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National Lung Cancer Screening Programs Worldwide; An Emerging Call for Early Diagnosis

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Abstract

Short abstract: National Lung Cancer Screening programs have evolved in their implementation worldwide. This manuscript is delivered by a multidisciplinary panel in lung cancer screening. It aims to identify and present existing evidence regarding similarities and differences as well as teachable moments that have arisen through national implementation of lung cancer screening programs.

Structured abstract

Background: Lung cancer screening (LCS) programs have emerged over the last years around the world. There are marked differences in program delivery, inclusion criteria and resources allocation.

Objective: This review aims to provide a comprehensive overview of current national LCS programs worldwide, identify similarities and differences as well as any teachable moments that may have arisen through national implementation.

Methods: A multidisciplinary Task Force experts' panel conducted a systematic literature search leading into this narrative review. We searched PubMed and Cochrane databases (January 2011-December 2023), international radiology societies, centers for disease control and national health ministry websites worldwide using a combination of appropriate MeSH keywords and headings.

Results: There is significant variation among current national LCS programs stemming from variable national epidemiological data, funding resources and existing healthcare systems. There is variability in the inclusion criteria, LCS intervals, imaging management protocols. The optimal imaging and case management protocol is yet to be defined and currently countries adhere to already established national practices. Quality assurance allegedly underpins all programs however there is no detailed information about the quality criteria, the quality assurance processes and external review mechanisms.

Conclusions: National LCS programs have been mostly influenced by the results of large LCS trials. Future data is anticipated from ongoing national LCS programs to inform program delivery, case management and optimal allocation of resources.

Keywords: lung cancer screening; national screening program; inclusion criteria; quality assurance; implementation

Abbreviations: ACR American College of Radiology; CCDC Chinese Centre for Disease Control; CDC Centre of Disease Control; ECDC European Centre for Disease Control; ESR European Society of Radiology; ESTI European Society of Thoracic Imaging; HTS Hellenic Thoracic Society; HSR Hellenic Society of Radiology; HSTCVS Hellenic Society of Thoracic, Cardiac and Vascular Surgeons; LC lung cancer; LCS lung cancer screening.

Background

Lung cancer attracts increasing attention as the most common cause of cancer worldwide and the leading cause of cancer death among both men and women [1]. Interestingly, the majority of diagnosed lung cancers (79%) is preventable [2]. Although lung cancer screening (LCS) is not an alternative option to smoking cessation which is essential, it can prevent a substantial number of lung cancer–related deaths [3-8].

Therefore, LCS raised big hope and several countries have proceeded with this public health intervention in combination with participants' access to smoking cessation programs where required [9-13].

There is a noticeable variation in national LCS programs among various countries with regard to inclusion criteria, funding, quality assessment etc. Strategies for maximizing its benefits and minimizing harms are continuously informed during LCS implementation as a public health intervention.

This focused narrative review aims to provide an overview of current national LCS programmes worldwide, identify similarities and differences as well as teachable moments that have arisen through national implementation. We present this article in accordance with the narrative review reporting checklist.

Methods

PubMed and Cochrane databases were searched using a combination of appropriate MeSH keywords and headings and search results were limited to 1st January 2011- 31st June 2023 including publications in English, French and German. Additional searches were performed in ACR (American College of Radiology), ESTI (European Society of Thoracic Imaging), ESR (European Society of Radiology), Centre of Disease Control (CDC), European Centre for Disease Control (ECDC), Chinese Centre for Disease Control (CCDC), national health ministry websites worldwide and in the dedicated national LCS programs websites where applicable.

An additional search was conducted for the period 1st July 2023-31st December with the same methods as stated above.

