- fumante (< 15 anos)
Idade: 55 - 74 anos

TC tórax com baixa carga de radiação
1,5 mSv x Rx tórax

Intervalo de 1 ano entre as imagens (T0,T1,T2)

Aberle, DR et al. NEJM 2011



CA pulmão TC tórax : 3,6%

Redução do risco relativo de morte em 20%

Int. J. Cancer: 120, 868–874 (2007)
© 2006 Wiley-Liss, Inc.

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)

Carola A. van Iersel[1,2*], Harry J. de Koning[1], Gerrit Draisma[1], Willem P.T.M. Mali[3], Ernst Th. Scholten[4], Kristiaan Nackaerts[5], Mathias Prokop[3], J.Dik.F. Habbema[1], Mathijs Oudkerk[6] and Rob J. van Klaveren[2]

- TC tórax X nenhum screening
- Intervalo entre as TCs: 1 – 2 – 2,5 anos
- Volumetria e tempo de duplicação do nódulo

Indeterminado

positivo

Table 1 NELSON classification of the different non-calcified nodules according to size at baseline screening

NODCAT baseline	Definition
I	Benign nodule (fat/benign calcifications) or other benign characteristics
II	Any nodule, smaller than NODCAT III and no characteristics of NODCAT I
III	Solid: 50–500 mm^3 Solid, pleural based: 5–10 mm d_{min} Partial solid, non-solid component: ≥8 mm d_{mean} Partial solid, solid component: 50–500 mm^3 Non-solid: ≥8 mm d_{mean}
IV	Solid: >500 mm^3 Solid, pleural based: >10 mm d_{min} Partial solid, solid component: >500 mm^3

Alto risco

Estudo Nelson	
Idade	50 - 74 anos
História de fumo	> 10 cigarros/dia por ≥ 30 anos > 15 cigarros/dia por ≥ 25 anos
Cessação do tabaco	≤ 10 anos

NLST	
Idade	55- 74 anos
História de fumo	≥ 30 maços/ano
Cessação do tabaco	≤ 15 anos

