Lung Cancer in Poland

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Epidemiology and Tobacco Control

In 2017, over 22,000 Poles have been diagnosed with lung cancer. Incidence rates among men and women are 93 and 38 per 100,000, respectively, based on the European Standard Population (2013).[1] Lung cancer ranks as the most prevalent malignancy overall, with approximately 18% of cancer cases among men and 10% among women. Lung cancer is also the main cause of cancer-related deaths in both sexes (almost 30% among men and 17% among women) and is the cause of almost 6% of all deaths in Poland. Similar to many European countries, tobacco epidemics was on the rise since the beginning of the 20th century and peaked in the early 1990s (Fig. 1).[1,2] Since then, the increasing trend of lung cancer incidence in Polish men reversed. Despite predicted further decrease in incidence rates, the absolute number of lung cancers among men in Poland will continue to rise. This increase results from demographic changes, predominantly the aging of the population.

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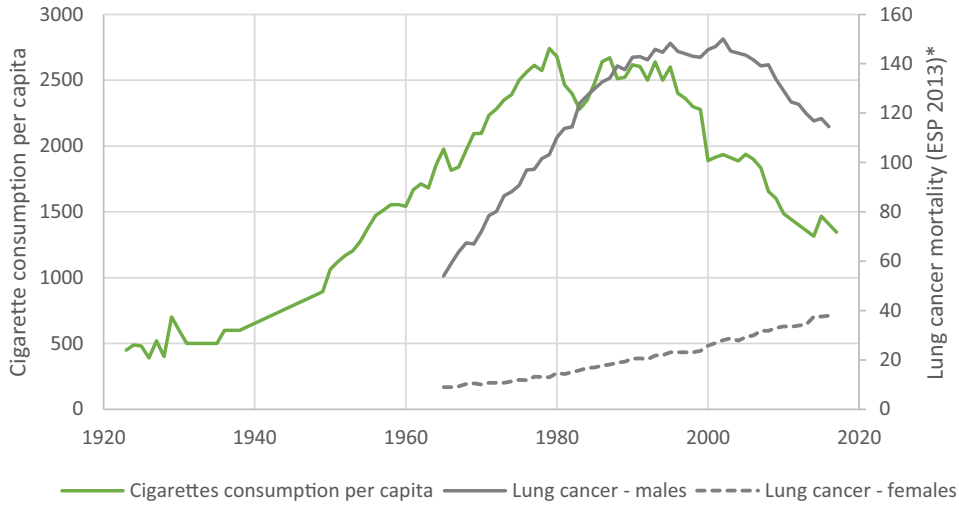
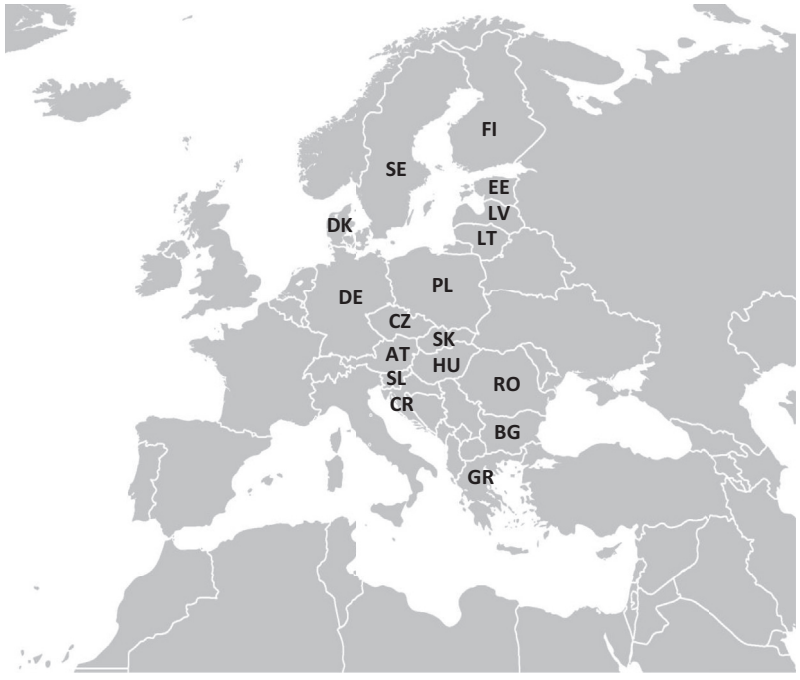


** Standardization on European Standard Population 2013*

Figure 1. Cigarette consumption and lung cancer mortality in Poland. ESP, the European Standard Population.

