

# GoldNet Research Network

## Virtual Journal Club Meeting

The GoldNet Research Network is pleased to invite you to an online journal club meeting. We invite you to join us in this session and look forward to your participation and insightful discussion.

### Panellists

**A/Prof. Nicole Rankin**

Head, Evaluation and Implementation Science Unit  
Centre for Health Policy  
University of Melbourne

**Prof. Nick Zwar**

Executive Dean of the Faculty of Health Sciences and Medicine, Bond University and Chair of GoldNet Steering committee

**Dr Krishna Bajee Sriram**

Staff Specialist – Respiratory Medicine, Department of Respiratory Medicine, Gold Coast University Hospital

**Professor Mark Morgan**

Professor of General Practice, Associate Dean External Engagement, Faculty of Health Sciences and Medicine, Bond University

**Date:** Thursday 7<sup>th</sup> April, 2022

**Time:** 6-7 PM (Evening) AEST

*Lung cancer screening*

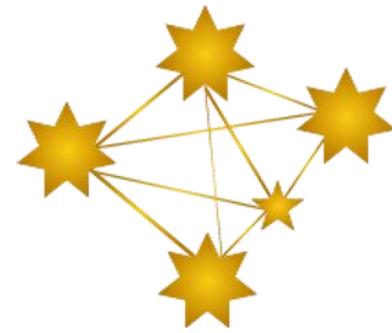
**Article:** [Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung Cancer Screening with Low-Dose CT in Smokers: A Systematic Review and Meta-Analysis. Diagnostics \(Basel\). 2021 Jun 5;11\(6\):1040. doi: 10.3390/diagnostics11061040. PMID: 34198856; PMCID: PMC8228723.](#)

If you are interested in joining this journal club, please register through Eventbrite. After registration, you will receive a confirmation email containing information about how to join the Journal Club – including Zoom invite details.



INSTITUTE FOR  
Evidence-Based Healthcare

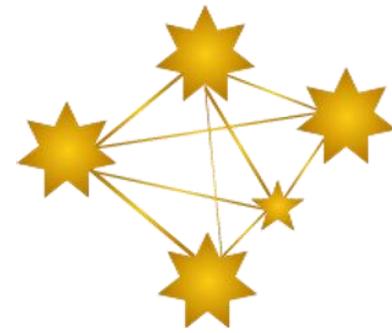




# Journal Club Agenda

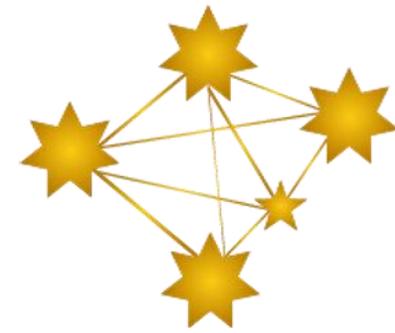
- **Welcome & case scenario**
  - Nick Zwar
- **Analysis of the research evidence**
  - **Loai Albarqouni** (article: [Hunger T et al. Lung Cancer Screening with Low-Dose CT in Smokers: A Systematic Review and Meta-Analysis](#))
- **Expert discussion**
  - Nicole Rankin (Implementation),
  - Krishna Sriram (Clinical),
  - Mark Morgan (RACGP)
- **Conclusion**

# Case Study



- 62 year old man
- Long-term smoker – over 40 pack years
- Stopped smoking after coronary artery bypass graft and pacemaker insertion in 2019
- Relapsed to smoking during COVID-19
  
- Problem list
  - Hyperlipidaemia
  - Gout
  - Obesity
  - Newly diagnosed type 2 diabetes

# Analysis of Research Evidence



Review

## Lung Cancer Screening with Low-Dose CT in Smokers: A Systematic Review and Meta-Analysis

Theresa Hunger \*, Eva Wanka-Pail, Gunnar Brix and Jürgen Griebel

Department of Medical and Occupational Radiation Protection, Federal Office for Radiation Protection, Ingolstaedter Landstrasse 1, 85764 Oberschleissheim, Germany; ewanka-pail@bfs.de (E.W.-P.); gbrix@bfs.de (G.B.); juergen-griebel@gmx.de (J.G.)  
\* Correspondence: thunger@bfs.de; Tel.: +49-30-18333-2253