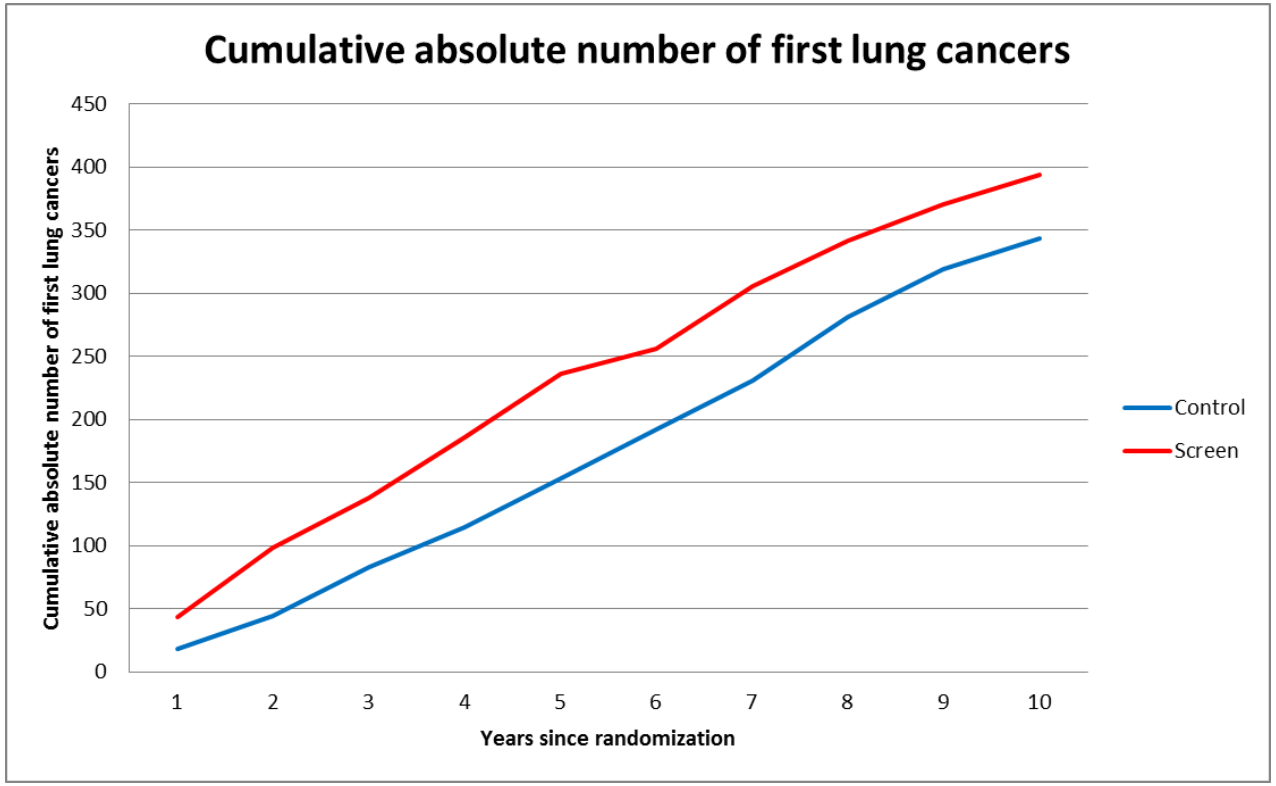
Resultados positivos

NLST	
T0	27,3%
T1	27,9%
T2	16,8%
Total	24,2%

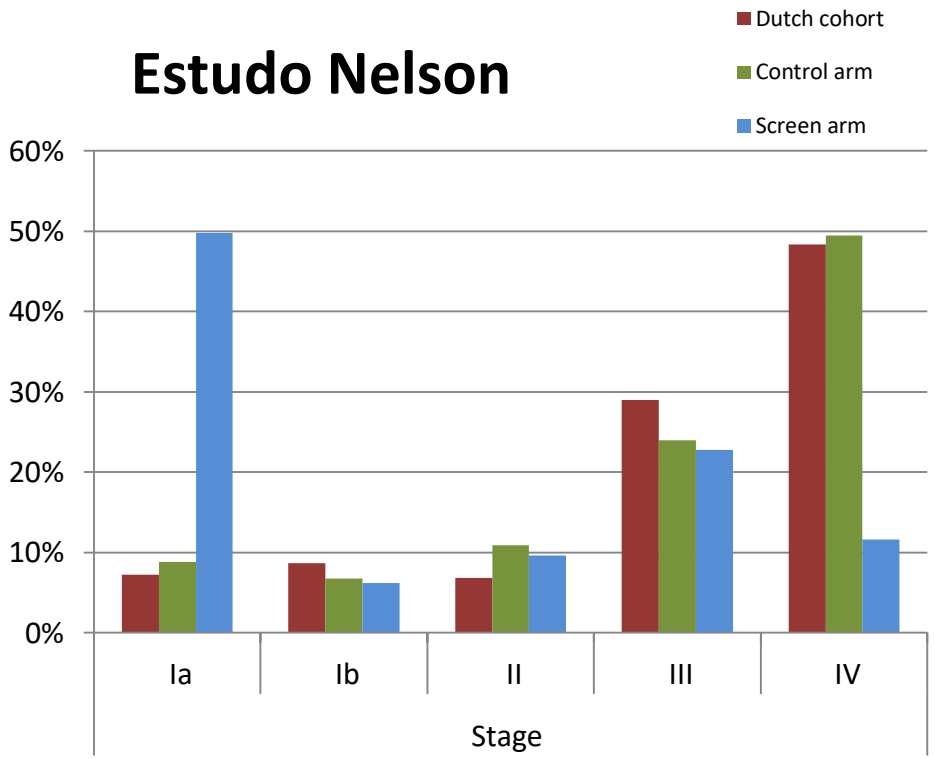
Nelson	
R1	2,6%
R2	1,8%
R3	2,4%
R4	2,0%
Total	2,2%

