4-IN THE LUNG RUN: towards INdividually tailored INvitations, screening INtervals, and INtegrated co-morbidity reducing strategies in lung cancer screening

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27422

Source
NTR

Brief title
4-IN-THE-LUNG-RUN

Health condition

lung cancer

Sponsors and support

Primary sponsor: ErasmusMC
Source(s) of monetary or material Support: EU - Horizon2020

Intervention

Outcome measures

Primary outcome

stage I-II lung cancer incidence

Secondary outcome

1: The rate of (late stage) interval cancers in each arm.
2: The rates of informed uptake of (sub-group) participants
3: The rates of smoking cessation within individuals in the trial smoking at the baseline screening.
4: The crude costs and cost-effectiveness of each arms.
5: Policies for risk-stratification through biomarkers.
6: The external validation and update/extension of various lung cancer risk-prediction models in 4-IN-THE-LUNG-RUN
7: Guidelines and training programmes for CT screening and pulmonary nodule management.
8: Overview of sex and gender differences in lung cancer risk and screening effectiveness.
9: Overview of SES and gender representativeness within the trial.
10: Comparison and merging of results with other ongoing European studies.

Study description

Background summary

With 338,000 EU-deaths annually, lung cancer is a devastating problem. CT screening has the potential to prevent ten-thousands of lung cancer deaths annually. The positive results of the Dutch-Belgian screening trial (NELSON), with relatively low referral rates, and the NLST in the US, with annual screens only, provided conclusive evidence on the benefits (and possible harms). However, EU-implementation is likely to be limited, slow and of variable quality throughout European countries, and current international guidelines could easily require up to 25 million CT screens annually. The most optimal strategy in risk-based lung-thoracic screening is still unknown regarding the optimal and most cost-effective (e.g., targeted) strategy 1) to recruit high-risk individuals, 2) to integrate smoking cessation and co-morbidity-reducing services, and 3) to determine the preferred personalised (risk-based) screening interval. Personalised regimens based on the baseline CT result can potentially retain 85% of the LC mortality reduction achievable through screening at 45% less screens, thus potentially saving much unnecessary harm associated with screening, and 0.5-1 billion Euros per year.

The heart of 4-IN-THE-LUNG-RUN is a European randomised controlled multi-centred implementation trial amongst 24,000 individuals, at high risk for developing lung cancer, evaluating whether it is safe to have risk-based less intensive screening intervals after a negative baseline CT.
Various methods to improve participation of hard-to-reach individuals will be assessed in five different healthcare settings/countires. Innovative co-morbidity reducing strategies will be tested including other markers on CT imaging, as Calcium Score and COPD. Cost impact and cost-effectiveness analyses using a natural history model will steer implementation. The experienced consortium will strongly interact with key stakeholders, and discuss interim results with key other international initiatives on CT screening, biomarkers, and smoking

cessation practices. This proposal will form the evidence base for risk-based lung cancer screening with huge benefits for the EU, on health outcomes, cost savings, and innovation in the long run.

Study objective

European randomised controlled multi-centred implementation trial amongst 24,000 individuals, at high risk for developing lung cancer, evaluating whether it is safe to have risk-based less intensive screening intervals after a negative baseline CT.

Study design

The primary analysis will compare the cumulative hazard functions of stage I/II cancers between the two randomized groups using a logrank test at 5-years of follow-up. The rate of stage I/II cancers for each arm will be estimated as the number of stage I/II cancers detected either clinically or through screening out of the total person-years of follow-up in their respective arm.

The primary analysis will be performed on the per-protocol (PP) population, which will include all randomized and eligible participants in the arm they were randomized to, who complied with their screening recommendations. Intention-To-Treat (ITT) analyses will be performed as a sensitivity analysis.
The per-protocol definition will be used for the primary analysis of the trial and is as follows per arm:
- Standard arm: Having received a negative baseline screening, and then adhering to an annual interval between screening (up to two CT screens after baseline).
- Risk-based arm: Having received a negative baseline screening, and then adhering to a biennial interval between screening (up to one CT screen after baseline).

The secondary endpoints are:
1: The rate of (late stage) interval cancers in each arm. --> measures by linkage national cancer registry at 5-years of follow-up
2: The rates of informed uptake of (sub-group) participants --> measured by questionnaire with validated questions about Informed-Decision Making from before randomization till after screening rounds.
3: The rates of smoking cessation within individuals in the trial smoking at the baseline screening. --> measured by a health questionnaire with validated questions about smoking behaviour, comparing recruitemnt data and baseline screening data.
4: The crude costs and cost-effectiveness of each arms.--> by using MISCAN modelling at 5-6 years of follow-up

Intervention

CT lung cancer screening

Contacts

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Eligibility criteria

Inclusion criteria

men and women, aged 60-79 years, at high risk for developing lung cancer, who gave written informed consent to participate

Exclusion criteria

1. Recent abnormal pulmonary findings under work-up of standard care.
2: Having had a computed tomography scan of the thorax <1 year before potential entry into the study.
3: Current or prior history of lung cancer.
4: Inability to provide signed informed consent.
5: Insufficient understanding of the languages in which trial information is available.
6: Unable to be followed-up for at least 5-years.
7: Body weight over 140 kg

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2020
Enrollment:	26000
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	31-08-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9710
Other	Minitry of Health (due to Population Screening Act) : 2379962-1011169-PG

Study results