



Could we continue chest X-ray(CXR) screening for lung cancer?:Re-evaluation of CXR screening with background consideration

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Background

- Lung cancer has been a heavy burden worldwide, and an efficient screening program is needed.
- Low-dose CT screening has become mainstream for lung cancer screening after publication of positive results from the NLST and NELSON studies.
- We re-evaluated the effectiveness of chest X-ray (CXR) screening and compared the histological distribution of the target population for lung cancer screening studies between the US and Japan.

Methods

- We performed a systematic review and meta-analysis for CXR screening for lung cancer. The study design included RCT, cohort study, and case-control study (CCS) that evaluated the efficacy/effectiveness of CXR screening.
- Literature searches were conducted using PubMed, Cochran Library, Web of Science, and Ichushu-web until April 2022. We examined the reference lists of systematic review and guidelines.
- Backgrounds of RCTs and CCSs were compared between the US and Japan.

Lung cancer screening in Japan

- In Japan, CXR screening has continued since 1987 based on the original guidelines, whose recommendation was on the base of the Japanese CCSs conducted around 2000.
- The screening method is CXR for average-risk, asymptomatic persons, with sputum cytology added for current smokers.
- Annual screening is provided for inhabitants aged 40 years and over, with no upper age limit.

Results

- From over 3,000 articles as candidates, 6 RCTs, 1 cohort study, and 6 CCSs were selected.
- Five RCTs were conducted from the 1960s to 1970s, except for the PLCO (Figure 1). All RCTs suggested there was no reduction in lung cancer by CXR screening.
- Six CCSs in Japan reported mortality reduction from lung cancer (Figure 2). The meta-analysis results showed a 43% mortality reduction from lung cancer (adjusted odds ratio 0.53, 95%CI: 0.50-0.63). Although the RCTs included only men, except for the PLCO and KFS, the Japanese studies included women (20% of the case groups).

Figure 1. Meta-analysis of RCTs for CXR screening (CTFPHC,2016)

