CATCHING GAPS WITH HEALTHCARE MAPS

CARDIOLOGY AND ONCOLOGY

Medical treatment in Poland – analysis and models

Volume I: Oncology

Edited by

Barbara Więckowska

Publication co-financed by the European Union under the European Social Fund

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Warsaw 2015 r.

PUBLISHER:
Ministry of Health, Department of Analyses and Strategy
Contact data:
Ministry of Health,
ul. Miodowa 15, 00-952 Warsaw,
Phone: 22 634 96 00,
www.mz.gov.pl;

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ISBN: 978-83-941589-3-4

In this publication, the authors present their own views, supported by in-depth analyses and many years of experience. The publication cannot be considered an official position of state authorities and bodies. The authors and the editing team are not liable for the application of guidelines, examples, information and solutions presented in this publication to specific medical cases.

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Translation prepared by GTC AMG Sp. z o.o.
www.invenire.pl

Typesetting:
Centrum Poligrafii Sp. z o.o., Warsaw, ul. Łopuszańska 53
Printing:
Centrum Poligrafii Sp. z o.o., Warsaw, ul. Łopuszańska 53

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Foreword

Barbara Więckowska

The book you are holding in your hands focuses on the use of quantitative methods in the area of cancer care in Poland. It is the first such detailed paper on malignant neoplasms, linking the data from the National Cancer Registry and the data of the public payer (National Health Fund). This publication is one of three volumes compiled by the team of experts working on the project "Improving the quality of management in health care by supporting the process of creating regional maps of health care needs as a tool streamlining the management processes in the health care system – training in estimating health care needs", implemented by the Department of Analysis and Strategy of the Ministry of Health, co-financed from the European Union funds under the European Social Fund. The expert working group on cancer care, composed of physicians, epidemiologists, experts in social policy, health economists, demographers, statisticians, econometrists, and big data specialists, performed an in-depth analysis of the Polish oncological care system, focusing at first on the reported and projected number of oncological patients.

This publication summarises the work of the expert working group in this area. Its purpose is to present a systematic approach to analysis of data collected by the Polish health care system in the area of malignant neoplasms in a way that ensures that maps of health care needs for individual voivodeships and Poland as a whole are based on reliable data and projections.

Maps of health care needs are being developed by a number of countries such as Austria, Czech Republic, and France. They are an important tool that supports evidence-based management in the health care system, in terms of both ensuring durability of actions (partial independence from the political process and making decisions based on objective analysis) and supporting the process of explaining social policy to citizens, which is more difficult in the area of health care policy. For this reason, the European Commission significantly supports mapping of health care needs through introduction of the so-called ex ante requirements. According to Regulation (EU) No 1303/2013 of the European Parliament and of the Council of 17 December 2013 laying down common provisions on the European Regional Development

Fund, the European Social Fund, the Cohesion Fund, the European Agricultural Fund for Rural Development and the European Maritime and Fisheries Fund and laying down general provisions on the European Regional Development Fund, the European Social Fund, the Cohesion Fund and the European Maritime and Fisheries Fund and repealing Council Regulation (EC) No 1083/2006 (OJ L 347, 20.12.2013, p. 320), disbursement of structural funds will depend on meeting the ex ante conditionality requirements, or ensuring fulfilment of specific entry conditions that allow efficient implementation of programmes co-financed from European funds. According to Annex XI to the above General Regulation, these conditionalities concern *inter alia* "The existence of a national or regional strategic policy framework for health within the limits of Article 168 TFEU ensuring economic sustainability" (conditionality 9.3)[1]. This framework should result from maps of health care needs.

Regardless of European Union's requirements, Poland planned a systemic solution for development and use of maps of health care needs. The obligation to develop maps of health care needs in Poland was introduced by the Act of 22 July 2014 amending the Act on health care services financed from public funds and certain other acts (Journal of Laws of 2014, item 1138).[2] According to the Act, first maps of health care needs are to be developed by 1 April 2016 at the latest and will cover hospital treatment[3].

It does not mean, however, that the mechanism is new in Poland or that there had been no previous attempts to develop maps of health care needs. There were initiatives of this kind in previous years. In 1997, i.e. when regional health care funds were in place, Article 55a of the Act of 6 February 1997 on universal health insurance stipulated that local government bodies, having obtained the opinion of medical professions' self-governments and in consultation with the regional health care fund, shall develop a plan of securing outpatient health care[4]. Article 101 of the Act of 23 January 2003 on universal insurance in the National

[1] Under thematic objective 9 of the Partnership Agreement (PA) – Promoting social inclusion, combating poverty and all forms of discrimination.
[2] The content of maps of health care needs is regulated by the Regulation of the Minister of Health of 26 March 2015 on the scope of contents of maps of health care needs (Journal of Laws of 2015, item 458).
[3] Pursuant to Article 19 of the Act, the first two editions of the maps will be developed by the minister responsible for health. As to maps of health care needs beyond 2021, they will be developed by voivodes and by their Voivodeship Councils for Health Care Needs, with significant support from the National Institute of Public Health – National Institute of Hygiene.
[4] The rules and conditions to be followed by a plan have been defined by Regulation of the Minister of Health of 10 October 2001 on the rules and conditions to be followed by a minimum plan of securing outpatient health care (Dz.U.01.121.1315).

Health Fund (Journal of Laws of 2003, No 45, item 391, as amended) introduced the obligation of voivodeship authorities to develop voivodeship health care plans and the obligation of the Minister of National Defence, the Minister of Justice, and the minister responsible for internal affairs to develop a plan of securing health care services for uniformed services[5].

This paper is not a direct attempt at developing a map of health care needs for oncology. Its purpose is to prepare data concerning a selected area of oncology, namely prevalence, i.e. to determine the incidence and 5-year prevalence of malignant neoplasms in Poland (current and projected values). Correct determination of current and historical values is the first necessary condition of correct estimation of future health care needs.

In many countries and in Poland registers of malignant neoplasms are kept[6]. The registers contain detailed information on oncological disease cases. The list of diagnoses on which data are gathered has been defined in line with the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems. The Polish register of neoplasms was established in 1952. It covers diagnoses C00-C97 (malignant neoplasms) and in situ neoplasms D00-D09. Generally, these are solid tumours as well as haematopoietic system and lymphatic system neoplasms. This volume focuses on solid tumours as the dominant group in cancer care[7], redefining it for the needs of international comparisons. This definition includes malignant neoplasms except NMSC (non melanoma skin cancers) and excludes malignant neoplasms of the haematopoietic system and lymphatic system (i.e. it includes diagnoses C00-C43, C45-C80, D05 according to the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems).

To prepare a projection of incidence (the number of newly diagnosed cases of cancer) and 5-year prevalence (the number of cases diagnosed in the previous 5 years), it is necessary to: (i) define methodology, in particular define the level of detail, and (ii) prepare the necessary historical data as the basis of projections. Because, as already mentioned, the results are to

[5] The rules and conditions to be followed by a plan have been defined by Regulation of the Minister of Health of 16 June 2003 on the conditions to be followed by voivodeship health care plans and on the scope of data necessary to develop such a plan (Dz.U.03.115.1087).
[6] For example in Finland (Suomen Syöpärekisteri), U.S. (SEER – Surveillance, Epidemiology and End Results), the Czech Republic, and England.
[7] Neoplasms of the haematopoietic system and lymphatic system, which are significantly different from the group in question, will be covered by one of the future volumes in this series.

be used towards the development of maps of health care needs, in line with the Regulation, the main objective of this volume is to determine the current value of incidence and 5-year prevalence of solid tumours in Poland with the highest possible degree of precision, considering available data. In other words: knowing that the obligation of physicians to send in a malignant neoplasm notification card for each oncological patient[8] is not always followed[9], the analyses are aimed at determining the number of cancer cases not registered in the National Cancer Registry.

The publication is divided into two main parts: theoretical (Chapters I-V) and empirical (Chapters VI-XII). Chapter I by Hanna Saryusz-Wolska presents the basic terminology used to talk about cancer care. The author presents the wide range of causes, symptoms, and techniques of diagnosing and treating malignant neoplasms. The chapter is a point of departure for further discussions. It emphasises the need for a more extensive analysis of modalities as cancer is treated through surgical treatment, radiotherapy, systemic therapy (including chemotherapy), and multi-modality treatment (surgical, radiotherapy, and systemic therapy).

The demographic and sociological factors influencing cancer incidence, such as age, sex, education level, and place of residence, are analysed in Chapter II. The author, Anita Gębska-Kuczerowska, argues that ageing of the population and changes in the social structure will result in a higher number of cancer cases, and thus will constitute an increasing challenge to the Polish heath care system.

Chapters III and IV are devoted to presentation of international experience in the methods of modelling cancer care. Chapter III by Filip Premik presents approaches to modelling epidemiological indicators in oncology. The author argues that regardless of the chosen study concept (statistical models vs. simulation models), it is of the utmost importance to apply scenario analyses at the same time to reduce projection uncertainty. In turn Chapter IV, by Barbara Więckowska and Margot Gralińska, presents models related to managerial decisions

[8] Article 32a(5) of the Act of 27 August 2004 on health care services financed from public funds (Journal of Laws of 2015, item 581, as amended).

[9] It should be noted that frequent failures to comply with such obligations are not characteristic of the Polish heath care system alone. This is the case also in health care systems of other countries, and in other areas of the [social] security system: for example, some vehicle owners fail to take out motor insurance.

in planning the health care service capacity required to meet the demand for oncological treatment. Decision trees, which constitute quantitative description of medical standards and evidence-based guidelines, are a popular tool used by a number of countries to assess demand for surgical treatment, radiotherapy, and systemic treatment. The authors claim that the model that constitutes a simplified description of reality is only a tool supporting, not replacing, the decision-making process. At the same time results of the model allow for gap analysis of availability of services (the difference between current and optimal use) and to verify the degree of adherence to medical guidelines.

The point of departure for forecasting incidence and prevalence is information on the current value of these indicators. The information is present in registries, of which cancer registers seem the most accurate and frequently kept registers in the majority of developed countries. As already mentioned, other national registers and the Polish Cancer Registry do not necessarily include information on all oncological patients (diagnosis and stage). For this reason, information in the registers should be supplemented. This topic is covered by Chapter V, which presents an original approach to linkage analysis of information in the National Cancer Registry and in payer's settlement database (National Health Fund). On the basis of information from these databases concerning treatment pathways and death following diagnosis, the Authors from the Department of Analyses and Strategy of the Ministry of Health describe the way in which algorithmic rules confirming a malignant neoplasm in a given person are defined (incidence) and then assign cancer stage (also in the case of individuals notified to the National Cancer Registry whose stage has not been entered). This action did not consist in simply merging the two data sets. Some patients were removed from the database of the National Cancer Registry as they were qualified as patients diagnosed in previous years (follow-up patients) on the basis of the services they received. Patients from the NHF database were removed if reported diagnosis was different from the National Cancer Registry (NCR database's precedence over the NHF database) or who, despite first entry, were qualified as follow-up patients on the basis of the services they received, and patients whose treatment did not indicate oncological treatment. The chapter ends with a description of methods applied to create a projection of cancer incidence and 5-year prevalence.

Chapters VI-XI belong to the group of chapters that concern empirical descriptive models for individual cancer streams. In other words, they constitute the practical application of

decision trees described in the theoretical part. Chapter VI describes models for lung cancer, Chapter VII – for breast cancer; the models for the other gynaecological neoplasms (cervical, endometrial, ovarian cancer) are covered in Chapter VIII. Chapter IX concerns cancer of the lower sections of the digestive tract, while Chapter X discusses bladder cancer. Finally, Chapter XI covers prostate cancer. The idea behind these chapters is to merge medical knowledge with statistical and IT knowledge. Therefore, each chapter has been drafted by experts: in medicine (Beata Freier – Chapters VII and IX; Iwona Włodarska-Polińska – Chapters VI and VIII; Iwona Skoneczna – Chapters X and XI) and in statistics (Beata Koń – Chapters VI and X, Filip Urbański – Chapters VII and VIII, Janusz Dagiel – Chapters IX and XI , Barbara Więckowska – Chapters VI, VII, IX). The structure of the chapters' contents is also similar: discussion of medical aspects of diagnostics and treatment of a given cancer stream and presentation of international experience in creating decision trees are followed by a description of a theoretical decision tree for Poland. As already mentioned, the trees are the result of effort on the part of an expert working group for oncology on the basis of available foreign models, Polish treatment standards, and expertise. Contrary to decision trees from other countries (separate ones for chemotherapy and radiotherapy with surgical treatment), the decision trees presented herein cover all oncological treatment techniques in aggregate. Descriptive treatment models based on 2012 data form the final part of each chapter.

The last chapter of the book, co-authored by staff of the Department of Analysis and Strategy of the Ministry of Health, presents the projected incidence and 5-year prevalence of solid tumours in Poland for the years 2015–2025. The methodology described in Chapter V was used to estimate total incidence of solid tumours except NMSC and excluding malignant neoplasms of haematopoietic system and lymphatic system (i.e. including diagnoses C00-C43, C45-C80, D05 according to ICD-10) in Poland in the years 2010-2012 at approximately 164,000 cases annually, i.e. almost 34% more than in the National Cancer Registry (approximately 123,000 cases annually); of which only 11% present at stage I, and most patients present in stage II and IV (approximately 33% each of all cases). The forecast of both incidence and 5-year prevalence for 2025 shows a significant increase of both epidemiological indicators – up to 204,000 new cases (+24%) and of 5-year prevalence to 533,000 cases (+16%), and thus point to significant challenges faced by the Polish health care system in the area of oncological treatment.

We hope that the readers will find this publication inspiring and that it will contribute to greater understanding of quantitative methods used in the area of healthcare and thus that it will contribute to popularisation of those quantitative tools as basis for governance. This is very important since the health care system should be developed in a well-planned manner, based on thorough analyses of the current situation and on reliable forecasts, and not only based on political decisions that can vary over time.

The authors would like to thank the reviewers of the publication namely Professor Maciej Krzakowski and Professor Bogumił Kamiński, for their valuable comments that resulted in enriching the topics presented in individual chapters.

Characteristics of cancer – diversity of causes, symptoms and treatment

Hanna Saryusz-Wolska[10]

Introduction

Today, it is widely believed that cancer is an acquired genetic disease resulting from accumulation of molecular damage in somatic cells leading to cancer progression (DeVita et al. 2009). The knowledge about mutations (molecular abnormalities) in cnacer cells is rapidly increasing[11].

Neoplasms can occur in almost any bodily organ and at every age, though certain locations are more frequent (e.g. lung, large intestine, breast in women, prostate in men), and incidence of the disease increases with age (DeVita et al. 2009; Didkowska 2014). The causes of neoplasm formation and development are complex and not fully understood. We know numerous carcinogenic agents inducing the disease and risk factors increasing the likelihood of cancer development. Symptoms of neoplasms are late and non-specific (may occur also in other diseases), and depend on location and stage of the disease. Therefore, screening is extremely important for early diagnosis of the disease. Depending on location, appropriate diagnostic algorithms are used to diagnose cancers. Histopathological type of cancer and stage of the disease as the moment of diagnosis (TNM staging system and clinical staging) serve as the basis for determining the treatment by a multi-specialist team of physicians. The treatment of cancers involves surgery, radiotherapy and chemotherapy, often as combination therapy, i.e. therapy including several of those methods in different combinations and sequences.

Characteristics of oncological diseases that distinguish them from other disorders include:

- varied and complex causes;
- difficult primary prevention due to their unknown causes;

[10] For Professor Leszek Woźniak, on the occasion of his 90th birthday.
[11] In 1985, 15 human oncogenes (DNA mutations) were known, in 2002 – 100, in 2009 – 410, while in 2011 – over 145,000 (COSMIC – *Cancer Gene Census Database*, cancer.sanger.ac.uk/cancergenome/project/census).

- complex, multi-stage and not fully understood development and progression of the disease (initiation, promotion and progression);
- various locations (place where the cancer develops first);
- various age of patients diagnosed with cancer, with the likelihood of the disease increasing with age (except for childhood cancers);
- late and non-specific symptoms;
- necessary constant monitoring to identify the tumour early;
- complex and difficult therapy (early and late side effects);
- uncertain treatment results, necessary constant monitoring;
- significant progress in research on pathogenesis (genetic diseases, we can identify numerous molecular abnormalities) and treatment (targeted therapies, cancer increasing often becomes a treatable chronic disease).

The purpose of the article is to present the diversity of causes, symptoms and diagnostic and therapeutic methods used in cancer care.

Ethiopathogenesis of cancers

Biological mechanism of formation and stages of development of oncological diseases

The causes of neoplasms are complex and still not fully understood. The key feature of cancer is the uncontrolled cell proliferation that grow locally and then infiltrate the surrounding tissues (expansion) and result in metastasis through spread by lymph nodes or by blood vessels (spread) (DeVita et al. 2009).

At every moment and during the entire life, human cells are affected by various agents (mutagens, carcinogens) causing disruptions and changes in genetic information included in the DNA of cells[12]. Cancer is a disease consisting in the change (mutation) of the activity or a

[12] DNA (deoxyribonucleic acid) consisting of deoxyribose, adenine (A), guanine (G), cytosine (C), thymine (T) and phosphate groups) is a carrier of genetic information in a cell. The chain of double-stranded DNA may be compared to a twisted ladder (helix shape), with base bonds forming its steps (always C-G and A-T). Human DNA consists of 3 billion base pairs in a specific sequences. Gene is a DNA fragment encoding a specific protein (sequence of amino acids in a polypeptide chain). Depending on the size of the encoded protein, a gene may consist of 1000 to one million base pairs. Human beings have 70,000 gene pairs. Chromosome is an organised structure of genetic material – DNA in a cell (human beings have 23 pairs of chromosomes). Mutation is a change in the genome (a change of only several bases in the DNA chain may lead to cancer development).

single gene or numerous genes regulating complex reproduction processes of somatic cells (DeVita et al. 2009). Neoplasm development process is a cascade of erratic signals, where mutated genes[13] initiate the production of inappropriate proteins (pathological signals). Cytokines[14], characterised by pleiotropy, i.e. the ability for multi-directional activity, are an example of cell signal regulation. Cytokines may act synergistically, antagonistically, as positive or negative feedback (triggering or suppressing the release of cytokines by another cell). A complex system regulating the transfer of signals between the cells, i.e. a signalling network (DeVita et al. 2009), is established.

The multi-stage process of cancer formation and development is called carcinogenesis (oncogenesis). It consists of the following stages: a. initiation (occurrence of a single mutation which may initiate the cancer development process), b. promotion (acquisition of the ability by the mutated cell to reproduce and transfer the inappropriate features to daughter cells), c. progression (the resulting clone of cancer cells behaves dynamically, other mutations occur, cancer cells have increasingly distorted functions regulating proliferation and increased capacity to infiltrate and build metastases) (DeVita et al. 2009).

Major carcinogens and risk factors

Carcinogens are substances or agents involved in cancer initiation or promotion. Substances inducing carcinogenesis are alkylating or acylating agents that are able to directly bind and damage DNA. Most cancer-causing chemical substances are pro-carcinogens which require metabolic activation in the body (DeVita et al. 2009).

Carcinogens are usually divided into:

- chemical agents (e.g. alkylating substances, polycyclic aromatic hydrocarbons, aromatic amines and azo dyes, nitrosamines, aflatoxins of plant origin, as well as asbestos and polyvinyl chloride – PVC occurring in the work environment);
- physical agents (ionising and ultraviolet radiation);

13 There are oncogenes (mutation activates a proto-oncogene, e.g. c-ERB-B (HER2), which participates in development of breast cancer) and anti-oncogenes (e.g. p53, which encodes the protein stabilising the DNA structure; the lack of this protein distorts DNA repair processes and contributes to the development of numerous cancers).
14 Currently over 100 cytokines are known, including interleukin (IL); hematopoietic cytokines; erythropoietin; SCF (stem cell factor); interferons (IFN type I and II); TNF (tumour necrosis factor).

- virus and bacterial agents (e.g. human papilloma virus – HPV, in particular its types 16 and 18 related to formation of cervical cancer, hepatitis B virus – HVB, Helicobacter pylori is a potential carcinogen causing chronic inflammation);
- hormonal factors (e.g. np. hormone replacement therapy – HRT[15]; hormonal contraception[16]).

Risk factors are individual characteristics and/or lifestyle elements increasing the risk (likelihood) of cancer. The most common risk factors include smoking, viruses, chronic inflammation, chemical and physical agents, diet, obesity and insufficient physical activity (DeVita et al. 2009). Knowledge about those factors allows modification of risk behaviour (primary prevention) and select people for screening (tests are performed in risk groups). Cancers occurring in different locations have different risk factors, e.g. (Krzakowski, Warzocha et al. 2014):

- lung cancer – smoking (active, but also passive), exposure to asbestos;
- colon cancer (obesity, high-fat and low-fibre diet, Crohn's disease, genetic risk factors – FAP[17]);
- breast cancer – family history (female relatives had breast cancer before menopause), BRCA 1 and BRCA2 gene mutation[18], hormonal factors (first period before 12 years of age and menopause after 55 years of age), long-lasting hormone replacement therapy.

Pathology of cancers

Anatomical pathology allows to differentiate malignant neoplasms based on an microscopic image, to determine its stage and to predict course of the disease, response to treatment and prognosis. A great diversity of anatomopathologic images is always accompanied by the principle of establishing histoclinical classifications, i.e. classifications where a given morphological image corresponds to a specific clinical process. Enormous diversity of cancer

[15] Depending on the hormones used, HRT increases the risk of endometrial, breast or ovarian cancer.
[16] Hormonal contraception slightly increases the incidence of breast cancer, and reduces the incidence of ovarian and endometrial cancer.
[17] FAP – familial adenomatous polyposis.
[18] Only approximately 5% of breast cancers are related to the mutation of BRCA 1 and BRCA2.

locations, microscopic images, molecular features and clinical course are the reasons for creation and constant modification of classifications of oncological diseases.

The International Classification of Diseases for Oncology (ICD-0)[19] has been in place for almost 30 years and is used for coding the site (topography) of cancers and their histological form (morphology) based on histopathological reports. The terminology used in ICD-O-3 is consistent with the International Histological Classification of Tumours, developed by WHO, however the ICD-O is not a system for determining the clinical staging.

