DOI: 10.4149/BLL_2023_016

Bratisl Med J 2023; 124 (2)
109 – 115

EPIDEMIOLOGICAL STUDY

Lung Cancer Screening Initiative in Slovakia: Guidelines of screening implementation

Dominik JUSKANIC[1,2], Frantisek SANDOR[3,4], Lucia DENKOVA[5], Peter JUHOS[6], Miroslav JANIK, Jonathan HONTZAS[7], Jana POLAKOVA MISTINOVA[2], Michal SENITKO[7], Martina ONDRUSOVA[8,9]

Department of Preventive and Clinical Medicine, Faculty of Public Health, Slovak Medical University, Bratislava, Slovakia.
martina.ondrusova@hotmail.com

ABSTRACT
Lung cancer (LC) represents a major healthcare issue worldwide. It is the leading cause of cancer-related mortality in Slovakia and European Union. Data from multiple randomized controlled trials have shown significant evidence of a mortality benefit in LC using screening with low-dose computed tomography of the chest (LDCT). Therefore, European healthcare authorities, relevant expert societies, and professional organizations recommend implementing national LC screening (LCS) programs in their member countries. This article outlines the basic methodology, guidelines, and practical aspects of LCS implementation strategies in Slovakia. We describe fundamental principles to identify asymptomatic high-risk patients reduce false positive and false negative results, decrease benign resection rates, and avoid unnecessary invasive procedures. The efficacious utilization of public resources to secure the highest possible quality standards of LDCT plays a crucial role in successfully implementing a nationwide LCS program *(Tab. 1, Fig. 4, Ref. 31)*.
Text in PDF *www.elis.sk*
KEY WORDS**:** lung cancer, screening, early detection, smoking cessation.

Introduction

Lung cancer (LC) often presents as a locally advanced/disseminated disease, thereby limiting the curative intent therapy. Stages IIIB-IV have a 5-year survival rate of < 25 % (1). Although immunotherapies have shown promising results (2), early diagnosis is the first step to improve cancer fatality rate.

The National Lung Screening Trial (NSLT) results provided evidence of a 20 % relative reduction in LC-specific mortality and 7 % reduction in all-cause mortality (3), favoring low-dose CT screening (LDCT) compared to chest x-rays. A total of 53,452 current/former smokers aged 55-74, with at least a 30 pack-year cigarette smoking history were included. For every 1,000 persons screened, approximately three LC deaths were prevented (3, 4).

Nederlands-Leuvens Longkanker Screenings Onderzoek Study (NELSON) trial showed 26 % and 61 % reductions in mortality in men and women, respectively (5). This study included 13,195 men and 2,594 women aged 50–74. The risk group was defined as smokers with 15 cigarettes/day for 20 years or ten cigarettes/day for 30 years and have been smoking within the past ten years. Patients were randomized to undergo four CT screening scans or no screening scans.

The results of the International Early LC Action Program (IELCAP) and National Lung Screening Trial (NLST) showed, that successive annual rounds of screening resulted in the detection of a higher proportion of stage I LC than those found in the baseline rounds (6). Therefore, the success of programs relies on the longevity of the screening process and simple clinical pathway to evaluate positive findings.

In 2017, the European position statement recommended implementing LC screening (LCS) programs in European countries (7). The European Society of Radiology and the European Respiratory Society have mutually reiterated (2015, 2017, 2020) recommendations for centrally steered LCS programs by national expert societies (8). The European Commission Expert Group and Europe's Beating Cancer Plan committed to implementing such programs in EU countries (9). The leader in implementing LCS is the USA. In Europe, each national randomized controlled trial has stood the test of time and has been gradually translated into clinical practice. The Czech Republic has laid out a 4-year pilot

[1]JESSENIUS – diagnostic center, Nitra, Slovakia, [2]Department of Radiology, Comenius University, Faculty of Medicine & Slovak Medical University, University Hospital, Bratislava, Slovakia, [3]Department of Pneumology and Phthisiology, Comenius University, Faculty of Medicine, University Hospital, Bratislava, Slovakia, [4]Penobscot Respiratory Associates, Northern Lights Eastern Maine Medical Center, Bangor (ME), United States of America, [5]Pneumo-oncology Unit, Department of Pneumology and Phthisiology, University Hospital, Bratislava, Slovakia, [6]Department of Thoracic Surgery, Slovak Medical University, University Hospital, Bratislava, Slovakia, [7]Departments of Medicine and Surgery, University of Mississippi Medical Center, Jackson (MS), United States of America, [8]Department of Epidemiology and Statistics, Pharm-In, Bratislava, Slovakia, and [9]Department of Preventive and Clinical Medicine, Faculty of Public Health, Slovak Medical University, Bratislava, Slovakia

Address for correspondence: Martina ONDRUSOVA, Assoc Prof, RNDr, PhDr, PhD, MPH, Department of Preventive and Clinical Medicine, Faculty of Public Health, Slovak Medical University, Limbova 12, Sk-833 03 Bratislava, Slovakia.
Phone: +421.905925298

project in 2022. Hungary has had a pilot study since 2014, which was then translated into a national program (2019). Poland has executed several regional EU-funded programs that translate into a centrally organized national program.