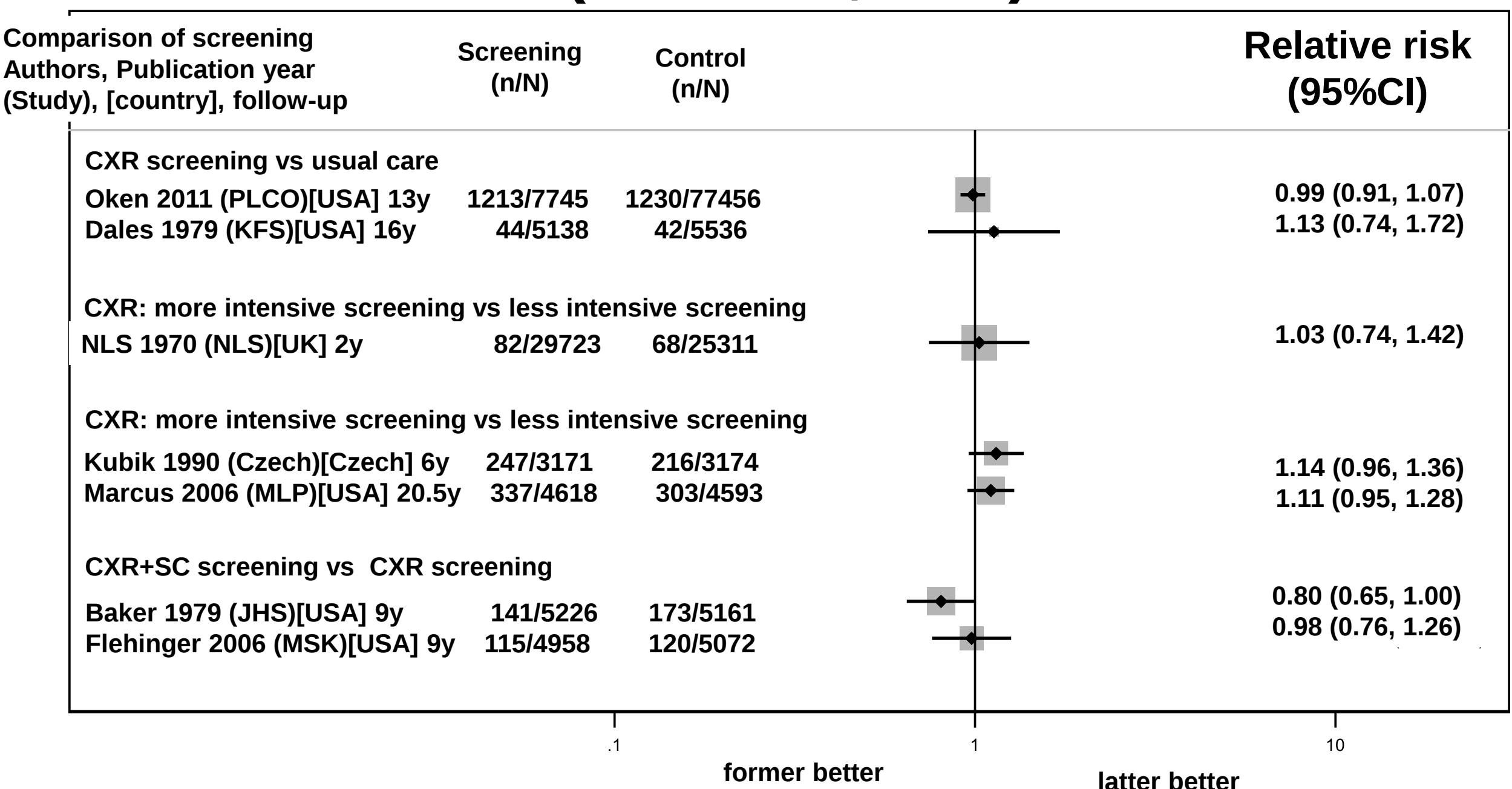
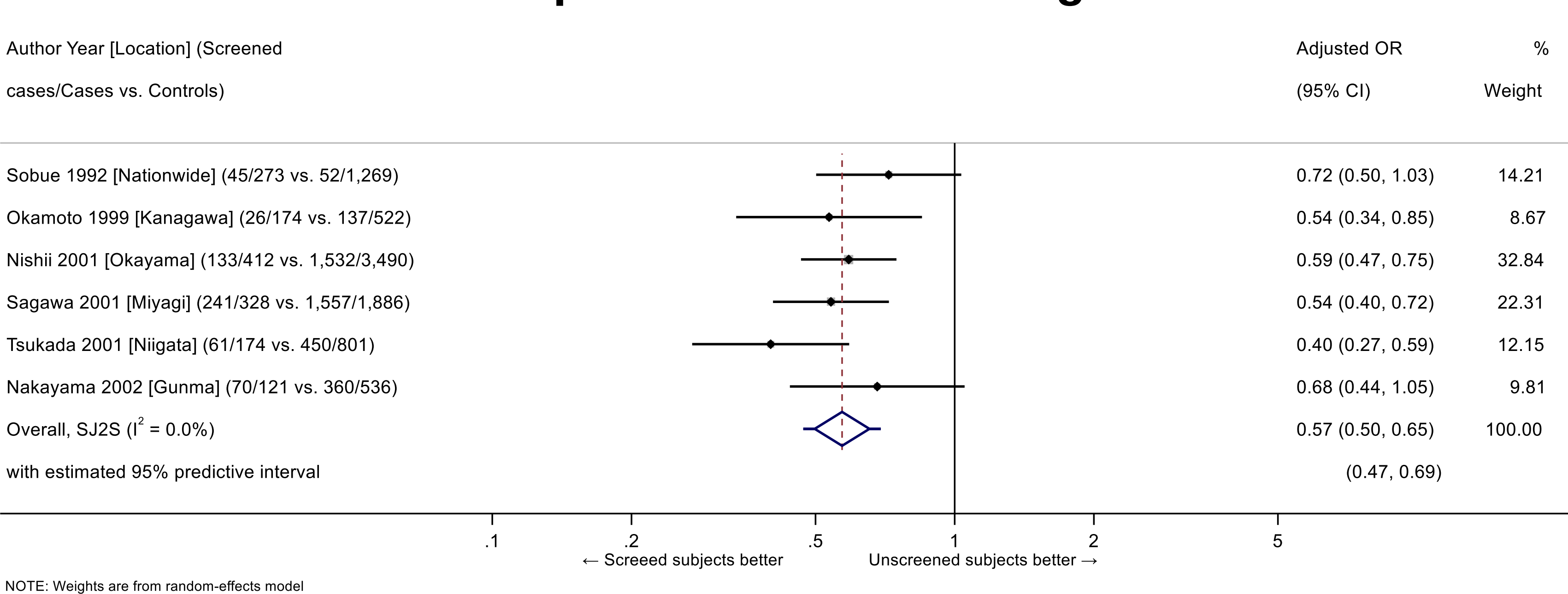