WHO International Histological Classification of Tumours (currently WHO/IARC[20] Classification) is the basis for anatomopathologic diagnosis and presents characteristics of histopathological types of cancers occurring in various organs. Since 2007, the fourth edition of the classification has been published (WHO/IARC Classification of Tumours 4th edition; www.iarc.fr/en/publication/list/bb/index.php).

Special classifications may be used for anatomopathologic analysis of cancers[21].

The assessment of molecular features is now used to identify new clinical and pathological groups of cancers with a significant impact on treatment and prognosis. One example may be the classification of breast cancer subtypes according to the recommendations of St. Gallen Conference 2013[22].

The TNM Classification (UICC – Union Internationale Contre le Cancer, from 1997 UICC/ WHO[23] classification, currently AJCC/UICC[24] classification, 7th edition from 2009) was developed by the UICC in 1953 and allows for assessing the clinical progression of cancer (anatomical spread). The TNM Classification includes the assessment of the size of the tumour and whether it has invaded nearby tissue, the condition of lymph nodes and the presence of distant metastases (**T**umour – primary tumour from T0 to T4; **N**odus – lymph node from N0 dt N3; **M**etastasis – metastasis M0 or M1). The classification of progression is specific for

[19] International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3).
[20] WHO (World Health Organization); IARC (International Agency for Research on Cancer).
[21] E.g. REAL/WHO classification from 2008 is used in Hodgkin's lymphoma, the Ann Arbor staging system in non-Hodgkin lymphoma, the Gleason grading system in prostate cancer, the IASLC (International Association for the Study of Lung Cancer) – www.iaslac.org in adenocarcinoma.
[22] St. Gallen classification defines five subtypes of breast cancer based on ER, PgR, HER2, Ki-67, i.e. luminal A, luminal B, non-luminal HER2+, basal-like and special histopathological types.
[23] UICC/WHO (Union Internationale Contre le Cancer/World Health Organization).
[24] AJCC/UICC (American Joint Committee on Cancer/Union Internationale Contre le Cancer).

locations, therefore, there are TNM classifications for head and neck, breast, lung, prostate, liver cancers, etc.

The TNM system (classification – tumour, lymph nodes, distant metastases) provides the basis for classification into appropriate clinical stages. For cancers in some locations, other clinical progression classification systems are used[25]. Therapeutic recommendations always refer to the TNM classification and to a specific clinical stage.

The uniform TNM cancer staging system allows to: a. plan the treatment and determine its effectiveness, b. formulate the prognosis, c. compare treatment results, d. exchange information between oncologists (Kordek et al. 2013).

Diagnosis of cancer

Early detection and diagnosis of cancer, which is a prerequisite for effective treatment, requires using appropriate methods and algorithms of diagnostic procedures.

Screening consists in using a specific method (diagnostic test) to identify early stages of the disease or conditions posing a risk of disease development (pre-cancer stages) in healthy or apparently healthy (asymptomatic) individuals and to start appropriate treatment. Screening relies on the knowledge about the course of oncological diseases where the period between the onset of the diseases and the occurrence of clinical symptoms (called pre-clinical, asymptomatic stage or disease latency period) may last many years.

The European Union recommendations on screening include[26]:

- Smear test screening of cervical cancer (which largely detects precancerous conditions, not only neoplasm) should start between 20 and 30 years of age,
- Mammographic screening for women aged 50-60,
- Fecal occult blood test for people aged 50-74.

[25] E.g. Dukes' staging is used in colon cancers and Breslow's scale in melanoma.

[26] Report from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Implementation of the Communication from the Commission, from 24 June 2009, on *Action Against Cancer: European Partnership* [COM (2009) 291 final] and Second Implementation Report on the Council Recommendation of 2 December 2003 on cancer screening (2003/878/EC), Brussels, 23 September 2014, COM/2014/0584 final.

U.S. recommendations on screening are much wider[27].

Every diagnostic method has a specific sensitivity and specificity[28]. The results of tests applied in the framework of screening usually do not yield a final diagnosis, but rather divide the population into two groups: (a) no disease suspicion (negative result), and (b) with a disease suspicion (positive result) for further, in depth, diagnostics (Kordek, Pawlęga 2013).

The effect of a screening programme depends on many factors, such as seriousness and prevalence of a given disease, sensitivity and specificity of a test, possibilities for further diagnostics and treatment, improved prognosis thanks to early onset of treatment, universal participation in a test, and coverage of individuals from higher risk groups with the test (Zieliński 2002).

An *interview* allows determining: (a) risk factors (smoking, diet); (b) environmental exposure; (c) family history (genetic predisposition); (d) temporary symptoms (slightly raised temperature); (e) subjective symptoms (weakness).

A *physical examination*, which consists primarily of visual inspection and examination, is important for diagnosis of skin and soft tissue neoplasms, breast lesions, oral and nasopharyngeal lesions, female reproductive system neoplasm (standard gynaecological examination) and prostate neoplasm (*per rectum* examination). A physical examination determines, for example, the general condition of the patient, lesions of skin and subcutaneous layer, palpable lesions in breasts, and peripheral lymph nodes. The result of a physical examination, symptoms and risk factors (such as age, smoking) constitute the basis for initiating a relevant diagnostic algorithm (Krzakowski, Warzocha et al. 2014).

The most frequent symptoms suggestive of neoplastic disease are:

– skin or mucous membrane lesions (ulcerations that would not heal, birthmarks),

[27] NCCN *Guidelines version 1.2014 Breast Cancer Screening and Diagnosis* (the private insurance system operates according to commercial rules: a product must be sold, even if benefits to population health improvement are doubtful).

[28] Sensitivity of diagnostic tests is the ratio of true positive results to the sum of true positive and false negative results (100% sensitivity means that all sick individuals will be detected); specificity of diagnostic tests is the ratio on true negative results to the sum of true negative and false positive results (100% specificity means that no sick individual would be diagnosed as sick). In practice there are no 100% sensitive and specific tests.

- gastrointestinal disorders (difficulties in swallowing, digestion disorders, constipation, diarrhoea, presence of mucus and/or blood in stool),
- haematuria, difficulties urinating,
- haemoptysis, long-term hoarseness, change in character of cough or chronic cough,
- irregular menstruation (acyclic or after menopause),
- breast lump (nipple asymmetry or retraction) or lump in any other body part,
- enlarged lymph nodes,
- pain, weakness, considerable weight loss, slightly raised temperature (Kordek, Piekarski 2013).

Any of the above symptoms should be the reason for seeing a doctor and undergoing relevant diagnostic tests to confirm or rule out neoplasm. Symptoms of cancer are varied, poorly expressed, and unspecific, and full-blown cancers usually have pessimistic prognoses and are rarely treatable.

Assessment of patient's general condition is a significant factor affecting the decision on starting and/or selection of the method of therapy, as cancer treatment is a burden for patients and has many side effects (Fijuth 2014; Jeziorski, Nejc 2013; Potemski 2013). Currently[29] it is recommended to use the ECOG (Eastern Cooperative Oncology Group) scale that allows the determination of the general condition and quality of life of patients with cancer. The ECOG Performance Status is expressed in grades 0-5: 0 – Fully active, able to carry on all pre-disease performance without restriction; 1 – Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 – Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours; 3 – Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours; 4 – Completely disabled; cannot carry on any selfcare; totally confined to bed or chair; 5 – Moribound[30].

Diagnostic imaging is used for diagnosis, determination of its stage and monitoring treatment effects. Each neoplasm has a different spectrum of features that allow highlighting it using specific imaging methods (Krzemieniecki, Łuczyńska 2013: 58).

[29] In the past, the Karnofsky's scale or the Lansky's scale (in paediatric oncology) was used.
[30] www.ecog.org/general/perf-stat.html.

Imaging techniques include: classic X-ray, ultrasonography, computerised tomography (CT), magnetic resonance imaging (MRI), nuclear magnetic resonance imaging (NMRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), and hybrid imaging (SPEC-CT, PET-CT, SPEC-MR) (Stefańczyk, Majos 2013).

There are precise guidelines on diagnosing neoplasm in various localisations (recommendations of the Polish Society of Clinical Oncology (PTOK) concerning diagnostic algorithms) (Krzakowski, Warzocha et al. 2013).

a. An anatomopathologic *examination* constitutes a basic element of diagnostics, therapy planning, and prognosis determination in neoplasms, and cooperation of a pathologist with a clinician is a principle of today's oncology (Kordek et al. 2013).
b. An anatomopathologic examination is based on microscopic examination of: (a) a tissue sample (histopathological examination – sample, thick-needle biopsy, surgical biopsy, postoperative material), or (b) cell smear (cytological smear – aspiration thin-needle biopsy, cytological smear of spit and pleural exudate, cytological uterine cervix smear, blood smear). A routine anatomopathologic examination continues to be the most specific method of malignant neoplasm diagnosis (Olszewski, Prochorec-Sobieszek 2014). Currently, molecular tests have considerably expanded the assessment of neoplasm predictive factors and constitute an integral part of anatomopathologic diagnostics (Olszewski, Prochorec-Sobieszek 2014; Kordek et al. 2013).
c. An anatomopathologic examination allows to: (a) determine a precancerous lesion; (b) recognise neoplasm on the basis of morphological malignancy criteria (cellular atypia, mitotic index, i.e. high number of cells undergoing mitosis); (c) conclude on histogenesis (tissue from which neoplasm developed[31]); (d) determine prognostic factors (degree of histological malignancy and clinical staging according to pTNM); (d) determine predictive factors; (e) evaluate

[31] Although the colloquial use of the terms 'cancer' is tantamount to 'malignant neoplasm', in correct medical vernacular 'cancer' (carcinoma) stands for a malignant neoplasm that developed from epithelial tissue; sarcoma – malignant neoplasm from soft tissues (such as bone tissue, cartilaginous tissue, vascular tissue); melanoma – from pigment cells, lymphoma – from lymphoid tissue).

completeness of resection in radical surgery (resection margin) (Kordek et al. 2013; Olszewski, Prochorec-Sobieszek 2014).

d. Standardised anatomopathologic examination protocols are used. Full histopathological diagnosis should include: (a) neoplasm location and macroscopic description; (b) histopathological form; (c) grade; (d) stage, (e) other information important for a given neoplasm (e.g. in breast cancer: ER, PgR, HER2 and proliferation factor Ki-67) (Krzakowski, Warzocha 2013).

Cancer treatment overview

General rules and indications for cancer care

a. The basic rule of treatment is evidence-based medicine (EBM) and not to harm the patient. In oncology these are of special importance due to: (a) a very high number of clinical trials and reports on new therapies (Potemski, Kordek, Jeziorski 2013); (b) strenuous treatment and numerous side effects (Potemski 2013; Fijuth 2014).

b. In oncology, treatment strategy is determined by a multi-disciplinary team composed of clinicians and diagnosticians (radiologist, pathologist). Therapy planning is a selection of optimum methods from the point of view of effects and application sequence. The decision on therapy is influenced primarily by: (a) the histopathological type of neoplasm; (b) clinical stage; (c) other predictive factors; (d) general condition of the patient and co-existing conditions. Oncological treatment standards result from continuously updated recommendations of national and international groups of specialists, such as the recommendations of the Polish Society of Clinical Oncology (PTOK) based on ASCO (American Society of Clinical Oncology) guidelines[32], recommendations of NCCN[33], FIGO[34] (reproductive system neoplasm treatment in women) and ESO-ESMO[35] (advanced breast neoplasm treatment) (Cardoso et al. 2014).

[32] www.onkologia.zalecenia.med.pl.
[33] NCCN –*The National Comprehensive Cancer Network – Clinical Practice Guidelines in Oncology – NCCN Guidelines*™, http://www.nccn.org/professional/physician_gls/f_guidelines.
[34] FIGO (*International Federation of Gynecology and Obstetrics*), www.figo.org.
[35] ESO-ESMO (*European Society of Oncology – European Society of Medical Oncology*).

Cancer treatment modalities

Surgical treatment

Surgery is the oldest treatment method, used for thousands of years. There are several basic rules of cancer surgery: (a) to operate as early after analysis of histopathological diagnosis as possible; (b) to operate radically, i.e. to resect tumour with a margin of healthy tissues and regional lymph nodes in a single block (Jeziorski, Nejc 2013). Such procedure requires expertise in surgery techniques, including plastic and reconstructive surgery, and ability to work in an oncological team with diagnosticians (pathologist, radiologist) and other oncology specialists (radiotherapists and chemotherapists). An experienced oncological surgeon can refrain from an extensive and mutilating surgery with no prospect of a positive effect for the patient (Jeziorski, Nejc 2013).

There are several types of surgical procedures in oncology:

- diagnostic procedures (to collect tumour tissue sample for a test and histopathological diagnosis, such as exploratory laparotomy, lymph node biopsy),
- radical procedures (planned to effectively cure the patient),
- sparing operations (reduced extent of the operation to preserve a part of an organ for a good aesthetic or functional effect, e.g. breast surgeries sparing a part of the organ or rectum surgeries with end-to-end intestine anastomosis and preservation of sphincter function) that require supplementary radiotherapy as local treatment,
- palliative operations (conducted to: (a) alleviate symptoms, such as bypass, feeding fistulas; (b) reduce tumour mass and improve the effects of radiotherapy or chemotherapy; (c) prevent direct threat of death due to e.g. bleeding from tumour disintegration) (Jeziorski, Nejc 2013).

Sentinel lymph node biopsy is important in determining a therapeutic strategy[36]. Diagnosis of metastases in a lymph node is an indication for regional lymphadenectomy (lymph node dissection) and potential systemic treatment.

Oncological surgery also includes various methods of destroying cancerous tissue (cryotherapy, electroresection and electrocoagulation, laser procedures) and increasingly

[36] Sentinel lymph node (SLN) is the closest node to which lymph from the primary neoplasm focus flows.

frequently applied endoscopic procedures that allow reaching lesions per rectum or through the urinary tract without the need to open the abdominal integument.

Radiotherapy

Radiotherapy is a local treatment method (i.e. in the area covered by radiation) using ionising radiation that triggers a cascade of physical chemical, biochemical, and biological changes that result in destruction of neoplasm in live organisms (Fijuth 2014).

The mechanism of ionising radiation's effect on live matter consists in destroying cell structure: (a) directly (mainly DNA); (b) indirectly (through radiolysis of water and emergence of hydroxyl radicals). Both mechanisms disturb DNA and RNA synthesis and cause numerous enzymatic changes in cells.

The use of ionising radiation in neoplasm treatment is connected with the following notions: (a) radiosensitivity; and (b) radiocurability. Both healthy and cancerous cells are sensitive to radiation, and this sensitivity is the higher, the greater proliferation activity and the lower cell maturity (malignant neoplasms have higher radiosensitivity, although it is diversified and depends on many factors). Radiocurability (so-called therapeutic indicator) is the quotient of radiation dose tolerated by healthy tissue and average dose lethal for cancerous cells of a given tumour (Dyczka, Jassem, Fijuth 2013).

The characteristics of radiation used in radiotherapy include: (a) radiation type – electromagnetic (photonic) or corpuscular radiation (electrons, protons, neutrons); (b) radiation energy – megavoltage[37] or conventional radiation; (c) radiation source location towards the patient – teleradiotherapy or brachytherapy[38]. To improve treatment efficiency, total radiation dose is divided into many parts (fractions). At present, dose fractioning methods are modified, for example by hyperfractionation (administering a single dose in a day instead of 2-3 smaller doses), accelerated fractionation (higher daily dose or shortened radiation time without weekend intervals), or accelerated radiation – hyperfractionation. Also

[37] Currently megavoltage (high energy) radiation is generated by special devices (linear accelerators) where electron or photon beams have energy of 4–20 MeV.
[38] Teletherapy (external beam radiotherapy, radiation source is away from the patient), brachytherapy (source of radiation is in direct contact with the patient).

unconventional radiotherapy techniques are used, such as stereotactic radiosurgery of central nervous system neoplasms or extracranial tumours[39] (Fijuth 2014).

Radiotherapy may be:

- radical, aimed at effective treatment of neoplasm, e.g. skin neoplasm, seminoma,
- adjuvant , e.g. following sparing breast cancer operations,
- inductive (neoadjuvant), e.g. it may precede surgical treatment of rectum cancer,
- palliative, for example to alleviate the symptoms in inoperable tumours and/or failed therapy of a different kind (Dyczka, Jassem, Fijuth 2014).

Indications for radiotherapy and treatment planning are complex decision-making and technical processes defined by a team of experts (with key role of radiotherapists and medical physicists) (Fijuth 2014; Dyczka, Jassem, Fijuth 2013). Radiotherapy involves the risk of side effects which are divided into: (a) severe and late; (b) local and systemic (Fijuth 2014).

Systemic treatment

Systemic treatment[40] includes: (a) chemotherapy (administering various cytostatic medicines); (b) hormone therapy (in treatment of hormone-dependent neoplasms, e.g. breast cancer, prostate cancer, endometrial cancer, thyroid gland cancer), (c) biological therapy (e.g. immunotherapy, inhibitors of proteins partaking in cancer development processes[41]) (Potemski, Stempczyńska 2013).

The types of systemic treatment are as follows: a. radical, b. supplementary (adjuvant), c. initial (pre-surgery, induction, neoadjuvant), d. regional (used locally, e.g. to hepatic artery, intrathecally, intraperitoneally), e. palliative (Potemski, Stempczyńska 2013).

[39] Brain tumour radiation technique that consists in one-off administration of a high dose of radiation to a specified tissue volume (special masks and stereotactic frames are used to achieve high repeatability of 3D positioning). At present, also stereotactic extracranial radiosurgery is employed with the use of a CyberKnife – a miniature accelerator mounted on a hydraulic arm that allows to point a radiation beam at multiple angles (Fijuth 2014: 102–103).

[40] The term "systemic treatment" refers to system-wide scope of therapy, as opposed to the local one, i.e. in the site where surgery is performed or where radiation is used. The aim of systemic treatment is to reach to sources of metastasis scattered in various parts of the body (metastatic cancers). Systemic treatment is a treatment of choice in haematopoietic system cancers and lymphomas.

[41] E.g. monoclonal antibodies – trastuzumab in breast cancer with over-expressed HER2; small-molecule drugs – imatinib, erlotinib, sunitinib (tyrosine kinase inhibitors); cytokines – interferons, interleukin IL-2.

Chemotherapy consists in using cytostatic drugs for:

- radical treatment (full recovery or long-lasting remission in cancers with high chemosensitivity);
- palliative treatment (extension of survival and/or improvement of the quality of life, when benefits from treatment exceed the risk of deterioration of the patient's overall condition due to adverse effects of individual drugs (Krzakowski, Wyrwicz 2013).

Cytostatic drugs are classified on the basis of their chemical structure and mechanism of impact on cell cycle stage. Cytostatics are divided into: a. alkylating drugs, b. antimetabolite drugs, c. anticancer antibiotics, d. podophyllotoxin derivatives, e. plant alkaloids, f. taxoids, g. camptothecin derivatives (Krzakowski, Wyrwicz 2013). Names of chemotherapy treatment schemes are usually abbreviations of first letters of international or commercial names of individual cytostatic drugs.

Sensitivity of individual cancers to cytostatics is established empirically based on clinical trial results. In general, the less mature the cancer (i.e. more different from the regular cell from which it originates) and the more frequent cell divisions, the more sensitive the cancer is to chemotherapy (Potemski, Stempczyńska 2013).

The decision on using chemotherapy should be based on the following:

- type of cancer (organ where it originates, histological type, clinical stage, sensitivity to cytostatic drugs);
- overall condition of the patient (objective assessment according to standardised classifications, history of diseases and/or co-existing diseases, drugs used);
- possibility to obtain benefits compared to the likelihood of adverse effects of the planned treatment (Krzakowski, Wyrwicz 2013).

The response to systemic treatment is classified as: a. complete remission (CR), b. partial remission (PR), c. stabilisation of the disease (SD), d. progression (Potemski, Stempczyńska 2013). A significant progress in treatment was achieved by using the so-called targeted therapy[42] with targeted molecular drugs (Dziadziuszko, Jassem 2014; Potemski, Stempczyńska

[42] Systemic treatment is also called targeted molecular therapy, personalised medicine. The current list of drugs approved by the FDA for use in molecular therapy is available at www.fda.gov.

2013). Systemic treatment, mainly chemotherapy, may have numerous undesirable effects (Potemski 2013).

Combination treatment

Combination treatment includes surgery, radiotherapy and systemic treatment in various combinations and sequences (Jassem 2013).

Types of strategies in combination treatment:

- sequential treatment – initial (induction, neoadjuvant), e.g. pre-surgery radio- or chemotherapy; adjuvant, e.g. post-surgery radio- or chemotherapy, or chemotherapy after radiotherapy;
- simultaneous treatment – combining various methods at the same time, e.g. intraoperative irradiation, systemic treatment in parallel with irradiation (radiochemotherapy).
-

Prognosis and monitoring of the patient after cancer treatment

Prognostic factors

Prognosis in cancer patients is usually measured with 5-year survival rate after treatment. The result of cancer treatment is never certain and may only be estimated. According to estimates, lasting recovery may currently be obtained in approximately 50% of all patients (Jassem 2013). Detection of cancer at an early stage (i.e. smaller tumour, without extensive infiltration of surrounding tissues or metastases in lymph nodes) results in a greater chance for recovery (Kordek, Piekarski 2013). Factors affecting the prognosis (risk of recurrence and death) include: a. features of the cancer (location, histopathological form, grade, molecular characteristics), b. stage (size of tumour, metastases to lymph nodes and distant organs), c. patient related factors (overall condition, age, co-existing diseases). The main prognostic factors in e.g. breast cancer include: a. size of tumour, b. histopathological type and grading, c. number of affected armpit lymph nodes, d. infiltration to lymphatic vessels and veins around the tumour, e. ER, PgR, HER2 and proliferation marker Ki-67 (Olszewski, Prochorec-Sobieszek 2014; Krzakowski, Warzocha et al. 2013).

As a result of the progress in cancer treatment, 5-year survival rates for patients diagnosed in the years 2000-2002 are of historical value. The value of anticancer treatment is assessed based on numerous indicators, such as a. overall survival (OS), b. disease-specific survival (DSS), c. progression-free survival (PFS), d. time to progression (TTP)[43], e. disease-free survival (DFS) (Płużański, Socha 2014).