There is no national program for systematic detection of early stages of LC in the asymptomatic population in Slovakia. A collaborative Slovak-Polish regional early LC detection project was performed a couple of years ago. A multidisciplinary consensus was settled in the document "Memorandum on Screening Lung Carcinoma in Slovakia" (10).

Epidemiology of LC and smoking habits in Slovakia

LC represents major healthcare issues worldwide (11). The last statistically processed year regarding the incidence of LC in Slovakia was 2012. With a proportion of 12.03 % of all malignancies, LC represented the second most frequently diagnosed malignancy in men and with a proportion of 4.2 %, the fifth in women. In absolute numbers, there were a total of N = 2,652 cases (1.969 men and 683 women) of newly diagnosed LC in Slovakia. This represents a crude rate (CR) of 74.76/100,000 for men and 24.62/100,000 for women, and a standardized incidence (to the World Standard Population – ASR-W) of 50.41/100,000 for men and 12.89/100,000 for women. The prediction of newly diagnosed LC represents for both sexes together for the year 2022 N = 3,154 cases, of which N = 2,191 cases are in men (CR of 81.00/100,000, ASR-W of 42.88/100,000) and N = 963 in women (CR of 34.20/100,000, ASR-W of 14.68/100,000) (12).

In 2012, Slovakia ranked 20th in men and 22nd in women in the list of countries with the highest incidence among European countries (12). 2012 was the last statistically processed year regarding the mortality of LC in Slovakia. In men, the value of 19.37 % represented the highest mortality among all malignancies while women with mortality of 10.05 % came second (13). In absolute numbers, there were 2,035 deaths in Slovakia (1,451 men and 584 women), which represents crude death rates (CDR) of 54.48/100,000 and 20.92/100,000 in men and women, respectively and ASR-W death rates of 30.50/100,000 and 9.28/100,000 in men and women, respectively (12). The estimated number of deaths from LC in 2022 represents 1,405 cases (CDR of 52.38/100,000 and ASR-W mortality of 27.43/100,000) in men, and 641deaths among women (CDR of 22.92/100,000 and ASR-W mortality of 9.84/100,000) in women (12).

Time trends of ASR-W incidence of LC in men in Slovakia were relatively heterogeneous: During 1968-1971, the incidence increased, in year 1986 the peak was recorded, from this moment only a slight, but statistically significant, decrease in annual percentage change (APC) by –1.93 % is registered ($p < 0.05$), which continues until the end of observed period (year 2012) (Fig. 1) (12).

In women, the ASR-W incidence in the period of 1968–1980 showed a nonsignificant decrease with APC of –0.77 % ($p > 0.05$). Then in the period of 1981–1984the incidence increased nonsignificantly with APC of 6.15 % while in the period of 1984–2001 the incidence increased with APC of 0.24 %)However, since 2001, a very sharp continuous increase in the trend with APC of 5.06 % ($p < 0.05$) was recorded, which persisted throughout the rest of the statistically processed period ending in 2012 (Fig. 2) (12).

Within the 1968–1981 period, there was a statistically significant increase in ASR-W mortality in men with APC of 4.10 %

