

The Swiss Approach – feasibility of a national low-dose CT lung cancer screening program

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Summary

BACKGROUND: Lung cancer is the leading cause of cancer-related deaths in Switzerland. Despite this, there is no lung cancer screening program in the country. In the United States, low-dose computed tomography (LDCT) lung cancer screening is partially established and endorsed by guidelines. Moreover, evidence is growing that screening reduces lung cancer-related mortality and this was recently shown in a large European randomized controlled trial. Implementation of a lung cancer screening program, however, is challenging and depends on many country-specific factors. The goal of this article is to outline a potential Swiss lung cancer screening program.

FRAMEWORK: An exhaustive literature review on international screening models as well as interviews and site visits with international experts were initiated. Furthermore, workshops and interviews with national experts and stakeholders were conducted to share experiences and to establish the basis for a national Swiss lung cancer screening program.

SCREENING APPROACH: General practitioners, pulmonologists and the media should be part of the recruitment process. Decentralisation of the screening might lead to a higher adherence rate. To reduce stigmatisation, the screening should be integrated in a "lung health check". Standardisation and a common quality level are mandatory. The PLCOm2012 risk calculation model with a threshold of 1.5% risk for developing cancer in the next six years should be used in addition to established inclusion criteria. Biennial screening is preferred. LUNG RADS and NELSON+ are applied as classification models for lung nodules.

CONCLUSION: Based on data from recent studies, literature research, a health technology assessment, the information gained from this project and a pilot study the Swiss Interest Group for lung cancer screening (CH-LSIG) recommends the timely introduction of a systematic lung cancer screening program in Switzerland. The final decision is for the Swiss Cancer Screening Committee to make.

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Introduction

Lung cancer is a major public health burden. In Europe, it ranks third among the most common cancers and has the highest cancer-related death rate [1]. A large share of the burden of this disease would be preventable through behavioural changes in the population as well as the detection of lung cancer at earlier stages [2].

There is increasing scientific evidence that low-dose computed tomography (LDCT) lung cancer screening (LCS) reduces lung cancer mortality [3]. In the US, the National Lung Screening Trial could prove a relative reduction of mortality of 20% [4]. In Europe, the NELSON trial which is the largest randomized controlled trial on LCS in Europe with more than 13,000 screened persons, showed a mortality reduction of 24% in men and 33% in woman compared with the unscreened control group [5].

Literature on implementation of LCS is limited, mainly because lung cancer screening programs have not often been implemented on a large scale. In January 2020, Croatia was the first European country to launch a national lung cancer screening program; the program targets all active smokers (or who have stopped smoking within the last 15 years) between 50 and 70 years of age. In total, eleven health facilities across Croatia provide screening [6]. Poland initiated a lung cancer early detection program within its National Cancer Plan funded by the Ministry of Health [7]. Experiences and reports from Poland are very encouraging for introducing LDCT cancer screening locally and building up facilities gradually [8]. Furthermore, the UK has established regional Lung Health Checks, which is a new service that aims to diagnose early lung cancer when treatment may be more successful. Although the lung health checks are not primarily labelled as screening, it is described as a "community-based, targeted, low-dose CT (LDCT) lung cancer screening pilot" [9].

Field et al. (2019) published the results of a roundtable discussion of experts on the implementation of LCS in Europe [10]. The authors recommended that national health policy groups start implementing CT screenings as evidence of their effectiveness becomes available; therefore, LCS should become a priority in Europe.

In the United States, private hospitals have implemented LCS. Thus, even though LCS is widely available in the country, there is no national cancer screening program in place [11]. However, most major medical organizations in the US recommend annual LCS for high-risk individuals. The American Thoracic Society and American Lung Association have published an implementation guide for LCS [12]. This guide describes a variety of existing LCS models and gives an overview of topics that should be considered when clinics are planning to implement LCS.

For example, the implementation guide provides guidance on how to centrally organize a LCS program. In this case, program coordinators are responsible for the organization of the program, e.g., recruitment, smoking cessation, and tracking of clinical outcomes. In contrast, a decentralised approach shifts all responsibilities to the referring provider. Furthermore, the implementation guide describes how to approach the introduction of LCS, starting with engaging local leadership, forming a governance structure, and establishing a business plan (or the definition of quality met-

rics) to be followed in the program. In 2021, the US Preventive Services Task Force (USPSTF), the government's influential guidelines panel, updated its 2013 recommendations on LCS, broadening eligibility to include younger and lighter smokers [13].