A multidisciplinary group of lung cancer experts (respiratory physicians, chest radiologist, thoracic surgeon) representing the Hellenic Thoracic Society (HTS) Lung Cancer Group, the Hellenic Society of Radiology (HSR) and the Hellenic Society of Thoracic, Cardiac and Vascular Surgeons (HSTCVS) worked closely with a dedicated Health Sciences' Librarian to identify relevant literature and independently screen their allocated abstracts and full papers based on the search criteria. Disagreements were virtually discussed among all team members where a consensus was reached. Table 1 summarizes the search strategy summary.

Table 1: The search strategy summary

Items	Specification
Date of search (specified to date, month and year)	01.01.2011-31.12.2023
Databases and other sources searched	PubMed and Cochrane databasesAdditional searches were performed in ACR (American College of Radiology), ESTI (European Society of Thoracic Imaging), ESR (European Society of Radiology), Centre of Disease Control (CDC), European Centre for Disease Control (ECDC), Chinese Centre for Disease Control (CCDC), national health ministry websites worldwide and in the dedicated national LCS programs websites where applicable
Search terms used (including MeSH and free text search terms and filters)Note: please use an independent supplement table to present detailed search strategy of one database as an example	(((LUNG CANCER SCREENING PROGRAMMES[Title]) OR (LUNG CANCER SCREENING PROGRAMME[Title])) OR (LUNG CANCER SCREENING PROGRAM[Title])) OR (LUNG CANCER SCREENING PROGRAMS[Title]) Filters: English, French, GermanSearch: ((((LUNG CANCER SCREENING PROGRAMMES[Title]) OR (LUNG CANCER SCREENING PROGRAMME[Title])) OR (LUNG CANCER SCREENING PROGRAM[Title])) OR (LUNG CANCER SCREENING PROGRAMS[Title])) OR (EARLY DETECTION[Title]) Filters: Randomized Controlled Trial, English, French, German
Timeframe	Jan 2011-December 2023
Inclusion and exclusion criteria (study type, language restrictions etc.)	Inclusion criteria: English, German French language manuscripts, Exclusion criteria: case reports, abstracts, letters to the editor, congress reports, reviews, meta-analysis, studies<40 patients, case series<40 patients, any other language than the ones stated above
Selection process (who conducted the selection, whether it was conducted independently, how consensus was obtained, etc.)	Abstract screening: 1st screening conducted by all authors. 2nd screening conducted by GH and IG as safety netting.Data extraction: All authorsData extraction review, analysis and synthesis: GH, IG, DB, MSConsensus was reached on virtual meetings
Any additional considerations, if applicable	N/A

Results

The Current LCS Situation in Europe

Europe has 3 National LCS programs: In January 2022 the Czech Republic initiated a five-year national LCS program, which is led and funded by the Czech Ministry of Health (2022-2026) [14-17]. Preliminary results meant to be published in April 2023 and are still awaited. The LCS recruitment is conducted by general practitioners (GP). The LCS program includes access to smoking cessation services and the inclusion criteria are age between 55-74 years old and current or past smoking history of 20 pack years. There is no reference to the minimum/maximum timeframe from smoking cessation to LCS enrollment. The time interval between the

LDCTs is annual or biennial based on imaging results stratification as negative/indeterminate/positive [14-17].

Croatia started a national LCS program in October 2020, the *National Program for Early Detection of Lung Cancer (CNLSCP)* [18-26]. The screening program is linked with access to smoking cessation services and it is funded by the Croatian Health Insurance Fund. Its first term will conclude in 2024 and the final results will be anticipated. The program was initiated on the basis of international studies without any preceding national pilot study. Recruitment is conducted by GPs following a mass media campaign and a Quality Control Committee has been appointed. The inclusion criteria for the Croatian LCS program are age between 50-75 years old, 30 pack years smoking history and ≤15 years since smoking cessation. The LCS intervals are variable (annual, biennial) depending on the individualized lung cancer risk [27].