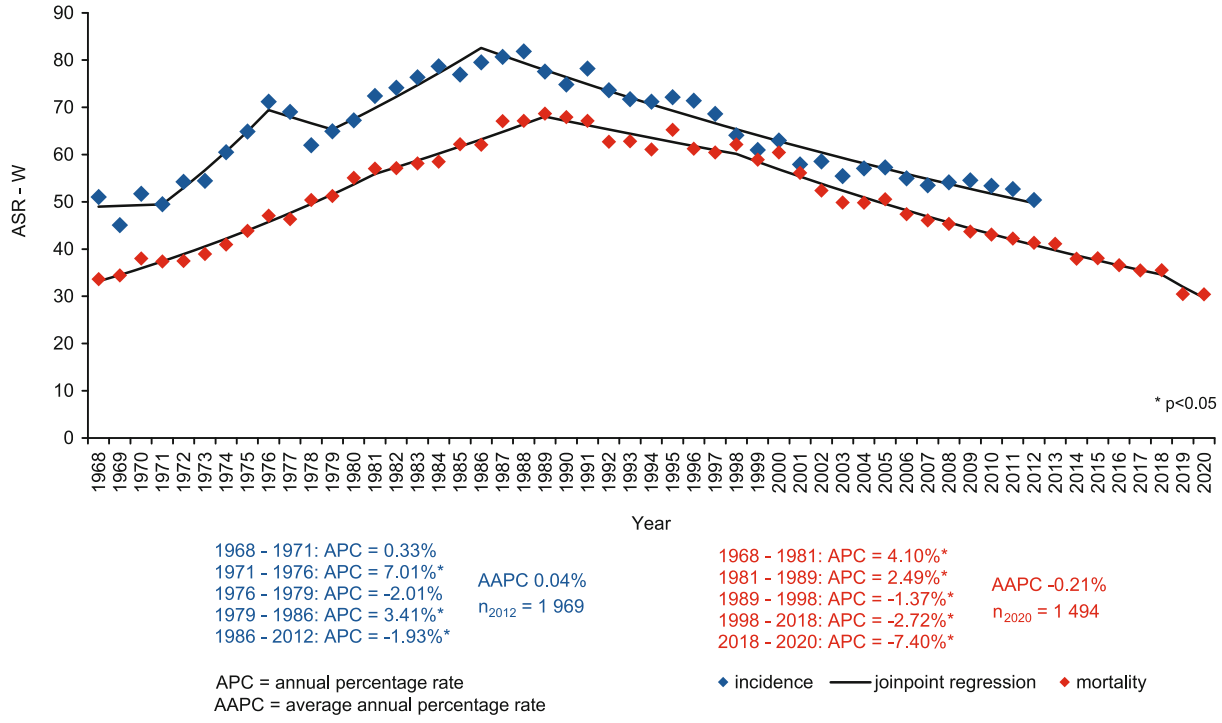

Fig. 1. Trends in World Age-Standardised (ASR-W) Incidence (1968–2011) and Mortality (1968–2019) Rates among Males in the Slovak Republic.

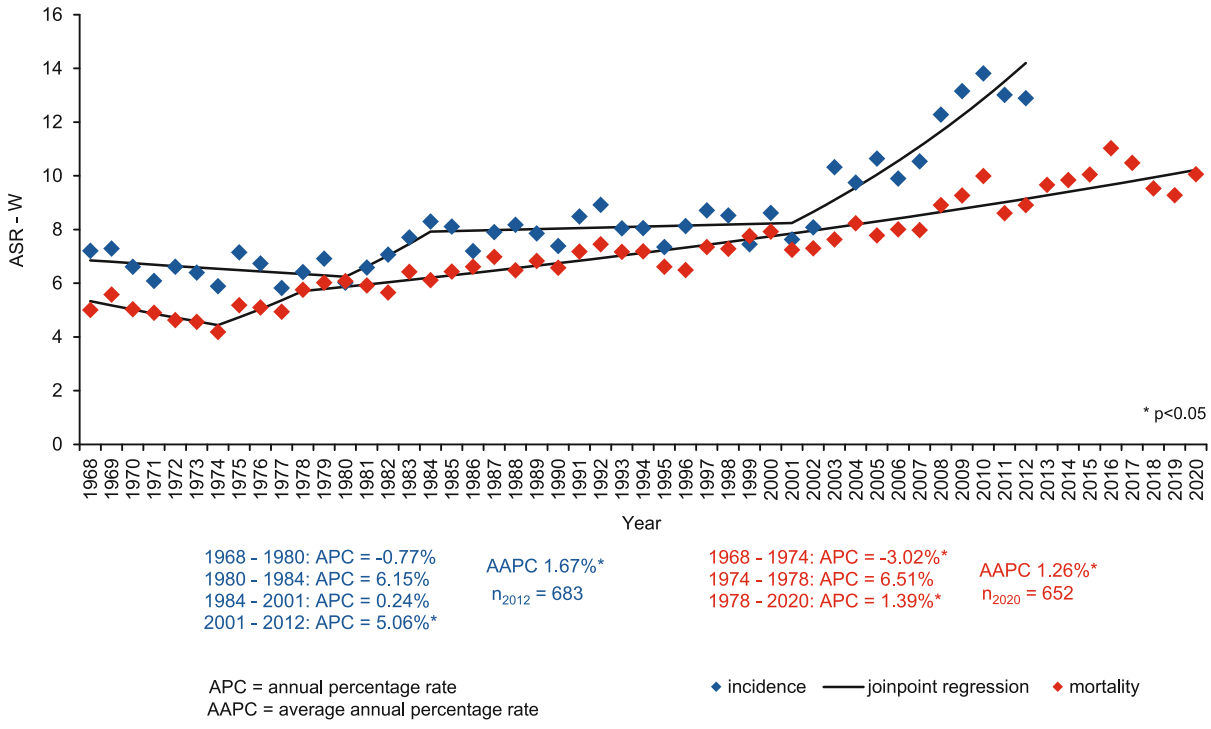

Fig. 2. Trends in World Age-Standardised (ASR-W) incidence (1968–2011) and mortality (1968–2019) rates among females in the Slovak Republic.