In Switzerland, on average, about 2,500 men and 1,500 women were diagnosed with lung cancer per year between 2008 and 2012 [14]. Lung cancer accounts for 11.8% of all cancers in men and 8.5% in women. It is the second most common cancer in men and the third most common cancer in women [14]. During 2008–2012, an average of about 2,000 men and 1,100 women died from lung cancer per year. Further, it is the most common cause of cancer death in men, accounting for 22.3% of all cancer deaths, and the second most common cause of cancer death in women (accounting for 14.9%). The risk of dying from lung cancer is 5.5% for men and 2.7% for women [14]. This means that almost 6 out of 100 men and 3 out of 100 women die from this cancer [14]. The European Society for Medical Oncology (ESMO) has not yet made a recommendation on the implementation of lung cancer screening. The ESMO has expressed concern that there is insufficient proof of mortality reduction and that the risk cohort has not yet been precisely defined as well as about the cost-effectiveness. However, the high burden of lung cancer as well as the increasing evidence of the benefit of LCS has triggered activities internationally and in Switzerland. The CH-LSIG is a national expert group for early cancer detection. The committee has looked into the topic of LCS and has currently mandated a health technology assessment (HTA) on LDCT-LCS [15]. Furthermore, the Swiss Lung Association has funded a feasibility study to establish a LCS program. The objective of this project was to assess feasibility of introducing LDCT-LCS in Switzerland through a bottom-up approach and propose and describe characteristics for implementation a LCS program in Switzerland. Finally, an ongoing pilot study, which will be published in near future has already delivered preliminary results in a Swiss screening cohort, which emphasise the benefits of screening.

Framework

Literature review

First, we conducted a review of the most recent literature [5, 16–23]. This review included scientific literature on the effectiveness and cost-effectiveness of LCS [24–37], recommendations and position statements of international associations [13, 20, 38–43] and grey literature on the implementation of LCS. This literature review served as a basis for further development of the project [18].

Interviews with national and international experts

In 2019, we conducted eight interviews with international experts. The interviews provided timely information on how other European countries plan and implement LDCT cancer screening. This allowed us not only to benefit from their experiences, but also to compare initiatives at different implementation stages. We carried out six interviews were as part of a site visit in Manchester, UK. The Manchester screening site takes a slightly different approach than other programs. The program consists of a mobile unit

of several trucks that go into regions with high tumour incidence to perform on-site screening [9]. They call their program a "lung health check" and assess the lungs as a whole, thus eliminating the stigmatization of term "lung cancer screening".

Next, we discussed these insights with a wide range of stakeholders in the Swiss context. This included all national stakeholders along the patient pathway from the beginning of the project in the design period through the assessment of the study. In total, 23 stakeholder interviews were conducted in two stages. The first stage was conducted in autumn 2019, and the second stage in spring 2020. The interview guide included questions about the patient pathway, organization, funding, and quality assurance of the screening program (table 1).

Workshops

At the beginning of 2020, after the first stage of the interviews was completed, a workshop of the Swiss Interest Group for LCS (CH-LSIG) was held in Bern. Preliminary results of the study were discussed with the members of the group. A second workshop with the CH-LSIG took place in late fall 2020. The goal of the workshops was to collect feedback from the national experts and to validate the latest developments of the project. To reach a broader audience for feedback on the progress of the project and to disseminate the idea of a potential model of LDCT screening, we also organized a workshop and presented our conclusions in a parallel workshop at the Public Health Con-

ference in Switzerland in 2020. A flowchart showing the step-by-step framework is given in figure 1.

Screening approach

Recruitment strategy

Reaching out to the individuals who are potentially at risk is a major challenge in LDCT-LCS [44]. Health professionals, like general practitioners (GPs), pulmonologists and pharmacists are potential actors in the recruitment process. Additionally, health associations such as "Lungenliga Schweiz", Krebsliga Schweiz" or "Swiss Cancer Screening" could play a leading role in the recruitment of the persons to be screened. Specific lung health associations are a feature of the Swiss healthcare system not seen in most other countries, but they play an important role in certain fields of health care and prevention. They are organized at the regional level and are also involved in the early detection of lung diseases. Despite this regional structure, screening should be equally implemented.