Survival rates differ between the countries for many reasons, with most important being the organisation and functioning of the health care system, as well as oncological knowledge and health behaviour of the society. Late diagnosis, advanced clinical stage of the disease at the moment of treatment, unequal access to health care and modern treatment methods results in shorter survival of patients (Wojciechowska, Didkowska, Zatoński 2010).

Monitoring tests recommended after cancer treatment

Due to few prospective clinical trials, recommendations for optimal monitoring test regimes are mostly based on retrospective observations or expert opinions. Depending on the location and type of cancer, specific tests and their frequency are recommended (they are more frequent right after the treatment, and usually performed every 12 months after 5 years from the treatment) (Jassem et al. 2014). Studies show that the effectiveness of monitoring tests performed by specialists in oncology and appropriately trained family physicians is comparable (Jassem et al. 2014). Five-year survival after cancer treatment without recurrence and/or distant metastases is considered to be effectively a cure. Due to the risk of late recurrence (after more than 5 years from the first treatment), monitoring tests are performed for many years.

Summary

Today, it is widely believed that cancer is an acquired genetic disease resulting from accumulation of molecular damage (mutations) in somatic cells.

[43] Progression is the progress, development of the disease.

The European Code Against Cancer[44] points to two main strategies in oncology: a. some cancers can be prevented by modifying lifestyle[45], b. possibilities to effectively treat cancer increase, when it is detected at an early stage.

Cancers are a large group of diseases, varying in location, symptoms, methods of diagnosis and treatment, as well as prognosis. Early detection and diagnosis of cancer, which is a prerequisite for effective treatment, requires using appropriate methods and algorithms of diagnostic procedures that are specific for a given cancer location. Screening is increasingly important in early detection of the disease.

Anatomopathologic examination (e.g. biopsy collected during endoscopy) is the basis for cancer diagnosis. The stage of the disease (TNM classification, staging) is determined using primarily imaging techniques (e.g. RTG, USG, MMG, KT, PET, PET-KT), which assess the extent of cancer (infiltration of surrounding tissues, metastases in lymph nodes and distant organs). Location and histopathological of cancer, clinical stage and overall condition of the patient affect the choice of treatment.

Treatment standards in oncology, developed by national and international groups of experts (recommendations of the Polish Society of Clinical Oncology) are based on research results (evidence-based medicine, EBM). The decision on the choice of therapy regime in oncology is made by a multi-specialist team, since treatment may involve surgery, radiotherapy, systemic treatment (chemotherapy, hormone therapy) and combination treatment (various combinations and sequences of surgery, radiotherapy and systemic treatment). Progress in biological and clinical sciences related to the natural progression of the oncological disease, assessment of molecular predictive factors (response to treatment) and use of new, targeted molecular drugs has significantly improved prognosis in some groups of patients. In future, algorithms of diagnosis and therapy will be subject to further modifications resulting from progress in knowledge.

[44] http://cancercode.eu/.
[45] http://www.who.int/cancer/prevention/en/.

Bibliography

American Joint Committee on Cancer (AJCC). (2009) *AJCC Cancer Staging Manual*. 7th edition. Ed. Edge S.B., Byrd D.R., Compton C.C. et al. New York: Springer.

Cardoso, F. et al. (2014) ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2), *The Breast*, 23, pp. 489–502.

Curtis, Ch. et al. (2012) The genomic and transcriptomic architecture of 2,000 breast tumours reveal novel subgroups. *Nature*, 486, pp. 346–352.

DeVita, V.T., Lawrence, T.S., Rosenberg, S.A. (2014) *DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology*. 10th edition. Philadelphia: Lippincott Williams & Wilkins.

Didkowska, J. (2014) Epidemiologia i profilaktyka. in: *Onkologia kliniczna*, vol. 1., ed. Krzakowski, M., Potemski, P., Warzocha, K., Wysocki, P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 1–15.

Dyczka, J., Jassem, J., Fijuth, J. (2013) Radioterapia nowotworów. in: *Onkologia. Podręcznik dla studentów i lekarzy*. ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 74–84.

Dziadziuszko, R., Jassem, J. (2013) Terapie ukierunkowane molekularnie w onkologii. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 97–101.

Fijuth, J. (2014) Radioterapia in: *Onkologia kliniczna*, vol. 1. Red. Krzakowski, M., Potemski, P., Warzocha K., Wysocki P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 87–106.

Jassem, J. et al. (2014) Badania kontrolne po leczeniu w najczęstszych nowotworach litych u dorosłych. *Nowotwory Journal of Oncology* 64 (5), pp. 415–435.

Jeziorski, A., Nejc, D. (2013) Podstawy chirurgii onkologicznej. Biopsja węzła wartowniczego. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 85–88.

Kordek, R., Pawlęga, J. (2013) Badania przesiewowe (skrining). in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 52–61, 74–84.

Kordek, R., Jesionek-Kupnicka, D., Kusińska, R. (2013) Podstawy patologii onkologicznej. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 112–117.

Krzakowski, M., Wyrwicz, L. (2014) Leczenie systemowe. in: *Onkologia kliniczna*, vol. 1. ed. Krzakowski, M., Potemski, P., Warzocha, K., Wysocki, P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 107–134.

Krzakowski, M. (ed.), Warzocha, K. (ed.) et al. (2013). Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych 2013, vol. 1. Gdańsk: VM Media sp. z o.o. VM Group sp.k.

Krzemieniecki, K., Łuczyńska, E. (2014) Rozpoznanie i określenie stopnia zaawansowania. in: *Onkologia kliniczna*, vol. 1. ed. Krzakowski, M., Potemski, P., Warzocha, K., Wysocki, P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 58–78.

Międzynarodowa Klasyfikacja Chorób dla Onkologii. 3rd edition. Centrum Onkologii – Instytut, Warsaw 2007.

Olszewski, W.T., Prochorec-Sobieszek, M. (2014). Patomorfologia. in: *Onkologia kliniczna*, vol. 1. ed. Krzakowski, M., Potemski, P., Warzocha, K., Wysocki, P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 39–57.

Płużański, A., Socha, T., Ocena wartości przeciwnowotworowego leczenia. in: *Onkologia kliniczna*, vol. 1. ed. Krzakowski, M., Potemski, P., Warzocha, K., Wysocki, P. Gdańsk: VM Media sp. z o.o. VM Group sp.k., pp. 400–401.

Potemski, P., Kordek, R., Jeziorski, A. (2013). Nowe leki i metody w onkologii. in: *Onkologia…* ed. Kordek R. Wyd. IV. Gdańsk: Via Medica, pp. 348–350.

Potemski, P., Stempczyńska, J. (2013) Systemowe leczenie nowotworów. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 89–96.

Potemski, P. (2013) Objawy niepożądane systemowego leczenia nowotworów. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 102–108.

Stefańczyk, L., Majos, A. (2013) Diagnostyka obrazowa w onkologii. in: *Onkologia…* ed. Kordek, R. Wyd. IV. Gdańsk: Via Medica, pp. 118–125.

WHO (2008) *International Statistical Classification of Diseases and Related Health Problems*. 10th revision. Vol. 1.

Wojciechowska, U., Didkowska, J., Zatoński, W. (2010) Pięcioletnie przeżycia chorych na nowotwory złośliwe w Polsce. *Nowotwory Journal of Oncology*, 60 (2), pp. 122–128.

Zieliński, A. (2002) Najczęściej spotykane błędy w badaniach przesiewowych. *Przegląd Epidemiologiczny*, 56, pp. 193–198.

Impact of socio-demographic factors on epidemiology of cancers

Anita Gębska-Kuczerowska

Introduction

Cancer poses a great challenge for the organisation of the health care system in Poland, as in other European countries (Allmeni 2010; Bielska-Lasota 2012, Gehlert 2014; Government Population Council 2014). It is not only the fact that the scale of the phenomenon is increasing in epidemiological terms, but also it concerns its components, i.e. demographic transformation and economic and social implications, i.e. direct and indirect costs (Nakanotani 2014; Valsecchi 2014). In order to minimize the damages caused by this phenomenon, the state must intensify its actions, also by changing the approach to health, including by wider inclusion of all its determinants and paying attention to the possibility of preventing oncological diseases in terms of environmental and genetic risk factors, as well as factors related to specific lifestyles (Arnold 2012; Vineis 2014). Equally important for cancer control within the health care system are well-planned and coordinated primary, secondary and tertiary prevention, e.g. rehabilitation of patients after remission, recovery from cancer (White 2014; Coleman 2011; Dacus 2014).

The aim of the article is to present the possibilities of forecasting the epidemiology of cancer through better understanding of the mechanisms of impact of the demographic structure on health situation of the population. Descriptive studies discussed further on constitute the beginning of analyses illustrating the links between health situation and demographic factors. However, it must be remembered that they require further, in-depth studies using different methods to evaluate the actual causative link.

Oncological epidemiology in Poland and in selected regions

According to the data of Globocan, in 2012 there were 14.07 million new cases of cancer reported around the world, while 8.20 million people died of those diseases. The number of

new diagnosed cases of cancer in the EU[46] was 2.64 million, while the number of deaths for 1.28 million.

Data from the National Cancer Registry (hereinafter referred to as the NCR) show that in the same year Poland recorded 0.15 million new cancer cases and 0.095 million deaths of oncological patients. Based on the NCR it is estimated that in 2011 about 154,000 people developed cancer in Poland. Not all cases were entered into the register[47], only 71,800 new cases of neoplasm diagnosed in men and 72,600 cases in women were registered. In 2011 the standardised incidence ratio for the total population was estimated at 222.2/100,000. For men, the ratio was 251.5/100,000 and was higher than for women (207.3/100,000). The above values are estimates, which will be presented in the following chapters that discuss the National Cancer Registry. Compared to other EU countries, Poland belongs to those with relatively low incidence (registered) and high malignant neoplasm-related mortality. Relative 5-year survival ratios were estimated at 38.8% for men and 48.3% for women. 5-year prevalence was 323,600 in Poland (54% – breast, prostate, large intestine, lung) (Bielska-Lasota 2012).

Change dynamics – time trends

According to WHO statistics, Poland (similar to many EU countries[48]) has recorded systematic increase in cancer incidence since the beginning of the 1980s: in 1980 the indicator was 219/100,000 in Poland and 414/100,000 in EU. This increase in the incidence in the period under analysis proves not only that the scale of cancer problem increases, but also gives reasons to believe that the increasing trend will continue.

WHO data show that in Poland standardised cancer mortality rates for all age groups increased from the beginning of 2000 to 218/100,000 and from 2001 they decreased to 191/100,000 (in 2011). In EU countries standardised death ratios until 1983 reached higher values than in Poland (202/100,000), but they decreased regularly in time, for example in 2011 to 160/100,000.

[46] 28 EU Member States, IARC, accessed on: 21 April 2015.
[47] More in Chapter 1. Material and methods in chapter 3. Voivodeship analysis. Assessment of registration completeness and quality, pp. 28-29 (Didkowska 2011).
[48] 15 EU countries, as before May 2004, WHO, HFA-db, accessed on: 15 April 2015.

In younger age groups (up to 64) in both EU countries and Poland the values of standardised death ratios decreased: for example in 2011 in Poland the value was 87/100,000 and in EU countries the figure was 64/100,000[49].

Age – individual ageing process (chronological ageing) and risk of oncological disease development

For the majority of oncological diseases, the values of age-standardised incidence and death ratios are higher in subsequent (older) age groups. According to Globocan[50] data, in Poland in 2012 raw incidence ratios for both sexes displayed an increasing trend and were as follows in various age brackets: 0–14: 12.4/100,000; 45–49: 257/100,000; 55–59: 699.4/100,000; above 75: 1,626.8/100,000. The death rate values also displayed an increasing trend in subsequent age groups: for children aged 0–14 it was 2.7.100,000; for adults it was: 45–49: 109.6/100,000; 55–59: 367.2/100,000; and above 75: 1,344.8/100,000. Similar trends of the number of diagnoses and deaths due to an oncological disease are observed for the global and Europe's population.

The above differences in neoplasm epidemiology depending on age are spectacular and also recorded in other countries. For example in 2012 for children aged up to 14 living in Europe the raw cancer incidence ratio was 14.3/100,000 and the death rate was 2.4/100,000, while for people aged 75+ the incidence ratio was 1,924.5/100,000 and the death rate was 1,386.7/100,000.

As more and more oncological diseases become chronic[51], due to better detectability and accumulation of various risk factors throughout a long life, the probability of diagnosing neoplasm in older people is higher (Allmeni 2015; White 2014). It is not solely the result of ageing, i.e. genetically programmed biological apoptosis. With individual ageing, the mechanism becomes more complex through accumulation of the risk of development and death due to an oncological disease (Niccoli 2012). Thus, multi-stage oncogenesis is triggered by complex genetic mechanisms (i.e. biological ageing) and mechanisms resulting

[49] In the 1980s they were: 88/100,000 in the EU and 117/100,000 in Poland.
[50] The data do not include melanoma statistics.
[51] Due to improved survival rate.

from chronological ageing, such as length of exposure to various risk factors (Nitsche 2014). Potential risk factors are: exposure at work (occupational exposure), lifestyle exposure (e.g. smoking, physical activity inadequate to supply of calories, incorrect diet), and environmental factors (pollution, e.g. with carcinogens) (Ott 2011).

Epidemiological data of the U.S. National Cancer Registry for 2007-2009 show that the risk of being diagnosed with neoplasm and the risk of death due to neoplasm increases with age, regardless of race. It was estimated that the risk of developing neoplasm increases nearly two times for individuals aged 30-40, and the risk of death was the highest for people aged 50[52]. The question on the risk of an oncological disease attributed solely to ageing was postulated by the telomere hypothesis that explained common mechanisms of biological ageing and oncogenesis. Yet, it plays a role in understanding neoplasia combined with age only to a limited extent. It does not offer unambiguous answers to many questions concerning this complex process at the level of genes and their modification by external factors[53], nor does it take into account the complexity of all pathomechanisms, self-regeneration problems and accumulation of carcinogenic mutations (Finkel 2007).

Neoplasm prevention and prophylaxis increasingly frequently highlights so-called modifiable risk factors, or factors related to the environment and lifestyle that significantly modify and shape the risk resulting from genetic factors, i.e. BMI, smoking, etc. (Sasco 2014; Supic 2013). They are important due to the possibility of modification, the scale of their spread in the Polish population and frequently intensity that increases with age.

An example of a relationship between higher malignant neoplasm development risk and exposure to modifiable risk factors connected with lifestyle that is important for epidemiological reasons covers observations and conclusions from assessment of the impact of excessive weight (BMI). The impact of excessive weight and resulting health consequences is complex: it links hyperinsulinaemia and increasing insulin resistance with induction of neoplasia processes (Niccoli 2012). In-depth clinical and laboratory analyses in this respect were triggered by earlier epidemiological observations concerning the link between excessive weight and obesity and higher neoplasm risk. It is estimated that 3-6% of new neoplasm

[52] SEER Cancer Statistics Review 1975–2009, Devcan version 6.6.1. April 2012, National Cancer Institute (http://surveillance.cancer.gov.pl/devcan).
53 Epigenetic mechanisms.

cases diagnosed in individuals above 30 is caused by excessive weight. A particularly strong cause and effect relationship is observed for endometrial neoplasms, post-menopausal breast cancer, and colorectal cancer (Arnold 2015).

Among other modifiable risk factors (and length of exposure to them) is chronic inflammation, which frequently creates conditions favourable to oncogenesis together with their own defensive mechanisms. A classic example is the relationship between chronic HPV infection and development of uterine cervix cancer, HBV and HCV infection with development of underlying liver cancer, *Helicobacter pylori* infection with development of stomach cancer, etc. (Belpomme 2007; Ott 2011).

Considering the complex oncogenesis mechanism and information on risk factors and their distribution in the population[54] and exposure time, it is difficult to unambiguously state which neoplasms have direct cause and effect relationship with age (White 2014). Undoubtedly we can only observe increase of the value of incidence indicators for the majority of neoplasms, and an increase in the risk of multiple morbidities and death, with age (Nitsche 2014).

Gender and neoplasms

Basically, from the anatomical point of view male-only neoplasms are neoplasms of male reproductive organs, i.e. testicles and prostate, and female-only neoplasms are endometrial, cervical, and ovarian neoplasms. Other neoplasms can develop in both sexes with various frequency and change their epidemiological expression with a change in risk factors, e.g. an increase in lung cancer incidence in women with increased tobacco addiction or very rare breast neoplasm in men.

Globocan statistics show that in 2012 the most frequent newly diagnosed neoplasms in men globally were: lung, prostate, and colorectal neoplasms. In men in Europe, the most frequently diagnosed neoplasms were: prostate, lung, and colorectal, respectively. Globally,

[54] I.e. risk differentiation due to differences in environmental exposure, related to sex, socio-economic status, profession, etc.

the highest mortality rates of men were recorded (in decreasing order) for lung, liver, and stomach cancers, while in Europe for lung, colorectal, and prostate cancer.

In 2012 women globally most frequently developed breast, colorectal, and cervical cancer. Among European women, the most frequent diagnoses concerned breast, colorectal, and lung cancers. The highest death rate of women in Europe was recorded for breast, lung, and colorectal neoplasms.

The above epidemiological data show that for women in Europe the greatest fatal health threat was breast cancer, while for men it was lung cancer, followed by prostate cancer. Globocan statistical data show that in the case of men the malignant neoplasm death rate is affected by lifestyle to a greater extent than by sex. Similar trends of increasing significance of lifestyle to the health situation in terms of civilisation disease epidemiology (including neoplasms) apply to digestive tract neoplasms.

Oncological diseases in Poland by gender in the last decade

Data from the National Cancer Registry database show that five most frequent malignant neoplasms developed by men in Poland in 2002 were: lung and bronchus cancer (22.7%), prostate cancer (12%), bladder cancer (6.6%), and large intestine cancer (6.5%). In 2012 two most frequent cancers were still lung and bronchus cancer and prostate cancer (19.9% and 14.3%, respectively). In addition, a higher share of skin cancers (7.7%) was recorded, followed by large intestine cancer (6.8%) and bladder cancer (6.7%).

In the case of women in 2002 the most frequent morbidities were: breast cancer (21.9%), lung cancer (8.2%), endometrial cancer (7.1%), skin cancer (7.1%), large intestine cancer (6.1%), and ovarian cancer (5.2%). In 2012 the most frequent cancer was breast cancer (22.2%). Similar to men, a higher share of skin cancers was recorded (8.8%) – it was the second most frequent oncological diagnosis. Third place as occupied by lung cancer (8.7%), followed by endometrial cancer (7.1%), large intestine cancer (6%), and ovarian cancer (4.6%).

According to the NCR Report, assessing incidence trends for all neoplasms in last decades it should be noted that in the male population in the 1980s and 1990s an increasing trend was

recorded, while past the 1990s the situation has been stable (Didkowska 2011). In the case of the female population, a disturbing increasing trend in neoplasm incidence is observed.

According to the NCR in 2011 cancer care caused death of 92,140 people, of which 56% were men. The standardised death rate for men was 173.5/100,000 and it was nearly two times higher than for women: 97.6/100,000. The most frequent cause of death of men and women due to neoplasm was lung cancer. The second most frequent cause of deaths among men was prostate cancer, and among women it was breast cancer (Didkowska 2011).

In the last decade the most frequent causes of deaths of men due to neoplasm were lung and prostate cancers (Didkowska 2011). Lung cancer is strongly linked with tobacco smoking (duration and volume of exposure), while prostate cancer is related to age (Quinn 2002). In the case of women, in the analogous period the main reasons for cancer-related deaths were lung and bronchus and breast cancers.

Neoplasm epidemiology – age and gender

According to NCR data, in Poland time trends of men's and women's mortality remain stable, but differ in various age groups, also due to causes (i.e. neoplasm location and type). Neoplastic disease expression varies not only by sex, but also by age. Epidemiological data for 2011 from the NCR for various age groups can serve as an example here (Didkowska 2011).

Deaths of children aged 0-19 due to neoplasm constituted 6.5% of total deaths for boys and 6.7% for girls. In this age group, the most frequent causes of newly diagnosed neoplasms and of deaths were leukemias, lymphomas, and brain neoplasms.

For people aged 20-44, incidence ratios for women were twice as high as for men, but from the beginning of the 1990s the values have reduced. The most frequent cause of deaths of young men in 2011 were brain neoplasms, the most frequently diagnosed morbidity was testicular cancer, while young women most frequently developed breast cancer and died of it most frequently.

Education level and occupation and cancer

Education level frequently determines occupation, and these two demographic parameters involve certain risk. The occupation determines a list of risk factors (physical, chemical and biological), while education specifies general possibilities of modifying these risk factors through knowledge and skills, acquired and own predispositions (Belpomme 2007; Shariff-Marco 2014). Information about the working time and occupation provide more precise information about the health risk rather than information about education alone. Epidemiological data regarding the health risk come from studies, in which both time and exposure dose precisely determine the health risk. Along with the development of knowledge the information resource about carcinogens and their number expands (Belpomme 2007; IARC 2015; Wilczyńska 2005). The evaluation of time and kind of occupational exposure is important in case of monitoring the risk factors at work for the prevention and prophylaxis of diseases, as well as in case of judicial decisions about an occupational disease (Rushton 2010). In the current situation on the labour market education is a very general indicator, which is often analysed together with other socio-economic indicators, e.g. income from work, working time, living conditions and lifestyle (Boscoe 2014; Mohaghegh 2015; Muirhead 2014). Epidemiological studies do not provide an explicit answer to the question, if education has an impact on the risk of developing specific types of neoplasms, while undoubtedly the socio-economic situation has an influence on incidence and chances of survival in case of some types of cancer (Boscoe 2014; Goss 2009; Kogevinas 1997; Ramsay 2014; Shariff-Marco 2014).

Simplifying at the same time at the level of the whole population the education has an impact on the value of HDI[55] and this indicator translates into socio-economic and health conditions[56] (Vineis 2014). According to Globocan statistics in 2012 the standardised death rate in the countries with high HDI was 278.1/100 000 and the death rate was 105.3/100 000, while in the countries with low HDI incidence ratio was 112.8/100 000 and death rate was 86.7. In case of the division from an economic perspective into areas/regions according to the accepted levels of economic prosperity the Globocan data show that in 2012 standardised death rate in less developed countries was 147.7/100 000 and death rate was 98.4/100 000,

[55] Human Development Index.
[56] For example because of the connection of education with the health condition, age, economic status and social relationships.

while in developed countries incidence ratio was 267.2/100 000 and death rate was 108.5/100 000.