**Abstract:** Lung cancer continues to be one of the main causes of cancer death in Europe. Low-dose computed tomography (LDCT) has shown high potential for screening of lung cancer in smokers, most recently in two European trials. The aim of this review was to assess lung cancer screening of smokers by LDCT with respect to clinical effectiveness, radiological procedures, quality of life, and changes in smoking behavior. We searched electronic databases in April 2020 for publications of randomized controlled trials (RCT) reporting on lung cancer and overall mortality, lung cancer morbidity, and harms of LDCT screening. A meta-analysis was performed to estimate effects on mortality. Forty-three publications on 10 RCTs were included. The meta-analysis of eight studies showed a statistically significant relative reduction of lung cancer mortality of 12% in the screening group (risk ratio = 0.88; 95% CI: 0.79–0.97). Between 4% and 24% of screening-LDCT scans were classified as positive, and 84–96% of them turned out to be false positive. The risk of overdiagnosis was estimated between 19% and 69% of diagnosed lung cancers. Lung cancer screening can reduce disease-specific mortality in (former) smokers when stringent requirements and quality standards for performance are met.

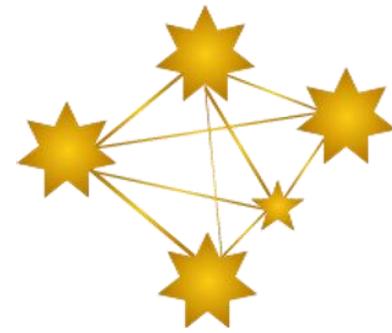
**Keywords:** screening; lung cancer; low-dose CT; systematic review



**Citation:** Hunger, T.; Wanka-Pail, E.; Brix, G.; Griebel, J. Lung Cancer Screening with Low-Dose CT in Smokers: A Systematic Review and Meta-Analysis. *Diagnostics* **2021**, *11*, 1040.

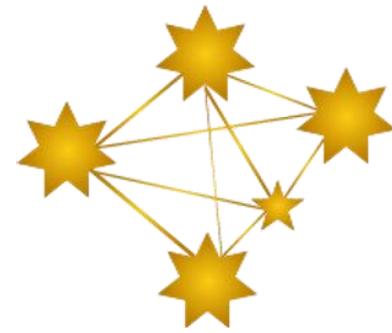
- [Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung Cancer Screening with Low-Dose CT in Smokers: A Systematic Review and Meta-Analysis. \*Diagnostics\* \(Basel\). 2021 Jun 5;11\(6\):1040. doi: 10.3390/diagnostics11061040. PMID: 34198856](#)

# Evidence Summary



- **Question:**
- **Population:** Adult (49-75 years old) current or former smokers (>20 pack-year)
- **Intervention:** Low-dose CT screening
- **Comparison:** No screening or Chest X-ray screening
- **Outcomes:** Benefits and Harms – 1ry outcomes: Lung cancer mortality and overall mortality. 2ry outcomes: incidence of lung cancer, false positives, overdiagnosis, complications associated with diagnostic work-up.

# Evidence Summary cont.



- **Methods:** This is a systematic review and meta-analysis of randomised controlled trials.
- **FAITH**

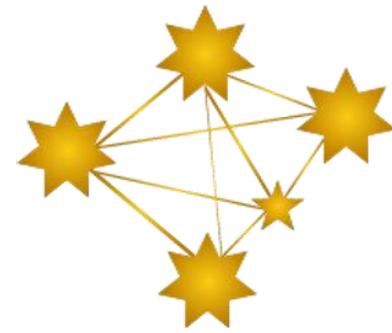
## **F** did the search **FIND** all relevant studies?

- The authors of this systematic review searched 3 electronic databases (Medline, Embase, Cochrane CENTRAL) using a combination of free-text and mesh terms. They also supplemented search by screening the reference list of included trials. There was no restriction on publication date.
- However, authors limited their search to articles published in English or German languages which can potentially lead to language bias (i.e., systematically missing important relevant pieces of evidence) – especially that countries like China that have high rate of smoking and might conducted trials to evaluate lung cancer screening programs. In addition, authors did not clearly report the terms/search strategy used in this review.