A steady growing lung cancer mortality has been reported for Polish women (Fig. 1), consistent with the ongoing increase in the frequency of smoking. Two phenomena are responsible for this picture: (1) the aging of the female population; and (2) entry into the "cancer age" by women born after World War II, characterized by relatively high tobacco consumption. Within the past few years, this growing tendency toward smoking has slowed down; however, the forecasts do not indicate that the growing incidence of lung cancer among women will stop in the next decade. The 5-year lung cancer survival rates between 1999 and 2010 increased only slightly, from 11.3% to 12.6% for men and from 16.8% to 18.5% for women. Lung cancer mortality rates in Poland and



	Age standardized rate Europe (ESP2013)	
	LCMM	LCMF
FI/FINLAND	53.7	27.4
SE/SWEDEN	39.5	37.3
DK/DENMARK	82.6	63.2
DE/GERMANY	76.4	36.7
AT/AUSTRIA	66.3	35.9
EE/ESTONIA	109.7	22.6
LV/LATVIA	94.3	19.0
LT/LITHUANIA	100.3	14.1
PL/POLAND	117.1	44.9
CZ/CZECH REP.	76.1	30.3
HU/HUNGARY	134.2	62.2
RO/ROMANIA	95.1	22.6
BG/BULGARIA	88.7	21.0
SK/SLOVAKIA	95.3	24.9
SL/SLOVENIA	88.2	37.2
CR/CROATIA	112.3	31.4
GR/GREECE	125.1	25.6

Figure 2. Map of Europe including Poland. Age-standardized lung cancer mortality rates in males and females are indicated for selected countries. ESP, European Standard Population; LCMF, lung cancer mortality rates in females; LCMM, lung cancer mortality rates in males; PL, Poland.

selected European countries are presented in Figure 2 (data standardized for European Standard population 2013).

Comprehensive antitobacco measures were undertaken in the early 1990s after Poland gained its democracy. "Kazimierz Declaration" was a milestone for the successful enforcement of tobacco control legislation in central and eastern Europe. This document included increased taxation, warnings on cigarette packs, and other measures.[3] Owing to these efforts, the number of cigarettes sold in Poland decreased from astonishing 101 billion yearly in 1995 to 47 billion in 2013 and 32 billion in 2016. Strong legislation bills on smoking ban in public places were introduced in 2010, thanks to the perseverance of Prof. Jacek Jassem who was its lead author and one of its strongest promoters in the Polish parliament. Despite these achievements, Poland still faces many challenges, such as increasing tobacco consumption among middle-aged women, the strong position of the tobacco industry in the country (Poland ranks third in the production of tobacco products in Europe, most of which are exported), and the lack of comprehensive antitobacco educational programs in schools. Major problems related to lung cancer have been addressed in a specific lung cancer control strategy plan recently developed by the Polish Cancer League, Polish Lung Cancer Group, and the Institute of Tuberculosis and Lung Diseases in Warsaw (document available in Polish at www.ligawalkizrakiem.pl). According to the recent analysis of lung cancer policies across Europe published by the Intelligence Unit of The Economist, out of 11 analyzed European countries, only Poland has developed such document.[4]

Organization of Health Care

Poland has a universal nationwide public health insurance system, which allows almost all citizens fully reimbursable care including modern diagnostic and therapeutic procedures, such as positron emission tomography–computed tomography (CT) imaging, video-assisted thoracic surgery, stereotactic body radiotherapy, targeted agents, and immunotherapy. In contrast, there is a shortage of specialists, particularly pathologists, radiation oncologists, and medical oncologists. This shortage may lead to a lengthy diagnostic process lasting up to 3 to 4 months in some cases and constitutes one of the most important organizational targets for improvement (Table 1). The reimbursement decisions of new agents approved by the European Medicines Agency are preceded by centralized health economic evaluation, including health budget impact, which, on average, take around 14 months.