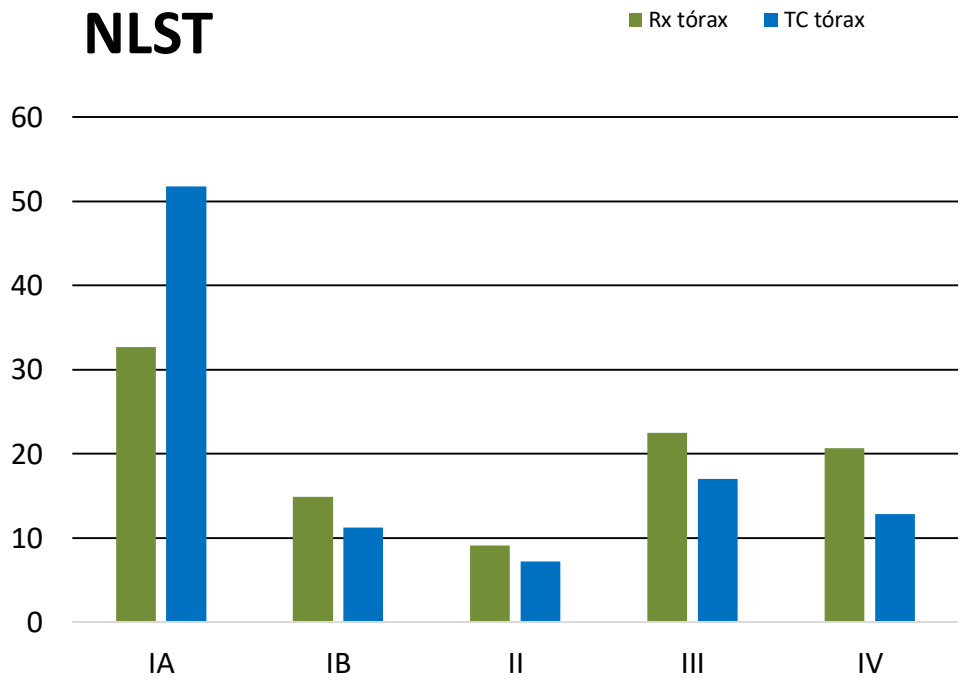
Redução do numero de falso positivos

CA pulmão - Estudo Nelson



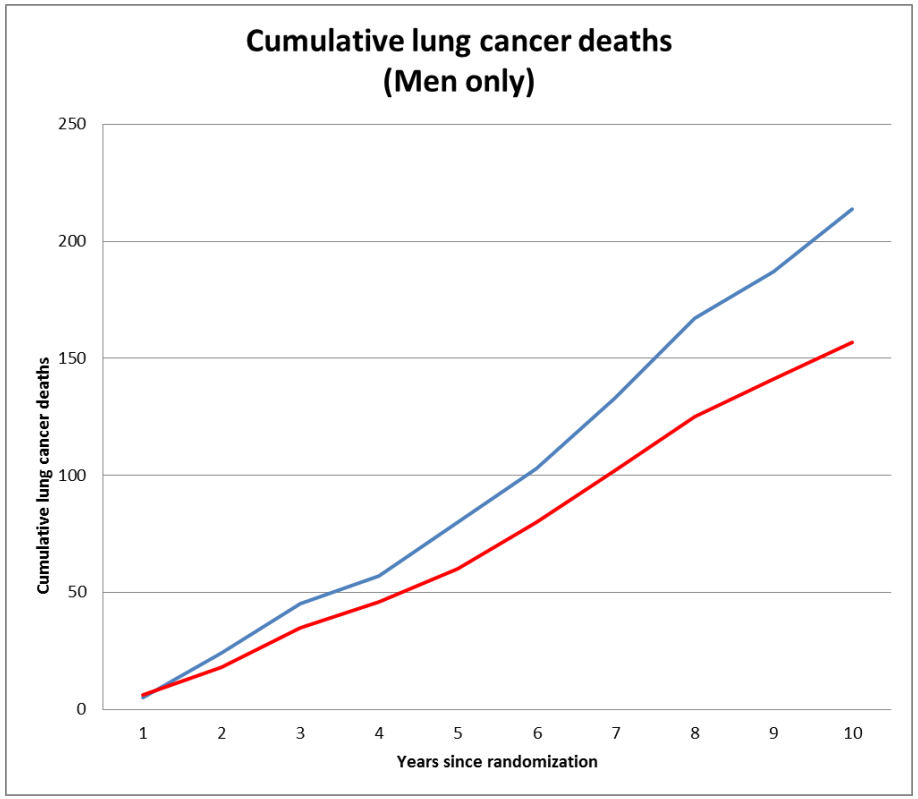
Diagnósticos por estadio





Aberle, DR et al. NEJM 2011
Yousaf-Khan et al., in preparation

Mortalidade CA pulmão - Estudo Nelson



Controle: 214 mortes

Screening: 157 mortes

Redução na mortalidade

Male v Female ratio	
NLST⁺	41/59
NELSON	16/84

Percent LC Mortality Decrease			
Trial	Men	Women	50:50 M/F
NLST*	8%	27%	18%
NELSON**	26%	39-61%	33 – 44%

Pinsky et al. The National Lung Screening Trial:. *Cancer* 2013; **119**(22): 3976-83. ⁺Aberle, et al. The National Lung Screening Trial: overview and study design. *Radiology* 2011; **258**(1): 243-53.
**Effects of Volume CT Lung Cancer Screening: Mortality Results of the NELSON Randomised-Controlled Population Based Trial De Koning et al 2018

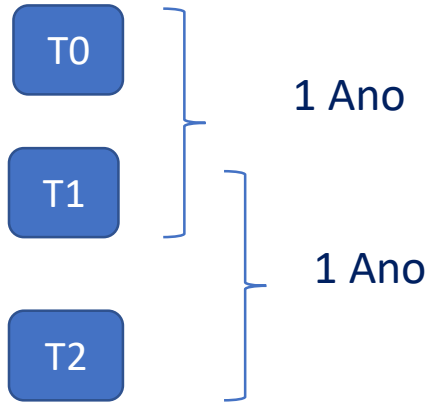
Intervalo entre as tomografias

NLST

Table 3. Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.*

Variable	Low-Dose CT				Chest Radiography			
	T0	T1	T2	Total	T0	T1	T2	Total
	number (percent)							
Total positive tests	7191 (100.0)	6901 (100.0)	4054 (100.0)	18,146 (100.0)	2387 (100.0)	1482 (100.0)	1174 (100.0)	5043 (100.0)
Lung cancer confirmed	270 (3.8)	168 (2.4)	211 (5.2)	649 (3.6)	136 (5.7)	65 (4.4)	78 (6.6)	279 (5.5)
Lung cancer not confirmed†	6921 (96.2)	6733 (97.6)	3843 (94.8)	17,497 (96.4)	2251 (94.3)	1417 (95.6)	1096 (93.4)	4764 (94.5)
Positive screening results with complete diagnostic follow-up information	7049 (100.0)	6740 (100.0)	3913 (100.0)	17,702 (100.0)	2348 (100.0)	1456 (100.0)	1149 (100.0)	4953 (100.0)