In Poland a national LCS program commenced in 2020, the *National Program of Early Lung Cancer Detection (WWRP)* [28-33]. The WWRP is a three-year LCS program (2020-2023) which is centrally administered and covers all 16 provinces of Poland. The recruitment is based on Family Physicians and it is supported by participant information leaflets. The program seeks to enroll 16,000 participants aged 50–74 from across 21 different sites in cooperation with 40 family physicians per region. A platform for LCS has been designed and created with the support of the International Early Lung Cancer Action Project (I-ELCAP). A cloud-based data management system has been provided to all participating sites. Eligibility criteria include age between 50-74 years old, a 20-pack year smoking history and ≤15 years since smoking cessation [34].

The Current LCS Situation in North and South America

The US National LCS program (US-NLCSP) started in 2015 (35-39) with more than 4,000 centers offering LDCT screening to date. LCS guidelines in the US were recently updated twice; in 2021 by the US Preventive Services Task Force 2021 (USPSTF) [40] and in 2023 by the American Cancer Society [ACS] [41].

The USPSTF 2021 guidelines recommend screening for people aged 50-80 years, current or ex-smokers (equivalent to 20 pack--years), and ≤ 15 years since quit smoking [40]. The ACS guidelines issued in 2023, maintained the same age criteria and quantification of smoking habit but were the first to include all ex-smokers regardless of the time passed since their smoking cessation [41].

There is considerable variation in LCS implementation in practice. LCS program structure, eligibility criteria and reimbursement differ among various US states. The LCS is accompanied by a smoking cessation program. The imaging protocol is based on Lung RADS method with annual intervals but the recruitment is still low between 6-15% despite the resources dedicated to it [42].

Canada runs a regional LCS Program, called OLSP (Ontario Lung Screening Program) since March 2021. The eligibility criteria include individuals aged between 55-74 years old who are current and former smokers over 20 pack years with a ≥2% risk of developing lung cancer in the next 6 years. The program is based on recruitment by primary physicians, patient navigators and nurse practitioners. The imaging protocol used is the same as in the US (Lung RADS). The LCS program in Canada includes smoking cessation services linked to it and there is also a quality control service [43]. In South America there are no national LCS programs. Four implementation studies run in Brazil [44-52]

The Current LCS Situation in Asia

There is no national LCS program in Russia however six implementation studies are reported [53-61]. South Korea runs a national LCS program, *the Korean National Lung Cancer Screening Programme (KNLCS)* which started in 2019 and it is ongoing [62-67]. This program is based on the results of a pilot trial named K-LUKAS (Korean Lung Cancer Screening) [68]. A total of 82,061 people participated in the KNLCS in 2019, followed by 80,499 in 2020 (24.7% and 22.4% of the population invited each year). In 2020, the baseline positive (unconfirmed) results for lung cancer were 8.73%. To support program delivery, radiologists require accreditation, including training on use of the Lung-RADS nodule management protocol and evaluation system that has been adapted for

a Korean population. Eligible participants are invited with invitation letters. Enrolled participants who are current smokers are offered free access to smoking cessation programs and pharmacotherapy. From 2019 to 2020 approximately 23% of the 690,000 eligible participants underwent screening with LDCT. The National Health Insurance Service (NHIS) in Korea supports 90% of the cost and the examinee pays the rest 10% [68].

Taiwan runs a national LCS program, which is the first program worldwide including non-smokers with a family history of lung cancer. *The National Lung Cancer Screening program (NLCSP-TW)* started in 2022 and it will last until 2030 [69-71]. The authorities followed a step-wise approach by initially setting the scientific network for the national LCS program. The Health Promotion Administration (HPA) of the Ministry of Health and Welfare has held strategic meetings on the topic with several organizations: Taiwan Lung Cancer Society, Taiwan Society of Pulmonary and Critical Care Medicine, Taiwan Radiological Society, Taiwan Society of Thoracic Surgeons, and relevant professional groups. The groups reviewed available scientific evidence and applied a cost-effectiveness analysis as the foundation for discussions regarding resources required, eligibility and potential benefits of LCS [72].