Figure 2. Meta-analysis of case-control studies for Japanese CXR screening



McMaster Evidence Review and Synthesis Center Team,
 Screening for lung cancer : Systematic Review and meta-analysis, 2015

Table 1. Comparison of lung cancer histology for the period for PLCO and Japanese CCS

	Period for Japanese CCSs	Period for PLCO in the US
	1990-94	1998-2010
Male		
Squamous cell carcinoma (%)	37.9	38.3
Adenocarcinoma (%)	36.4	35.9
Small cell carcinoma (%)	17.4	16.3
Others (%)	8.4	9.5
Female		
Squamous cell carcinoma (%)	18.3	19.7
Adenocarcinoma (%)	61.3	59.5
Small cell carcinoma (%)	13.6	13.5
Others (%)	6.8	7.4

Kinoshita FL, et al. J Epidemiol. 2016 Nov 5;26(11):579-586 Meza R, et al. PLoS One. 2015 Mar 30;10(3):e0121323

Change of target lung cancer for cancer screening

- The histological distribution of lung cancer was similar in the period when the PLCO and Japanese CCSs were performed (Table 1).
- During that period, squamous cell carcinoma decreased with a decrease in the smoking rate, but adenocarcinoma increased, particularly in Asian women.
- Although CXR was used for lung cancer screening, the target disease differed between old RCTs and Japanese CCSs. The PLCO is a contemporary study, and the results reflected the same background as the Japanese studies.

Table 2. Comparison of the result of PLCO for lung cancer by study design and follow-up periods

Study design defined by Duffy SW (JMS, 2015)	PLCO (CXR vs usual care)	
	6 y	13 y
Follow-up continuing beyond the screening phase	0.91 (0.81-1.03)	0.99 (0.87-1.22)
Follow-up continuing beyond the screening phase, but with only deaths from cancers diagnosed during the screening phase included (Dilution analysis)	0.89 (0.80-1.00)	-

Oken, et al. JAMA 2011

Discussion

- The lead time of CXR screening was estimated to be 2-4 years, and then 13 years follow-up might be too long to evaluate mortality reduction of lung cancer. The dilution effect might affect the PLCO results (Table 2).
- At 6-year follow-up, mortality reduction by 9% was observed, but it was not statistically significant.
- When the outcomes was defined only deaths from cancers during the screening phases included, mortality reduction of 11% was found with CXR screening.

Conclusion

- The target disease were different between the old RCTs and cotemporally studies including PLCO and Japanese CCSs.
- Although evidence of CXR screening is limited, it might be adopted in Japan considering the change of the screening target for lung cancer screening.