	T0				T1				T2			
	LDCT		CXR		LDCT		CXR		LDCT		CXR	
	N	%	N	%	N	%	N	%	N	%	N	%
Stage IA	133	45.4	46	24.5	87	47.5	31	23.5	116	50.4	35	24.5
Stage IB	27	9.2	24	12.8	21	11.5	11	8.3	31	13.5	13	9.1
Stage IIA	10	3.4	3	1.6	11	6.0	7	5.3	8	3.5	9	6.3
Stage IIB	12	4.1	10	5.3	7	3.8	5	3.8	5	2.2	3	2.1
Stage IIIA	34	11.6	30	16.0	14	7.7	14	10.6	15	6.5	18	12.6
Stage IIIB	30	10.2	28	14.9	19	10.4	12	9.1	20	8.7	21	14.7
Stage IV	47	16.0	47	25.0	24	13.1	52	39.4	35	15.2	44	30.8
Unknown	4	-	5	-	3	-	1	-	7	-	1	-
Total	297	100.0	193	100.0	186	100.0	133	100.0	237	100.0	144	100.0



Aberle, DR et al. NEJM 2011

Nelson trial

ORIGINAL ARTICLE

Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval

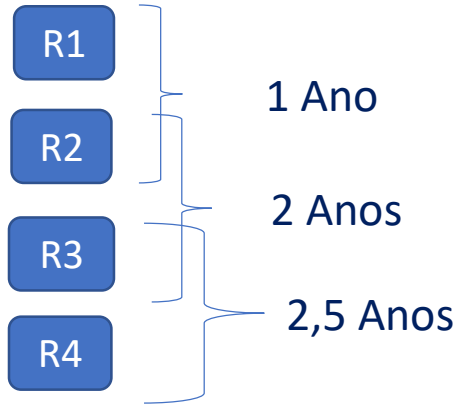


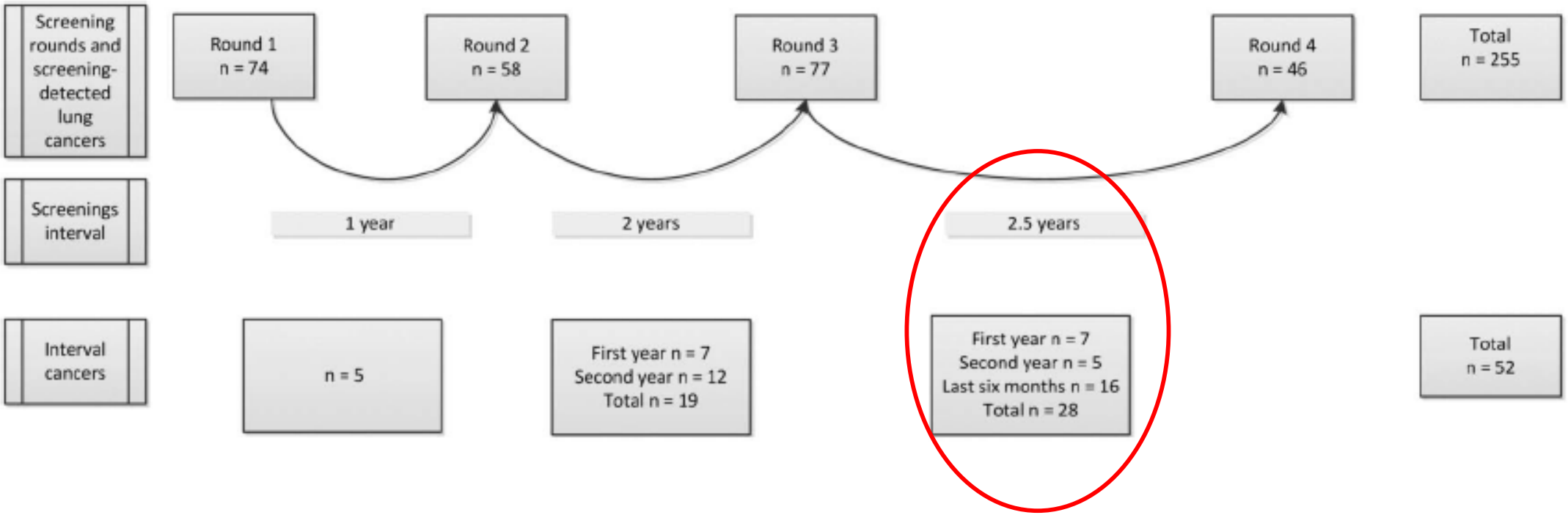
Table 3 Stage distribution of screening-detected lung cancers of all rounds