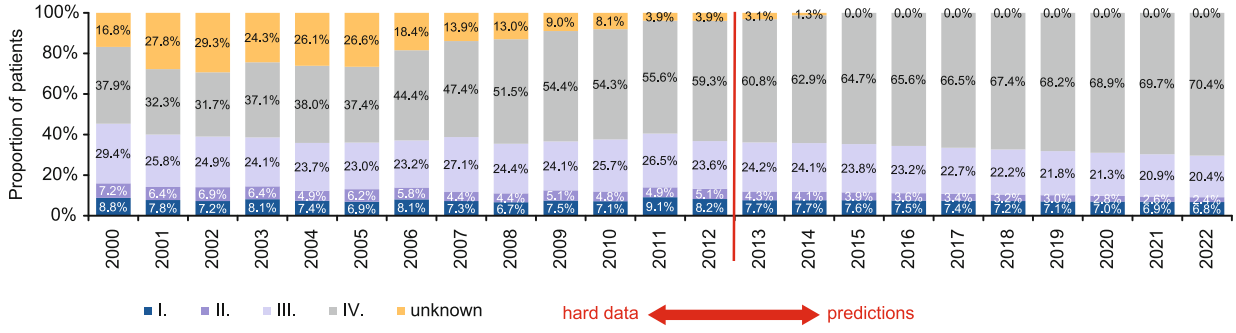

Fig. 3. Trends in lung cancer clinical stages among males in the Slovak Republic.

per year ($p < 0.05$) which subsequently decreased to the value of 2.47 % ($p < 0.05$). In 1989 it further decreased with APC of –1.30 % ($p < 0.05$) per year. The decline in the curve in the 1998–2019 period became steeper, with APC of –2.80 % ($p < 0.05$) (Fig. 1) (12). Up to 2016, the mortality in women was increasing significantly with APC of 1.09 % ($p < 0.05$). During the period of 2016–2019, a clinically positive but statistically nonsignificant decrease was observed with APC of –4.22 % ($p > 0.05$) (Fig. 2) (12).

The latest published data showed the exact prevalence of LC in Slovakia in 2012 to be n = 4,862 (both sexes together) (12). In order to predict the exact prevalence for 2021, a Weibull distribution-based statistical model was used to approximate the survival of LC patients. The number of surviving LC patients in Slovakia in 2021 is assumed to be in the range of 5,305–6,056 (for both sexes together) (12).

The predicted proportions of newly diagnosed LC in men with clinical stages I, II, III and IV for the year 2021 are 6.9 %, 2.6 %, 20.9 % and 69.7 %, respectively (Fig. 3). In Slovak women, the prediction of the proportions of newly diagnosed LC in clinical stages I, II, III and IV for the year 2021 are 12.4 %, 4.1 %, 21.5 %, and 62.0 %, respectively (Fig. 4) (12).

Time-dependent variations of incidence and mortality caused by LC are affected by the change in smoking habits. Trends in men generally are of declining or stabilized nature. This is in contrast to the almost constant increase in the number of women smoking (14). In Slovakia, the prevalence of smokers reached 54 % in the 1970s. After a temporary decline in the 1980s, there was a slight increase in smokers in the 1990s. Since this period, the prevalence of smoking has decreased in the age group of 25–64 years. However, with an age-related division into specific

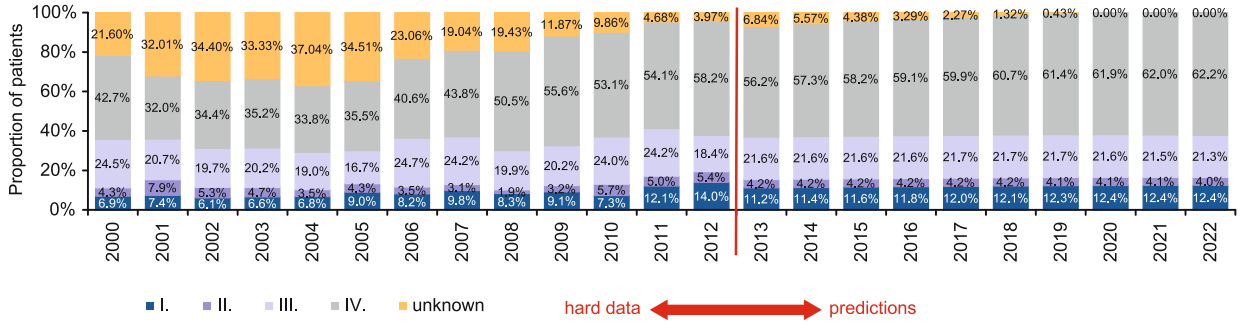

Fig. 4. Trends in lung cancer clinical stages among females in the Slovak Republic.

decades, an increase in prevalence can be observed in the oldest of observed age groups (55–64 years). In a study from 2005, the proportion of smokers in the cohort of 16,748 persons representing the population of Slovakia was 20.1 % (24.6 % of men and 17.6 % of women) (14). The highest proportion of smokers was in the youngest age group under 25 years (39.7 % of men and 25.6 % of women). In the age group of 25–34 years, smoking women were more represented (33.6 % of women, 31.6 % of men). The proportion of smokers in the population declines with age, with the lowest number of smokers in the age group over 75 years (3.6 % of men, 2.8 % of women) (14)

Although there are other exogenous and endogenous risk factors for LC, smoking remains the most significant one (15).