The media may be also employed to raise awareness for LCS and to recruit patients for screening. Magazines, newspapers, and social media platforms have widespread reach throughout all social classes and age groups. Strong et al. have shown that social media can be used to increase knowledge of lung cancer screening [45]. Recruiting participants through media requires a comprehensible description of the screening program and contact information. If there is available data for the risk assessment participants, they could also be contacted directly via telephone or email. Hinshaw et al. analysed recruitment methods in

Table 1:
Characteristics covered in the stakeholder interviews.

	Characteristics	Operationalisation (examples)
1	General Information	Screening program (name), country, year of program initiation
		Program type, geographical scope, implementation status
		Estimated target population (no. of persons), participation (no. of persons)
		Costs, human and financial resources
2	Organisation	Which stakeholders are involved? How is the program organized? For example, does it incorporate smoking cessation programs?
3	Institutional capacities	Screening centres, radiology centres, recruitment centres
4	Eligibility/ inclusion criteria	Target age (years), smoker: pack-years, quit (years), further criteria (last CT scan, risk stratification approach such as incorporation of potential biomarkers and susceptibility genes)
5	Recruitment strategy	Who is responsible for recruitment? How is recruitment performed?
6	Training of providers	How are providers educated/ informed? What kind of educational material is available?
7	Screening protocol	Screening interval (years) and duration
		CT performance (requirements, protocols, training of technician)
8	Informed decision/ decision aid	Does the program require signed informed consent? Is written information on benefits and harms of screening provided?
9	Management of abnormalities detected in screening	What is measured by the algorithms on lung nodule management? Information to include: standardise diagnostic criteria, a nodule-characterisation method, semi-automatically derived volume measurements/ volume-doubling time, management tracking, radiation exposure limits, communication approach between the ordering provider and the patient; data collection on the use and outcomes;
		Who is involved in follow-up diagnostic tests? Are there different protocols for newly-detected incident screening and detected nodules in clinical practice?
		For internal communication, does the program use multidisciplinary boards?
10	Reading strategies	How many reading centres; single- or double-read, requirements on expertise for reading, use of CAD (computer-aided detection), training/certification of radiologist
11	Quality assurance	Program monitoring including screening registry, structured reporting of program, quality control of data and if so, the kind of data; National quality assurance board
12	Financing/ reimbursement	Is the program publicly funded? Is health insurance a source of funding?
		Are the screening tests provided free of charge? Are the diagnostic tests provided free of charge?
13	Ethical issues and Equity	How are ethical issues and equity taken into account?

the course of the NLST and found out that emailing was the most efficient method, but printed media like magazines and brochures have also been proven to be effective [46]. Health insurers also have information on individuals' backgrounds as well as their treatments, medications, and laboratory data [47]. Therefore, health insurers would have all the necessary information to recruit individuals. However, the legal situation would need to be assessed to determine if this data could be employed for the recruitment of the target population.

A short interview can verify whether potential patients meet the requirements for the pre-screening. If the individual meets the inclusion requirements, an appointment can then be set for a more detailed risk assessment within a lung health check.

Framing of the LDCT-LCS program as a lung health check

In the UK, a pilot study determined the importance of patient perception in the design of an LCS program, resulting in the presentation of a Lung Health Check [48] that addresses the issue of lung health more broadly. From the stakeholder consultation and based on the Manchester experience, framing the LCS as a Lung Health Check is favourable, as it focuses on health instead of the disease. Furthermore, the term Lung Health Check can help minimise stigmatisation related to lung cancer.

Centralisation vs. decentralisation

A screening program can only be successful if it reaches as many eligible people as possible.

Restricting the number of screening institutions may be helpful to ensure quality, but it increases the travel distance to the next screening centre. This in return may hamper the adherence rate.

Several stakeholders were in favour of mobile screening. The Manchester trial achieved participation rates of over 50% by implementing a community-based program focusing on areas with a higher risk of lung cancer, bringing mobile medical trucks into communities for screening (including LDCT), and incorporating initial counselling for helping patients quit smoking [9, 49]. However, mobile screening may generate extra costs, and the CT density is assumed to be high in Switzerland. The degree of centralisation can vary based on the levels of pre-screening, screening, and radiology reading. A possible approach is to perform diagnostics in a decentralised manner and organize radiology and treatment centrally.

Risk assessment

Lung health checks and risk assessments will be conducted by paramedical health professionals such as nurses in specifically-equipped buses, outpatient centres, or private practices. The efficiency of a LCS program directly depends on risk stratification. Only individuals with a significant risk of lung cancer should be eligible for LDCT screening.

