

Table S1: Characteristics of identified studies											
Trial name	Population characteristics	Intervention (screening interval in months/n rounds)	Control	N total (intervention/control)	Definition abnormal screening	Intervention group cumulative incidence (N screen-detected)	Control group cumulative incidence	Follow-up after last screen (years)	Contamination rate (%)	Participation rate (%)	RoB (overall)
Included studies											
DLCST(1)	Men, women age 50-70, smokers and former smokers, at least 20 pack-years. Former smokers must have quit <10 years prior	Low-dose CT (12/5)	Usual care	4104 (2052/2052)	Nodules > 5 mm in maximal diameter	96 (64)	53	5	20.3	95.5	Low
ITALUNG(2)	Men, women age 55-69, smokers and former smokers, at least 20 pack-years in past 10 years	Low-dose CT (12/4)	Usual care	3206 (1613/1593)	At least one NCN ≥ 5 mm or a non-solid nodule ≥ 10 mm or the presence of a part-solid nodule.	67 (38)	71	5	No data provided	81	Some concern
LUSI(3)	Men, women, age 50-69, smokers and former smokers (cessation <10 years) with at least 25 years of smoking at least 15 cigarettes/day or 30 years of smoking 10 cig per day.	Low-dose CT (12/5)	Usual care	4052 (2029/2023)	Nodules >5mm in diameter	85 (No data provided)	67	3	8.7	>90	Low
MILD(4, 5)	Men, women, age 49-75 years, current or former (cessation <10 years) with at least 20 pack-years	Low-dose CT (12 or 24/6 or 3) Median duration of screening was 6.2 years	Usual care	4099 (2376/1723)	Nodules >4.8 mm in diameter	98 (71)	60	The follow-up since last screening round is unclear.	1.2	95.1 in the biennial and 96.1 in the annual LDCT group.	High

Excluded studies											
DANTE(4, 6)	Male, age 60-74 years, current or former smoker with >20 pack-years, cessation <10y	Low-dose CT (12/5)	Baseline CXR and usual care	2450 (1264/1186)	Non-calcified pulmonary nodules ≥10 mm in diameter or smaller but showing possible signs of malignancy	104 (66)	72	3	100%#	93	NA
NELSON(7)	Men, women, age 50–75 years, who had smoked ≥15 cigarettes per day for ≥25 years or ≥10 cigarettes per day for ≥30 years, and who were current smokers or former smokers with cessation ≤10 years ago	Low-dose CT (12-24-36/4)	Usual care	15822 (7915/7907)	Nodules 50–500 mm ³ was indeterminate and >500 mm ³ was positive.	307 (255)	Not reported	0	Not reported	At least 87.5% participated in round 1-3, 80.7% in round 4	NA
UKLS(8)	Men, women, age 50-75 years, current or former smokers (high risk population)	Low-dose CT (0/1) ^f	Usual care	4055 (2028/2027)	Nodule measuring >3 mm diameter	52 (52)	Not reported	0 ^g	Not reported	98.3	NA
NLST(9)	Men and women aged 55-74, smoking history of at least 30 pack-years, with either current smoking status or having quit within the past 15 years	Low-dose CT (12/3)	CXR (12/3)	53454 (26722/26730)	Nodule measuring ≥ 4 mm	1089 (649)	969	2-4	4.3	95	NA

Chinese trial (Yang et al) (10)	Men and women, aged 45-70 years, current or former smokers (cessation <15 years) with at least 20 pack-years or non-smokers with at least one high risk factor for lung cancer*	Low-dose CT (0/1) [£]	Usual care	6717 (3550/3167)	Non-calcified nodules or masses with longest diameters of ≥4 mm identified on LDCT images	52 (51)	10	0 ^ø	Not reported	98.9	NA
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⌘ Most had 3-4 years follow-up after last round of screening, but study completion date is reportedly October 2016 and end point for follow-up April 2018

Entire control group received CXR at baseline

£ Only at baseline. A follow-up LDCT after a pre-determined interval (based on diameter of the nodule) was made in case of "indeterminate result"

*Cancer history of any kind in close family members; cancer history of any kind for the participant; occupational exposure to carcinogenic agents (asbestos, dust or radiation); long history of passive smoking (> 2 h every day in homes or indoor workplaces for at least ten years); and/or long-term exposure to cooking oil fumes (cooking history of stir frying, frying or deep frying > 50 dish-years)

ø No reporting of cancer incidence after baseline screening

1. Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al. 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.
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3. Becker N, Motsch E, Trotter A, Heussel CP, Dienemann H, Schnabel PA, et al. Lung cancer mortality reduction by LDCT screening-Results from the randomized German LUSI trial. *International journal of cancer Journal international du cancer*. 2019.
4. Infante M, Sestini S, Galeone C, Marchiano A, Lutman FR, Angeli E, et al. Lung cancer screening with low-dose spiral computed tomography: evidence from a pooled analysis of two Italian randomized trials. *Eur J Cancer Prev*. 2017;26(4):324-9.
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6. Infante M, Cavuto S, Lutman FR, Passera E, Chiarenza M, Chiesa G, et al. Long-Term Follow-up Results of the DANTE Trial, a Randomized Study of Lung Cancer Screening with Spiral Computed Tomography. *Am J Respir Crit Care Med*. 2015;191(10):1166-75.
7. 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.

8. Marcus MW, Duffy SW, Devaraj A, Green BA, Oudkerk M, Baldwin D, et al. Probability of cancer in lung nodules using sequential volumetric screening up to 12 months: the UKLS trial. *Thorax*. 2019;74(8):761-7.
9. Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer*. 2013;119(22):3976-83.
10. Yang W, Qian F, Teng J, Wang H, Manegold C, Pilz LR, et al. Community-based lung cancer screening with low-dose CT in China: Results of the baseline screening. *Lung cancer*. 2018;117:20-6.