## **A** Have the included studies been critically **APPRAISED**?

- The authors assessed the risk of bias in included studies using Cochrane Risk of Bias tool – standard practice for systematic reviews of interventions.

# Evidence Summary cont.



**I** Did the review **INCLUDE** the right type of studies and assess their risk of bias?

- The authors included RCTs that compared CT screening with no screening or screening with chest radiogram (CXR) in current or former smokers - studies should report results on benefits and/or harms of LDCT screening.

**T** Have the results of included studies been **TOTALLED** up with appropriate summary tables and plots?

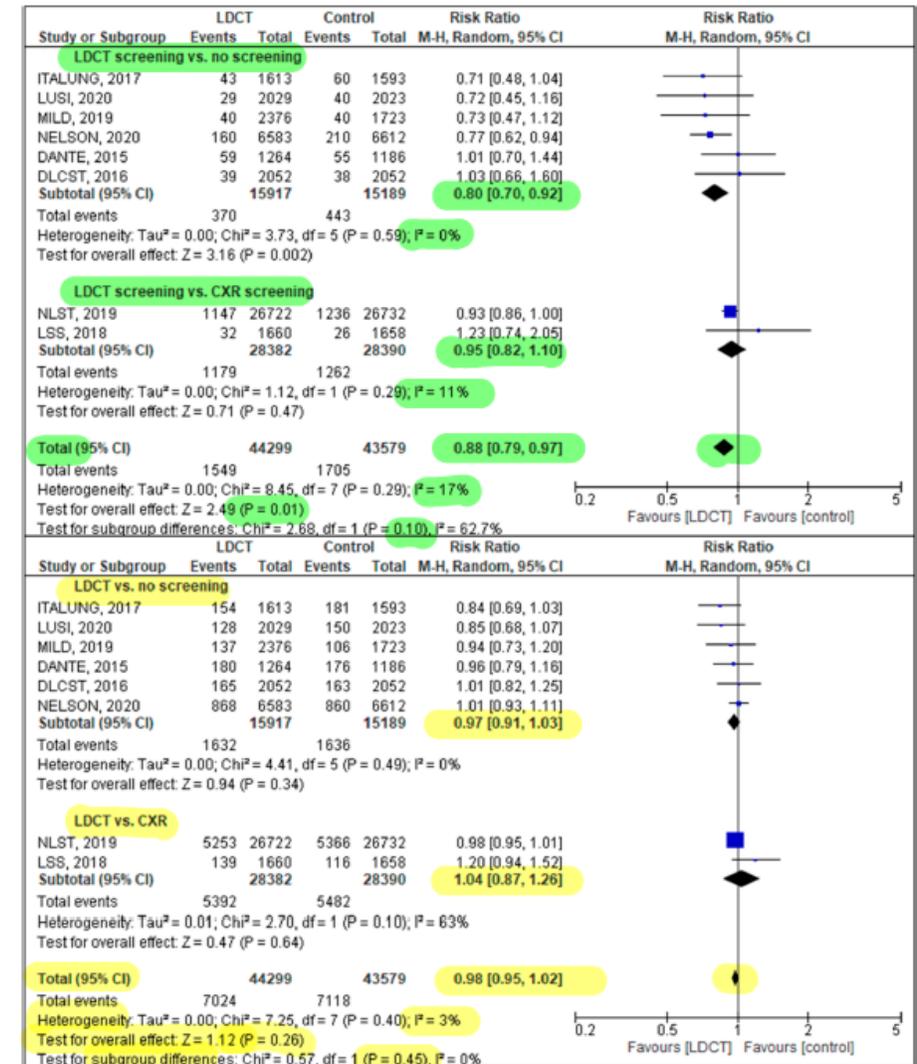
- Authors reported the results using figures and tables appropriately.

**H** Has **HETEROGENEITY** between the studies been assessed and explained?

- Authors assessed the heterogeneity among included studies using I<sup>2</sup> and conducted prespecified subgroup analysis.