Place of residence and the risk of cancer development

The data about the place of residence provide information about local determinants of health, i.e. the risk of developing a disease and death, both in terms of factors related to the environment and connected with living conditions, e.g. socially-conditioned lifestyle, access to achievements of modern civilization (Muirhead 2014). It means, that living in a place, where there is a constant exposure to carcinogenic agents will over time result in an increase of specific neoplasm incidence. Often the increase of epidemiological indicators values including the factor of time and place (i.e. information about the change dynamics concerning the health condition of a population living on a specified area) is a signal to undertake further, extended analyses. The physico-chemical or biological contamination of human habitat often causes greater risk of developing diseases (e.g. neoplasms) and congenital genetic damages. Important for the evaluation of the causative link is considering a lot of data, concerning both the kind of a risk factor and duration and volume of exposure – they determine dynamics of exposure state attributed only to a specific area. In practice it means, that it is necessary to include in the evaluation of health risk also the impact of other demographic phenomena, which could change the epidemiological indicators values, e.g. due to natural movements in the population and migratory movements (i.e. migration in the population and thus "migration of risk") (Blepomme 2007). The place of residence could have an impact on the increase of the mortality rate in case of significant disparities concerning the access to the health care system, and thus limited possibilities of diagnosis and therapy (Coleman 2011).

Demographic ageing and cancer epidemiology

The socio-economic changes, including changes in the family model, have a significant impact on procreative behaviours in the population, and they in turn on the socio-demographic transformation. The demographic ageing is a complex process, still occurring in populations

of many European countries, including Poland[57]. The complexity of the demographic transformation process is caused by a number of phenomena, such as decrease in fertility rate, lack of replacement of generations guarantee, emigrations, as well as premature deaths of persons of working age and of reproductive age, longer life expectancy and increase of number of elderly people. Each of the above-mentioned phenomena, which form part of demographic ageing process, can have an impact on the population's state of health and health risk. For example late age of marriage and early initiation of sexual activity (and thus promiscuity) increase risk of sexually transmitted infections (including HPV) and at the same time increase risk of cervical cancer. The childlessness could have an impact on the development of ovarian and endometrial cancer and breast cancer. Taking into consideration the difference in average life expectancy of men and women in developed and developing countries, the demographic ageing is often accompanied by the phenomenon of feminisation due to longer life expectancy of women. Both above mentioned phenomena, i.e. the feminisation and ageing of population may have an impact on the health situation of the population, e.g. greater accumulation of neoplasms characteristic for older women, and thus greater epidemiological expression of specific health problems (Nakanotani 2014). The escalation of health problems is accompanied by increasing expectations concerning social benefits, including medical services. The expectations with regard to the healthcare system concern both the necessity to guarantee an effective monitoring system of the epidemiological situation, e.g. keeping registers of chronic diseases (neoplasms) in order to ensure an appropriate quality of functioning of the

[57] This process is defined as exceeding the percentage of the elderly in the population structure above the arbitrarily accepted limit, e.g. 7% people aged at least 65 years.
According to the United Nations one can distinguish young, mature and old populations, based on the criterion of percentage of people aged 65 years or more. When in the population this percentage constitutes less than 4%, it is classified as a young population. If the percentage of people aged 65 years and more is between 4–7%, then a given population is defined as a mature population. When the percentage is higher than 7%, the population is called an old population.
According to S. Klonowicz the age of populations shall be evaluated on the basis of five-point scale. The scale, which was created on the basis of E. Rosset scale, distinguishes:

- young population – the percentage of the elderly does not exceed 4%,
- population in an early transitional phase between demographic youth and demographic old age – the percentage of the elderly is between 4–6.9%,
- population in a late transitional phase between demographic youth and demographic old age – the percentage of the elderly is between 7–9.9%,
- population in a real old age phase – the percentage of the elderly is between 10–12.9%,
- population in an advanced demographic old age phase – the percentage of the elderly is higher than 13%.

healthcare system (Valsecchi 2008), as well as undertaking actions in the healthcare system, which are justified on the basis of scientific evidence (Kontis 2014).

Another real challenge in case of ageing populations is determining reasonable and ethical premises in selecting and choosing the most effective and safe diagnostic and therapeutic methods (Mohaghegh 2015; Renzi 2015; Whitaker 2015). The social expectations are growing both due to the demographic and epidemiological situation and the development knowledge. This phenomenon can be observed in many countries, where the demographic change – the ageing of population and increasing number of the elderly – is accompanied by parallel changes in the epidemiology of civilisation diseases, i.e. cardiovascular diseases and neoplasms. It is also accompanied by a stronger involvement of ageing and conscious societies in the prevention, treatment and rehabilitation.

Summary

The described parameters and demographic phenomena have an important impact on the health situation of the population and are often a signal for further analyses aimed at finding a causative link. The observed changes and health disparities are caused by risk factors, the knowledge of which is important not only for understanding the pathomechanism of diseases development, but also their prevention, prophylaxis, diagnostics and more effective treatment (Zonderman 2014).

Bibliography

Allmeni C. et al. (2015) Global surveillance of cancer survival 1995–2009: analysis of invidual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2), *Lancet*, 385, pp. 977–1010.

Arnold M. et al. (2015) Global burden of cancer attributable to high body-mass index in 2012: a population-based study, *Lancet Oncol*, 16, pp. 36–46.

Belpomme D. et al. (2007) The multitude and diversity of environmental carcinogens, *Environmental Research*, 105, pp. 414–429.

Bielska-Lasota M., Car E., Rzepczak-Zacharek E. (2012) Obciążenie nowotworami złośliwymi w Polsce na tle krajów Unii Europejskiej. Sytuacja zdrowotna ludności Polski i jej uwarunkowania, Warsaw, NIZP-PZH, pp. 153–171.

Boscoe F.P. et al. (2014) The Relationship Between Area Poverty Rate and Site-Specific Cancer Incidence in the United States, *Cancer*, 120 (14), DOI:10.1002/cncr.228632.

Coleman M.P. et al. (2011), Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership):an analysis of population-based cancer registry data, *Lancet*, 377, pp. 127–138.

Dacus H.L.M. et al. (2014) The Role of a State Health Agency in Promoting Cancer Prevention at the Community Level Examples from New York State, *American Journal of Preventive Medicine*, vol. 46, No 3, supl. 1, pp. S81–S86.

Didkowska J., Wojciechowska U., Zatoński W., *Nowotwory złośliwe w Polsce w 2011 roku*.

Finkel T., Serrano M., Blasco M.A. (2007) The common biology of cancer and aging, *Nature*, vol. 448/16, 762773.

Gehlert S. (2014) Forging an Integrated Agenda for Primary Cancer Prevention During Midlife, *American Journal of Preventive Medicine*, vol. 46, No 3, supl. 1, pp. 104–109.

Goss E. et al. (2009) American Society of Clinical Oncology Policy Statement: Disparities in Cancer Care, *Journal of Clinical Oncology*, vol. 27, No 17, pp. 2881–2885.

IARC (2015) Agents classified by IARC Monographs, vol. 1–112.

Kogevinas M., Porta M. (1997)*Socioeconomic differences in cancer survival: a revive of the evidence. Social Inequalities and Cancer*, IARC, pp. 177–206.

Kontis V. et al. (2014) Contribution of six risk factors to achieving the 25x25 non-communicable disease mortality reduction target: a modelling study, *Lancet*, 384, pp. 427–437.

Mohaghegh P. et al. (2015) Relationships between Family Levels of Socioeconomic Status and Distribution of Breast Cancer Risk Factors, *Iranian Journal of Cancer Prevention*, 1, pp. 53–59.

Muirhead L., DNP, APRN, ANP-BC (2014) Cancer Risk Factors Among Adults with Serious Mental Illness, *American Journal of Preventive Medicine*, 46(3SI), pp. 98–103.

Nakanotani T. et al. (2014) Characteristics of Elderly Cancer Patient's Concerns and Their Quality of Life in Japan: A Web-based Survey, *Japanese Journal of Clinical Oncology*, 44(5), pp. 448–455.

Niccoli T., Partridge L. (2012) Ageing as a Risk Factor of Disease, *Current Biology*, 22 Sept, pp. 741–752.

Nitsche U. et al. (2014) Colorectal cancer surgery remains effective with rising patient age, *Int J Colorectal Dis*, 29, pp. 971–979.

Ott J.J. (2011) Global cancer incidence and mortality caused by behaviors and infection, *Journal of Public Health*.

Quinn M., Babb P. (2002) Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons, *BJU International*, 90, pp. 162–173.

Ramsay S.E. et al. (2014) Time trends in socioeconomic inequalities inequalities in cancer mortality: results from a 35 year prospective study in British men, *BMC Cancer*, 14, pp. 474.

Renzi C., Whitaker K.L., Wardle J. (2015) Over-reassurance and under support after a 'false alarm': a systematic review of the impact on subsequent cancer symptom attribution and help seeking, *BMJ Open*, 5, e007002.doi10.1136/bmjopen-2014-007002.

Rushton L. et al. (2010) Occupation and cancer in Britain,*British Journal of Cancer*, 102, pp. 1428–1437.

Rządowa Rada Ludności (2014) *Zachorowalność i umieralność na nowotwory a sytuacja demograficzna w Polsce*, sci. ed. Petrykowska A., Strzelecki Z., Szymborski J., Witkowski J., Warsaw.

Sasco A.J., Secretan M.B., Straif K. (2004) Tabacco smoking and cancer: a brief review of recent epidemiological evidence, *Lung Cancer*, 45, supl. 2, pp. S3–S9.

Shariff-Marco S. (2014) Impact of Neighborhood and Individual Socioeconomic Status on Survival after Breast Cancer Varies by Race, *Cancer Epidemiology, Biomarkers & Prevention*, pp. 793–811.

Supic G. et al. (2013) Epigenetics: A New Link Between Nutrition and Cancer, *Nutrition and Cancer*65(6), pp. 781–792.

Valsecchi M.G., Steliarova-Foucher E. (2008) Cancer registration in developing counties: luxury or necessity?, *Lancet Oncol.*, 9, pp. 159–167.

Vineis P., Wild Ch.P. (2014) Global cancer patterns: causes and prevention, *Lancet*, 383, pp. 549–557.

Whitaker K.L. et al. (2015) Help seeking for cancer 'alarm' symptoms: a qualitative interview study of primary care patients in the UK, *British Journal of General Practice*, 65 (631).

White M.C. et. al. (2014) Age and Cancer Risk: A Potentially Modifiable Relationship, *American Journal of Prevention Medicine*, vol. 46, No 3, supl. 1, pp. S7–S15.

Wilczyńska U., Szeszenia-Dąbrowska N. (2005) Nowotwory pochodzenia zawodowego w Polsce w latach 1995–2003, *Medycyna Pracy*, 56(2), pp. 113–120.

Zonderman A.B. et al. (2014) The Influence of Health Disparities on Targeting Cancer Prevention Efforts, *American Journal of Preventive Medicine*, 46(3SI), pp. S87–97.

The quantitative approach to prevalence process modelling in oncology – the overview of international research

Filip Premik

Introduction

The empirical analysis of factors such as incidence (percentage of newly diagnosed diseases in the population), prevalence (the number or percentage of disease occurrence in the population) or mortality (the number or percentage of patients, who died because of neoplasm) is usually focused on achieving at least one of two objectives. First, studies focus on identification of factors significantly affecting the values of the discussed characteristics in the specific population and quantification of those relations. Second, answering a number of research questions requires projecting the values of variables beyond the scope of the observable sample, both in the categories of forecasting future realisations and through analysis of counterfactual scenarios (extensive discussion on tools for analysing the said phenomena may be found in Manton, Akushevich i Kravchenko 2008).

This article is a short review of approaches and methods used in the analysis of the above epidemiological indicators. It begins with the discussion on two quantitative approaches to modelling, presenting their indications and limitations. Then, the scenario analysis is discussed as a method for reducing uncertainty of projection and counterfactual considerations are presented. The subsequent part includes a description of variables used in research, with a particular focus on the APC model. The last two parts described the practices of modelling incidence and prevalence (MIAMOD and PIAMOD models) and survival curves.

Basic quantitative terms in modelling of oncological prevalence in international research

Quantitative modelling of oncological prevalence is based on two concepts – statistical analysis and simulation analysis. The purpose of statistical modelling is to estimate unknown

numerical values describing relations between characteristics of a given group in the population using estimators, i.e. random functions reproducing a set of (observable) variables into the space of (unobservable) parameters[58], describing relations between variables in the analysed population. This approach builds primarily on empirical data collected for the purpose of analysis and thus the availability of good quality data determines the possibility of performing appropriate statistical modelling (De Angelis, De Angelis, Frova and Verdecchia 1994; Habbema, van Oortmarssen, Lubbe and van der Maas 1985).

If the researcher has a set of data created as a result of an experiment (which means that all factors affecting the resulting variable were controlled – in general, it means that all features determining the regression are observable and may be included in the analysis), statistical inference is an extremely useful tool enabling unbiased identification of the analysed relationships. However, for numerous economical, practical and ethical reasons, in epidemiological research it is impossible to perform an experiment and obtain, as a result, the so-called randomised sample (divided into two groups: an experimental group – usually consisting of patients with a given diseases and a control group with observations about healthy subjects[59]). Therefore, statistical analysis relies on non-experimental sets of data, which results in numerous risks for the quality of conclusions. Methodological foundations for the statistical approach when faced with the lack of experimental data in epidemiological research were proposed by Cornfield (1951) and Mantel and Haenszel (1959).

The most useful types of data set structure in epidemiological research include mainly data from cohort studies and case studies (Singh and Salaheddin 2009). The first consist in tracking the history of individual patients through regular measurements in the same observation units (so-called follow-up studies). They provide the main basis for identification of carcinogens, in particular in rare diseases (Breslow, Day and Heseltine 1987). However, they require large investments in terms of finance and time. The second method of forming a statistical data set for modelling consists in randomly selecting patients with the disease (cases) and healthy subjects (controls) from the population and making comparisons between the two groups. The resulting set of data presents the population at a specific time and generates significantly lower

[58] It concerns parametric analysis, i.e. the most common statistical estimation method in literature.
[59] The fact that the observed individuals should have identical probability of being classified into the two groups (or the probability may be dependent on observable factors) is of key importance for further analysis.

costs for the organiser, thus enabling simultaneous analysis of various causal relationships between pathogenic factors and main variables. In contrast to cohort studies, modelling on such sets of data is strongly exposed to bias resulting from non-random selection of subjects for the sample and from other biases leading to erroneous statistical inference (Sackett 1979). Breslow and Day present extensive discussion on both approaches and potential benefits and threats related to estimation of models based on cohort data (Breslow, Day and Heseltine 1987) and case studies (Breslow and Day 1980).

The quality of statistical data set is sometimes queried due to missing data, inconsistencies, non-random nature of the sample and other factors. As a result, conclusions from statistical models become debatable. Furthermore, statistical modelling is rather an ex post analysis, and in most cases prevents consideration of counterfactual scenarios for a priori optimisation of decisions. The possibilities of forecasting are also limited, in particular in the long-term, due to the lack of exogenous explanatory variables with respect to the model, which should also somehow be forecast in parallel. Sometimes the information necessary for the study is dispersed in several sets of data. It is risky to combine data from various sets, since they do not always depict similar populations, which has a negative impact on reliability of the obtained results (Heckman, Ichimura, Smith and Todd 1998). Of course, there are cases where the variables that should be included in the statistical analyses are not measured at all, and thus the appropriate statistical model cannot be estimated. When the above factors prevent reliable statistical analysis, simulation models come in useful. They consist of repeated simulation, for example using the Monte Carlo simulation, of the history of the diseases at the level of a patient, depending on the patient's various characteristics, such as risk factors for a given type of cancer, age, sex, etc. Then numerous, e.g. 100,000 so created unit data are aggregated to replicate the process of generating data about prevalence in a population (Manton, Akushevich and Kravchenko 2008). Simulation techniques are increasingly often employed to evaluate the policy making in health care in such areas as prevention and control of the number of cancer cases by organising screening, estimation of effectiveness (Gustafsson and Adami 1990) and cost efficiency (Pignone, Saha, Hoerger and Mandelblatt 2002) of health care programmes, or projection of prevalence (Alberg, Brock and Samet 2005). Algorithms generating recommendations for intervention programmes are also used (Hunter, Drake, Shortt, Dorland and Tran 2004). They play an important role in

policy making, since they enable reliable synthetisation of data from various sources and to estimate the effects of intervention in the situations where clinical samples are unavailable for such reasons as time, cost or ethical considerations (Baker 1998). Another advantage of simulation methods compared to the statistical analysis is the fact that the statistical approach can only assess the reality in which the observed individuals from the sample are found. In particular, this hampers the identification of optimal values, among others the lowest cost of the implemented intervention. Simulations are useful tools for support and evaluation of potential consequences for implementing appropriate strategies and interventions in health care (Rutter, Zaslavsky and Feuer 2010).

The description of the disease development in simulation models is based on parametric mathematical equations. The values of parameters must be explicitly provided to conduct simulations, but they most often are unknown. Therefore, the formulation of simulation models is strongly arbitrary on the part of the researcher, which does not take place in statistical research (or at least to a lesser extent). Statistical analyses involve formal procedures for verifying the compliance of the researcher's assumptions with empirical data. The values of the needed parameters in simulation modelling may be determined in two ways: through calibration and through estimation. Calibration consists in arbitrary selection of the parameter value to most accurately replicate the empirical data. The correctness of calibration is verified by comparing the results of prediction from the model with actual data for different values of parameters. It is a complex task and there is no consensus in literature as to the selection of effective verification procedure (Stout, Knudsen, Kong, McMahon and Gazelle 2009). Parameters may also be estimated directly from data, e.g. using the maximum likelihood method. Estimation is usually separate from simulation. This approach, which combines the functionality of statistical and simulation methods, does not consider replicability of empirical data due to estimated parameters. Literature provides examples of purely analytic models based only on estimation, micro-simulation models based only on calibration, and numerous hybrids of both types where some parameters are estimated and some calibrated (Stout, Knudsen, Kong, McMahon and Gazelle 2009).

Simulation modelling is an extensive category combining models based on various methods, for example on Markov chains at the mechanisms of the patient's progression from one stage of the disease to another. Among numerous available programmes for building simulation

models, the MISCAN package deserves a mention (Habbema, van Oortmarssen, Lubbe and van der Maas 1985). It is used in particular in the simulation of models for assessment of quality and effects of the policy of popularising control examinations. Rutter, Zaslavsky and Feuer (2010) proposed a more exhaustive description of simulation models.

Role of scenario analysis in international research on oncological disease prevalence

Scenario analysis concerns the part of research related to uncertainty. It is used in both statistical and simulation modelling. It consists in repeated analyses of the problem with various assumptions concerning the value or dynamics of variables affecting the result of modelling which are unknown at the time of analyses. In the discussed methodology, there are two approaches that are not necessarily mutually exclusive. Firstly, highly probably scenarios are implemented to maximise the reliability of obtained results. Secondly, extreme variants, i.e. the most pessimistic and the most optimistic, are analysed. Despite the lack of realism, the approach is useful in numerous contexts, since it allows estimating the maximum and the minimum value of the analysed (often projected) parameter, regardless of the scenario that will take place in reality.

In statistical modelling, uncertainty justifying the use of scenario analysis is related mainly to prediction. Sometimes it is almost embedded in estimation procedures. In the PIAMOD model (described more extensively further in the publication), appropriate assumptions on survival probability of cancer patients must be adopted to generate projections. Two extreme scenarios are analysed. The first one assumes that the survival probability of a cancer patient will be constant in the years of projection. The assumption is usually contrary to the observations from empirical data and excludes the progress in using increasingly effective drugs. The second scenario consists in adopting a constant pace of improvement of survival rate at the level estimated from empirical data (Verdecchia, De Angelis and Capocaccia 2002).

The projecting itself requires additional assumptions about exogenous variables that influence the projected indicators within the projection horizon. Various scenarios in this case will concern different trend trajectories of such factors as e.g. demographic changes. Population growth and changes in demographic structure of the society may beyond any

doubt have an impact on projected prevalence. For example, the PIAMOD model assumes constant values in the projection horizon for the newborn babies in subsequent years and for patients who die of other causes than the analysed cancer. The specific values are calculated based on historical data. Similar assumptions are applied to age and quantity structure in cohorts. Demographic changes are a particularly important predictor in research focusing on prevalence among the elderly. Prevalence in those groups is particularly sensitive to the increasing expected life expectancy, which provides the basis for deliberations on various scenarios (Yancik 1997).

In practice, in statistical analyses the scenarios are most often defined with the assumed fixed level of a given variable from the end of observations or constant dynamic of changes from the end of the sample over the entire time horizon of the projection. For example, Mariotto et al. adopted the established levels of incidence, survival and treatment costs as the base scenario to which the results of others were subsequently compared. Subsequent scenarios included the variation of at least one of those categories by means of trend extrapolation (Mariotto, Yabroff, Shao, Feuer and Brown 2011). A similar approach was adopted by Maddams et al. (Maddams, Utley and Møller 2012). In both publications, the only group of variables for which the zero-dynamics scenario was not considered consisted of demographic characteristics the trend of which is extrapolated based on separately estimated models.

Maddams et al. noted that for a long time horizon of the projection (e.g. 30 years) the assumptions on continuation of trends with the dynamics estimated on the basis of a historical sample may not be reliable due to progress in medicine (Maddams, Utley and Møller 2012). Moreover, more subtle dependencies must also be taken into account. Popularisation and wider availability of control examinations in recent years resulted in the increased detection of cancers, which translated into an abrupt surge in incidence. The analogous growth rate should not be expected in the longer time horizon, since the increase is a direct result of intervention programmes. The nature and scope of health care policy, the elements of which will be introduced in the future, is seldom known.

Risk factors increasing the likelihood of having a given type of cancer are yet another area for generating and analysing various projection scenarios. In research on lung cancer,

the importance of the dynamic evolution of social habits regarding smoking is emphasized (Hakulinen and Pukkala 1981). The scenario analysis in this case may build on not only assumptions concerning the expected trends in tobacco consumption, but also on other risk factors, such as air pollution, particulate matter and exposure to other dangerous substances e.g. asbestos (Alberg, Brock and Samet 2005). In the analysis of breast cancer incidence and prevalence, the role of control examinations (their availability, intensity, etc.) is often considered (Newman et al. 1995).