We propose the use of the established inclusion criteria from the NLST study [4] as well as the use of a risk prediction model based on data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) [50]. PLCOm2012 is a validated lung cancer risk prediction model incorporating 15 predictors, including medical history, sociodemographic characteristics, and smoking exposure. An additional predictor is a diagnosis of chronic obstructive pulmonary disease (COPD), which may rely on the results of pulmonary function testing (spirometry). Individuals with a probability of suffering from lung cancer within the next 6 years of 1.5% or higher will be eligible for LDCT-LCS, even if they do not meet the established NLST inclusion criteria. Different approaches in risk assessment and defining inclusion criteria are shown in table 2.

Eligibility criteria:

- Age from 55 to 74 years
- Willingness and ability to undergo LDCT

Figure 1: Framework for a country specific screening pathway.



- >30 pack-years
- Former smoker <15 years
- Never diagnosis of lung cancer
- No major medical problems
- No CT scan in the last 18 months
- No haemoptysis or weight loss >7 kg in the last year
- OR Risk of lung cancer of at least 1.5% over the next six years (according to the PLCOm2012 prediction model)

Individuals' risk for lung cancer should be assessed at 2-year intervals, which would allow the identification of individuals who may become eligible for LDCT-LCS, e.g., due to accumulated pack-years of smoking or increased age.

Informed decision making

Information must be available for all program stages. The flow of information is key for the successful implementation of an LDCT-LCS program. The necessary information and the flow of the information depend on the detailed participant pathway (figure 2).

Participants eligible for screening must receive informational material describing the benefits and risks of an LDCT-LCS program. To support informed consent, several decision tools from other countries can be used. Unisanté (Lausanne) is currently developing such informational material for LCS in Switzerland [51]. If requested, written information can be complemented with a question and answer (Q&A) session with a health professional. This discussion will allow the potential patient to resolve open

questions about the screening process. Based on the informational material and the discussion, the participant will

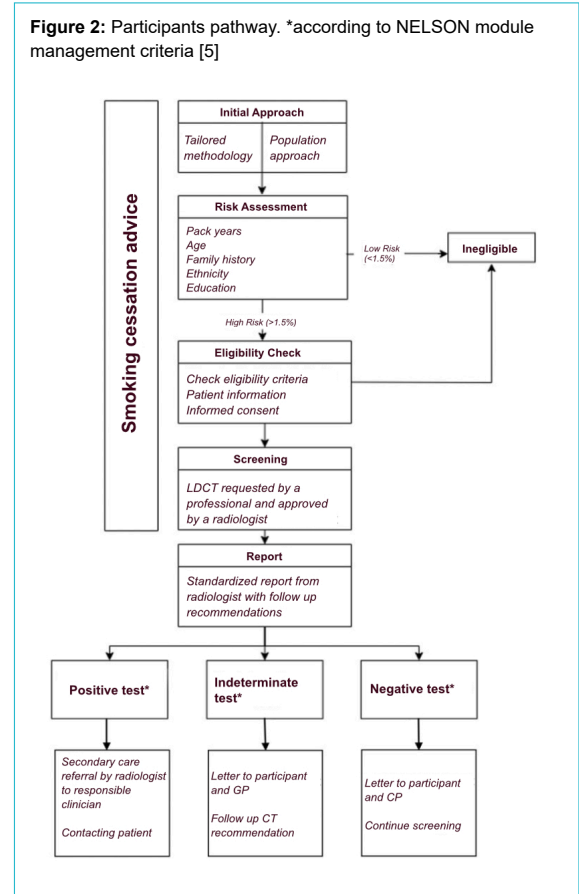


Table 2: Inclusion criteria and nodule management of different screening programs [4, 19, 55–60].

Trial	Age	Inclusion criteria		Nodule interpretation
		Tobacco	Other	
NLST (US)	55–75	>30 PY Ex <15 Y		NLST >4 mm
DANTE (IT)	60–75	>20 PY EX <10 Y		NLST ≥10 mm
DLCST (DK)	50–70	>20 PY EX <10 Y	FEV1 >30%	NELSON
ITALUNG (IT)	50–70	>20 PY EX <10 Y		NELSON
MILD (IT)	50–75	>20 PY EX <10 Y		NELSON
LUSI (GE)	50–70	>15 cig/d >25 Y OR >10 cig/d >30 Y EX <10 Y		NELSON
NELSON (NL/BE)	50–70	>15 cig/d >25 Y OR >10 cig/d >30 Y EX <10 Y		NELSON
UKLS (UK)	50–70		LLP ≥5%	NELSON
Swiss Pilot Study (CH)	55–74	>30 PY	Lung cancer risk >3% (PLCOm 2012)	Lung-RADS 1.1, NELSON+

py: packyears; FEV: forced expiratory volume

be able to make an informed decision for or against screening.

