



Population screening study
for lung cancer

Information

4-IN-THE-LUNG-RUN

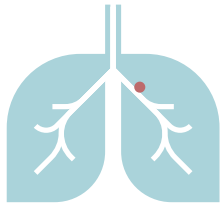
Scientific research into the early detection of lung cancer in Europe



This brochure contains information about the scientific population screening study into lung cancer. This is our way of helping you to decide whether or not you want to take part in this study. You will learn about the background of the study, how the study will be carried out and what taking part means for you. You can personally decide whether you wish to participate.

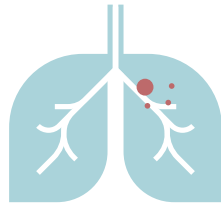
Lung cancer

Lung cancer is a serious health issue. Over the past year, approximately 10,000 people died from lung cancer in the Netherlands. Once lung cancer-related symptoms start to appear, the lung cancer is normally at an advanced stage. Treatment then becomes difficult. Of 100 people with such an advanced stage of (metastasised) lung cancer, almost all die within 5 years.



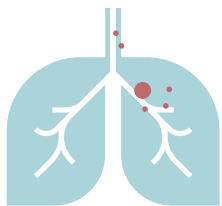
Stage I

Tumour smaller than 3 cm without metastases



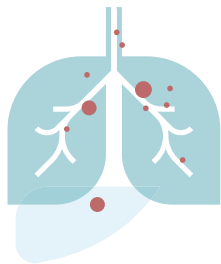
Stage II

Tumour 3-5 cm and/or one-sided metastases in the lymph nodes



Stage III

Tumour larger than 5 cm and/or metastases in the lymph nodes of the lung and/or between the lungs

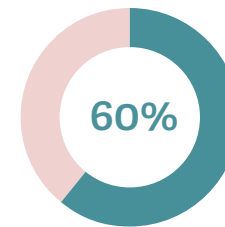


Stage IV

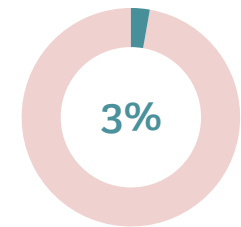
Tumour larger than 7 cm and/or metastases in the other lung and/or other organs

Early detection of lung cancer

Lung cancer can be detected at an early stage using a CT scan. If lung cancer is detected at an early stage (stage I), there tend to be more treatment options. The lung cancer is still small in stage I and cancer cells are only located in one lung. Of 100 people with lung cancer in an early stage (stage I), approximately 60 people are still alive after 5 years following treatment. In stage IV, only 3% of people are still alive after 5 years.

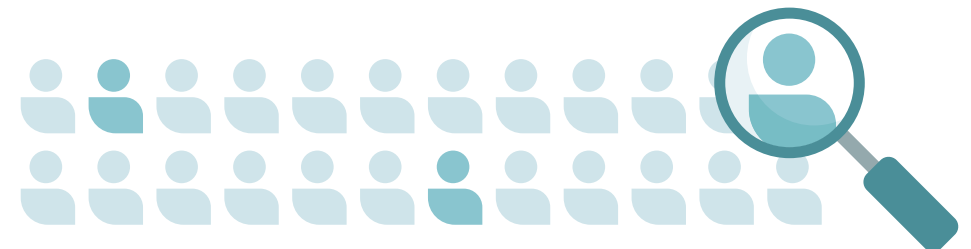


Lung cancer discovered in stage I
60% still alive after 5 years



Lung cancer discovered in stage IV
3% still alive after 5 years

Lung cancer screening involves detecting lung cancer in people with a high risk of lung cancer. This is also referred to as population screening. In approximately 1 in 4 people with lung cancer, lung cancer screening can prevent people dying from lung cancer because it leads to early detection and treatment. Nonetheless, population screening for lung cancer is still not taking place. Some important questions first need to be answered. Only then can a decision be made about whether population screening for lung cancer can be introduced.



What is 4-IN-THE-LUNG-RUN researching?

Lung cancer often grows quickly. That is why people with a high risk of lung cancer should be examined every year. And over a period of 20 years. But this is demanding for the people themselves, as well as the healthcare system. In the meantime, we know that abnormalities are not found during the first examination (namely the first CT scan) of 8 in 10 people. These people are also slightly less likely to suffer from lung cancer in the years that follow. Such people, where abnormalities are not encountered, could possibly wait slightly longer for their next CT scan. The main aim of our study (4-IN-THE-LUNG-RUN) is to examine whether it is in fact safe to wait 2 years to examine people who did not encounter abnormalities on their first CT scan. We would also like to know how we can best help people when deciding whether or not they want to be examined. We expect there to be 26,000 participants in 5 European countries.