	Round 1			p Value*	Round 2			p Value†	Round 3			p Value‡	Round 4		
	n	Per cent	Cumulative %		n	Per cent	Cumulative %		n	Per cent	Cumulative %		n	Per cent	Cumulative %
				0.37				0.02				0.10			
Stage															
Ia	44	59.5	59.5		43	74.1	74.1		50	64.9	64.9		22	47.8	47.8
Ib	4	5.4	64.9		1	1.7	75.9		6	7.8	72.7		6	13.0	60.9
IIa	7	9.5	74.3		4	6.9	82.8		–	–	76.6		3	6.5	67.4
IIb	–	–	–	6,8%	–	–	–	5,2%	3	3.9	–	17,3%	4	8.7	76.1
IIIa	10	13.5	87.8		6	10.3	93.1		14	18.2	94.8		3	6.5	82.6
IIIb	4	5.4	93.2		2	3.4	96.6		1	1.3	96.1		2	4.3	87.0
IV	5	6.8	100		2	3.4	100		3	3.9	100		6	13.0	100
Total	74	100	–		58	100	–		77	100	–		46	100	–

*p Value: comparison of stage distribution of the screening-detected lung cancers of round 1 vs round 4.
†p Value: comparison of stage distribution of the screening-detected lung cancers of round 2 vs round 4.
‡p Value: comparison of stage distribution of the screening-detected lung cancers of round 3 vs round 4.

Yousaf-Khan U, et al. Thorax 2017

Incidência de câncer entre os exames



Yousaf-Khan U, et al. Thorax 2017

Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial

Edward F Patz Jr, Erin Greco, Constantine Gatsonis, Paul Pinsky, Barnett S Kramer, Denise R Aberle

T0 negativo e T1 positivo: 0,34%

Tempo médio de detecção: 3,3 anos

Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening

Nódulo < 100 mm3
Ou < 5 mm

Risco de malignidade de 0,4% em 2 anos

Lancet Oncol 2016; 17: 590–99
Lancet Oncol 2014; 15: 1332–41

Benefícios adicionais

NLST

Redução de mortalidade global: 6,7%

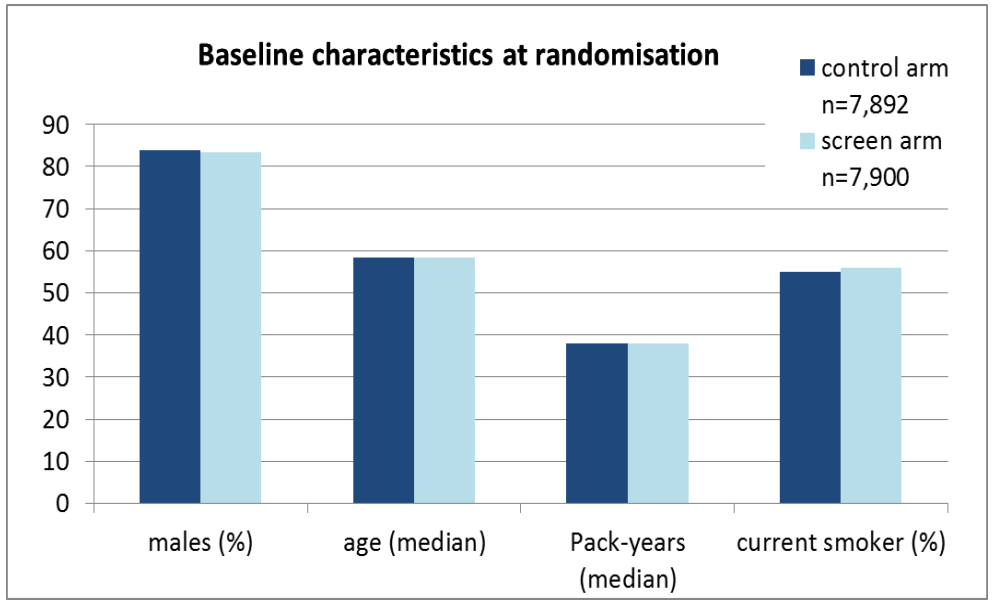
Redução de mortalidade global (exceto CA pulmão): 3,2%

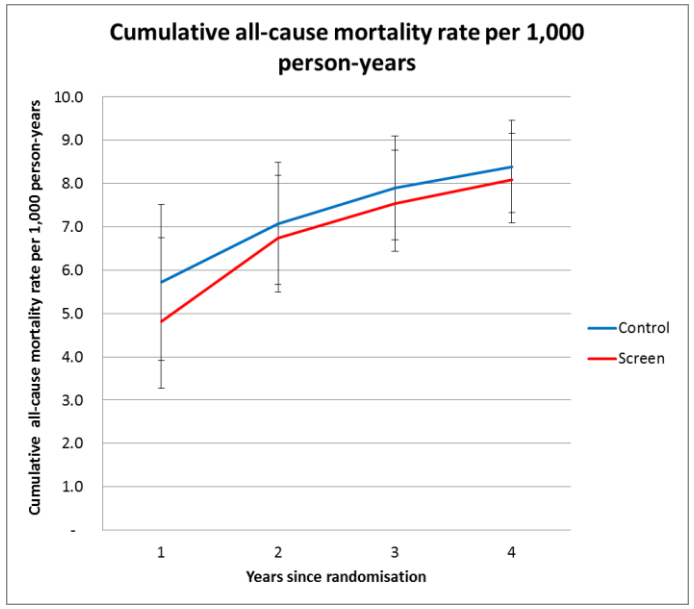
Table 7. Cause of Death on the Death Certificate, According to Screening Group.*