All participants eligible for screening and willing to undergo screening must give written informed consent. Participants must confirm that they have been informed about the goal of the screening as part of a scientific implementation study and the potential positive and negative consequences and limitations of screening. By providing informed consent, the patient also agrees to the use of the anonymised clinical data and radiological images for research and quality assurance.

Smoking cessation program

As part of the risk assessment and lung health check, smokers will be offered access to a smoking cessation program. Smoking cessation advice will be independent of eligibility for LDCT screening. The advice on smoking cessation should be face-to-face between the participant and a dedicated health professional. Pharmacotherapy may be offered as part of the smoking cessation program to enhance the possible effect on quitting smoking.

LDCT screening protocol and technical requirements

The screening protocol is based on the newest available scientific evidence from large studies such as MILD, NELSON and the NLST trial [4, 19, 52]. Following the ALARA (“as low as reasonably achievable”) principle, a non-contrast low-dose CT is recommended. To ensure quality and simplicity, the number of screening institutions within a certain area should be restricted.

The recommended radiology requirements advise reports to be read twice, with at least one reading by an experienced (>1,000 thoracic CTs annually) board-certified radiologist.

Additionally, a computer-assisted diagnosis (CAD) program should be used for proofreading. The readers should regularly attend their local lung cancer multidisciplinary team (MDT) meetings and must regularly attend national or international education programs on nodule management and LDCT screening as endorsed by the European Society of Thoracic Imaging (ESTI).

When performing LDCT, the standards and minimum technical requirements provided by ESTI should be followed [53]. Across the screening institutions, the CT scanners must be calibrated to minimise variations between the institutions and scanners. A volumetric CAD software must be employed for a second reading to assess images and pulmonary nodules, respectively. Volumetric software should be comparable regarding accuracy across the screening institutes and should be calibrated to ensure comparable results across the different scanners and screening institutions.

Reporting

The report itself must be standardised and must contain the parameters proposed by ESTI [53]. These parameters include a summary of the screening findings with the suggested management, extranodular findings and information about detected nodules as used in the Lung CT Screening Reporting and Data System [54]. Furthermore, the record

must include participant background characteristics and date of LDCT.

The nodules should be categorised, reported and managed according to the nodule management protocol used in the NELSON trial [55] or the 2019 Lung-RADS version 1.1 [54]. Recently, the protocol of NELSON has been adapted by Oudkerk et al. to NELSON+ [16].

Screening interval

Based on current data and evidence, we propose biennial screening based on evidence from the MILD study, which proposes that in the case of no or benign findings, screening can be repeated every other year [56]. In the future, scores based on individual risk assessments will further stratify the screening follow-ups [16]. The screening program management will coordinate follow-up invitations.

Communication of results and patient coordination

Health professionals involved in the screening program will directly communicate screening results. The communication approach will be based on the results of screening:

- *Negative results* will be communicated by letter directly to the patient and GP. In the case of queries, the patient can contact a support line for the screening program. The support line will be operated by experienced health professionals.
- Individuals with *indeterminate or positive findings* will be invited by the health professional to discuss the results and further actions, e.g. additional investigations. Such invitations will be communicated by telephone.

Furthermore, positive (malignant) findings are discussed at a multidisciplinary board including chest radiologists, pulmonologists, oncologists, radio-oncologists, and thoracic surgeons.

Incidental findings will be managed by GPs who will refer the patient to an appropriate medical specialist, if necessary. Table 3 shows the role of the different institutions, who may be involved.

Data management/registry

A predefined set of variables will be gathered for every patient. The data will be used for quality assurance, administrative management of the program, and research.

The reports on readings will be automatically stored within the data management system of the screening program. The registry will include information on the provider, the health professionals, and the patient, including:

- Identifier of the screening institute
- Identifier of the (reading) radiologist
- Patient identifier (social security number)
- Information on the CT scanner (manufacturer and model)
- Information on the radiation dose
- System used for nodule identification and the reporting system
- Address of the patient

In signing an informed consent form, participants will also agree to the data collection and the intentions for the use of the data. The collected data will be handled anonymously, and privacy will be ensured at all points in time.