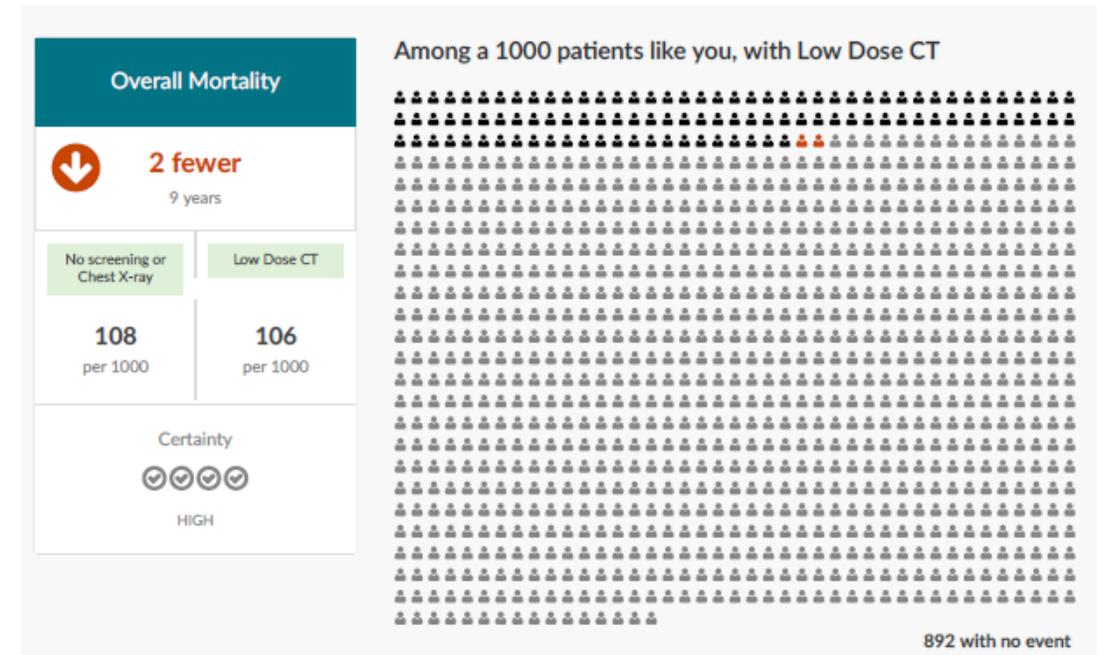
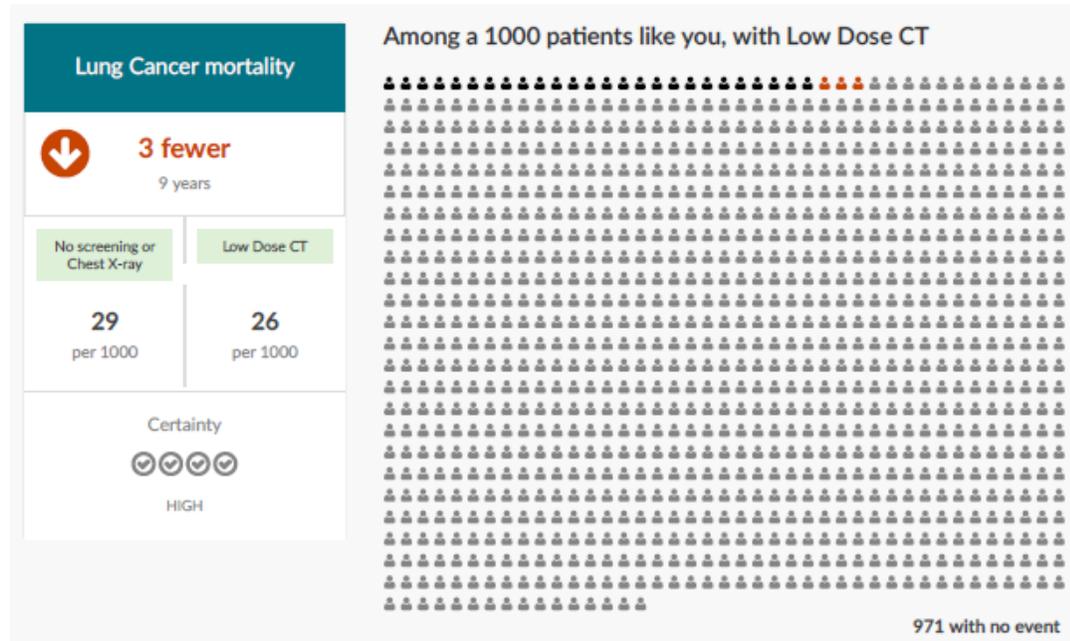
# Findings