Cause of Death	Low-Dose CT Group	Radiography Group	Total
		number/total number (percent)	
Neoplasm of bronchus and lung†	427/1865 (22.9)	503/1991 (25.3)	930/3856 (24.1)
Other neoplasm	416/1865 (22.3)	442/1991 (22.2)	858/3856 (22.3)
Cardiovascular illness	486/1865 (26.1)	470/1991 (23.6)	956/3856 (24.8)
Respiratory illness	175/1865 (9.4)	226/1991 (11.4)	401/3856 (10.4)
Complications of medical or surgical care	12/1865 (0.6)	7/1991 (0.4)	19/3856 (0.5)
Other	349/1865 (18.7)	343/1991 (17.2)	692/3856 (17.9)

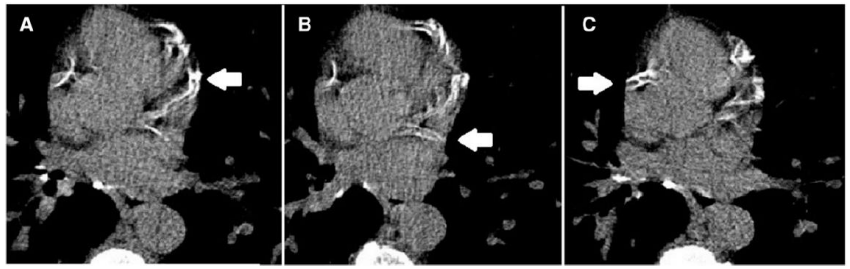
Aberle, DR et al. NEJM 2011

Estudo Nelson





Frequency of Incidental Findings and Subsequent Evaluation in Low-Dose Computed Tomographic Scans for Lung Cancer Screening



	Respiratory (*n* = 223)		Cardiovascular (*n* = 216)		Endocrinological (*n* = 23)		Gastrointestinal (*n* = 79)		Genitourinary (*n* = 14)		Other Systems (*n* = 78)		Total
Incidental findings	Emphysema	162 (50.6)	Coronary calcification	182 (56.0)	Adrenal nodule	12 (3.8)	Hiatal hernia	30 (9.4)	Renal cyst	8 (2.5)	DJD	74 (23.1)	
	Bronchial wall thickening	126 (39.4)	Aortic calcification	66 (20.6)	Thyroid nodule	11 (3.4)	Liver cyst	22 (6.8)	Renal stone	4 (1.3)	Compression fracture	3 (0.9)	
	Atelectasis	52 (16.3)	Aortic dilation	26 (8.1)			Dilated esophagus	7 (2.2)	Renal mass	2 (0.6)	Breast nodule	1 (0.3)	
	GGO	26 (8.1)					Gallstone	6 (1.9)					
	Bronchiectasis	14 (4.4)					Diaphragmatic hernia	5 (1.6)			Splenic lesion	1 (0.3)	
	Mediastinal adenopathy	9 (2.8)					Other	9 (2.8)					
	Fibrosis	5 (1.6)											
Evaluation and treatment	Pulmonary	2 (0.6)	Cardiology	33 (10.3)	Endocrine	7 (2.1)	GI	3 (0.9)	Urology	2 (0.6)			49 consultations
	ENT	1 (0.3)	Vascular surgery	1 (0.3)									
	Imaging	3 (0.9)	Imaging	7 (2.1)	Imaging	7 (2.1)	Imaging	6 (1.8)	Imaging	4 (1.2)	Imaging	1 (0.3)	28 imaging studies
			ECG	6 (1.8)									
			Echocardiogram	9 (2.8)									
	PFT	3 (0.9)	Stress test	9 (2.8)	Laboratory tests	6 (1.8)							33 various testing
	Laryngoscopy	1 (0.3)	Cardiac catheterization	4 (1.2)	Thyroid FNA	5 (1.5)							10 procedures
			PCI	1 (0.3)									
			CABG	1 (0.3)	Total thyroidectomy	1 (0.3)			Robotic partial nephrectomy	2 (0.6)			4 surgeries

Definition of abbreviations: CABG = coronary artery bypass grafting; DJD = degenerative joint disease; ENT = ear, nose, and throat; FNA = fine-needle aspiration; GGO = ground-glass opacity; GI = gastrointestinal; PCI = percutaneous coronary intervention; PFT = pulmonary function testing.