LC early detection program in Slovakia

The primary goal of the LCS program is to maximize the number of curative resections of malignant lesions, hence saving lives and providing the best possible quality of life (QoL). We have identified seven major preconditions which have to be fulfilled to operate the Complex Multidisciplinary LC Early Detection Program in Slovakia (CM-LCEDP):

1. Systematic support for smoking prevention, treatment of smoking addiction, and maintaining smoking-free lifestyle choices
2. Clear communication about screening benefits and harms to provide a shared decision-making process with patients as a cornerstone of credibility and future adherence to the program
3. Preemptive and proactive solutions to address geographical and socio-economic disparities
4. A sustainable and simple pathway of screening participants throughout the entire process, including timely evaluation of positive screening findings in pneumo-onco-surgical centers
5. High-quality control processes with the scope on minimizing radiation exposure, identifying gaps in screening organizations, and updating future policies based on collected data
6. Development of the national image and tissue biobank to support research
7. Implementation of artificial intelligence algorithms into diagnostic and therapeutic pathways.

To implement the CM-LCEDP in Slovakia, we recommend an involvement and support of Slovak healthcare authorities and propose a three-phase process:

1. Planning phase – forming an expert committee/panel, identifying the target population, setting centralized and decentralized algorithms
2. Pilot phase – identifying several pilot centers with a centralized approach to referrals.
3. Launch phase – expanding to multiple dedicated screening centers of excellence with an option to join a centralized program and its pathways.

This publication's primary intention is to initiate a discussion in related professional societies and target providers' communities. Implementing established efficacious screening protocols and procedures published in multiple international studies should guide early national LC detection strategy.

A. Target population

LC incidence dominates in patients > 50 years of age. All randomized clinical trials included high-risk population with severe smoking history per age group. The reason for focusing on the high-risk population lies in the very high sensitivity of low-dose chest CT and its ability to recognize a variety of benign/indolent lung pathologies.

Age and pack-year smoking history are considered the minimal inclusion criteria for any LCS program. The US Preventive Services Task Force (USPSTF) recently updated their screening criteria to include individuals ≥ 50 years old who have at least 20 pack-year smoking history and quitted smoking no sooner than 15 years ago (16). Individual risk assessment in the screening recruitment process should also be considered (Tab. 1).

Most of the scans with positive findings of nodules in size of 6mm to 10mm need subsequent scans to establish the annual growth rate of nodule. The growth rate is the best non-invasive indicator of potential malignancy (17). Serum biomarker testing and an artificial intelligence system with a malignancy scoring tool helps to further risk-stratify positive findings and leads to a more straightforward pathway to biopsy/resection. Moreover, present co-morbidities, socio-economic status, and psychological aspects should also be considered prior enrollment to the screening pro-

Tab. 1. Proposed inclusion, exclusion criteria, and individual risk assessment.

Inclusion criteria:
1. Age at least 50 years
2. 20 pack-year smoking history for current or former smokers that quitted smoking later than 10–15 years ago.
Individual risk assessment:
1. Exposure history to other carcinogens, specific family history regarding lung cancer occurrence.
2. At least 5-year life expectancy with absence of major co-morbidities
3. Outlook for successful screening program adherence
Exclusion criteria:
1. Diagnostic chest CT within last year
2. Clinical symptoms of lung cancer

gram. Patients with life expectancy shorter than 5 years due to co-morbidities should not be enrolled.

B. Early detection of LC and pathway through the screening program

The sustainable and straightforward paradigm of the LCS program is defined by:

1. Recruitment of eligible participants and support for smoking cessation
2. Low-dose chest CT
3. Structured reporting according to the screening protocol and further management recommendation
4. Multidisciplinary team assessment of positive screening findings in pneumo-onco-surgical centers
5. Histological evidence of malignancy, treatment of LC according to the standard of care (SoC), and ongoing oncologic surveillance

1. Recruitment of eligible participants and support of smoking cessation

In Slovakia, smoking cessation programs and LCS awareness are poor. One of the crucial components of information availability is the elevation of awareness among experts, population and healthcare policymakers. The inclusion of general practitioners along with pneumologists into the recruitment process is crucial.

The success of Slovak screening programs begins with governmental support and the involvement of primary care physicians.

2. Low-dose chest CT examination

The geographically heterogeneous location of pneumo-onco-surgical centers has been identified as one of the most severe barriers for the LCS process in Slovakia. Implementing a two-step hybrid model seems plausible to secure a successful screening program. Firstly, a primary care physician reviews the eligibility, orders a scan and makes a referral to an accredited radiology department. Secondly, a centralized data collection algorithm is utilized in appointed pneumo-onco-surgical centers and further steps are recommended. This two-step hybrid model should make screening tests available for the majority of the Slovak population. The local radiology acquisition centers would have to comply with the minimum requirements for LCS standard protocols based on international guidelines and in line with Slovak legislation on auditing examinations that utilize medical ionizing radiation. The provision of professional radiology support at centers should be under central governing surveillance.