The scenario analysis is also used in the context of the simulation approach. Assuming that the model is correct, i.e. it reproduces the process of generating data in a reliable way, scenarios are a tool enabling to simulate reality in case of a concrete realisation of various factors, similar in a certain sense to conducting experiments. Quaranta et al. noted that in this way mathematical models enable to analyse "what would happen if" and therefore allow counterfactual considerations (Quaranta, Weaver, Cummings and Anderson 2005). The simulations scenario analyses have a unique added value as a tool of *ex ante* analysis of planned reforms and interventions, e.g. implementing control examinations. At the same time they are relatively easy to implement, because usually they are based only on a model calibration. They also show the impact of specific assumptions adopted at the stage of model formulation on the final results (Rutter, Zaslavsky and Feuer 2010). Therefore, predictions based on the scenarios can be used to warn the decision-makers to undertake specific preventive actions or regulatory measures so that the results projected by a given scenario do not happen (Bray and Møller 2006).

Literature describes scenario analyses in simulation models concerning various kinds of problems. Vogelaar et al. (2006) analysed colorectal neoplasms incidence on the basis of data from the United States using the MISCAN model (Habbema, van Oortmarssen, Lubbe and van der Maas 1985). They distinguished many simulation scenarios based on changes in the structure and intensity of human exposure to risk factors, such as smoking, obesity or lack of physical activity (appropriate parameters were calibrated on the basis of results of different research), quality and availability of control examinations and improvement of treatment efficiency. Pignone et al. (Pignone, Saha, Hoerger and Mandelblatt 2002) estimated the cost efficiency of treating colorectal neoplasms. The scenarios were formulated as combinations of examinations offered under *screening* and age brackets of patients, who would potentially

participate in such examinations. They estimated the cost of life saved at 10,000–25,000 USD, but did not point out any strategy that would be significantly more cost-efficient than the rest. Zauber et al. (Zauber, Lansdorp-Vogelaar, Knudsen, Wilschut, van Ballegooijen and Knutz 2008) distinguished in a similar way on the basis of *inter alia* MISCAN model (Habbema, van Oortmarssen, Lubbe and van der Maas 1985) cumulatively 145 scenarios. In case of this study the analysis was focused not on the cost of saving life, but the expected number of additional years of patient life in comparison to no-change scenario, assuming lack of any interventions (in this case: control examinations).

Description of decision-making variables

A set of predictors for prevalence, incidence and many other epidemiological variables widely used in literature consists of age, cohort and period. On the basis of these features a whole category of APC models (age-cohort-period models) was constructed. It is worth noticing that all of them refer to evolution in trends of epidemiological variables over time. The analysis of time trends has a long history in public health research. The origins of this kind of analysis are connected with a well-known epidemiological study concerning tuberculosis (Frost 1940). The time trends are important in the analysis, because they enable to extrapolate values out of sample in a quite easy way, which plays a key role in projecting. They are also useful in analyses aimed at understanding the aetiology of a specific disease. Currently they serve as the basis for many research and models. They are commonly used in modelling of mortality rate, incidence, prevalence and many other epidemiological indicators at the level of population *inter alia* in MIAMOD model (Verdecchia, Capocaccia, Egidi and Golini 1989) and PIAMOD model (Verdecchia, De Angelis and Capocaccia 2002) described later in this document.

In case of monitoring a given cohort from birth until death, it is easy to notice that the risk of a disease changes with age. The consecutive age groups are exposed to the various degrees of individual risk factors, which result in differences in incidence for a specific disease in case of individuals born in different years, i.e. coming from various cohorts. For example people born in the period, when diethylstilbestrol was prescribed for pregnant women, have a higher risk of developing some kinds of neoplasms throughout life than patients born in a

period, when this medicine was not prescribed (Holford 1991). The effects related to cohort can also have another dimension. It is worth noticing that the individuals in the cohort usually start smoking tobacco products as a teenager or young adult. Therefore the habit of tobacco smoking is characteristic for people of a certain age. Thus the risk of developing diseases caused by smoking increases rapidly, when a given cohort exceeds an exact number of years. This effect is again specific for a cohort, despite the fact that smoking tobacco products, and thus an increased exposure to this risk factor is not related to the date of birth.

The subsequent factors having an impact on the time trends in case of incidence and prevalence are connected with a particular year of diagnosing a disease and the age of patient. Another aspect of describing trends in case of incidence is an analysis of the period, in which a disease was diagnosed. The aim is to capture the unique effects for a specific point in time that changes the risk of developing a disease for all people. The examples of this type of factors are pollution of air and drinking water or the consumption of highly processed food. They are affecting everyone in the population at a given time and causing an increased risk of developing a given type of neoplasm. Another example of effects related to the time of diagnosis are changes in the medical technology causing increased incidence due to the decrease in number of undiagnosed or wrongly diagnosed patients.

The easiest way to understand APC analyses is by using the example of age-by-period table, in which rows contain information about age groups (e.g. 5-year age groups) and columns contain information about periods of monitoring (5-year time intervals), whereas the diagonal contains information about cohorts (Kupper, Janis, Karmous and Greenberg 1985). The modelling of APC effects in its simplest version consists in the regression of a given indicator, e.g. mortality, incidence, prevalence, etc. with respect to binary variables, inducing age groups, time intervals and cohorts respectively. The problem of lack of traceability arising in this kind of modelling is solved *inter alia* by applying appropriate standardisation restrictions for estimated parameters (Holford 1991). Using APC models for modelling of time trends is very useful in case of projecting (Bray and Møller 2006). Kupper et al. (Kupper Janis, Karmous and Greenberg 1985) have on the other hand a critical attitude towards described methodology and indicate possible shortcomings and risks. Osmond gives an example of applying APC in analysing and projecting lung cancer mortality in the United Kingdom (Osmond 1985).

The application of APC concept requires transforming continuous variables, such as age, into discrete variables. Literature provides several standards relating to this issue. In general the greater the number of generated age groups, the greater chance to capture more detailed relations. On the other hand the excess of categories can lead to problems with interpreting the results and the preciseness of estimation. While designing the APC table Holford (1991) applied 5-year cohorts beginning at the age of 15 and ending with the category 85+. Corazziari (Corazziari, Quinn and Capocaccia 2004) on the other hand distinguished three groups of neoplasms due to the age patters of incidence. The first group consists of neoplasms occurring usually among young people (e.g. testicular cancer), the second consists of diseases, the incidence of which does not generally depend on the age of potential patient (such as thyroid gland cancer), the third group concerns neoplasms typical for the elderly. For each of these groups different categorisation of age has been proposed. The main differences concerns the length of the first category (15–44, 15–54 etc.). It is then followed by ten-year periods.

Apart from the variables described in the APC concept, other predictors of epidemiological indicators are also applied in literature. Wright et al. enumerate a number of variables, which could help explain mortality (Wright, Kucharczuk, O'Brien, Grab and Allen 2009). Among them there are variables describing the health condition of patient, including hypertension, diabetes, weight, medical history etc. In literature it is frequently emphasised that the analysis should also take into account the exposure to risk factors specific for each type of neoplasm. In case of lung cancer the obvious predictors are indicators informing if and how much does the patient smoke. However there are also other factors that are worth taking into consideration in the analysis, such as diet, environmental pollution and occupation (Doll and Peto 1981). The extensive description of applying various factors of prevalence in the context of epidemiological analyses can be found in the study of Manton (Manton, Akushevich and Kravchenko 2008).

Methods of cancer incidence and prevalence estimation applied in international research

Incidence and prevalence are basic measures applied in a description of neoplasm occurrence, therefore they are of a key importance from the perspective of epidemiological

research (De Angelis, De Angelis, Frova and Verdecchia 1994). Data about mortality is usually available in official statistics at the national level, whilst incidence and prevalence come from follow-up studies, thus it is frequently impossible to make a direct generalisation on the population level. However, parameters in the population can be estimated. Among models used to estimate and project incidence and prevalence rates worth mentioning are primarily MIAMOD concept – *Mortality and Incidence Analysis Model* (Verdecchia, Capocaccia, Egidi and Golini 1989) and PIAMOD concept – *Prevalence and Incidence Analysis Model* (Verdecchia, De Angelis and Capocaccia 2002). They are based primarily on combination of numerical methods and statistical adjustments.

MIAMOD is a procedure used to estimate incidence and prevalence in a sample and to extrapolate their values out of sample. The data about mortality and the so-called survival curves are used in the estimation. The estimation is based on the assumption of incurability of analysed diseases, thus incidence can be expressed as regular, deterministic function of demographic variables inducing age, cohort and time of the measurement (it is worth noticing that this variables come from APC methodology). The assumption of incurability, according to which the patient having a given disease will die without being cured, is not really controversial in case of neoplasms (Verdecchia, Capocaccia, Egidi and Golini 1989). Moreover, this assumption has rather technical character in the context of conducted analysis.

The MIAMOD model is classified as an indirect procedure, which means that it uses information about mortality and survival in order to estimate incidence and prevalence. If incidence is available, it is not necessary to use indirect estimation (in such cases the described below PIAMOD estimation strategy is applied, which does not require additional estimation of incidence). However often the incidence, survival and mortality data come from different sources, which are not always compatible as regards data collection methods, excluded observations, data completeness and even the described population. In such case, the additional estimation of incidence enables, the verification of conformity in analysed sets of data as well as obtaining estimations and projecting incidence and prevalence rates. MIAMOD is a method broadly used in Europe (EC BIOMED-II EUROPREVAL project) and United States of America (Verdecchia, De Angelis and Capocaccia 2002), *inter alia* due to positive statistical features and availability of software (De Angelis, De Angelis, Frova and Verdecchia 1994).

PIAMOD was constructed in order to provide estimators and to project incidence, prevalence and mortality on the basis of data from cancer registries. It requires the availability of incidence data. On the basis of this data and taking into account the survival curves the model provides updated information about prevalence, thus it is especially useful in the context of the allocation of health care resources and control of the number of cancer cases (Verdecchia, De Angelis and Capocaccia 2002). Unlike the MIAMOD model it is classified as a direct method, which means that it uses individual data from the population concerning incidence and survival probabilities in order to calculate a number of diagnosed neoplasm patients living in a given population in a specific period of time. PIAMOD is projecting incidence similarly to MIAMOD on the basis of deterministic relationship between mortality and incidence, and survival and prevalence.

The implementation of both procedures requires data from the population about causes of death, incidence or mortality for a given type of neoplasm and survival curves estimated under a separate model.. With the exception of the survival curves the data should be appropriately divided according to age (cohort), calendar year and sex. The projections are calculated on the basis of the assumption that impact of age and cohorts on mortality/ incidence will remain stable in the projection period. Bray and Møller (Bray and Møller 2006) indicate on the one hand some disadvantages of this type of trend extrapolation, on the other hand they recognise the usability of projections for the allocation of health care resources and point out statistical models, which can improve the quality of obtained projections.

MIAMOD and PIAMOD have many practical applications. One of the most frequent applications is projecting incidence and prevalence in order to estimate future expenditure on cancer care. Therefore it becomes relevant not only to estimate total prevalence in the future, but also the division of patients according to various stages of disease, since patients in different stages of disease generate different costs. Mariotto et al. (Mariotto, Yabroff, Feuer, De Angelis and Brown 2006) distinguished, on the basis of data coming from the United States of America, three categories of medical services in case of colorectal carcinoma treatment: initial care, last year of life and other, indicating that the first two are generating the highest costs. Then, they repeated the study for several types of neoplasms (13 for men, 16 for women) analogously divided into categories of medical services (Mariotto, Yabroff, Shao, Feuer and Brown 2011). Yu et al. (Yu, Clements and O'Connell 2013) pointed out the significant

heterogeneity of patients in the group *other* and estimated future costs for five groups of patients, using data about Australian colon cancer patients. It was assumed that share of patients in groups concerned was stable over time, which allowed forecast procedures. It may be also useful to provide prevalence results at the regional and not national level, especially if data at the national level may be unreliable, for example due to the concentration of medical centres only in several regions or the incompleteness of registers. Verdecchia et al. (Verdecchia A., De Angelis, Francisci and Grande 2007), used the MIAMOD procedure and the example of Italian data to show that despite an increase in the cancer survival rate, there are still marked differences between Southern and Northern Italy.

Other methods of incidence and prevalence estimation are also worth mentioning. The counting method (Feldman, Kessler, Myers and Naughton 1986; Gail, Kessler, Midthune and Scoppa 1999) consists in estimating prevalence on the basis of data from cancer registries. Patients living in a given period are counted and the sum is adjusted for likelihood of a given patient's exit from the sample as most frequently cohort data sets are used. Also survivorship curves in cohorts should be taken into account. Depending on the registry length, it is possible to model partial prevalence (the number of people who have lived for *x* years after diagnosis) or total prevalence (all people living with a diagnosis). The completeness index is a statistical method that estimates total prevalence on the basis of partial prevalence (Capocaccia and De Angelis 1997) (Merill, Capocaccia, Feuer and Mariotto 2000). The method of calculating the index has been implemented in the ComPrev package. The completeness index concept is used to estimate cancer prevalence in the U.S. Estimation of childhood prevalence concerns individuals diagnosed between 0 and 19 or 0 and 14 years of age, depending on a study. It is a solution to the problem of missing data when estimating partial prevalence. It is distinguished because patients diagnosed at an early age have high chances of living long after the diagnosis. When calculating prevalence, considering 20-year survival from the diagnosis, only observations of patients older than 39 can be used, which leads to the missing observations problem. It is a semiparametric method based on the completeness index and implemented in the ComPrev package (Simonetti, Gigli, Capocaccia and Mariotto 2008).

Cancer survival rate estimation methods in international research

Survival analysis (Klein, van Houwelingen, Ibrahim and Scheike 2013) assumes homogeneity of individuals, meaning there is exactly one survivorship curve type. It means that for each patient under analysis the survivorship curve, or a function that maps time in terms of survival likelihood, is the same. However studies show that cancer patient cohorts are heterogeneous. Some patients die for causes directly or indirectly related to cancer, some recover and die for completely different reasons, frequently many years after their therapy is completed. Therefore, cancer patients can be divided into at least two groups. For one group, the risk of death is similar to the risk of death of all individuals with the same characteristics in the population, while for the other group the risk of death is much higher due to cancer. If heterogeneity of cancer patients is not taken into account, it may result in incorrect identification of main survivorship determinants and shift the survivorship curve trends. This is particularly undesirable, especially as they are used for further analyses, such as projecting incidence and prevalence in MIAMOD and PIAMOD models.

To take this heterogeneity into account, it was suggested (Ederer, Axtell i Cutler 1961; Hakulinen 1982) to apply the notion of relative survival that is the quotient of observed survival (classic measure estimated by standard procedures on a sample) and survival in the population, i.e. unburdened by the effects of a disease. Comparability of units for which both survivals were estimated should be ensured, at least in terms of demographic characteristics such as age, sex, etc. It is assumed that the relative survival ratio constitutes an objective measure of the proportion of patients who will die for reasons directly or indirectly related to a disease, i.e. a survival measure adjusted by non-disease factors (Esteve, Benhamou, Croasdale and Raymond 1990). Using this approach a net survival curve was calculated that constitutes the net effect of cancer against the likelihood of survival. In many studies it flattened out at the right end, as if it tended to a fixed positive value. The value was interpreted as a long-term percentage of those who survived cancer. Yet, the result was obtained by censoring observations of patients who died for reasons other than cancer. There is no objective measure to see whether death was actually caused by cancer. Therefore the percentage of patients who won the war with cancer calculated in this way was unreliable. Nonetheless, the methods described in this section are still popular, e.g. De Angelis et al. (2009) based their study on the Hakulinen approach to calculating relative survival (Hakulinen 1982).

Despite numerous improvements, the Ederer method did not work well as it overestimated long-term survival in groups with heterogeneous values of life expectancy (Esteve, Benhamou, Croasdale and Raymond 1990). Thus, a number of methods were suggested (Hakulinen and Tenkanen 1987; Esteve, Benhamou, Croasdale i Raymond 1990; Dickman, Sloggett, Hills and Hakulinen 2004) which assume that survival is the product of two components: survival in the population and excess rate survival, or a factor that takes into account additional risk related to cancer. It is subject to estimation and does not require defining which patient died from cancer and which did not, which is one of the main advantages of this method. Estimation is usually based on the most probable method. In modelling practice, the function of hazard in the population is usually taken from published life expectancy tables concerning units with similar characteristics as the cohort under analysis. It should be noted that the model is based on the assumption that the hazard function, and thus the function of survival in the population, does not depend on cancer-related factors, such as for example cancer stage at diagnosis, etc. (Dickman, Sloggett, Hills and Hakulinen 2004). To carry out additional estimation, connected with hazard function cancer, it is suggested to use standard survival function estimators, such as the parametric Cox model or non-parametric methods (Pohar-Perme, Henderson and Stare 2009). This way, net survival curve estimators can be obtained without indicating the cause of death. An example of this method's application in empirical research is the paper by Bossard et al. (2007).

Another range of models that take into consideration heterogeneity in the risk of death for cancer patients is the mixture cure (MC) approach (De Angelis, Capocaccia, Hakulinen, Soderman and Verdecchia 1999). In a sense, it is a method close to the one discussed in the previous paragraph, but it allows estimating both the risk of death in fatal cases and the percentage of patients who recovered. MC models are used to describe the health condition of patients treated for multiple stage diseases, where for each stage the survival time is estimated on the assumption of varied survival time distributions. Of course, they are also useful in the case under analysis, where there is a percentage of patients whose likelihood of death caused by the analysed cancer tends to nil, as they allow its estimation. The survival function resulting from additional risk induced by disease depends on many factors, such as age, sex, stage at diagnosis, therapy efficiency, and access to health care. Two main currents of MC estimation have developed. One focuses on parametric models, based on standard distributions of survival

time (log-normal, exponential, Weibull, Gompertz). In this case, the most reliable method is the correct estimation method. The other current is the non-parametric approach based on the empirical Kaplan-Meier distribution procedure or its generalisations. Improved availability of cancer registries allowed estimation of MC models for entire populations, thanks to which model results can be compared to life tables for the population to check result resilience. Introduction of MC models to the analysis allowed simultaneous estimation of the impact of the same factors on both likelihood of cancer survival and the time of death. Heterogeneity in a given variable's effects on the indicators should not be surprising. For example age plays various roles in recovery likelihood and life expectancy in fatal cases. Examples of MC models in literature are provided *inter alia* by Phillips et al. (Phillips, Coldman and McBride 2002), and Mariotto et al. (Mariotto, Yabroff, Shao, Feuer and Brown 2011).

The above-mentioned methods of conditional estimation of the survival function are available in standard statistical software, e.g. in Stat (*strel* package) and in R (*relsurv* package) (Pohar and Stare 2006).

Conclusion

The quantitative approach to prevalence modelling in oncology consists of two leading concepts: statistical modelling and simulation. Each concept is applied in empirical research extensively, with certain criteria met that are specific to each approach to obtain reliable results. Despite apparent similarity, they concern different research areas. Regardless of adopted research strategy, a useful analysis tool is consideration of scenarios that reduce uncertainty (through the possibility of defining the expected variability range of the characteristic under analysis between the lower and upper limit resulting from extreme scenarios – e.g. extremely optimistic and extremely pessimistic scenarios, but still real in the opinion of the researcher), providing a potential reflection of reality in the case of fulfilling certain assumptions. In the context of correct modelling, selection of adequate variables is very important. Relatively simple APC models provide a wide range of opportunities. Modelling and projecting major epidemiological indicators can be based on MIAMOD and PIAMOD models, which, due to favourable statistical characteristics and software availability, have become the standard analysis tool. Finally, considering the cancer survival curves one should take into account

heterogeneity of cohorts resulting from the fact that some patients will surely survive treatment. It is particularly important as the results of survival analysis are frequently used as data in further calculations.

Description of quantitative approach methods in modelling pathogenic processes proposed herein is rather aimed at familiarising the readers with various research concepts, rather than providing technical details of analysis. An extensive review of quoted literature will provide the interested readers with more details relating to analysis of cancer-related indicators.

Bibliography

Alberg, A., Brock, M. and Samet, J. (2005) Epidemiology of Lung Cancer: Looking to the Future. *Journal of Clinical Oncology*, 23(14), pp 3175–3185.

Baker, R. (1998) Use of a mathematical model to evaluate breast cancer screening policy. *Health Care Management Science*, 1(2), pp. 103–113.

Bossard, N., Velten, M., Remontet, L., Belot, A., Maarouf, N., Bouvier, A. et al. (2007) Survival of cancer patients in France: A population-based study from the Association of the French Cancer Registries (FRANCIM). *European Journal of Cancer*, 43(1), pp. 149–160.

Bray, F. and Møller, B. (2006) Predicting the future burden of cancer. *Nature Reviews Cancer* (6), pp. 63–74.

Breslow, N.E. and Day, N.E. (1980) *Statistical methods in cancer research. Vol. 1: The analysis of case-control studies.* International Agency for Research on Cancer.

Breslow, N. E., Day, N. E. and Heseltine, E. (1987) *Statistical methods in cancer research. Vol 2: The design and analysis of cohort studies.* International Agency for Research on Cancer.

Capocaccia, R. and De Angelis, R. (1997) Estimating the Completeness of Prevalence Based on Cancer Registry Data. *Statistics in Medicine*, 16(4), pp. 425–440.

Corazziari, I., Quinn, M. and Capocaccia, R. (2004) Standard cancer patient population for age standardising survival ratios. *European Journal of Cancer*, 40(15), pp. 2307–2316.

Cornfield, J. (1951) A Method of Estimating Comparative Rates from Clinical Data. Applications to Cancer of the Lung, Breast, and Cervix. *Journal of the National Cancer Institute*, 11(6), pp. 1269–1275.

De Angelis, G., De Angelis, R., Frova, L. and Verdecchia, A. (1994) MIAMOD: a computer package to estimate chronic disease morbidity using mortality and survival data. *Computer Methods and Programs in Biomedicine*, 44(2), pp. 99–107.

De Angelis, R., Capocaccia, R., Hakulinen, T., Soderman, B. and Verdecchia, A. (1999) Mixture models for cancer survival analysis: application to population-based data with covariates. *Statistics in Medicine*, 18(4), pp. 441–454.