Lung Cancer Screening

The lung cancer screening programs conducted in the United States and Europe have led to the initiation of lung cancer early detection pilot studies in Poland in 2008. These nonrandomized programs using low-dose chest CT in high-risk individuals were introduced independently in a few major clinical centers: Szczecin, Gdańsk, Poznań, and Warsaw—the latter focusing on regions of the country with lowest rates of operable NSCLC at diagnosis. Gdańsk early detection program was accompanied by complementary biomarker projects. The above protocols, involving approximately 50,000 individuals, were based on the Early Lung Cancer Action Program study with linear measurements of detected lung nodules or NELSON (Nederlands-Leuvens Longkanker Screenings Onderzoek) and the modified United Kingdom Lung Cancer Screening projects using volumetric assessments of the nodule growth. Consistent with the literature, lung cancer was detected in approximately 1% of the individuals (from 0.86% in Szczecin to 2.0% in Gdańsk). Stage I was diagnosed in 64% to 70% of detected cancers.[5] The results of these studies contributed to the awareness of the risk of lung cancer in society and established a knowledge-base on the low-dose CT for early lung cancer detection. The final results of the National Lung Screening Trial[6] and NELSON trial[7] prompted the development of the first Polish large-scale lung cancer early detection program.[8]

Table 1. Ongoing Lung Cancer National Initiatives

Initiative	Target	Coordinating Organizations
Primary prevention: increase in taxation of cigarettes	Decreasing lung cancer incidence and mortality	Ministry of Health, Ministry of Finance
Introduction of pilot lung cancer early detection projects	Decreasing lung cancer mortality	Ministry of Health selected institutions, European Union-funded POWER Program
National lung cancer database (currently only includes surgical treatment)	Benchmarking procedures and outcomes, providing data for clinical research	National Institute of Tuberculosis and Lung Diseases, Warsaw
Lung cancer units	Shortening the time from symptoms to diagnosis and treatment	Ministry of Health, National Health Fund, Medical Societies
Pathology standards and accreditation	Improving the quality of pathologic results and materials for translational research	Ministry of Health, Polish Society of Pathology

This pilot program, covered by public funds, is currently being implemented in six main regions and will be carried out within the next 3 years.

Lung Cancer Diagnosis and Staging

Patients with suspected lung cancer are diagnosed and staged in pulmonary hospitals, pneumonology, or thoracic surgery departments. The diagnostic and staging process is often lengthy and suboptimal (e.g., inadequate access to endobronchial ultrasound and mediastinal staging, repeated biopsies, inadequate material for molecular tests). A special pathway, including obligatory multidisciplinary meetings to optimize treatment strategy, was introduced for newly diagnosed patients with cancer in 2015; yet many institutions lack all the modern multidisciplinary lung cancer diagnostic options. Planned development of dedicated lung cancer units is expected to improve this situation (Table 1).

Surgery

Thoracic surgery is performed only in accredited thoracic surgery units independent of cardiac surgery units. All centers are obliged to keep detailed treatment records and their results. The records of thoracic surgeries have been collected in a nationwide lung cancer registry since 1983, and detailed lung cancer treatment outcomes since 2007. The ministry advisor in thoracic surgery and the Thoracic Surgeons Club, including the heads of all thoracic surgery units, have been meeting regularly since 1983 to set up and monitor the quality of surgical treatment. Out of 27 accredited Polish thoracic surgery units, 18 are high-volume centers performing over 100 anatomical resections yearly. In 2017, 4031 anatomical resections of lung cancer were performed in Poland, of which 41%, 23%, and 12% were in stage I, II, and III, respectively, according to the eighth Union for International Cancer Control lung cancer classification. Video-assisted thoracic operations were performed in 36% of all patients with lung cancer operated for stage I and II in 2018 (Orłowski, National Institute of Tuberculosis and Lung Diseases, personal communication, 2019). Pneumonectomies accounted for 7.9% of all resections, compared with 17.9% in 2008. Nationwide perioperative 30-day mortality is 0.94%. Thoracic surgeons are instrumental in the development of innovative surgical procedures[9] and the preparation of the national pilot lung cancer early detection program.