3. Structured reporting according to the screening protocol and further management recommendations

The results of LDCT should be reported in a structured way reflecting the European Position Statement and American College of Radiology LungRADS classification (7, 18). Reports need to include information about localization, morphological characterization, size, follow-up doubling times of the nodules, and extranodular findings. Referring physicians receiving LDCT reports will proceed in the following manner:

A. Negative finding – scheduling of the patient for the following standard round of LDCT chest screening according to the protocol
B. Indeterminate finding – scheduling of the patient for early LDCT follow-up according to the recommendations.
C. Positive finding – direct referral to the pneumo-onco-surgical center

The LUNG-RADS reporting system provides a crude estimate of malignancy and helps to guide further nodule management. Those with positive findings are denoted with Lung-RADS score of 2–4 A-B while the scan is recommended to be repeated after 3 months up to a year. For instance, a yearly follow-up is recommended for the solid and part-solid nodules in size smaller than 6 mm, perifissural nodules in size smaller than10 mm (score 2). On the other hand, LDCT repeated quarterly up to semiannually is recommended for patients with categories 3 and 4A, i.e., for those with solid and semi-solid nodules in size ≥ 6 mm < 15 mm. Patients with nodules scored 4B or 4X (category 3 or 4 of nodules with additional features increasing the suspicion for malignancy) should undergo further imaging or tissue sampling/resection. Different size limits and management guidelines apply for non-solid nodules, also called ground-glass nodules, as they often represent a benign process/slow-growing malignancy (19).

4. Multidisciplinary team assessment plan of positive LCS findings within a tertiary cancer center.

Slovakia should plan for several complex multidisciplinary teams strategically positioned in different regions, who will guide the further management of suspicious cases of early LC following the current guidelines and SoC. A complex and interdisciplinary approach to patients with LC is required to adhere to the pathway from the nodule to treatment speedily and accurately. The multidisciplinary team needs to include radiology, pulmonology, oncology, thoracic surgery, and radiation oncology specialties. In our model, we advocate utilizing a virtual lung nodule clinic led by coordinators responsible for nodule risk stratification, tracking, and further diagnostic management. The positive effect of an automated tracking registry on the rate of tracking failures has been described (20).

Data from the largest I-ELCAP registry containing more than 250,000 LDCT studies combined with long-term follow-up can quantify malignancy risk. Based on those data, a single time-point lung nodule measurement of 6–15 mm is not a sufficient predictor

of malignancy. Nodules measuring 10–15 mm have a malignancy probability of 15–18 %. The European position statement on LCS recommends invasive workup for nodules larger than 10 mm by employing a biopsy or surgical resection (7). Volume doubling time (malignant doubling time 30–400 days) evaluation and other risk stratification methods reduce such a high false positivity rate. Screened patients should be aware that they could undergo subsequent serial LDCT examinations.

Variability of volumetric software can reach an interval of 370 % against the referenced software used in the NELSON trial (20). Such a high degree of variability in accuracy directly impacts the amount of invasive workup. Thus, the central surveillance and quality control of nodule measurements are crucial. Establishing and monitoring of a rigorous unified methodology across the centers must be implemented to avoid unintentional reporting of misleading growth rate measurements.

Risk stratification of intermediate nodules using artificial intelligence software has been recently validated. This approach has been shown to outperform traditional risk prediction models (21). Genomic sequencing classifiers performed from blood serum (22) or nasal or bronchial mucosa (23) are also finding their everyday use in clinical practice.

5. Histological evidence of malignancy, LC treatment according to the SoC and oncology surveillance.

LC diagnosis should be obtained by the least invasive methods available with simultaneous invasion staging. A multidisciplinary discussion determines the optimal invasive diagnostic procedure being carefully weighed against the possible risk of complications. The overall risk remains negligible against the benefit of establishing an accurate histologic, immunohistochemical and molecular marker profile of the tumor. CT-guided transthoracic biopsies and computer-assisted bronchoscopy biopsies complemented by radial endobronchial ultrasound and augmented fluoroscopy with or without cone-beam CT are both heavily utilized tools for performing biopsy of nodules with a high pre-test probability of cancer.

Mediastinal staging plays a crucial role; PET/CT should not be used as a sole method for staging the nodules in size ≥ 2 cm due to low specificity (59.8 %), which leads to a significant risk of upstaging or downstaging (24). Endobronchial ultrasonography /esophageal ultrasonography with fine-needle aspiration is the first choice since it is minimally invasive and has a high sensitivity in mediastinal nodal disease. If negative, surgical staging with nodal dissection or biopsy is indicated. Video-assisted mediastinoscopy is preferred to mediastinoscopy (25).

High-risk nodules smaller than 2 cm in diameter with absent mediastinal lymphadenopathy on PET/CT or enlarging pure GGN should be evaluated for a potential surgical resection (26, 27).