De Angelis, R., Francisci, S., Baili, P., Marchesi, F., Roazzi, P., Belot, A. et al. (2009) The EUROCARE-4 database on cancer survival in Europe: data standardisation, quality control and methods of statistical analysis. *European Journal of Cancer*, 45(6), pp. 909–930.

Dickman, P., Sloggett, A., Hills, M. and Hakulinen, T. (2004) Regression models for relative survival. *Statistics in Medicine*, 23(1), pp. 51–64.

Doll, R. and Peto, R. (1981) The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *Journal of the National Cancer Institute*, 66(6), pp. 1192–1308.

Ederer, F., Axtell, L. and Cutler, S. (1961) The relative survival rate: a statistical methodology. [in:] *End Results and Mortality Trends in Cancer*, vol. 6. National Cancer Institute Monograph, pp. 101–121.

Esteve, J., Benhamou, E., Croasdale, M. and Raymond, L. (1990) Relative survival and the estimation of net survival: elements for further discussion. *Statistics in medicine*, 9(5), pp. 529–538.

Feldman, A., Kessler, L., Myers, M. and Naughton, M. (1986) The Prevalence of Cancer. *New England Journal of Medicine*, 315(22), pp. 1394–1397.

Frost, W. (1940) The age selection of mortality from tuberculosis in successive decades. *The Milbank Memorial Fund Quarterly*, pp. 61–66.

Gail, M., Kessler, L., Midthune, D. and Scoppa, S. (1999) Two Approaches for Estimating Disease Prevalence from Population-Based Registries of Incidence and Total Mortality. *Biometrics*, 55(4), pp. 1137–1144.

Gustafsson, L. and Adami, H. (1990) Cytologic screening for cancer of the uterine cervix in Sweden evaluated by. *British Journal of Cancer*, 61(6), pp. 903–908.

Habbema, J., van Oortmarssen, G., Lubbe, J. and van der Maas, P. (1985) The MISCAN simulation program for the evaluation of screening for disease. *Computer Methods and Programs in Biomedicine*, 20(1), pp. 79–93.

Hakulinen, T. (1982) Cancer survival corrected for heterogeneity in patient withdrawal. *Biometrics*, pp. 933–942.

Hakulinen, T. and Pukkala, E. (1981) Future Incidence of Lung Cancer: Forecasts Based on Hypothetical Changes in the Smoking Habits of Males. *International Journal of Epidemiology*, 10(3), pp. 233–240.

Hakulinen, T. and Tenkanen, L. (1987) Regression analysis of relative survival rates. *Applied Statistics*, pp. 309–317.

Heckman, J., Ichimura, H., Smith, J. and Todd, P. (1998) Characterizing selection bias using experimental data. *Econometrica*, 66(5), pp. 1017–1098.

Holford, T. (1991) Understanding the effects of age, period, and cohort on incidence and mortality rates. *Annual review of public health*, 12(1), pp. 425–457.

Hunter, D., Drake, S., Shortt, S., Dorland, J. and Tran, N. (2004) Simulation modeling of change to breast cancer detection age eligibility recommendations in Ontario, 2002–2021. *Cancer Detection and Prevention*, 28(6), pp. 453–460.

Klein, J., van Houwelingen, H., Ibrahim, J. andi Scheike, T. (2013) *Handbook of Survival Analysis.* Chapman and Hall/CRC.

Kupper, L., Janis, J., Karmous, A. and Greenberg, B. (1985) Statistical age-period-cohort analysis: a review and critique. *Journal of chronic diseases*, 38(10), pp. 811–830.

Maddams, J., Utley, M. and Møller, B. (2012) Projections of cancer prevalence in the United Kingdom, 2010–2040. *British Journal of Cancer*, 107(7), pp. 1195–1202.

Mantel, N. and Haenszel, W. (1959) Statistical Aspects of the Analysis of Data From Retrospective Studies of Disease. *Journal of the National Cancer Institute*, 22(4), pp. 719–748.

Manton, K., Akushevich, I. and Kravchenko, J. (2008) *Cancer Mortality and Morbidity Patterns in the U.S. Population: An Interdisciplinary Approach.* Springer.

Mariotto, A., Yabroff, R., Feuer, E., De Angelis, R. and Brown, M. (2006) Projecting the number of patients with colorectal carcinoma by phases of care in the US: 2000–2020. *Cancer Causes & Control*, 17(10), pp. 1215–1226.

Mariotto, A., Yabroff, R., Shao, Y., Feuer, E. and Brown, M. (2011) Projections of the Cost of Cancer Care in the United States: 2010–2020. *Journal of the National Cancer Institute*, 103(2), pp. 117–128.

Merill, R., Capocaccia, R., Feuer, E. and Mariotto, A. (2000)Cancer prevalence estimates based on tumour registry data in the Surveillance, Epidemiology, and End Results (SEER) Program. *International Journal of Epidemiology*, 29(2), pp. 197–207.

Newman, B., Moorman, P., Milikan, R., Qaqish, B., Geradts, J., Aldrich, T. et al. (1995) The Carolina Breast Cancer Study: integrating population-based epidemiology and molecular biology. *Breast Cancer Research and Treatment*, 35(1), pp. 51–60.

Osmond, C. (1985) Using Age, Period and Cohort Models to Estimate Future Mortality Rates. *International Journal of Epidemiology*, 14(1), pp. 124–129.

Phillips, N., Coldman, A. and McBride, M. (2002) Estimating cancer prevalence using mixture models for cancer survival. *Statistics in Medicine*, 21(9), pp. 1257–1270.

Pignone, M., Saha, S., Hoerger, T. and Mandelblatt, J. (2002) Cost-Effectiveness Analyses of Colorectal Cancer Screening. A Systematic Review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*, 137(2), pp. 96–104.

Pohar, M. and Stare, J. (2006) Relative survival analysis in R. *Computer Methods and Programs in Biomedicine*, 81(3), pp. 272–278.

Pohar-Perme, M., Henderson, R. and Stare, J. (2009) An approach to estimation in relative survival regression. *Biostatistics*, 10(1), pp. 136–146.

Quaranta, V., Weaver, A., Cummings, P. and Anderson, A. (2005) Mathematical modeling of cancer: The future of prognosis and treatment. *ClinicaChimicaActa*, 357(2), pp. 173–179.

Rutter, C., Zaslavsky, A. and Feuer, E. (2010) Dynamic Microsimulation Models for Health Outcomes: A Review. *Medical Decision Making*, 30(3).

Sackett, D. (1979) Bias in analytic research. *Journal of Chronic Diseases*, 32(1–2), pp. 51–62.

Simonetti, A., Gigli, A., Capocaccia, R. and Mariotto, A. (2008) Estimating complete prevalence of cancers diagnosed in childhood. *Statistics in Medicine*, 27(7), pp. 990–1007.

Singh, H. i Salaheddin, M. (2009) Different Study Designs in the Epidemiology of Cancer: Case-Control vs. Cohort Studies. in: M. Verma, *Cancer Epidemiology*. Humana Press, pp. 217–225.

Stout, N., Knudsen, A., Kong, C., McMahon, P. and Gazelle, G. (2009) Calibration Methods Used in Cancer Simulation Models and Suggested Reporting Guidelines. *PharmacoEconomics*, 27(7), pp. 533–545.

Verdecchia, A., Capocaccia, R., Egidi, V. and Golini, A. (1989) A method for the estimation of chronic disease morbidity and trends from mortality data. *Statistics in Medicine*, 8(2), pp. 201–216.

Verdecchia, A., De Angelis, G. and Capocaccia, R. (2002) Estimation and projections of cancer prevalence from cancer registry data. *Statistics in Medicine*, 21(22), pp. 3511–3526.

Verdecchia, A., De Angelis, R., Francisci, S. and Grande, E. (2007) Methodology for estimation of cancer incidence, survival and prevalence in Italian regions. *Tumori*, 93(4), pp. 337–344.

Vogelaar, I., van Ballegooijen, M., Schrag, D., Boer, R., Winawer, S., Habbema, J. et al. (2006) How much can current interventions reduce colorectal cancer mortality in the U.S.? *Cancer*, 107(7), pp. 1624–1633.

Wright, C., Kucharczuk, J., O`Brien, S., Grab, J. and Allen, M. (2009) Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. *The Journal of thoracic and cardiovascular surgery*, 137(3), pp. 587–596.

Yancik, R. (1997) Cancer burden in the aged. *Cancer*, 80(7), pp. 1273–1283.

Yu, X., Clements, M. and O'Connell, D. (2013) Projections of cancer prevalence by phase of care: a potential tool for planning future health service needs. *Journal of Cancer Survivorship*, 7(4), pp. 641–651.

Zauber, A., Lansdorp-Vogelaar, I., Knudsen, A., Wilschut, J., van Ballegooijen, M. and Knutz, K. (2008) Evaluating Test Strategies for Colorectal Cancer Screening: A Decision Analysis for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*, 149(9), pp. 659–669.

Decision-making models in oncological care – international experience

Barbara Więckowska, Margaret Gralińska

Introduction

Virtually all countries in the world carry out planning to ensure health care services, but the methodology of planning may vary significantly. It may vary from using prognostic quantitative models (econometric, statistical and stochastic) based on data, using the historical "value of service provision and service model" to subjective central planning.

The majority of developed countries that want to ensure the most fair and effective services for the entire population plan their health services potential. The planning may take place at the national, regional or local level[60]. The so-called strategic planning is always centralised and defined at the national level (Ettelt et al. 2008) – this indicates the health care services to be provided by the government (i.e. to be financed from the budget) and/or social insurance. The operational planning translates this highest level vision into the allocation of budgets and resources, organisational model of services, facilities and equipment, as well as personnel. The second, equally important, aspect is education and training of medical and paramedical personnel.

In the past, operational planning focused on hospital care (Ettelt et al. 2008)[61], since this part of the health care sector required high capital outlays in the existing and new facilities, expensive equipment and specialist technologies. The planning usually builds on the estimation of the future number of beds, but within the last decade the majority of countries started to predict the expected number of health care services and their types as well as the expected results of service providers (both outputs and outcomes).

Until recently, planning in the outpatient sector and primary health care took place only in the countries defined by the OECD as systems financed primarily from tax revenues, with

[60] The decision-making level in each country is related to administrative decentralisation in the health care sector.
[61] The planning may cover only public hospitals, in line with the tradition of public service provision, or may include both public and private hospitals (both 'for profit' and 'not for profit' ones).

a strong component of the requirement to refer to specialist consultations – they include the United Kingdom, New Zealand and Norway (Wastgaf et al. 2009; Thomson et al. 2013). In view of the attempts to transfer the burden of care from hospitals to widely understood outpatient care, the importance of decision-making models in this field is expected to increase.

The approach to planning is a reflection of institutional, legislative and regulatory structures of the health care system of the country, but may also be a precursor and/or outcome of health care reforms. The Polish oncology reform should be coupled with a modern approach to planning, represented by regional demand maps in the field of oncological services.

Use of decision-making models for central and regional health care plans

Decision-making models are tools supporting the management decisions. They cannot, however, replace the responsibility of decision-makers for their choices, which will remain subjective. A good model will define the balance between the demand for and the supply of services, and will present the consequences of demand being higher than the potential supply and leading to queues and increasingly longer waiting times.

For the purposes of this article, the decision-making model is defined as a tool allowing the assessment of the impact of changes taking place in a given population and the incidence and prevalence of disease to determine the supply to fulfil such needs.

Demand forecasting and modelling allows the prediction of short and long-term changes in health care needs. The input data should depend on the type of analysed health care services. In oncology, the number of cancer cases (incidence) should be taken into account, while in obstetrics – the predicted number of births. The modelling systems may use both simple statistical tools and tools based on the Monte Carlo simulation method takes into account such factors as age or co-existing diseases in demand forecasting.

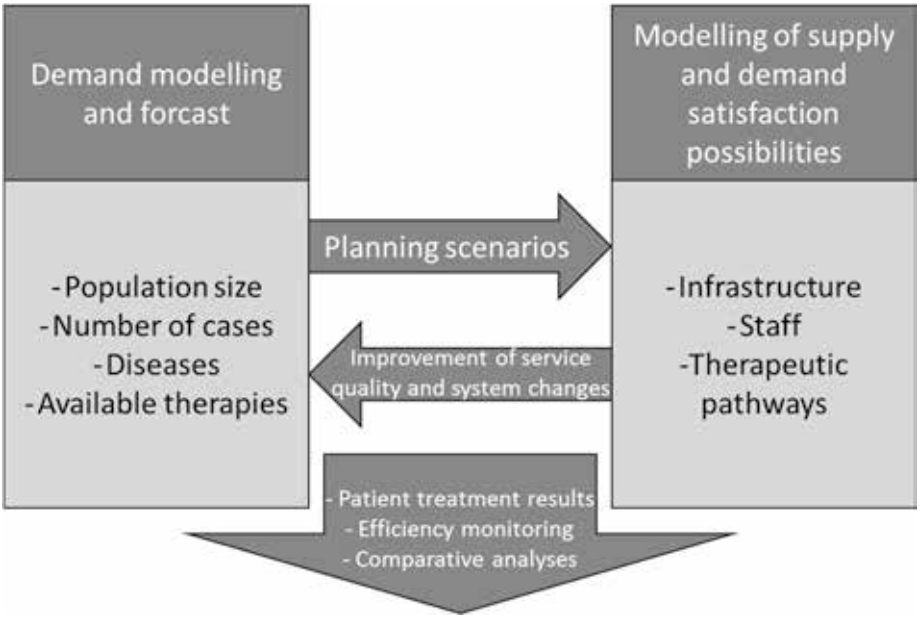
Another part of the model consists of resources required to satisfy the demand, i.e. appropriate infrastructure, qualified medical personnel and possibility to provide comprehensive medical treatment.

The widely used tools allow mapping the treatment path of the patient in the health care system as the map of processes. Such analysis may be modified by taking into account

the impact of different work methods or reorganisation of provided services, as well as by introduction of new technologies or procedures.

The tools for scenario planning and simulations enable interactive optimisation, which ensures that the demand is efficiently satisfied at the appropriate time, for example by defining the maximum waiting time. Such scenario planning may be used for various purposes, from short-term planning (daily or weekly action plan) to long-term planning of operational capacities or requirements for personnel training.

Decision-making models may also have additional functionalities allowing the measurement of the "process" – indicators such as the outcome of the patient's treatment, definition of various benchmarks or monitoring of treatment outcomes (accomplishment of objectives).



Flowchart 1. Decision-making pathway modelling in the health care system (source: own analysis)

The challenge is to use the tools (models) in a way ensuring the balance between decision-making at the regional and central level in the light of historical resources and the competition

among future service providers, legal regulations and the provision of fair, affordable and available health care services. The promotion of incentives for innovation and increased productivity with the use of strategies (such as decentralisation, competition and pluralism of service providers) may pose yet another challenge. In some cases, those difficulties cannot be overcome and lead to the complete lack of planning of services in some health care sectors or even in entire countries.

The second, and perhaps the more important, use of modelling is the assessment of the potential impact of health care sector reforms on the sector financing and on long-term changes in the model of health care provision. For example, modelling was used in Germany to assess planning and determining the hospital budget with introduction of resource groups related to diagnosis (correction of uniform patient groups by risk factors)[62] or financing based on the number of services (Obermann et al. 2013). Another example comes from the United Kingdom where the target number of planned day surgery cases to assess the reconfiguration of hospital infrastructure and development of dedicated day surgery centres (Light 2003).

The scope of planning tools is closely related to the characteristics of the health care system in a given country, most importantly the extent of vertical integration of service providers. The countries whose systems require referral for specialist consultation (United Kingdom, New Zealand) will have the plans covering the entire care process, starting from primary care, through outpatient sector (specialists and diagnosis) to the hospital sector. In this case, the models may be very detailed and even include the number of specialist wards and their geographic distribution in a given area. On the other hand, countries with developed market mechanisms on the part of service providers, but using public health insurance (Austria, France, Australia or Canada) usually make plans only for the hospital care sector for both public and private service providers, specifying the number of facilities and their location, usually based on the existing infrastructure. Those countries often use more specific planning tools for capital investment schemes (Thomson et al. 2013; Hofmarcher and Quentin 2013).

The interrelation between decision-making at the regional and the national level approaches a new balance: the countries which traditionally used central planning, such as

[62] The model of risk balancing applied currently in Germany is, along with the Dutch model, one of the most advanced analytical models in the world; see: Więckowska B. (2010), *Konkurencja między płatnikami w bazowym systemie zabezpieczenia zdrowotnego*, Ernst&Young.

France, concentrate decision-making at the regional level (Chevreul et al. 2010), while some countries with strong decentralisation traditions (e.g. Denmark or Finland) introduced a greater role of national supervision, which reflects the reduced social acceptance of regional inequalities in health care (Thomson et al. 2013; Vuorenkoski et al. 2008).

It should be noted that regional health care planning should take into account demography (and thus the demand for individual services), instead of following accurately the existing administrative boundaries. As we will argue further on in the article, in rare neoplasms the regional population is often insufficient to justify the existence of a regional highly specialist service provider. Therefore, the first step to be taken at the national level/strategic planning level is to define which health care services should be modelled on the national and/or supraregional scale, and which on the regional or local scale.

Large capital investments in hospital infrastructure and expensive equipment are usually regulated and prepared separately from plans and operational budgets of individual units. There are also various mechanisms to assess long and short-term investments, taking into account the required amount of funds to be invested. Expensive equipment, which in the majority of countries is planned and/or approved at the central level, includes MRI and PET for diagnosis, linear accelerators for radiotherapy, as well as specialist technologies, such as proton therapy.

The use of models and other planning tools requires defining the scope of a given map of health care needs. In the widest sense, the demand for health care services is a derivative of demand for health. Through demand for health care services, consumers aim at achieving the highest capital, i.e. health. Demand for health is not analogous to demand for other goods, since individuals allocate resources to both consume and produce health (Grossman 1972). Health is treated as a good produced for people using various measures. An important element of the model is distinguishing between health treated as the product and health care treated as a factor in health production.

In this context, regional maps of health care needs mean the demand of the population or the society for medical services, as well as medical services for which the society is able and willing to pay. Most of service capacity planning is based on matrices of use of key resources (such as operating theatres, other equipment and infrastructure, hospital beds, capacity of

service providers in terms of day care, medical and paramedical personnel), which may be used jointly (within the meaning of planning the treatment of various diseases) with specialisations and/or types of diseases.

For example, the planning concerning surgery wards will cover numerous specialisations concentrated around joint, shared resources, such as operating theatres.

Less frequently key resources are more strictly assigned and/or dedicated. Planning may be completely separated, since both equipment and personnel are linked only to a specific type of treatment or patient. For example, radiotherapy or intensive neonatal care may be planned as dedicated units.

History of decision-making models in oncology

Due to the fact of existence of cancer registries, both the incidence and the prevalence of cancer is relatively easier to define and model, while the outcomes, such as survival rate, may be measured. In cardiovascular diseases, for example, where severe symptoms, such as cardiac arrests (index cases), are visible and measurable, but the majority of cases are undiagnosed and may only be estimated, more comprehensive modelling and planning are required. Using methods enabling comparisons between individual epidemiological indicators and outcome indicators, many incentives appeared for preparing national oncology plans, oncological strategies and other strategic documents; their aim is to plan oncological care services, improve the survival rate and access to oncological services (WHO 2002, Albreht et al. 2011).

The planning of oncological services and infrastructure for a given population requires reliable estimation of demand for various services that are necessary for the population and depend on the number of new cancer cases, cancer stage upon diagnosis, required primary treatment method and the number of patients who require subsequent treatment cycles (repeated treatment) in the course of their disease. Examples and reference points for planning of oncological services may be based on:

- retrospective analysis of provided services and historically applied clinical practice;
- evidence-based medical guidelines;
- criterion-based models.

The first evidence-based models of services related to cancers were developed in 1974 in Sweden (Torgil et al. 2003; The Swedish Council on Technology Assessment in Health Care 1996). Following this approach, in 1991 the Swedish Council on Health Technology Assessment and Assessment of Social Services (SBU) issued directives on organisation of oncological care in Sweden. The Swedish models paid attention to the role to be played by regional medical centres that have to provide the most specialist services in the area of non-surgery oncological therapy, mostly radiotherapy and chemotherapy, but should also be involved in post-hospital treatment, continuation of therapy and home-based care, located as close as possible to the place where patients live.

The first evidence-based decision-making models were created for radiotherapy. Why was this the case, given that radiotherapy is only one of the three most often used cancer treatment procedures, others being surgery and chemotherapy? The answer to this question is linked to investment costs. Radiotherapy is the most capital-intensive method of cancer treatment, with a long implementation time, with the average time from a decision to invest in accelerators to introduction of radiotherapy services and to patient treatment amounting to several years. The cutting edge linear accelerators cost millions of euro and must be operated by qualified personnel. Therefore, radiotherapy services must be planned years in advance to obtain and maintain appropriate service capacity to meet the demand and to maximize the productivity of the purchased equipment[63].

In 2001, the Australian Department of Health and Ageing financed a project of the Collaboration for Cancer Outcomes Research and Evaluation (CCORE) entitled: *Radiotherapy in cancer care: estimating the optimal utilisation from a review of evidence-based clinical guidelines* (Delaney et al. 2003). The project involved a review of guidance on radiotherapy included in the clinical practice guidelines and other literature, which was then used to create trees of indications for radiotherapy for each type of cancer, referred to as decision trees. Although technically it is called a radiotherapy model, the model includes most types of radical surgical treatment[64]. The optimal radiotherapy utilisation rates for all types of cancers were calculated using the Australian reporting data on those services.

[63] By 2003, almost all EU Member States suddenly suffered a real decision of radiotherapy services and realised that radiotherapy offers "the appropriate cost to benefit ratio" (Barton et al. 2014).

[64] The data concerning indications for surgery are included in all decision trees. The decisions also take into account the patient health status and co-existent diseases, as well as the presence of focal lesions.

The results of the study were published in 2003 and the radiotherapy utilisation rate[65] for all cancer cases in Australia, based on optimal treatment pathways[66], amounted to 52.3%. This reference point for radiotherapy demand served as the basis for long-term planning of radiotherapy services in Australia. Since its publication, it has been adjusted for use in planning radiotherapy services around the world, including in England (Report to Ministers from National Radiotherapy Advisory Group 2007; A report for Cancer Research UK. Achieving a world-class radiotherapy service across the UK 2009), Scotland (Scottish Executive Health Department Report of the Radiotherapy Activity Planning Group 2005) and Europe (ESTRO-HERO Working Group) (Grau et al. 2014). It is also currently used by the International Atomic Energy Agency (IAEA) to estimate the demand for radiotherapy in developing countries (Rosenblatt et al. 2013).