Radiotherapy

During the past two decades, radiotherapy equipment has been successfully supplemented and modernized to meet the European Union standards. Between 2005 and 2018, the number of high-energy external beam units increased from 70 to more than 170, almost closing the historical infrastructure gap. This instrumental improvement, paralleled by an approximately threefold increase in the number of radiation oncologists and medical physicists, was possible owing to a dedicated national program carried out since 2006. Stereotactic radiotherapy, intensity-modulated radiation therapy, and volumetric arc therapy are being used in most (approximately 35) radiation oncology facilities. Challenges include inadequate endoscopic staging, considerable regional inequalities in the implementation of concurrent radiotherapy and chemotherapy for stage III NSCLC, and imperfect reporting of treatment results to benchmark treatment efficacy.

Systemic Therapies for Advanced Lung Cancer

Recommendations for systemic treatment of lung cancer are developed by the Polish Society of Clinical Oncology and published every 2 to 3 years. The updates follow international guidelines and consider Polish epidemiologic, clinical, and pharmacoeconomic features. Standard cytotoxic therapy is widely available in oncology centers, pulmonary hospitals, and medical oncology clinics. Reimbursed targeted agents include EGFR inhibitors gefitinib, erlotinib, afatinib, and osimertinib; although the last is available only for T790M-positive patients who relapsed after first- or second-generation EGFR tyrosine kinase inhibitors. Also, reimbursed are ALK inhibitors crizotinib, alectinib, and ceritinib, and the ROS1 inhibitor crizotinib. Programmed cell death protein 1 or programmed death-ligand 1 (PD-L1) inhibitors covered by the national insurance system include the first-line pembrolizumab (in patients with PD-L1–positive tumors) and the second-line nivolumab and atezolizumab. Nintedanib (antiangiogenic agent) combined with docetaxel is reimbursed as second-line treatments for patients with adenocarcinoma. These novel treatments are available in approximately 100 institutions across the country within special national insurance covered programs with restrictive inclusion criteria, monitoring requirements, treatment cessation rules, and reporting infrastructure. The proportion of patients receiving innovative agents in relation to the number of institutions reveals a scattered use of anti-EGFR agents and immunotherapy. The availability of modern targeted therapies and immune checkpoint inhibitors in Poland and selected European countries is provided in Figure 3.[10]

Predictive biomarker testing in Poland is well-aligned with available therapies, and therefore, offered mostly to patients with nonsquamous NSCLC. Typically, testing includes *EGFR* mutation assessment (predominantly by polymerase chain reaction with Cobas v.2) and *ALK*/