Alteração pulmonar: 69,9%

Alteração cardiovascular: 67,5%

Morgan L et al. Ann Am Thorac Soc 14:1450-1456, 2017

Interstitial Lung Abnormalities in the Queensland Lung Cancer Screening Study: Prevalence and Progression Over Two Years of Surveillance

John A Mackintosh ✉, Henry M Marshall, Richard Slaughter, Taryn Reddy, Ian A Yang, Rayleen V Bowman, Kwun M Fong

First published: 22 October 2018 | https://doi.org/10.1111/imj.14148

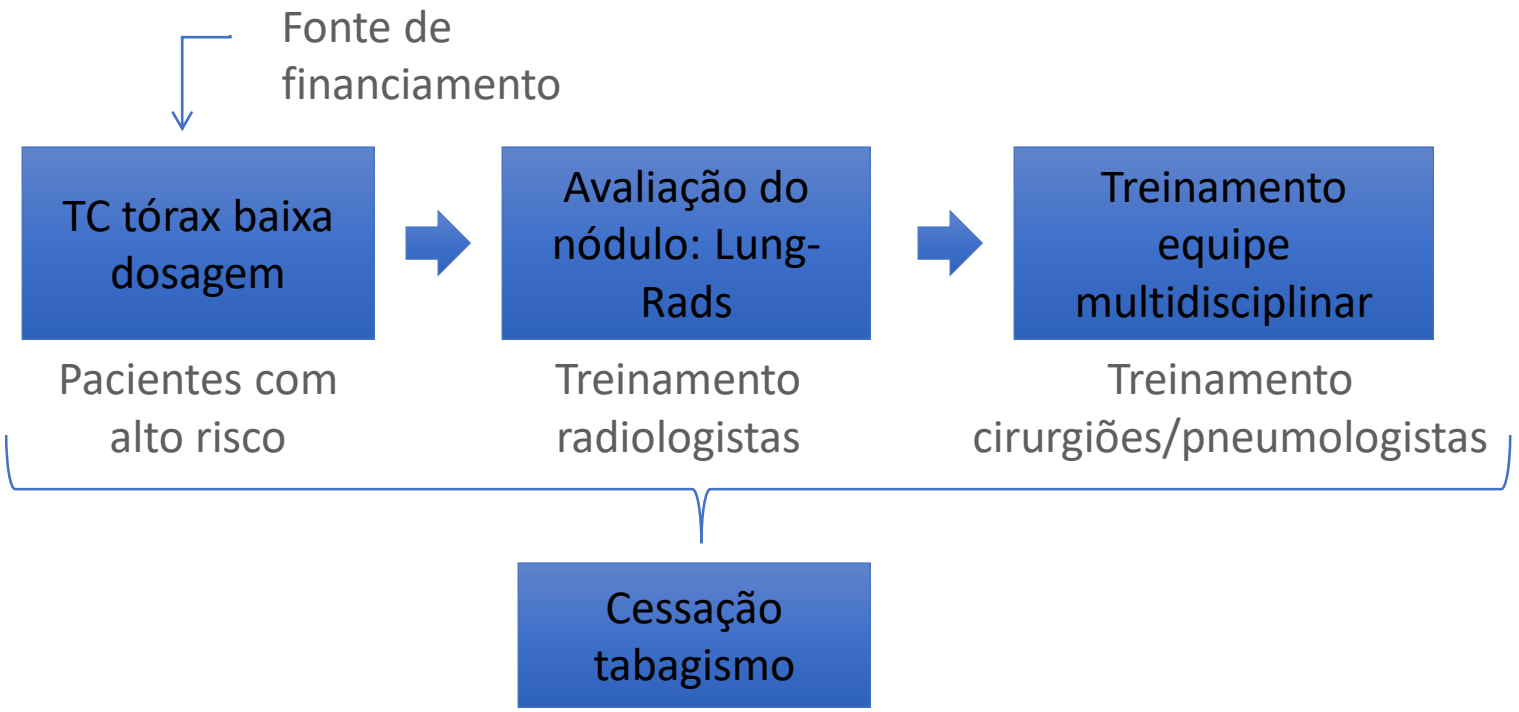


Incidência 7,8%

Study	Surveillance Interval (years)	ILA Prevalence	ILA Progression
Araki et al. 2016 [4]	6.4	8.3% (155/1867)	76.1% (118/155)
Tsushima et al. 2010 [13]	4	2.6% (80/3079)	43.8% (32/73)
Jin et al. 2013 [12]	2	9.7% (86/884)	20.3% (16/79)

Implementação

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LUNG CANCER SCREENING
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American Thoracic Society and American Lung Association