The continuation of this approach is found also in other planning tools. For example, a more detailed modelling tool – the Malthus Model – was developed in England. The model uses local data on the type of cancer and distribution of its stages to model the use of equipment and the number of fractions (Round et al. 2013; Jena et al. 2012).

Decision trees were also created for chemotherapy.[67] The CCORE team built the optimal chemotherapy utilisation model using evidence-based indications for this type of oncological treatment. The indications for chemotherapy and epidemiological data were consolidated using TreeAge Pro 2007 to calculate the optimal chemotherapy rate. The model, published in 2010, is used as reference to compare the patterns of chemotherapy use in oncological treatment (Ng et al. 2010).

Criterion-based benchmarking (CBB) methods were developed in Canada in 2007 and combines the appropriate decision-making and optimal accessibility of services (Kerba 2007). The criteria used to determine radiotherapy demand are as follows: no barriers to referrals, decisions on radiotherapy made by experts working in optimal conditions and no incentives to use radiotherapy when this is not advisable.

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[65] Also called the appropriate radiotherapy rate (ARR) in Europe.

[66] A decision tree illustrating the optimal therapy is based on scientific evidence from international analyses which further increases the value of the proposed therapy.

[67] Chemotherapy was defined as any anti-cancer systematic treatment, including targeted therapy and immunotherapy.

Models for individual cancer streams – at which decision-making level?

How can we model services for the groups of patients who require highly specialist personnel, skills, infrastructure or technology, or any combination of them all? Operational modelling is seldom used is those cases, since the main and the most important decision on modelling is made at the strategic planning level to determine which types of cancer and/or patient groups require a national approach at the highest strategic level. In this case the major challenge is to balance two contradictory pressures:

- pressure on concentration of services due to low incidence, complexity of therapy or scope of knowledge required to ensure safe, fair and comprehensive services;
- preference for a modern model of oncological service provision which gives priority to diagnosis, therapy and long-term care at the local level, i.e. as close as possible to the patient's place of residence.

The first group of neoplasms that require a special approach includes almost 200 neoplasms defined as rare, i.e. those with incidence lower than 5 persons per 10,000 and/ or with prevalence below 6 per 100,000 persons annually (Gatta et al. 2010). In Europe, rare neoplasms are those which cause problems at the level of making clinical decisions, organisation of health care and clinical studies due to their low incidence rate, and thus limited specialist knowledge thereon (Gatta et al. 2013). The group also covers all cases of neoplasms in children. Although in Poland we could expect approximately 2500 cases of rare neoplasms (including approximately 1000 in children), the number of new cases of each rare neoplasm may range from one to 100.

Rare neoplasms in adults are usually classified into larger groups using the ICD-10 classification (e.g. neoplasms of oesophagus, neuroendocrine neoplasms); in the majority of cases, in European countries with the population below 100 million, one reference centre for each subtype should be sufficient.

Regardless of the type, cancers in children should be referred to specialist centres, and the challenge is to determine the number of centres offering diagnosis and treatment for such patients in the country.

Strategic planning becomes slightly more complicated in the middle group of neoplasms, i.e. those classified between rare and common neoplasms. Two main trends were identified over the last decades.

- In some neoplasms, the cooperation of specialist services and not the specialisation itself is of greater importance; the example of malignant neoplasms of head and neck shows that otorhinolaryngologists, oral surgeons, plastic and reconstructive surgeons, endocrine surgeons and neurosurgeons must cooperate during surgeries and share operating tasks to perform them at the same time or subsequently. Access to paramedical specialists, such as speech therapists, dieticians and others is also essential (British Association of Otorhinolaryngology Head and Neck Surgery 2011).
- Research has shown that cancer treatment exhibits the quantity-quality relation, connected with, among others, the learning curve. Although evidence is coherent for all services related to cancers, the benefits in specific types of cancers in the case of service provides with a large groups of patients are very impressive (Hopper et al. 2007; Vickers et al. 2007; Tekkis et al. 2005; Eden et al. 2009).

For strategic planning for those "complex" cancers, the recommendation is to plan and contract the services at the level covering the sufficient number of cases, and thus the population, regardless of administrative boundaries. For example, in the case of head and neck cancers, the minimum population recommended by the NICE is over one million patients, which translates into at least 100 new cases a year. The minimum population may be bigger (3 to 4 million) in other cancers, e.g. oesophagus, pancreatic cancers or central nervous system tumours, to ensure the sufficient number of cases per centre (Guidance on Cancer Services, Improving Outcomes in Head and Neck Cancers 2004).

Use of decision-making models to plan oncological services in surgery, radiotherapy and chemotherapy

The quality of a model depends primarily on its input data. The creation of all models for cancers must begin with collecting accurate and verified data on cancer incidence, data on distribution of individual pathological subtypes and data on distribution of stages in various types of cancer. The majority of countries have models projecting cancer incidence trends,

which are defined as all cases of cancer, excluding non-melanoma skin cancers (ICD-10 codes: C00-97, excluding C44). There is very little data available on the procedure to be followed when the reference point for incidence in a country does not exist or is inaccurate, as is often the case in developing countries. According to CCORE recommendations, the GLOBOCAN estimates should be used (Delaney et al. 2003). Data on cancer staging are not always available and reliable, even in developed countries. Partial data from regional audits, from neighbouring regions or international reference points are used in the absence of available source data – both the English and the Scottish models used original Australian data in some cases.

At the same time, optimal treatment pathways ("decision trees") for each cancer subtype must be determined. The radiotherapy (surgery and radiotherapy) model and chemotherapy models may be developed separately or in combination. Optimal treatment pathways should be changed only in rare cases and only when there are solid scientific grounds for a significantly different clinical management, for example, in the Scottish model such change was made in less than 2% of cancer cases. Having been filled in, such trees should be verified by local physicians, although it needs to be ensured that the physicians see the difference between the optimal and the current clinical practice.

In order to ensure the focus on patients' needs, the maximum travel time for radiotherapy and chemotherapy (but not necessarily for surgery), must be determined. This maximum time will be then treated as the cut-off point, with special exceptions for remote areas. In Scotland, such cut-off point was set at one hour each way, and in England, which is more urbanised, it currently amounts to 45 minutes (Report to Ministers from National Radiotherapy Advisory Group 2007). The models usually incorporate special planning tools, such as the Geographical Information System (GIS), which model patient travel times and analyse the impact of introducing potential new patient treatment centres.

The main cancer treatment procedures, i.e. surgery, radiotherapy and chemotherapy, require assumptions that reflect the current work schedules, skill mix and competency models. If there are shortages of staff and/or obsolete methods are used, this must be taken into account in the time horizon of the models. Treatment options should have capacity limiting factors embedded in the models. It is of special importance for radiotherapy, while such limitations were rarely reported in the case of surgery and chemotherapy.

In radiotherapy, there are technical and capacity constraints that must be modelled:

- Top-level guidelines (historically it was the number of linear accelerators per 100 million population, currently it is a more precise number of linear accelerators per cancer cases).
- Estimates of potential workload per linear accelerator based on work methods and such variables as the number of patients (450 patients on average per linear accelerator, although the number may be lower in the case of new techniques, such as IMRT).
- The current fractionation methods (the way in which the treatment is divided into daily doses) and the impact of hyperfractionation (more frequent, smaller doses) and hypofractionation (higher doses over a short time). Particular attention must be paid to eliminating the current treatment practices that are not based on optimum and evidence based treatment pathways.

One of the key modelling outputs is gap analysis, i.e. comparison of optimal treatment and current clinical practice. Based on such analysis, the element of unmet needs should be incorporated in the model to promote equal access in all cancer treatment procedures.

At present, the majority of models include also sensitivity analyses to assess the changes that may result from errors in epidemiological data or may occur where there is a conflict between treatment guidelines. Most models use the multivariate analysis (such as a Monte Carlo simulation) to analyse the sensitivity of the entire tree. An example which takes into account the maximum diversity in the model is uncertainty related to the choice between treatment options offering the same clinical benefits, e.g. the selection of therapy in early stages of prostate cancer (radiotherapy, brachytherapy, radical prostatectomy and active supervision). In such cases, the patient choice may be used to determine the proportion of patients assigned to each treatment option.

As a final result, all well-designed models will present a balance between the demand for and capacity of services and clear patient pathways, which unambiguously describe what should happen, in which order and when. The models should calculate the maximum length of the waiting list corresponding to the demand and key pathway stages, e.g. maximum time between referral and initiation of treatment.

Advantages, disadvantages, and restrictions of decision models

The purpose of models is to improve understanding and support discussion on how service providers/region/country can predict demand and plan service delivery accordingly. Their specificity generates certain restrictions: models should be subordinate tools aiding decision making, and we must not forget that, due to their very nature, the modelled position will never adequately reflect the reality.

Modelling based on retrospective studies of clinical practice is not advisable, as in the past it has been proven that planning based solely on information from physicians and professional associations may bring about disastrous consequences. Until year 2000 professional societies in England predicted that demand for radiotherapy would decrease. In 2007 experts agreed that projected demand for radiotherapy was largely underestimated, leading to a 63% gap between activity levels at that time and optimum treatment levels – therefore experts advised that within the next 5 years radiotherapy delivery capacity was to increase in England by 91% (Radiotherapy in England 2012, November 2012). As an increase in radiotherapy capacity requires a long time, the NHS introduced urgent measures concerning planning of both equipment and personnel training; in particular the measures changed working methods and requirements as to services, which helped ensure improved access in a short time.

Currently all developed countries use decision models for oncological treatment planning. The main advantages of modelling are: objectivity and scenario planning. Most importantly, it allows analysis of gaps (difference between current and optimal use). Frequently gap analysis shows that actual use level seems much lower than the optimal level, which suggests that individual therapies are not used for cancer treatment to the full extent. On the other hand, gap analysis may reveal that currently applied practices no longer match optimal treatment pathways.

Modelling and planning the service capacity and demand are not a one-off task. Models should be checked regularly so that projections of cancer incidence are adjusted and updated systematically. All clinical decision trees must be regularly checked to reflect changing clinical practice. It is reassuring that the model constantly changes to reflect clinical progress, but if the model is well formed, changes to final guidelines should be slight. In 10 years total optimal RUR in Australia changed from 52.3% in 2003 to 48.3% in 2012 (Barton et al.).

Criterion-based benchmarking (CBB) has several advantages: its methodology is based on observation, it is relatively inexpensive, and can be repeated when indications change. Contrary to evidence-based modelling, it does not require an exhaustive list of indications or information on combination of cancer cases in the population. Nonetheless there are several restrictions, and the most important one is the fact that the utilisation rate prediction gets complicated if referral is required for specialised consultations and/or if there is limited financing. Other restrictions include: absence of relevant guidelines for surgical procedures, treatment results, care quality and means to improve efficiency.

The major disadvantage of evidence-based modelling is the time necessary for all stakeholders to understand the restrictions of decision models, which means that their implementation may require legislative amendments and, more importantly, a major culture change in health care services. It is easy to prove that 3 centres are sufficient to ensure a certain kind of service, but absence of correct incentives (for example by payment restrictions) means that a model alone cannot change clinical practice. Another major restriction is the use of international reference points that may largely differ from local practice. For example, radiotherapy models do not model hospitalisation because they are based on outpatient radiotherapy. Unless local requirements reflect such points of reference, models alone cannot ensure improved access.

Another major limitation is the structure of services that promotes cooperation to competition. Having in mind that surgical treatment should be centralised, while radiotherapy and chemotherapy should be decentralised (close to the patient), the basic condition of success is smooth transfer of patients between service providers in formal or informal networks. In the case of service providers competing for financing, incentives for offering joint care must be clear. It also leads to a conflict between major and regional/satellite centres. Ideally, each centre would develop its field of specialisation and some resources would be distributed between the centres equitably. Experience shows that it is possible: oncological care networks based on equal partners can be established, even if such networks would include three world-class cancer treatment service providers (such as the London group in the United Kingdom). Strategic planning should take into account choice between small satellite centres and new service providers/centres based on existing infrastructure, which in time can develop into larger oncological care centres that would inevitably compete with current

major players and thus face resistance from those players. If a health care system is focused on the needs of the patient, provision of local services is a priority. In such case, models can be very useful in planning additional service delivery capacity in places where the gap between demand and service provision is the greatest.

Bibliography

A report for Cancer Research UK (2009) *Achieving a world-class radiotherapy service across the UK*.

Albreht T., Borras J., Conroy F. et al. (2011) *European Guide for Quality National Cancer Control Programmes EPAAC*.

Barton M.B., Jacob S., Shafiq J. et al. (2014) Estimating the demand for radiotherapy from the evidence: A review of changes from 2003 to 2012. *Radiother. Oncol.*, 112(1), pp. 140–144.

British Association of Otorhinolaryngology Head and Neck Surgery. The Royal College of Surgeons of England Head and Neck Cancer (2011) *Multidisciplinary Management Guidelines*, 4th edition.

Chevreul K., Durand-Zaleski I., Bahrami S., Hernández-Quevedo C. and Mladovsky P. (2010) France: Health system review. *Health Systems in Transition*, 12(6), pp. 1–291.

Delaney G.P., Jacob S., Featherstone C., Barton M.B. (2003) *Radiotherapy in cancer care: estimating optimal utilisation from a review of evidence-based clinical guidelines*, Collaboration for Cancer Outcomes Research and Evaluation (CCORE), Liverpool Hospital, Sydney, Australia.

Eden C.G., Neill M.G., Louie-Johnsun M.W. (2009) The first 1000 cases of laparoscopic radical prostatectomy in the UK: evidence of multiple 'learning curves'. *BJU Int.*, 103(9), pp. 1224–1230.

Ettelt S., Nolte E., Thomson S., Mays N. and the International Healthcare Comparisons Network (2008) Capacity Planning in health care, a Review of International Experience.

Grau C., Defourny N., Malicki J. et al. (2014) Radiotherapy equipment and departments in the European countries: final results from the ESTRO-HERO survey. *Radiother. Oncol.*, 112(2), pp. 155–164.

Gatta G., Capocaccia R., Trama A. et al. (2010) The Burden of Rare Cancers in Europe. Volume 686, pp. 285–303.

Gatta G. et al. (2013) Rzadkie nowotwory złośliwe – narastający problem w Europie i w Polsce. *Medycyna Praktyczna – Onkologia* 1.

Guidance on Cancer Services (2004) *Improving Outcomes in Head and Neck Cancers. The Manual*, NICE.

Hofmarcher M., Quentin W. (2013) Austria: Health system review. *Health Systems in Transition*, 15(7), pp. 1–291.

Hopper A.N., Jamison M.H., Lewis W.G. (2007) Learning curves in surgical practice. *Postgrad Med J.*, 83(986), pp. 777–779.

Jena R., Round C., Mee T. et al. (2012) The Malthus programme – a new tool for estimating radiotherapy demand at a local level. *Clin Oncol (R Coll Radiol)*, 24(1), pp. 1–3.

Kerba M. (2007) *How Should We Estimate the Need for Radiotherapy in the General Population? A Criterion-Based Benchmarking Approach*, Cancer Care Ontario Symposium.

Lee J.H., Ryu K.W., Lee J.H. et al. (2006) Learning curve for total gastrectomy with D2 lymph node dissection: cumulative sum analysis for qualified surgery. *Ann Surg. Oncol.*, 13, pp. 1175–1181.

Light D.W. (2003) Universal Health Care: Lessons From the British Experience. *Am. J. Public Health*, 93(1) pp. 25–30.

Ng W.L., Jacob S., Delaney G., Barton M. (2010) CCORE. Optimal chemotherapy utilization rate in cancer care: Setting an evidence-based benchmark for quality improvement. *J Clin Oncol* 28, p. 15 (suppl.; abstr. 6099).

Obermann K., Müller P., Müller H.H. et al. (2013) *Understanding the German Health Care System*, Ratgeber Verlag.

Report to Ministers from National Radiotherapy Advisory Group (2007) *Radiotherapy: developing a world class service for England*.

Rosenblatt E., Izewska J., Anacak Y. et al. (2013) Radiotherapy capacity in European countries: an analysis of the Directory of Radiotherapy Centres (DIRAC) database. *Lancet Oncol.*, 14(2), pp. 79–86.

Round C., Mee T., Kirkby N.F. et al. (2013) The Malthus Programme: developing radiotherapy demand models for breast and prostate cancer at the local, regional and national level. *Clin Oncol (R Coll Radiol)*, 25(9), pp. 538–545.

Round C.E., Williams M.V., Mee T. et al. (2013) Radiotherapy Demand and Activity in England 2006–2020. *Clinical Oncology* Volume 25, Issue 9, pp. 522–530.

Scottish Executive Health Department Report of the Radiotherapy Activity Planning Group (2005) *Radiotherapy Activity Planning for Scotland 2011–2015*.

Tekkis P.P., Senagore A.J., Delaney C.P. et al. (2005) Evaluation of the learning curve in laparoscopic colorectal surgery: comparison of right sided and leftsided resections. *Ann Surg.*, 242(1), pp. 83–91.

Torgil R., Moller et al. (2003) Radiotherapy and Cancer Care in Sweden. *Acta Oncologica*, vol. 42, No 5/6, pp. 366–375.

The National Radiotherapy Implementation Group. Department of Health Cancer Policy Team (2012) *Radiotherapy in England 2012*.

The Swedish Council on Technology Assessment in Health Care (1996) Radiotherapy for cancer. The development of radiotherapy: physics, technology, methods. *Acta Oncol*, 35 (supl. 6), pp. 24–30.

Thomson at al. (2013) *International profiles of Health Care Systems*, New York: The Commonwealth Fund.

Vickers A.J., Bianco F.J., Serio A.M. et al. (2007) The surgical learning curve for prostate cancer control after radical prostatectomy. *J Natl Cancer Inst*, 99, pp. 1171–1177.

Vuorenkoski L., Mladovsky P., Mossialos E. (2008) Finland: Health system review. *Health Systems in Transition* 10(4), pp. 1–168.

Wagstaf A. (2009) *Social Health Insurance vs. Tax-Financed Health Systems – Evidence from the OECD*, The World Bank Development Research Group Human Development and Public Services Team.

Williams M.V., Drinkwater K.J. (2009) Radiotherapy in England in 2007: modelled demand and audited activity. *Clin Oncol (R Coll Radiol)*, 24(1), pp. 575–590.

World Health Organization (2002) *National cancer control programmes: policies and managerial guidelines*, Geneva.

Grossman, M. (1972), On the Concept of Health Capital and the Demand for Health, *Journal of Political Economy* 80 (2), pp. 223–255, doi:10.1086/259880.

Sources and Quality of Cancer Epidemiological Data in Poland - Data Analysis Methodology

Barbara Więckowska, Janusz Dagiel, Beata Koń, Filip Urbański

Introduction

When drafting analytical models, one thing is inordinately important - apart from a correct definition of a theoretical model which will reflect a phenomenon under research with acceptable accuracy - is to prepare an appropriate set of data to be used for empirical analyses and to forecast values estimations. The more detailed input data, the smaller sub-groups within a general population can be analysed (eg. 3 age groups vs 10-year age groups vs. one-year age groups). Conversely, the greater the aggregates used by a researcher, the bigger simplifications must be made in a theoretical model and the more general conclusions can be drawn. On the other hand, though, one should be careful that the sample for a given sub-group is not too small, otherwise in case of a great variability of the latter, it will be impossible for the study results to be interpreted unequivocally.

Limitations concerning the data scope, availability and quality may also result from the applicable legislation. Direct access to data included in the National Cancer Registry is limited to cross-sectional information which makes it impossible to conduct a cohort analysis; moreover - as it is demonstrated further - the data is incomplete. The second source of information about the number of patients and on health services provided to them is the reporting system of the National Health Fund[68]. However, also in this case it is quite problematic to define the number of services and the clinical pathway - it is primarily a database used for the purposes of funding health-care services, so the data therein is presented against products reimbursed rather than patients or groups thereof[69].

[68] The assumption behind the database is also that the number of cancer patients treated exclusively within the private health care system in Poland is statistically negligent.

[69] One should also not forget about the *up-coding* phenomenon (health-care provider or medical coder charging for a service which was not actually performed), which is the case in practically all health-care systems worldwide - European Observatory on Health Systems and Policies Series (2001), p. 72, and Silverman E., Skinner J. (2004), pp. 369–389.

This article aims at presenting a methodology for estimating cancer incidence rate in Poland (new cases) and 5-year prevalence. The methodology was used for making decision trees as tools for treating various cancer types and for the construction of a forecasting model for estimating the number of new cancer cases in Poland for the period 2015-2025 as well as for defining 5-year prevalence in that period.

Methodology for estimating cancer incidence rate in Poland

Data bases used

National Cancer Registry (NCR) is the first source of information on cancer incidence in Poland; it was established under a project „Establishing the first in Poland scientific IT platform for sharing knowledge concerning cancer risk in Poland". This project assumed the establishment of a central database of cancer knowledge with access by regional branches, instead of the dispersed system which operated earlier. Although NCR provides (since 2013) a possibility of recording cases on-line, paper records' system based on sending a cancer case report by mail to a relevant regional office is still in use. After the data submission the case was appropriately verified and entered into the data base. This type of reporting pathway resulted in obvious delays for the collection of complete data[70].