- 10 trials were eligible and 9 of those included in the evidence synthesis of this review (DANTE, Depiscan, DLCST, ITALUNG, LSS, LUSI, MILD, NELSON, NLST). UKLS was a pilot trial without full reporting of the results, therefore, excluded from the analysis.
- Table 1 summarise the study characteristics and Table 2 summarise the characteristics of participants enrolled in the included trials. Average age of participants 59.3 years and most of them male with long-standing smoking history (32-54 pack-years).
- The use of low-dose CT screening resulted in a 12% reduction on lung cancer mortality (RR 0.88; 95% CI 0.79 to 0.97; I<sup>2</sup> 17%) – statistically significant. However, the effect of low dose CT screening did not lead to statistically significant reduction in overall mortality (RR 0.98; 95% CI 0.95 to 1.02).



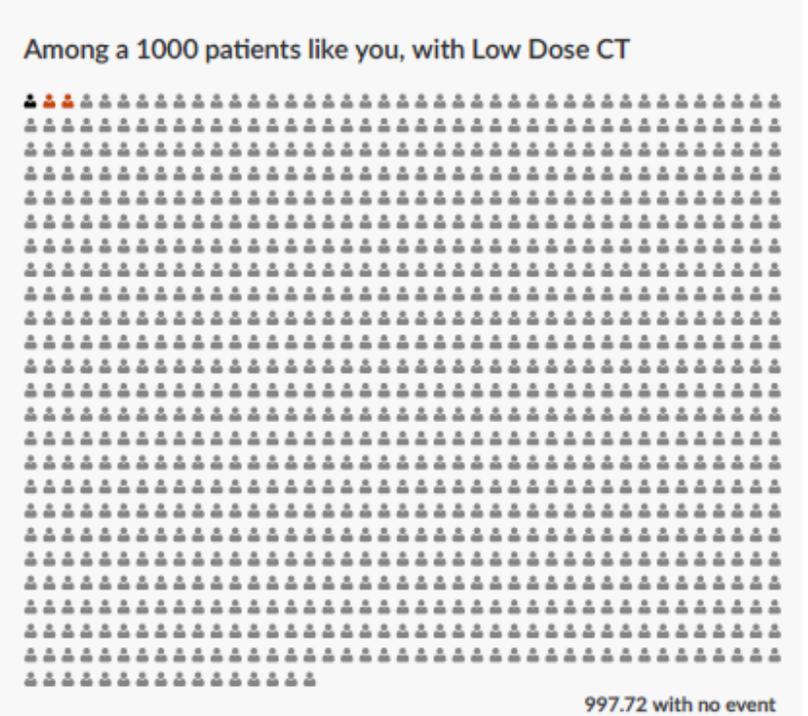
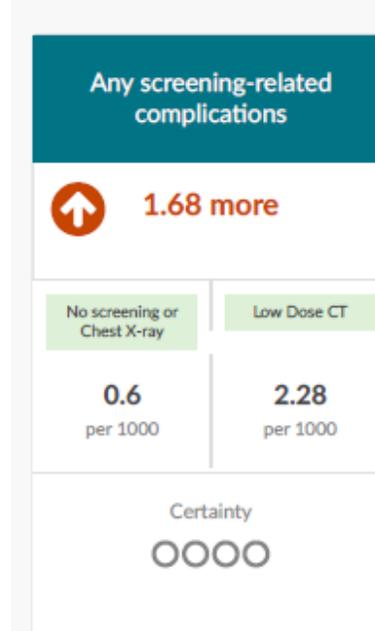
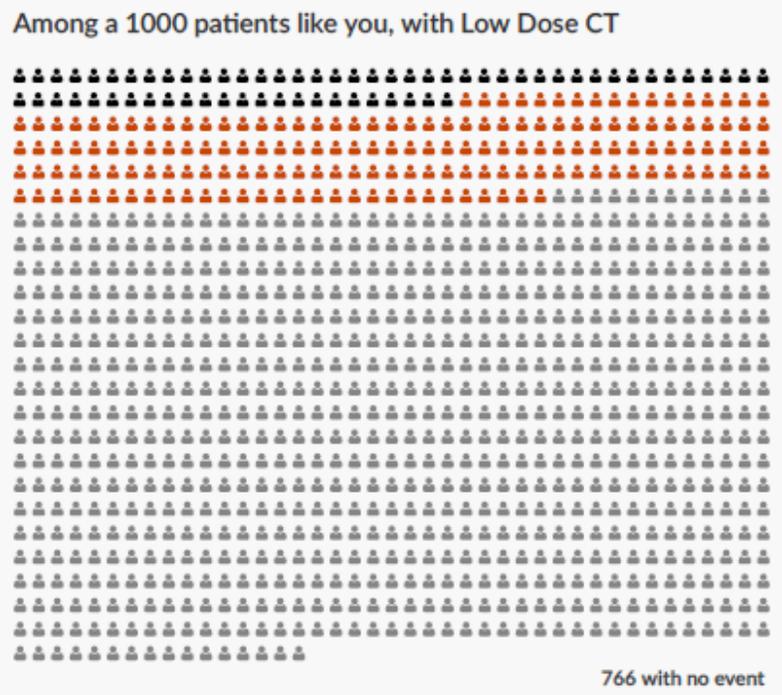
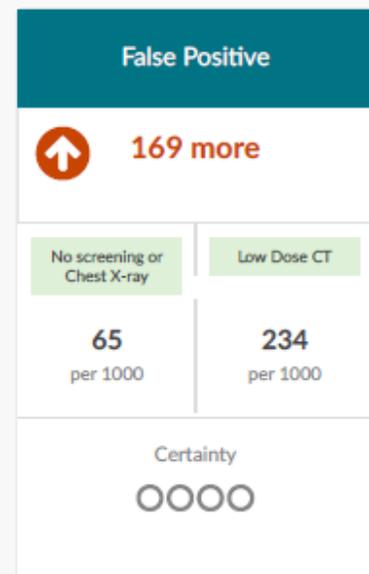
# Findings