For whom is this study intended?

Population screening for lung cancer will only be useful to people with a high risk of developing lung cancer. Lung cancer is mainly encountered in people who have smoked for a large part of their lives. The risk of suffering lung cancer continues to be high for a long period of time even after people have quit smoking.

For this study, we are looking for people who have smoked for a long time. For example, a pack a day for more than 20 or 30 years. Or 2 packs a day for 15 years. If people have stopped smoking, they should not have done so more than 10-15 years ago. As a result, it does not matter if you currently smoke or have already stopped. If you have never smoked cigarettes, you are not exposed to a high risk; this study is not intended for you and will also be of little use.

Are you being treated for lung cancer or have you been treated for lung cancer during the past 5 years? Then the study will also not be useful for you.

How did we get your details?

3 hospitals and regions in the Netherlands are taking part in this study. All men and women between 60 and 79 years who live near these hospitals will be invited to complete a questionnaire. Your details have been obtained from the Personal Records Database (BRP). Permission to do so was obtained from the Ministry of the Interior. Only authorised study staff will be able to access your details. We will destroy your details if you do not take part in the study.

What do we expect from you?

Please read the information brochure carefully. Decide for yourself if you want to take part in the study. If you still have questions, please feel free to visit our website (www.lungscreening.eu) or to contact us. The contact details can be found at the end of this brochure. Continue reading to see what else you must do.



I want to take part

If you want to take part, fill in the questionnaire and the informed consent, and return them to us. The study team will carefully examine the completed questionnaire. The study team will then determine whether you meet all requirements for participation. Besides smoking, we will also examine various other variables, which is why we are using a scientific questionnaire.



I am *eligible* for participation

You will be notified if your answers confirm that you are eligible for participation. Participation is always voluntary. This means you can stop participating at any moment in time. And there is no need to mention a reason. .



I am *not eligible* for participation

We will also notify you if your answers confirm that you are not eligible for participation. If you cannot participate, this does not mean that you cannot get lung cancer. That is why you should always consult your GP if you suffer symptoms that are associated with lung cancer. Further information can be found on our website, www.lungscreening.eu.



I do not want to take part

You do not have to do anything. We will no longer approach you.

How will we conduct the study?

The various steps in the study have been explained below.

Step 1 Allocation into study groups

Firstly, the computer will allocate all participants into one of two groups. It is not possible to switch between groups. This is the only way for us to compare the groups effectively. You will be sent a letter that informs you about your group.

Step 2 First CT scan of the lungs

All participants will undergo a CT scan of the lungs. This examination lasts approximately 10 minutes and is painless. You will not receive any medicines for this examination and a contrast medium will not be used. More information about the CT-scan examination can be found in the appendix. The CT scan can be used to look for abnormalities in the lungs that could point to lung cancer. You will receive the result within approximately 3 weeks.

There are three possible outcomes of this examination:

- A negative result

The CT scan showed nothing that points to lung cancer. This is the most commonly encountered result. Approximately 82 in every 100 people will receive a negative test result. A negative result does not guarantee that you will never get lung cancer. That is why you should always consult your GP if you suffer symptoms.