The primary goal should always be establishing the most efficacious and patient-centered plan for curative surgical resection. Hence defining an accurate diagnosis, staging, and nodule labelling during one interventional diagnostic session has become the SoC worldwide. After a histological diagnosis and molecular marker profile of LC, the multidisciplinary team outlines the specifications of the treatment plan. It considers imaging, staging, patient's performance status, and center-specific diagnostic and therapeutic circumstances; alternatively, minimally invasive thoracoscopic sub-lobar resections as a curative surgical method (28). For non-surgical patients, stereotactic radiotherapy or image-guided ablation techniques are discussed. In cases of locally advanced or disseminated disease, patients are referred for chemo-radiotherapy.

Structured tissue bank and database will provide insight into the LC epidemiology and serve as an essential source of information for future oncology healthcare policies and screening program adjustments.

C. LCS Benefits and risks

The beneficial impact of LCS on population survival will depend mainly on the staging status. Our prediction model showed that up to 70 % of patients diagnosed with LC in 2022 will be in clinical stage IV (Figs 3 and 4). Large cohort studies proved significant stage shifts after LCS programs had been initiated (29, 30). Based on the previously published data, we predict the average annual percentage shift change to be between 0.5 % and 2.5 %. This could result in an approximately 10 % increase in curative resection over ten years and have a tremendous impact on cancer-related mortality in Slovakia.

Screening-related psychological stress is known to accompany all screening programs. Imaging-related risks include overdiagnosis resulting in unnecessary procedures and surgeries. These phenomena are inherent in LCS due to the very high sensitivity of LDCT that accurately detects up to 90 % of lung nodules in size < 6 mm, with low probability of malignancy (19). To decrease false-positive findings, we suggest risk stratification of intermediate nodules by applying volumetric calculations, AI-based risk scores, and genomic classifiers

Conclusion

Sample evidence supports the efficacy and cost-effectiveness of early LC detection programs. While the implementation methods might differ, we have identified crucial steps pertinent to the specifics of the healthcare system in Slovakia. Neighboring countries with a similar healthcare system, demographic composition, and economic output, could serve as an example.

At first, it is necessary to form an expert panel to define the target population and centralized and decentralized algorithms. The panel will then identify and educate the key radiologists, pulmonologists, and smoking cessation specialists in each region of the country. Radiology departments in local hospitals should adopt and operate consistent low-dose chest CT imaging protocols.

Secondly, with the assistance of primary care physicians and pulmonary specialists, a clear and concise information package should be delivered to the above-identified high-risk group of patients.

Thirdly, information about high-risk nodules should be provided to major tertiary medical centers equipped with specialized pulmonary, oncologic, and surgical teams to formulate patient-centered diagnostic and treatment plans. Centralized LCS centers with multidisciplinary teams would accommodate patients with positive findings coming from smaller non-centralized healthcare facilities.

Informed consent enabling a participant to understand the benefits and possible harms of the screening program is the first important step in initiating the individual screening process (31). A comprehensive smoking cessation program must be an integral part of the early LC detection philosophy.

Discussions about cost-effectiveness should take place on the levels of the Ministry of Healthcare, including all insurance providers in Slovakia. With a coordinated approach among healthcare providers, institutions, governmental legal framework, and insurance providers' financial support, we can aspire to develop a sustainable and successful nationwide multidisciplinary LC early detection program. These efforts will improve overall cancer-related survival and enhance the QoL for the high-risk population group.

References

1. Detterbeck FC, Boffa DJ, Kim AW LT. The Eighth Edition Lung Cancer Stage Classification. Chest 2017 and 193–203; 151 (1): 193–203.

2. Steven A, Fisher SA, Robinson BW. Immunotherapy for lung cancer. Respirology 2016; 21 (5): 821–833.

3. Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: Results stratified by demographics, smoking history, and lung cancer histology. Cancer 2013 and 3976–3983, 119 (22).

4. Mazzone PJ, Silvestri GA, Patel et al. Screening for Lung Cancer: CHEST Guideline and Expert Panel Report. Chest 2018; 153 (4): 954–985.

5. De Koning HJ, van der Aalst CM, de Jong PA et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med 2020; 382 (6): 503–513.

6. Yip R, Henschke CI, Yankelevitz DF, Boffetta P, Smith JP; International Early Lung Cancer Investigators. The impact of the regimen of screening on lung cancer cure: a comparison of I-ELCAP and NLST. Eur J Cancer Prev 2015; 24 (3): 201–208.

7. Oudkerk M, Devaraj A, Vliegenthart R et al. European position statement on lung cancer screening. Lancet Oncol 2017; 18 (12): e754–e766.

8. Kauczor, HU, Baird AM, Blum TG et al. European Society of Radiology (ESR) and the European Respiratory Society (ERS). ESR/ERS statement paper on lung cancer screening. Eur Radiol 2020; 30 (6): 3277–3294.