- The impact of low dose CT screening on lung cancer mortality and overall mortality presented in absolute terms in the figures below.

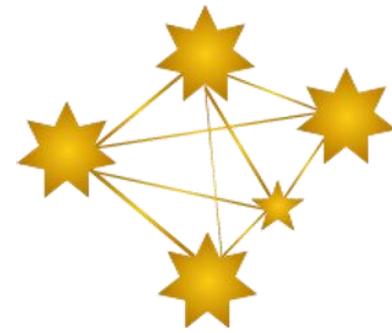


# Findings

- Unsurprisingly, low dose lung cancer screening resulted in an increase in lung cancer incidence (26% increase). More cancers were detected in stage I in the screening group than in the control group (mean of all diagnoses: 44% vs. 26%) and less in stage IV (29% vs. 43%).
- Low dose CT screening resulted in higher rates of false-positive test results, complications associated with unnecessary diagnostic work-up, and overdiagnosis (18.5% - 69.1%) (figures below).



# Comments from Journal Club



- The following points raised in the discussion of this article in the GoldNet Journal Club
  - **More relevant RCTs have been published** – so might change the findings of this review. For example, UKLS trial published showing similar findings in terms of reduction in lung cancer deaths. *Field JK, Vulkan D, Davies MPA, et al. Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis. Lancet Reg Health Eur. 2021;10:100179. Published 2021 Sep 11. doi:10.1016/j.lanepe.2021.100179*
  - **Incidental findings:** we discussed the frequency of incidental findings associated with lung cancer screening program and the consequences associated with these incidental findings. This article describe the implications of incidental findings from a pilot lung cancer screening program in the UK <https://www.nature.com/articles/s41533-021-00246-8>
  - **Opportunity cost:** we discussed how the time, energy and public resources (including Medicare benefits and PBS subsidies) might be much better spent in advising patients not to start smoking, and if they already smoke, in helping them to stop rather than in advising them to start lung cancer screening program.
  - **Patient preferences:** we discussed the importance of involving patient preferences in the decision-making process e.g. shared decision making and decision aids. In this analysis of the quality of shared decision making in consultations around lung cancer screening – this analysis showed it is of low quality <https://jamanetwork.com.ezproxy.bond.edu.au/journals/jamainternalmedicine/fullarticle/2696731>