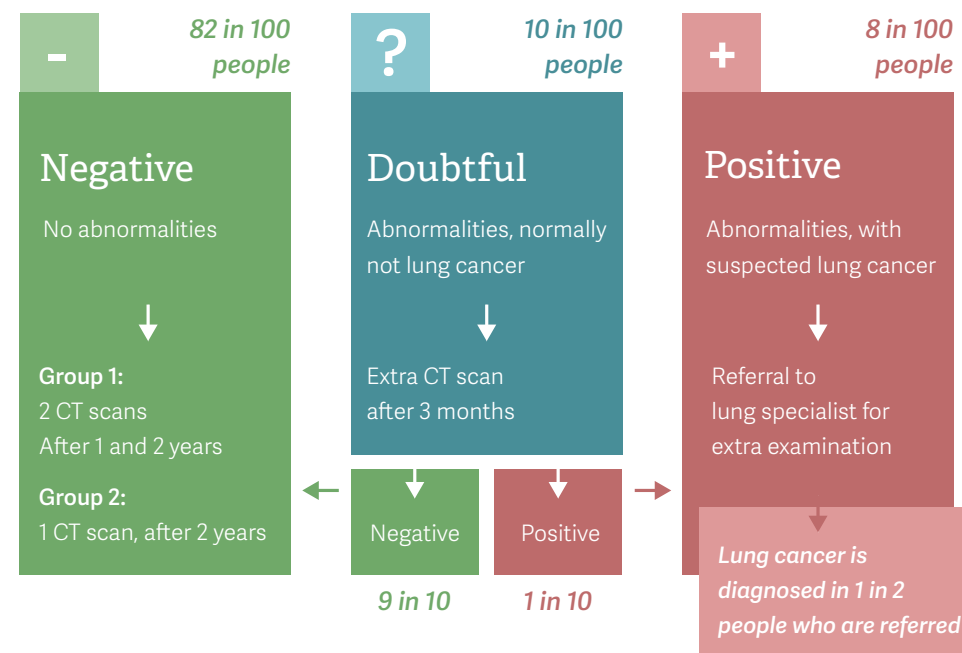
? A doubtful result

The CT scan showed a few minor abnormalities in the lungs, which do not immediately point to lung cancer but there are still doubts. This is often inflammation or scarring. To be on the safe side, an extra CT scan will be carried out after approximately 3 months. Approximately 10 in every 100 participants undergo a repeat CT scan. Minor spots that have not, or have barely, grown require no further treatment. This will lead to a negative result. Spots that grow quickly are more suspicious. They will result in a positive result.

+ A positive result

The CT scan shows abnormalities in the lung that point to lung cancer. Further examination by the lung specialist is needed to determine whether it actually involves lung cancer.

Approximately 8 in every 100 people receive a positive result. But not all people actually have lung cancer. Of every 2 people who are referred to the lung specialist, 1 person will effectively have lung cancer.



Step 3 The next CT scans in the 2 study groups

All people with a negative test result (no abnormalities) will be automatically invited for a new CT scan. Exactly when this will be, will be determined by the study group.

There are two groups:

Study group 1:

Participants in this study group will receive another 2 CT scans: one CT scan every year.

Study group 2:

Participants in this study group will receive another 1 CT scan; this CT scan will be carried out two years after the first one.

If (minor) abnormalities are actually found on the CT scan, they will also receive a CT scan every year until the end of the study. If lung cancer is suspected, people will be referred to the lung specialist for further examination.

What will we do once all CT scans have been carried out?

Once all CT scans have been carried out, we will ask the Netherlands Comprehensive Cancer Organisation to inform all participants that have lung cancer about the stage and type of cancer. To do so, we need you to provide written approval on the informed consent. You will not be able to take part in the study if you do not want to provide consent for this.

The stages of lung cancer that are encountered in the two study groups will be compared against each other. If there are no stage-related differences in the groups (which is positive), we will be able to increase the period of time between the two CT scans in people where no abnormalities were encountered during the first CT scan.

Extra measurements for scientific research only

The CT scan will show the area around the lungs. Besides lung cancer, the CT scan will also show the degree of artery calcification in the arteries around the heart: this is referred to as "the calcium score". The calcium score is an indicator for the risk of cardio-

vascular disease. We are also able to examine measurements that offer an insight into (chronic) respiratory diseases/lung emphysema. The use of these two measurements is something rather new. That is why we will measure and examine these values, but not share them with you or your GP. We first need to conduct more research before we know enough about how these measurements can be used. An exception will be made for an elevated calcium score because this may require further treatment. Your GP will be informed if you have an elevated calcium score.



What can you expect if you take part in the study?

Participating in the screening study can have advantages as well as disadvantages. You can find further information about the most commonly encountered advantages and disadvantages below.

Advantages

- Early detection of lung cancer reduces the risk (by approximately 24%) of dying from lung cancer
- Your prospects will improve if lung cancer is treated at an early stage
- Treatment is often less invasive if lung cancer is discovered early
- The CT scan is painless and is completed within 10 minutes. A contrast medium is not used.

Disadvantages

- You may start worrying or feel anxious when being examined or waiting for the result
- Even after further examination, it may transpire that you do not have lung cancer
- A CT scan is based on X-rays
- Lung cancer may be discovered that is growing so quickly that treatment is no longer possible
- Lung cancer may be discovered that is growing so slowly that it will not have caused you any inconvenience during your life

Coincidental discovery of other serious abnormalities

The CT scan will only show the area around the lungs. We will not look for abnormalities in other organs. However, sometimes the doctor may coincidentally discover another serious abnormality. For example, this could involve cancers other than lung cancer or dilation of the aorta. In this case, further examination will be important for your health. But it may also make you feel worried and uncertain. Treating a severe abnormality that is discovered coincidentally can have very intrusive consequences. However, the condition may also be beyond treatment, which means you will know that you are ill, and also know that doctors can do little to assist you.