Between July and December 2022, a total of 23,487 individuals received LCS and 319 cases of lung cancer were detected. The vast majority of individuals (87%) were diagnosed at an early stage (defined by the authorities as stage I-III). Taiwanese authorities anticipate that the eligibility criteria for the national LCS program will be further refined as necessary. These refinements will be based on the evidence being generated by the implementation of the national LCS program per se and also expansion to subgroups with other non-smoking risk factors, such as air pollution, oil fumes, occupational exposure and a history of lung disease [72].

China runs the oldest national LCS program in Asia since 2010. There is a great heterogeneity in funding resources depending on the geographic region. The National Health Committee of China leads on a Cancer Screening Program (CanSPUC) for its urban territories. The program targets 6 different types of cancer that are most prevalent in urban areas, including lung cancer. Eligible participants are over 50 years old, current smokers or ex- smokers who have quitted smoking for ≤15 years, those with a history of chronic lung disease or a family history of lung cancer. The current recommendation includes annual LDCT for LCS unless specific findings warrant different follow up or further investigations [73]. LDCT in China is relatively cheap and convenient. It costs less than 300 CNY (equivalent to less than 50 USD) and can be performed within a week after an appointment [74]. The Chinese authorities have established their own management protocols considering the specific imaging characteristics lung cancer has in the Chinese population. Therefore, a percutaneous needle aspiration biopsy is strongly recommended for all solid or sub-solid lung nodules more than 5 mm [74].

The Current LCS Situation in Australia

In Australia and New Zealand, even though lung cancer is also considered as the main cause of cancer mortality (Australian Institute of Health and Welfare. Cancer in Australia 2019. Canberra: AIHW; 2019. 174 p. Contract No.: CAN 123) there is a remarkable absence of LCS initiatives. However, the recent trend leans towards the support of such screening techniques. The previous policy recommendations initially advised against the implementation of LCS with LDCT [75] However, the results of the largest relevant US and European recent trials have updated the evidence base of screening, showing its numerous benefits nudging towards the change of policy discussion regarding implementation [3, 4, 76].

The Cancer Australia institution has committed to re-evaluate a pilot LCS, focusing on factors such as cost-effectiveness, customized target population, recruitment, and other areas of implementation concern that were raised during past trials.

Despite the initial approach, Cancer Australia committed to support a national LCS program. The Australian Ministry for Health and Aged Care announced a National LCS Program which will lead to the early detection of lung cancer in Australians and it will commence screening by July 2025. In the next 2 years, the Australian authorities will work towards determining workforce requirements including training and education and impact modelling, assessing screening infrastructure capacity and capability, determining program tools and resources as well as developing quality assurance frameworks [77].

Discussion

National LCS programs are advertised on national stakeholders' websites with limited information on implementation processes and scientific evidence leading to the programs' roll out. Despite limited data, it transpires there is ongoing mobility in LCS programs' implementation with variations in practice. All national programs integrate LDCT and smoking cessation services although there is no clarity regarding the referral process and the service interconnectivity.

To the best of our knowledge, this is the first review summarizing all existing national LCS programs therefore providing a collection of useful information to inform decision making in the design of future LCS programs globally (Table 2).

Table 2: List of national LCS programs per continent and their characteristics.