Implementation Guide for Lung Cancer Screenin



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Cessação tabagismo

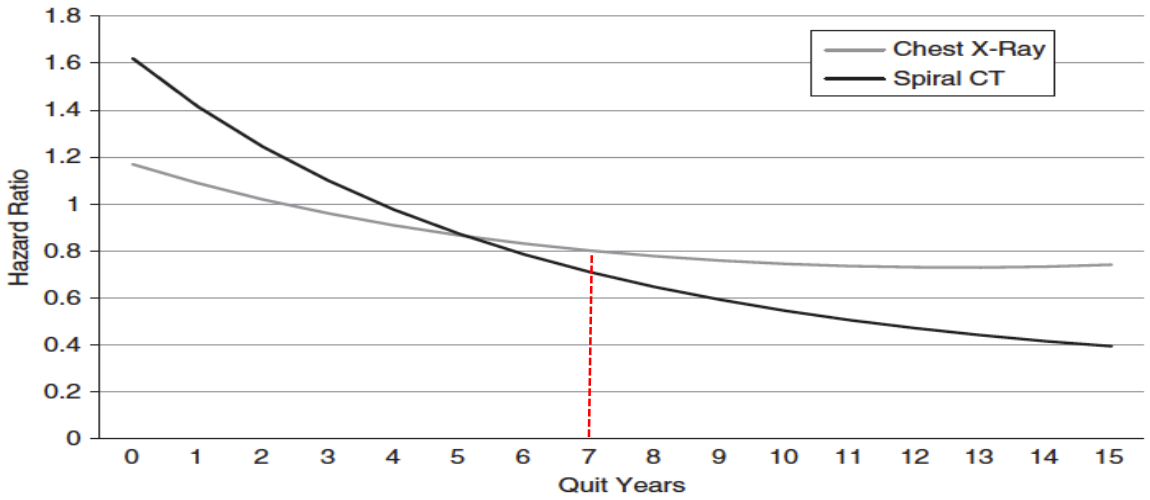
The Association between Smoking Abstinence and Mortality in the National Lung Screening Trial

Nichole T. Tanner[1,2], Neeti M. Kanodra[1], Mulugeta Gebregziabher[2,3], Elizabeth Payne[3], Chanita Hughes Halbert[2,4], Graham W. Warren[5,6], Leonard E. Egede[2,7], and Gerard A. Silvestri[1]

> Hazard Ratio > índice de mortalidade

Variable	Hazard Ratio	95% Wald CI	P-Value
Centered Age (by 5 years)	1.57	(1.47, 1.68)	<0.0001
Years Since Quitting			
< 5	1.66	(1.29, 2.13)	<0.0001
5 ≤ Quit Years < 10	1.16	(0.89, 1.50)	0.2843
10 ≤ Quit Years < 15	--	--	--
Pack Years			
30 ≤ Pack Years < 60	--	--	--
60 ≤ Pack Years < 90	1.55	(1.31, 1.84)	<0.0001
90+	1.93	(1.64, 2.28)	<0.0001
Cigarette Smoking Status			
Former Smokers (reference)	--	--	--
Current Smokers	1.69	(1.45, 1.96)	<0.0001

Alcançando 7 anos de cessação do tabagismo



Rx tórax: redução da mortalidade em 20%

TC tórax: redução de mais 10% na mortalidade

Conclusão

- Inegável benefício
  - Diagnóstico em fase inicial
  - Redução da mortalidade por cancer de pulmão
  - Redução da mortalidade por outras causas
- Seleção do paciente de risco
  - 55-74 anos
  - Carga tabágica: 30 maços/ano
  - Tabagistas ou ex-tabagistas < 15 anos
- Cessação do tabaco

Bibliografia

1.National Lung Screening Trial Research T, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395-409.
2.van Iersel CA, de Koning HJ, Draisma G, Mali WP, Scholten ET, Nackaerts K, et al. 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). Int J Cancer. 2007;120(4):868-74.
3.Yousaf-Khan U, van der Aalst C, de Jong PA, Heuvelmans M, Scholten E, Lammers JW, et al. Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval. Thorax. 2017;72(1):48-56.
4.Patz EF, Jr., Greco E, Gatsonis C, Pinsky P, Kramer BS, Aberle DR. Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial. Lancet Oncol. 2016;17(5):590-9.
5.Horeweg N, van Rosmalen J, Heuvelmans MA, van der Aalst CM, Vliegenthart R, Scholten ET, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. Lancet Oncol. 2014;15(12):1332-41.
6.Handy CE, Quispe R, Pinto X, Blaha MJ, Blumenthal RS, Michos ED, et al. Synergistic Opportunities in the Interplay Between Cancer Screening and Cardiovascular Disease Risk Assessment. Circulation. 2018;138(7):727-34.
7.Morgan L, Choi H, Reid M, Khawaja A, Mazzone PJ. Frequency of Incidental Findings and Subsequent Evaluation in Low-Dose Computed Tomographic Scans for Lung Cancer Screening. Ann Am Thorac Soc. 2017;14(9):1450-6.
8.Mackintosh JA, Marshall HM, Slaughter R, Reddy T, Yang IA, Bowman RV, et al. Interstitial Lung Abnormalities in the Queensland Lung Cancer Screening Study: Prevalence and Progression Over Two Years of Surveillance. Intern Med J. 2018.
9.Wiener RS, Gould MK, Arenberg DA, Au DH, Fennig K, Lamb CR, et al. An official American Thoracic Society/American College of Chest Physicians policy statement: implementation of low-dose computed tomography lung cancer screening programs in clinical practice. Am J Respir Crit Care Med. 2015;192(7):881-91.
10.Tanner NT, Kanodra NM, Gebregziabher M, Payne E, Halbert CH, Warren GW, et al. The Association between Smoking Abstinence and Mortality in the National Lung Screening Trial. Am J Respir Crit Care Med. 2016;193(5):534-41.

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