You are free to decide whether we should inform you if other severe abnormalities are encountered on your CT scan. You can mention this on the informed consent. If you provide consent, the study team will inform your GP about the matter. Your GP will then contact you and refer you to a specialist at the hospital.

However, the doctor may still decide to contact you even though you indicated that you do not wish to be contacted if an abnormality is discovered coincidentally. This may be done if the doctor believes that not telling you could be dangerous to your health or the health of people around you. Naturally, the doctor will consider this matter carefully and will not make the decision alone. In this case, advice will be requested from an independent committee. These people will have nothing to do with the study. Of course, these people will not be aware of your identity; they will only see a code.

What happens if you do not want to take part in the study or want to stop?

Participation in the study is voluntary. You can always drop out of the study, even if you have agreed to participate. There is no need to mention a reason in this case. Whether or not you take part in this study will have no impact on your medical care.

What if new information becomes available?

The study will last 5 years. We have compiled a plan for the study but also realise that things can change over the course of 5 years. For example, new information may become available that causes us to view the study differently. We will notify you if this is the case. You can then decide whether or not you want to continue with the study.

What will we do with your details?

Your details will be processed in pseudonymized form. This means we will use a personal study number instead of your name and address. Researchers will only see the study number and will thus never use your name in the articles or reports that they write. This ensures that researchers never know to whom the details belong.

Details like your name and address will only be accessible to a few employees within the study. This is needed to, for example, invite you for the CT scan or to send the result of the CT scan.

All employees comply with the General Data Protection Regulation and the Privacy Regulations of the Erasmus MC. All information about you will only be used for the 4-IN-THE-LUNG-RUN study. The Medical Treatments Agreement Act (WBG0) stipulates that all data must be retained for a period of 15 years after stopping the study. All data will be destroyed after this period.

Will your GP be informed about your participation?

GPs play an important role if indications of lung cancer are encountered. We think it is important for you to receive the right support and medical care. If you provide consent to do so, we will inform your GP about the results of your examination.

For what are we requesting consent?

The questionnaire is accompanied by an informed consent. For each part of the form, could you indicate whether or not you are in agreement? The consent form contains further information about each section that you consent to. Written consent is needed by law if you want to participate.

All (medical) information will only be used for the 4-IN-THE-LUNG-RUN study. Your medical information will not be shared with other organisations.

A separate question on the form asks you to provide consent for using the study data for other research into lung cancer. In this case, it will not be possible to use the data to trace your identity. For instance, your name, address and date of birth will never be sent. The concerned research must also have received ethical approval.

Will you be paid?

You will be able to claim your travel expenses.

Who will pay healthcare-related costs?

CT scans for the 4-IN-THE-LUNG-RUN study will be paid in full from study funding that the Erasmus MC has received from the European Commission.

If the CT scan shows abnormalities that require further examination, your GP will refer you to the lung specialist (happens to approximately 8 in every 100 people). From the moment that you are referred by your GP, all medical care will fall under your health insurance. This is also how things were arranged in other population screening programmes in the Netherlands. However, in this case, further examinations or treatment by the lung specialist may be (partly) charged against your deductible. Some medicines are also subject to a personal contribution.

Ethical approval

The Minister of Public Health, Well-being and Sport asked the Health Council to investigate whether the study is safe and whether careful consideration has been given to every aspect. The Health Council was positive about the scientific quality of the study as well as the harm-benefits ratio for participants. On 24 June 2021, the (outgoing) Minister of Public Health, Well-being and Sport issued a licence for executing the 4-IN-THE-LUNG-RUN study.




Smoking and quitting smoking

Smoking and passive smoking increase the risk of many illnesses, including cancer, cardiovascular diseases and chronic respiratory diseases. If you smoke, it is always important to try to quit smoking. However, we also realise that quitting can be very difficult. People that seek help are more likely to quit smoking for a longer period of time. 'Quit smoking' care will be covered under your basic health insurance.