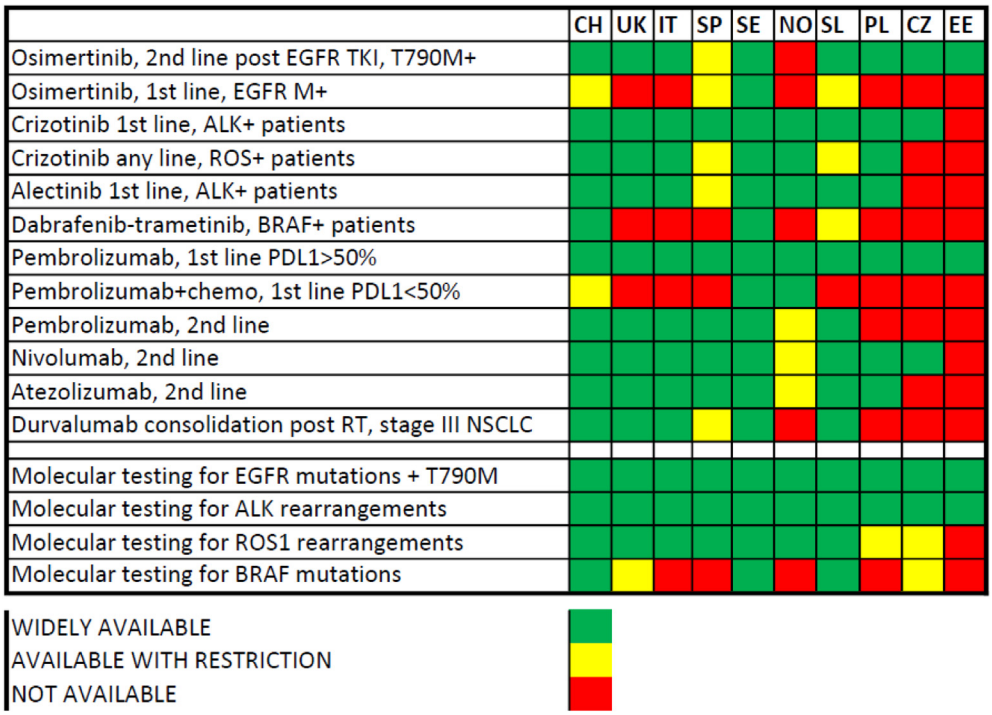


Figure 3. Availability of modern systemic therapies in Poland and selected European countries. CH, Switzerland; UK, United Kingdom; IT, Italy; SP, Spain; SE, Sweden; NO, Norway; SL, Slovenia; PL, Poland; CZ, Czech Republic; EE, Estonia; data as of September 2019. PD-L1, programmed-death ligand 1; TKI, tyrosine kinase inhibitor.

ROS1 rearrangement evaluation (predominantly by immunohistochemistry and break-apart fluorescence in situ hybridization assays). Several high-volume institutions have recently introduced next-generation sequencing with other targetable alterations, such as *BRAF*, *MET*, *RET*, *HER2,* and *NTRK1-3*, in conjunction with dedicated clinical research programs. National reimbursement selectively covers molecular biomarker testing but not protein expression assays (e.g., *ALK, ROS1*, PD-L1). This situation reflects some fundamental problems faced by Polish pathologists. Pathologic assessments have not been identified as separate reimbursable procedures, and are, therefore, financed in lump coverage for any in-hospital or outpatient diagnostics. Years of underfunding resulted in a substantial decline in the number of pathologists in Poland (one per 91,700 inhabitants versus a European average of one per 36,000 inhabitants), leading to protracted time to diagnosis in many clinical centers. This situation is currently being addressed on a national level (Table 1).

Clinical and Translational Research in Lung Cancer

Lung cancer academic research is conducted by two national cooperative groups: the Polish Lung Cancer Group (www.polgrp.org.pl) and the Central and East European Oncology Group (www.ceeog.eu). In addition, several oncological institutes and medical universities are involved in lung cancer academic studies, alone or in collaboration with other European partners, such as the European Thoracic Oncology Platform (www.etop-eu.org) or the Lung Cancer Group of the European Organization for Research and Treatment of Cancer (www.eortc.org/research_field/lung/). Basic and translational lung cancer research is supported by both the national governmental and nongovernmental agencies (National Science Center, The National Center for Research and Development, Foundation for Polish Science) and by international institutions. The importance of academic clinical research was recently recognized by the Polish Government, which established the Agency for Medical Research that offers grants for biomedical clinical research. Polish institutions also actively participate in pharmaceutical company–sponsored studies. Two large institutions have recently opened phase I units (Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw and Medical University of Gdańsk). Several institutions play a major role in the design and recruitment of phase II and III trials and some lung cancer–focused pharmaceutical companies have significantly enlarged their hubs in Poland. Within the reciprocal membership system of the International Association for the Study of

Lung Cancer and Polish Lung Cancer Group, many thoracic oncology professionals have access to the International Association for the Study of Lung Cancer resources and are involved in its activities.

Areas for Improvement and Future Perspectives

Although the results of lung cancer treatment seem to be slightly better than those of other countries in the central and eastern Europe, there is still an evident room for improvement.[4] With the overwhelming lung cancer burden in Poland, it is in the spotlight of many initiatives from both governmental and professional medical organizations, and also patient advocacy groups, aiming to address the most urgent issues. Current initiatives that will hopefully contribute to the improvement of lung cancer statistics are summarized in Table 1.

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