COUNTRY	ESTIMATED DURATION	FUNDING SOURCE	INCLUSION CRITERIA	SCREENING INTERVAL	PARTICIPATION RATES	RECRUITMENT	SMOKING CESSATION	IMAGING MANAGEMENT PROTOCOL	OBSTACLES	QualityAssurance
NORTH AMERICA										
ONTARIO/CANADAREGIONAL PROGRAM	2021-N/A	Health Sciences North Foundation	55-74 YO20P/Ys>2% risk of lung cancer next 6 years	Annual		General Practicioners patient navigators nurse practitioners	YES	N/A		YES
USA	2015-ongoing	Medicare/Medicaid	50-80 YO 20P/Ys ≤15Y Since Quitting to smoke	Annual	5.8%	written invitation	YES	Lung RADS	ADD LIST	YES
SOUTH AMERICA NO NATIONAL PROGRAM										
EUROPE										
CROATIA	2020-2024	CroatianHealth InsuranceFund	50-75YO30P/Ys≤15Y Since Quitting to smoke	Annual, BiennialFor people with 'normal' baseline scans, repeat scans are offered after a year, and then every two years until the age of 75.	8.875/12.000	Family Doctors	YES	Lung RADS		YES
CZECH REPUBLIC	2022-2026	Czech Ministry of Health	55-74YO20P/YsYSQ:N/A	AnnualBiennal		General Practitioner	YES	NegativeIndeterminatePositive		YES
POLAND	01.2020 -2023(ceased 1y due to COVID-19) -01.2024	EU- POWER grant through the Ministry of Health	50-74 yo ≥ 20PYor≤15YSQ	Annual	14.000/16.000	Family physicians,Leaflets	YES AT SOME SITES		N/A	YES
ASIA										
CHINA	2010-ongoing	National Insurance/local funds/research funding/NGO*/insurance bodies/self funded	50-75 YO with at least one of the following:- Current smoker (≥20PY)-Ex smoker (≥20PY), 15YSQ-Passive smoker-Professional exposure (asbestos, virillium, uranium, radonium)-Past medical history of cancer- Family history of lung cancer - Past medical history of COPD or IPF	Annual Biennial	33%	Unclear	YES in planning unclear in implementation	No	Not stated	Not stated
TAIWAN	2022-2030	Ministry of health and Welfare	45-74 (f)50-74 (m)with a family history of lung canceror 50-74 30PYs or ≤15Y SQ	Biennial	n/a	Not stated	YES	NoLung RADS		Not stated
SOUTH KOREA	2019-ongoing	National Health Insurance Service 90%Participant 10%	55-74 ≥30PYs≤15YSQ	Annual	n/a			Lung RADS		
AUSTRALIA NO NATIONAL PROGRAMME										
AFRICA NO NATIONAL PROGRAMME										
ANTARCTICA NO NATIONAL PROGRAMME										

There are significant differences in the duration of the current eight national LCS programs. The US LCS program is delivered on a continuous basis while in Europe equivalent LCS programs have limited duration (i.e. Croatia and Poland 2020-2024, Czech Republic 2022-2026). European authorities favor piloting national LCS programs over indefinite implementation with the view to reassess the initial impact following the first 4 years of implementation [15-17, 51-53, 56, 57, 62-65]. This approach may be affected by the variation in funding sources and their limited duration for LCS programs in Europe. However, the NELSON trial which inspired the national delivery of European LCS programs offered the longest follow up in high-risk participants in comparison with NLST (10 years versus 3 years) [3, 4] therefore one would expect European authorities to advocate for a continuous implementation due to the availability of favorable European data. The UK has set an example of advocacy for continuous implementation for LCS through the successful implementation of the Targeted Lung Health Check (TLHC) which is essentially a LCS program rolled out in England and following its success the authorities urge for implementation on a national level across all 4 UK nations (Eng-

land, Wales, Scotland and Northern Ireland) [78, 79]. All national LCS programs worldwide are funded by the state either directly or through donations/support funds except for the US which gives the option of extended access to the national LCS program through private insurance in addition to the national insurance funds [42] and Canada which funds the program through a non--governmental organization [Health Sciences North Foundation] [43].

National LCS programs have a predilection towards inclusion criteria over risk stratification models. They share the same inclusion criteria based on smoking habit and age with variations in cut-offs which are arbitrary and they do not seem to be based on national epidemiological data. Canada's national LCS program includes a risk stratification model (PLCOm12) in addition to age and smoking habit to complement the selection process [43]. China is the only country that extensively expanded its LCS inclusion criteria to occupational risk factors, family history of lung cancer, past medical history of any cancer/COPD/IPF [73, 74].