Are you thinking about quitting smoking? Our 'quit smoking' coaches are ready to assist you! It does not matter whether or not you want to participate in the study. Would you like to know how our quit smoking coaches can help you? Then enter your name, e-mail address and phone number at www.rookvrijookjij.nl/longkankerscreening and we will contact you without any obligation. If you currently smoke, you are eligible to have your risk of cardiovascular diseases measured by your GP. You can also request support for quitting smoking via your GP.

Contact

Would you like to know more? Feel free to visit the website for more detailed information. Please feel free to contact us if you have questions or comments. We will be pleased to assist you.

 **0800-0191** (free help desk I&O Research)

 **4.in.the.lung.run@erasmusmc.nl**

 **www.lungscreening.eu**



With help from
Longkanker Nederland



Independent doctor

Do you have doubts about participating and do you have a question that you would prefer to ask someone other than our researchers? Then you can phone or send an e-mail to an independent doctor:

Prof. Dr. Agnes van der Heide, Professor Public Health, Erasmus MC

tel. **010-7043719**, email: a.vanderheide@erasmusmc.nl

The independent doctor is not directly involved with the study but knows everything about it.

Do you have a complaint about the study? Then you have three options:

- 1** You can phone or send an e-mail to the researchers. Are you not satisfied with the response to your complaint? Then you can phone the Complaints officer at the day clinic of the Erasmus MC. The phone number is **010-704 41 08**. Ask for the Complaints officer.
- 2** You can immediately speak to the Complaints officer (**010-704 41 08**).
- 3** You can submit a complaint to the secretary of the Complaints Committee at the **Erasmus MC via Postbus 2040, 3000 CA Rotterdam** or via www.erasmusmc.nl.

The complaints regulations of the Erasmus MC and the complaint-handling brochure can be obtained from the Complaints officer.

Available brochures

Information about the study is available in various languages. You can request the brochure in Dutch, Turkish, Arabic or Italian.

Visit www.lungscreening.eu or phone the free help desk of I&O Research (**0800-0191**).

Appendix 1 The CT scan

More information about the CT scan (of the lungs) can be found below.

What is a CT scan?

A CT scan is an examination that is based on X-rays. You will lie on an examination bed while a thin x-ray tube moves around your body, creating images. It is possible to create a few images within a couple of seconds. The examination will take around 10 minutes in total.

What does the CT scan mean for you?

You do not have to take many things into consideration. You do not have to make preparations. There is also no need for you to avoid eating. If you take medicines, you can continue as usual.

You will experience no pain while the scan is being performed. You will not be administered any medicines or a contrast medium. You can also keep your clothes on. However, you do have to remove metal objects like jewellery or glasses. If you, for example, have a prosthesis or screws in your body, this will not cause issues when performing the CT scan.



What will happen during the examination?

You will lie on an examination bed for a few minutes. The lab technician will slightly insert the bed into the opening of the CT scanner. You must then remain as still as possible. You will spend a short while alone in the CT scan room, but can continue talking to the lab technician via the intercom. The lab technician can also see and hear you, and will check how you are doing. The lab technician will tell you exactly what you must do, for example, inhale, exhale, cough, and briefly hold your breath.

Which side effects can you expect?

There are no side effects to undergoing a CT scan. However, people who are claustrophobic may feel anxious or inconvenienced when undergoing a CT scan. Our employees will always guide you during the process and will be in continuous contact with you.

After the examination

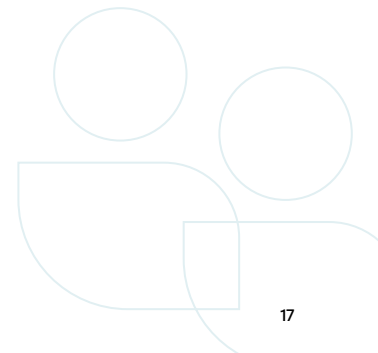
After the examination, you can simply go home and do everything as normal.

Is it dangerous?

The CT scan works with X-rays that can be harmful. However, the use of radiation is minimised, whereby the likelihood of harmful consequences is very low.

The result of the examination

After the examination, the radiologists will view your lungs on the CT scan. They will look for abnormalities that could indicate lung cancer. Both you and your GP will receive a letter containing the result of the examination. If abnormalities are encountered that require further examination, your GP will refer you to a lung specialist for further examination.



Appendix 2 Which hospitals are taking part, and in which countries?

The "4-IN-THE-LUNG-RUN" study will be carried out in various countries, namely the Netherlands, Germany, England, France, Italy and Spain. Experts in the field of lung cancer screening are working on this study.

The institutions in question can be found below.

The Netherlands



England



Germany



Spain



France



Italy