Quality board

An independent quality board consisting of international experts such as radiologists, pneumologists and epidemiologists will ensure the quality of the LCS. This independent board will oversee all steps of the screening pathway, especially CT screening and reading.

Financing

The mandatory health insurance currently does not reimburse LDCT-LCS. For reasons of equity and accessibility, out-of-pocket payments of participants should be discouraged. Potential financing sources may include the Federal Office of Public Health (FOPH), regions (cantons), health associations, Health Promotion Switzerland and the Tobacco Prevention Fund. In addition, raising taxes on tobacco products to support a screening fund should be explored to cover costs for a future screening program.

Tomonaga et al. suggested that LCS may be cost-effective in Switzerland, which is a high-income European country with high smoking prevalence [26]. They estimated the cost-effectiveness of LDCT screening for lung cancer to be below the threshold of €50,000 per life-year gained [26].

To ensure the sustainability of LDCT-LCS in the long term, it would be important for the screening to be covered by mandatory health insurance (KVG). According to Art. 12d KLV measures for the early detection of diseases in certain risk groups, mandatory health insurance covers certain preventive measures for the detection of illnesses in specific risk populations. However, only the measures currently listed are covered by mandatory health insurance. Any new screening measure needs to be assessed regarding its efficacy, appropriateness, and cost-effectiveness prior to coverage by mandatory health insurance. This assessment is performed by the Eidgenössische Kommission für allgemeine Leistungen und Grundsatzfragen (ELGK), after the relevant stakeholders have submitted an application to FOPH. Mandatory health insurance does not cover regional pilots of services. Screening mammography in the general population is listed in Art. 12e KLV and is thus covered by health insurance provided it is performed within a cantonal program. In any case, the medical indication for CT screening would need to be provided by a medical doctor to be covered by mandatory health insurance.

Summary points

- Decentralised screening has been shown to have a high adherence rate in the Manchester trial (>50 %) and is feasible due to a high density of CT scanners in Switzerland. Nevertheless, quality assurance must be applied to ensure a uniform quality standard.
- GPs, pulmonologists, employers, and the media play a central role in the recruitment process. To minimise stigmatisation and to make screening accessible, the program should be declared as a “lung health check”. During the recruitment process, eligibility criteria could be validated, and the patients should be referred to smoking cessation programs. Established inclusion criteria should be extended by the additional use of the PLCom2012 risk model, including factors like ethnicity, education, family history, and education.
- If the patient matches the inclusion criteria, a LDCT should be performed. To increase cost effectiveness, biennial screening is the preferred approach if there is no significant finding.
- Though there are no fundamental differences in the NELSON+ and LungRADS 1.1 classification system, further studies should aim to prove a superiority of one classification system to unify reporting.

Barriers

It should be noted that the financial resources used for screening implementation could also be invested in smoking prevention. Furthermore, due to increasing cost pressure, it might currently be difficult to establish new screening programs financed by health insurance providers. Apart from financial aspects, the human resources required for screening program activities must also be considered. Furthermore, the widespread perception that smoking is self-inflicted could represent an obstacle for the introduction of LDCT-LCS.

Conclusion

Based on the information gained from this project and from a pilot study, the CH-LSIG recommends the timely introduction of a systematic LCS program in Switzerland. The final decision will be made by the Swiss Cancer Screening Committee.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

Table 3:
Prospective institutions and their role.

Steps in the pathway	Involved institutions	Involved professionals
Information	Lung, cancer and patient associations, health insurer, cantonal health directorate, Federal Office of Public Health	Nurses, pulmonologists, GPs, administrative personnel
Invitation	Screening program, medical doctors, pharmacists, Lung League	Administrative personnel, nurses
Pre-screening	Mobile truck, hospital/screening centre	Nurses, lung function technicians, GPs, pulmonologists
Smoking cessation	GPs, Lung Association	GPs, nurses
Screening	Mobile truck, accredited hospital/ screening centre	Nurses, radiology technicians, radiologists
LDCT reading	Accredited hospital/screening centre	Radiologists Interdisciplinary Board: radiologist, pulmonologist, radio-oncologist, thoracic surgeon and oncologist
Patient information/coordination	Screening program, GPs	Administrative personnel, nurse, GPs

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