The frequency of LDCT screening varies among national LCS programs. Four countries (Canada, US, Poland, South Korea) implemented annual LDCT screening and Taiwan is the only country that implemented biennial screening intervals [42, 43, 28-34, 62-65, 69-71]. The remaining countries (Croatia, Czech Republic, China) seem to offer both annual and biennial screening intervals however participants' selection process for each option remains vague.

Worldwide, primary care plays an integral role in LCS participants' selection. Canada seems to have an intermediary healthcare professional between primary care and LCS centers (patient navigator, nurse practitioner) who leads the participant's pathway and coordinates the logistics [43]. Information leaflets, pamphlets, mass media seem to contribute to public awareness and are used by all countries.

There is scarce data regarding participation and adherence rates in the national LCS programs. Current evidence shows almost 5.8% participation rate in the US versus 33% in China [42, 73, 74]. This great variation raises the issue of optimal approach strategies in diverse high-risk populations and the impact of cultural background in the selection process. Adherence to annual screening has been investigated at the US national LCS program where recent real-world data showed that adherence is affected by education status, race, insurance cover and smoking status. Hispanic, Black participants, current smokers with low education and uninsured participants presented with lower adherence. In detail, general adherence to annual screening was 22.3% whereas adjusted analyses showed that Asian, Black, Hispanic participants were less likely to have at least 1 LCS examination following the initial screening (adjusted OR of 0.79, 0.84, 0.73) [42]. Adherence rates for LCS derived from this real-world data are much lower than for breast cancer screening where adherence can reach up to 80.2% [80]. On first glimpse, adherence to annual LCS seems low considering the resources invested in raising public awareness with regard to the benefits of LCS for high-risk population.

Similarly, cancer detection rates (CDR) after baseline screening CT have only been published for the national US LCS program while this data is anticipated by the European LCS programs following their completion in the coming years. The overall CDR at the US LCS program was 0.56%, which was significantly less than the CDR published by LCS trials (NLST 1.1%, Nelson 0.9%, UKLS 2.1%) therefore highlighting the significant differences between trial and real-world data [3-5].

The possibility of under-reporting confirmed lung cancer cases identified outside the national LCS program cannot be overlooked however there is lack of solid evidence to support this hypothesis.

There is scarce data regarding the use of imaging management protocols with Lung RADS being the most popular in the majority of national LCS programs [81]. Focused LCS reporting with Lung RADS protocol requires dedicated training by reporting radiologists however there is unclear evidence whether this is organized by the national LCS programs or by the Radiologists' individually.

Quality assurance is referenced as an underpinning principle by all national LCS programs although there is no detailed information about the quality criteria, the quality assurance processes and external review mechanisms.

Although published information alludes to the need for healthcare professionals' training in obtaining informed consent and running national LCS programs there is no specific training program published with the exception of the European Society of Thoracic Imaging (ESTI) that runs a dedicated LCS training program for Radiologists [82].

Conclusions

National LCS programs have emerged over the last few years and they have been mostly influenced by the results of large LCS trials. There is a remarkable diversity in the program delivery, inclusion criteria, frequency of screening intervals as well as funding resources. European LCS programs have adopted a pilot approach with limited funding lasting up to 4 years limiting the program duration as opposed to the US program which is indefinite. The optimal imaging and case management protocol is yet to be defined and currently countries adhere to already established national practices. Future data is anticipated from ongoing national LCS programs to inform program delivery, case management and optimal allocation of resources.

Declarations

Ethics Approval and Consent to Participate

None

Consent for Publication

None

Availability of Data and Materials

None

Competing Interests

None

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None

Authors' Contributions

(I) Conception and design: GH, IG

(II) Administrative support: EF

(III) Provision of study materials or patients: All authors

(IV) Collection and assembly of data: All authors

(V) Data analysis and interpretation: GH, IG

(VI) Manuscript writing: All authors

(VII) Final approval of manuscript: All authors

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