9. Field JK, Zulueta J, Veronesi G et al. EU Policy on Lung Cancer CT Screening 2017. Biomed Hub 2017; 2 (Suppl 1): 154–161.

10. Juskanič D, Lehotská V, Poláková Mištinová J et al. Memorandum skríningu karcinómu pľúc na Slovensku. Slov Radiol 2021; 28 (1–2): 65–70.

11. Kavcová E, Ondrušová M. Epidemiológia karcinómu pľúc. 19–35, In: Kavcová E, Halašová E, Dzian A (Eds). Karcinóm pľúc Martin: Univerzita Komenského, 2010. 647 s.

12. Ondrušová M, Bucek-Pšenková M, Suchanský M (Eds). Descriptive epidemiological, morphological, immunohistochemical and genetic indicators in primary lung cancer in the Slovak Republic. Bratislava, Pharm-In 2022www.pharmin.sk (17.06.2022.).

13. Príčiny smrti, Pramenné dielo. (2021). https://slovak.statistics.sk (accessed January 17, 2022).

14. Avdičová M, Francisciová K, Ďateľová M. Monitorovanie rizikových faktorov chronických chorôb v SR. Bratislava: Regionálny úrad verejného zdravotníctva, 2012.

15. Kimáková T, Bernadič Jr M, Bernadič M, Bielik I, Rovný I, Mácová Ž, Nevolná Z. Fajčenie ako jeden z najzávažnejších celospoločenských zdravotných problémov súčasnej doby. Psychiatria-Psychoterapia-Psychosomatika 2019; 19 (3): 19–26.

16. Krist AH, Davidson KW, Mangione CM et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. JAMA 2021; 325 (10): 962–970.

17. Henschke CI, Yankelevitz DF, Yip R et al. Lung cancers diagnosed at annual CT screening: volume doubling times. Radiology 2012; 263 (2): 578–583.

18. American College of Radiology Committee on Lung-RADS. Lung-RADS Assessment Categories version 1.1. https://www.acr.org/-/media/ACR/Files/RADS/Lung-RADS/LungRADSAssessmentCategoriesv1-1.pdf. Accessed on January 1, 2020.

19. Soo E, Edey AJ, Mak SM et al. Impact of choice of volumetry software and nodule management guidelines on recall rates in lung cancer screening. Eur J Radiol 2019; 120: 108646.

20. Massion PP, Antic S, Ather S et al. Assessing the Accuracy of a Deep Learning Method to Risk Stratify Indeterminate Pulmonary Nodules. Am J Resp Crit Care 2019; 202 (2): 241–249.

21. Nodules: Extended Analyses and 2-Year Follow-Up Results of the PANOPTIC (Pulmonary Nodule Plasma Proteomic Classifier) Trial. Chest 2021; 159 (3): 1283–1287.

22. Johnson MK, Wu S, Pankratz DG et al. Analytical validation of the Percepta genomic sequencing classifier; an RNA next generation sequencing assay for the assessment of Lung Cancer risk of suspicious pulmonary nodules. BMC Cancer 2021; 21 (1): 400.

23. Hwangbo B, Kim SK, Lee HS et al. Application of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration Following Integrated PET/CT in Mediastinal Staging of Potentially Operable Non-small Cell Lung Cancer. Chest 2009; 135 (5): 1280–1287.

24. De Leyn P, Dooms C, Kuzdzal J et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J Cardiothorac Surg 2014; 45 (5): 787–798.

25. Janík M, Lučenič M, Juhos P, Šiška D, Lauček P, Tarabová K. Torakoskopické sublobárne anatomické resekcie pľúc pre malígne nodulárne lézie. Onkológia (Bratisl) 2021; 16 (1): 52–54.

26. ESTI LCS structured report basic template. (n.d.). https://www.myesti.org/content-esti/uploads/ESTI-LCS-structured-report-basic-template_2019-07-09.pdf.

27. Migliore M, Fornito M, Palazzolo M et al. Ground glass opacities management in the lung cancer screening era. Ann Transl Med 2018; 6 (5): 90.

28. Detterbeck FC, Lewis SZ, Diekemper R, Addrizzo-Harris D, Alberts WM. Executive Summary: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013; 143 (5 Suppl): 7S–37S.

29. Wang Z, Hu Y, Wang Y et al. Can CT Screening Give Rise to a Beneficial Stage Shift in Lung Cancer Patients? Systematic Review and Meta-Analysis. PlosOne 2016; 11 (10): e0164416.

30. Flores R, Patel P, Alpert N, Pyenson B, Taioli E. Association of Stage Shift and Population mortality Among Patients With Non-Small Cell Lung Cancer. JAMA Netw Open 2021; 4 (12): e2137508.

31. Bernadič Jr M, Bernadič M. Príspevok k etiopatogenéze nádorových ochorení – superinformačný systém. Lek Obzor 2020; 69 (12): 483–485.

Received August 17, 2022.
Accepted September 21, 2022.