Pursuant to The Act of 28 April 2011 on health-care information system (Journal of Laws 2011 No 113 item 657) and Ordinance of the Minister of Health of 20 December 2012 on the establishment of the National Cancer Registry (Journal of Laws 2012 item 1497) entities are under obligation to report a cancer case or suspected cancer case. Legislative amendments passed in the form of a so called oncological package which entered into force on 1 January 2015 resulted in the establishment of a mechanism which conditioned a limitless settlement of payment for providing services to an oncological patient on i.a. the patient being reported to the National Cancer Registry (using an on-line application or by means of a direct XML communication generated by a hospital system). This solution should have a positive impact on the completeness of NCR database as well as reducing delays resulting from paper reporting. Considering the above, one can surmise that there is a risk that information collected in NCR

[70] see: http://onkologia.org.pl/system-rejestracji-nowotworow (access: 13 May 2015.

is incomplete (in terms of particular cases not being recorded and in terms of the recorded data being incomplete) and as a result it is necessary to complement the data from other sources. In the process of analysis a decision was made to use the records of the National Health Fund (NHF data base) as the second source of information on cancer incidence rate in Poland. One should remember, however, that the data base includes only patients who have been diagnosed and treated within the public health care system and that the period of the data base operation is significantly shorter than the period of NCR operation (Voivodeship Cancer Registers have been in operation since 1963, in order to process them at the national level, in 2012 a National Bureau for Cancer Registration was established, and the electronic records of NHF have been operating only since 2008). Due to this fact, uncritical linkage of NCR information with NHF data could result in the following errors:

- a patient was not recorded in NCR, but started treatment before 2008 - this is a patient under monitoring,
- a patient was not recorded in NCR, started treatment in a given year (under analysis), but the diagnosis presented for financial settlement is erroneous,
- a patient was not recorded in NCR, because he/she did not have cancer diagnosed, but due to some reason, a cancer diagnosis appeared in the NHZ data base.

Thus, it is necessary to define rules which structure the way information is used from both these sources. These rules have been described in the following sub-sections, however, due to a financial character of data included in the NHF database, in case of conflict (cancer diagnosis) the superiority of NCR data base is assumed.

Data obtained from Voivodeship Record Bureaus are verified at central level. Because of various delays resulting from paper reporting and because of time-consuming verification mechanisms, at the moment of conducting the analyses for the purposes of this publication, the results of which are going to be presented below, complete data for the year 2013 and later years were not available. This translates into the need to allocate the distribution of cancer disease stage for the majority of patients diagnosed post 2012. Due to this fact, analysis was conducted of the period 2010-2012 - the lower time limit results from limitations of the NHF databases (and a possibility to make a retrospection of the analysed year), and the upper time limit results from limitations of the NCR (data incompleteness resulting from delays in reporting).

The analyses conducted related to cancer diseases defined as solid tumours, i.e. excluding cancers of lymphatic and hematopoietic system (Table 1). The analysis excluded also non melanoma skin cancers (except for malignant melanoma, which was subject to analyses). Exclusion of this group of cancers was due to its specific character - regardless of its malignancy, only in rare cases are they life-threatening[71], and their treatment can often be conducted in ambulatory conditions (under local anaesthesia)[72]. In addition, non-melanoma skin cancers are excluded from international statistics (e.g. GLOBOCAN[73]) – and for the purposes of comparability with international results this was taken into account. Also, the analysis excluded tumours with very low incidence according to NCR data base (e.g. heart tumors, intraocular melanoma or thymoma) - too small annual number of cases would not allow making any inferences about trends. Therefore the results from the analysis have been extrapolated to the remaining 6.2% of the cases of solid tumours.

The analyses conducted ignored D00-D09 diagnoses (apart from D05 qualified as in-situ breast cancer). This decision resulted from practical reasons as there are insignificant number of patients with such diagnoses (apart from breast and cervical cancers).

International classification of diseases and health problems includes codes D37-D48 (neoplasms, the character of which is unknown or unidentified); in the analyses were taken into consideration only those patients who appeared in the system with the C (or D05) diagnosis. A reason behind this decision was that those codes are applied i.a. for reporting a service provided for which the histopathological results were not available at the moment of reporting. If a malignant cancer is confirmed, a patient returns to the system with the malignant cancer diagnosis (he/she will be taken account of in further analyses) for further treatment or monitoring. If the patient has not returned to the system with the C diagnosis, it has been assumed that the malignant cancer has not been confirmed. Services provided to patients with D37-D48 diagnoses, who returned to the system, were taken into consideration when defining the stage of cancer disease. Systematics of the analysed diagnoses according to ICD-10 has been presented in Table 1.

[71] 312 deaths a year with over 12 thousands cases a year – 2% mortality rate (NCR 2012).
[72] *Współczesna Onkologia* (2005) vol. 9; 10, pp. 429–435.
[73] See: http://globocan.iarc.fr/ia/World/atlas.html (access: 7.05.2015).

Table 1. Cancer groups analysed (source: own analysis DAiS)

Group		ICD10
Central Nervous System		C70, C71, C72
Melanoma		C43
Lower segment of gastrointestinal tract	Large intestine	C18, C19
	Rectum and anus	C20, C21
Gyneacological	cervix	C53
	corpus uteri	C54
	ovary	C56
Head and neck	lip	C00
	mouth	C01, C02, C03, C04, C05, C06, C09, C10, C14
	salivary glands	C07, C08
	nose cavity, sinuses	C11, C12, C13, C30, C31
	larynx	C32
Upper segment of gastrointestinal tract	oesophagus	C15
	stomach	C16, C26
	liver	C22
	gallbladder	C23, C24
	pancreas	C25
Testicle		C62
Kidney		C64, C65, C66
Bladder		C67
Breast		C50, D05
Lung		C33, C34
Prostate		C61
Thyroid		C73

First appearance of a patient in the system

The first step of analysis was to define a set of potential new cancer cases in Poland, based on NCR and NHF databases. This is why, for each of the analysed years 2010-2012 (YEAR* - analysed year: e.g. 2011) for a given diagnosis according to ICD-10 (ICD10* - analysed group of diagnoses for a given cancer: eg. C18-C19) the date of first appearance in each of the data bases is indicated. Possible combinations and resulting decisions concerning patient's disease are presented in Table 2, in which the label:

- “NEW” means a patient who is assumed to have appeared in the whole health-care system in the analysed year YEAR* and it includes all the patients who were recorded in the NCR data base and did not have a relevant diagnosis recorded in the NHF data base before YEAR*, as well as those who were recorded for the first time in the NHF data base in YEAR*, but were not recorded in the NCR data base or were recorded in it later than YEAR*,
- “OLD” means a patient who is assumed to have appeared in the whole health-care system prior to the year YEAR*, i.e. was recorded in any data base with an ICD10* diagnosis before YEAR*, i.e. is a *follow-up* patient,
- “FUTURE” means a patient who is assumed to have appeared in the health-care system after the analysed year YEAR*,
- “not recorded” means a patient who has not been recorded in an of the data bases. This is unobserved theoretical category, which by definition cannot be taken account of in further analysis.
-

Table 2. Definition of a new patient based on information from two data bases (source: own analysis DAiS)

ICD10=ICD10*		National Cancer Registry			
NHF		No data available	YEAR<YEAR*	YEAR=YEAR*	YEAR>YEAR*
	No data available	Not recorded	OLD	NEW	FUTURE
	YEAR<YEAR*	OLD	OLD	OLD	OLD
	YEAR=YEAR*	NEW	OLD	NEW	NEW
	YEAR>YEAR*	FUTURE	OLD	NEW	FUTURE

As it has already been mentioned, all the records in NCR were treated as substantially correct (i.e. the very fact of cancer confirmation as well as the type of cancer concerned). However uncritical consideration of data from the NHF database seems to be unjustified. Due to this fact further, necessary and in-depth analyses were made, in which only patients ascribed to the “NEW” category have been taken account of. These patients compose a set of potentially “first time” patients who determine the value of incidence ratio. Based on this set, following appropriate transformations, it will also be possible to estimate the value of 5-year oncological prevalence (see: Methodology for estimating 5-year oncological prevalence).

Correctness of diagnoses according to ICD-10

Due to a different character of the data bases used, in some cases there is a risk of unreliability of information originating from the NHF database. Settlement requirements may lead to erroneous diagnostic assumption - let us remember that the NEW group of patients included not all the oncological patients, but patients with a given group of diagnosis according to ICD10*. Due to this fact, in case of discrepancy between the databases as to diagnosis, information obtained based on NCR data base is accepted. Due to a specific process of information flow to NCR (significant delays) verification covers information from the year under analysis and the period up to 365 days of the first appearance in the system according to the NHS database. The decision-making sequence as a result of which patients are taken into consideration has been presented in Table 3 and Table 4.

Table 3. Decision-making sequence determining an ICD-10 diagnosis
(source. own analysis DAiS)

<table>
<tr><th colspan="4">Is a given patient with ICD10* recorded in the NCR in the year YEAR*?</th></tr>
<tr><td>TRUE

<u>Decision: 2</u></td><td colspan="3">FALSE

Is a given patient with ICD10* recorded in NCR in the period of 365 days of the first appearance in the system according to NHF?</td></tr>
<tr><td></td><td>TRUE

<u>Decision: 2</u></td><td colspan="2">FALSE

Was a given patient recorded in NCR in the year YEAR* (with a different diagnosis)?</td></tr>
<tr><td></td><td></td><td>TRUE

<u>Decision: 0</u></td><td>FALSE

Is a given patient recorded in NCR in the period of 365 days of the first appearance (with a different diagnosis)?</td></tr>
<tr><td></td><td></td><td></td><td>TRUE

<u>Decision: 0</u></td><td>FALSE

<u>Decision: 1</u></td></tr>
</table>

Table 4. Decision-making sequence determining a correct ICD-10 diagnosis (source. own analysis DAiS)

Decision:	Is the patient taken into account in the analysis?	Justification
2	YES	Information about ICD-10 is consistent with NCR database[1]
1	YES	No records in NCR in a period under consideration - information from NHF is taken into account (as the only available)
0	NO	Information about ICD-10 is inconsistent between the databases. Based on information from NCR data base, patient will be taken account of in the analysis of another ICD-10, in the year which is consistent with the date entered in the NCR.

Based on applying the above mentioned decision-making sequence, a set of data about potentially new oncological patients have been obtained, which includes: (1) patients recorded in a given year YEAR* in NCR with a given ICD10* and (2) patients recorded for the first time in NHF, who were not recorded in NCR with other diagnoses as ICD-10*. This set was subject to further analysis, in order to analyse the occurrence of three types of potential errors:

- despite a record in NCR in year YEAR* patient was treated prior to 2009 (i.e. a *follow-up* patient),
- despite the first appearance in the NCR database in year YEAR* with a given ICD10* the patient was treated prior to 2009 (i.e. a *follow-up* patient),
- despite the first appearance in the NCR database in year YEAR* with a given ICD10* the patient suffers from some other disease than cancer with a given ICD10* (i.e. wrongly coded patient),

Further set reduction - the use of information about services

In order to eliminate people who fall into one of the error groups described above from the group of potential new patients, information concerning the services provided to patients was used. The method applied at this stage includes three main steps:

1) collecting information about services provided for a given group of patients,

2) preparing dictionaries of service groups,

3) categorizing patients against types of services. The above described approach was applied to patients in relation to whom the stage of cancer development was not defined. Patients whose stage of disease development was defined in NCR were assigned to the group of new patients.

Ad. 1) Downloading all available information for the set of potentially new patients

For patients defined in the point, all[74] information from the NHF database was downloaded; also that which are not recorded with a given ICD10* diagnosis. This information was reduced to the period of 365 days of the moment the patient entered the system, i.e. as of the patient's appearance in the NHF database or NCR database up to 182 days prior to that date. A sequence for obtaining the set concerned looked as follows:

a) For each patient from the group of potentially new patients (ID_NEW) define:

$$Date_{Entry} = \min(Date_{NCR}, Date_{NHF})$$

where: $Date_{NCR}$ - date of first record of patient made in the NCR database with ICD10* diagnosis

$Date_{NHF}$-date of first record of patient made in the NHF database with ICD10* diagnosis

b) Download data from NHF database for all ID_NEW with type of services

- AOS, including ASDK or
- HOSPITAL or
- SOK

for YEAR*-1, *YEAR** and *YEAR*+1*

c) Save only data which fulfil the requirement:

$$Date_{Entry} - 182\ days \leq Date_{starting\ a\ service} \leq Date_{Entry} + 365\ days$$

This step means that the analysis will take account of services provided during 365 days of the moment of first appearance in the system (it is assumed that at that time in the majority of cases the main part of therapy is conducted) and services provided during 182 days prior

[74] i.e. concerning hospital services, specialized ambulatory services and services contracted separately.

to first appearance within the system (it was assumed that certain services, due to reporting procedure, could have been provided without the confirmation of oncological diagnosis, e.g. with suspected oncological disease)

d) Attach information about the stage of disease development from NCR

Ad. 2) Preparing dictionaries of service groups

NHF reporting data can be divided into two groups - data about reported financial products and data about reported medical procedures assigned to the products. Depending on the reported products one can define their character based on a product alone (e.g. administering of a chemotherapy drug informs about chemotherapy treatment implementation) or based on the reported procedures which were provided to a given patient (if a settlement products includes a Uniform Patient Group of too broad a scope - then the product may be settled in case of implementing diagnostic procedures as well as in case of smaller therapeutic treatments[75], because of this one cannot infer about a diagnostic or therapeutic character of a service based on the group alone).

On the basis of expert knowledge and medical standards for each of the types of ICD10* cancers, a glossary of ICD-9 procedures has been developed, which was followed by assigning each of the approx. 10 thousand procedures to one of the 10 following categories:

0. Zero procedures - procedures whose implementation does not supply any additional (material) information about the process of cancer treatment.
1. Diagnostic procedures - TK, PET, RM, RGT, ultrasonography, mammography, bronchoscopy, colonoscopy procedures, excluding biopsy, etc.
2. Diagnostic and therapeutic procedures - diagnostic procedures which, in particular cases, could also be a therapeutic procedure; for example: cervical conization in case of early cervical cancer, colonoscopic polypectomy at the early stage of colon cancer.

[75] A part of Homogenous Patient Groups requires a report on the implementation of procedures indicated in the product description - these are treatment UPGs. Apart from those there are also conservative UPGs, in case of which procedure reporting depends on the service provider's will. Due to a financial character of NHF reporting, not all procedures provided to a patient might have been recorded. Due to this fact one should assume that the data on procedures implemented will be more biased in case of conservative UPGs rather than procedural UPGs.

3. Radiotherapy/chemotherapy procedures - due to specific NHF reporting, information on chemotherapy or radiotherapy service provided was taken out for further analysis from the database of reported settlement products, rather than medical procedures.
4. Procedures involving lymph nodes; for example: sentinel lymph node resection, radical dissection of regional nodes.
5. Procedures of treating metastases to brain/bones.
6. Procedures belonging to palliative services; e.g. services provided by a nurse in palliative care.
7. Surgical procedures belonging to palliative services - surgical procedures indicating palliative treatment.
8. Major surgeries in the area not related with directly treated cancer - depending on a type of cancer, they are evidence of wrongly coded ICD-10* diagnosis or are an important service, which cannot, however, be qualified to group 9 (e.g. castration in prostate cancer).
9. Major surgeries - in many cases they meant a radical surgery service.

The order of listing of the above mentioned categories results from the informative value of the fact of the procedure being executed - a maximum of groups of procedures executed under a given service enables to define the character of service provided (i.e. the higher the value of service group, the higher the informative value of the reported procedure concerning the character of treatment). For example, in the combination (for one service) of Diagnostic procedures + Major surgeries the information, from the point of view of defining the stage of disease development, is conferred by the fact of performing a major surgical operation - diagnostic procedures are performed at any stage, also in follow-up patients. Domination of major surgeries over palliative services results from the analysis of how to qualify a patient who received such services - this usually means a performance of a major surgery and - as a consequence of change in the patient's condition - starting palliative treatment. In such a situation the treatment planned (i.e. the treatment after which one could make inferences about the stage at the moment of making a diagnosis) meant a major surgery. Due to the above, in case of a major surgery, information about simultaneous provision of palliative services does not change the decision concerning patient qualification.

In addition, a glossary of financial products subject to settlement was developed, which defined a character of service based on the service reported. It included the following services in particular:

- Chemotherapy - handling, substances, therapeutic regimens, drug regimes
- Palliative radiotherapy - a product of palliative radiotherapy
- Radical radiotherapy - teleradiotherapy (apart from palliative, intraoperative teleradiotherapy, in treating skin diseases), brachytherapy
- Nuclear medicine

The above glossaries enabled defining a character of the reported services.

Ad. 3) Categorizing patients against types of services

Using information on services provided for a selected group of patients and the glossaries of service groups, each patient for whom the stage of cancer development was not defined in NCR[76], was categorized to one of the groups in the following way. For each patient the following parameters were defined:

- whether the patient concerned was recorded in NCR,
- whether the patient concerned died within 365 days of being recorded in the system,
- whether the patient received chemotherapy services,
- whether the patient received radical radiotherapy services,
- what was the highest group of procedures provided to a given patient.

Based on experts' knowledge, for each combination of the above mentioned parameters probability was defined, that the patient was for the first time diagnosed in a given year (this probability is obviously higher for a patient who, since his/her appearance within the system, underwent a major surgery and was recorded in NCR than for a patient who, while not being recorded in NCR, entered the system only for the purpose of diagnostic tests and survived another year.)

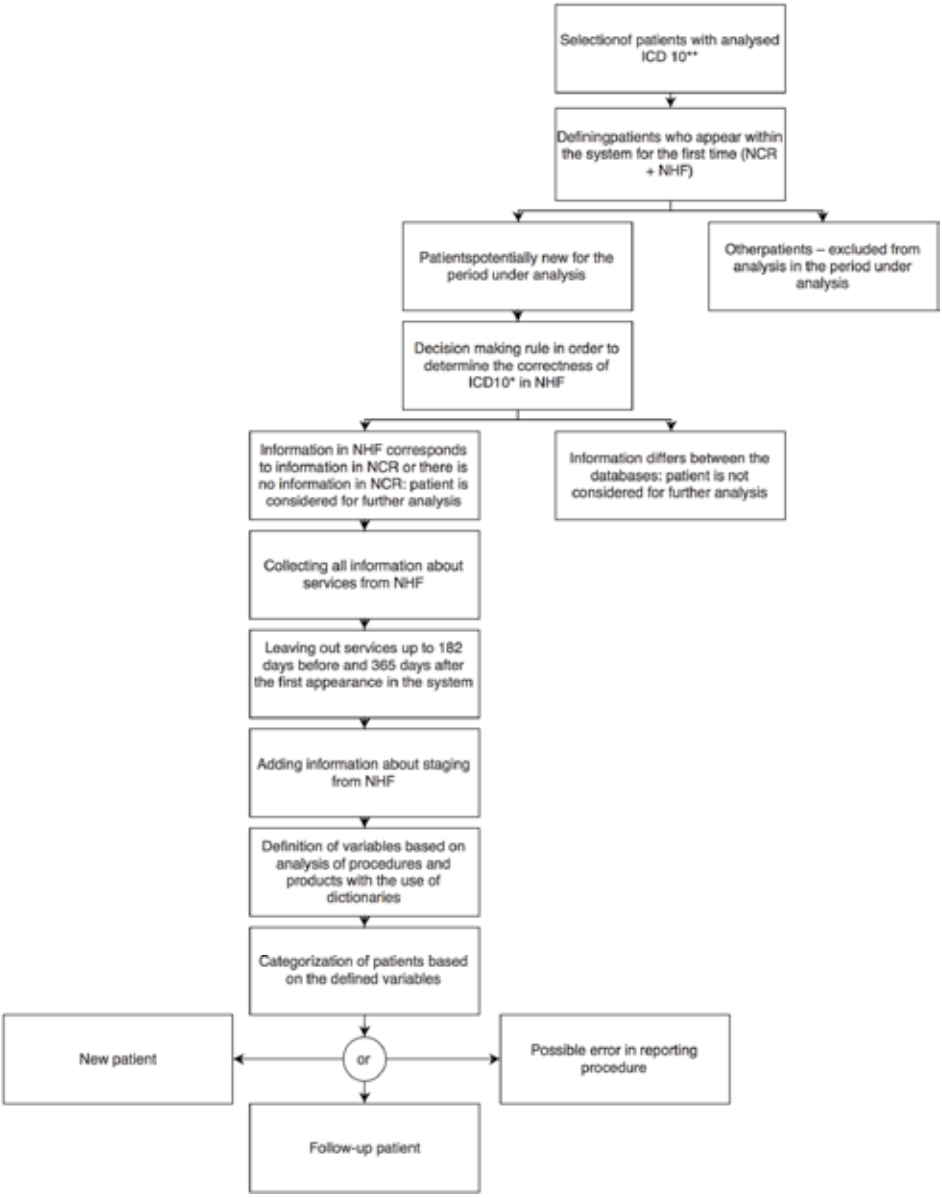
Based on the application of the above-mentioned algorithm, patients - in case of whom services and procedures provided to them did not show that they are new patients - were excluded from the group of potentially new patients. The group of excluded patients included

[76] More information concerning disease stage definition - see the following sub-chapter.

mainly patients who survived another year and underwent check-up (implementation of diagnostic or zero procedures). Decision-making procedure depended on the type of cancer (for example: prostate cancer analysis took account of new patients who received hormone therapy, even if the patients did not have radio- or chemotherapy provided, or did not have a surgery).

It has to be underlined that patients categorized as *follow-up* patients were not categorized to any of the newly diagnosed patients in the period 2010-2012. The algorithm applied forces the first appearance of patients under consideration in the system to occur in the year under analysis, so a possible earlier diagnosis of cancer must have occurred before 2008.

To sum up, by using the NCR database and the NHF database a set of patients was developed, who for the first time were diagnosed with a given ICD-10* cancer in the defined year YEAR*, and this action did not involve uncritical combination of the above mentioned sets. From the database of the National Cancer Registry, records were taken of patients who, despite the first record, were qualified as follow-up patients on the basis of the services provided to them. As far as the NHF database, records were taken from the database of patients reported with other type of cancer than that reported in the National Cancer Registry (NCR database's superiority over the NHF database) who, despite the first record, were qualified as follow-up patients on the basis of the services that were provided to them (Figure 1).



Flowchart 1. Categorization of patients based on NCR and NHF databases (source: own analysis DAiS)

Methodology for determining the stage of cancer development

Use of information from NCR database

Among a range of information about oncological patient that is entered in the NCR database[77], there is also data concerning the stage of cancer development. Data is collected concerning the stage of cancer development according to TNM, but also according to FIGO, Ann Arbor, Astler-Coller, Breslow/Clark or Gleason score. In addition, in a closed question, the reporter defines the stage of cancer (0-IV). Due to a close and uniform character of this field, the data collected there is the most useful.

The NCR database often includes a number of records concerning one patient - also concerning a given type of cancer. Those records differ by date of diagnosis or the stage of cancer. In order to select, for a given patient, a unique record to NCR with a given cancer, the record corresponding in the closest way to the date of entry in the system was selected. This means that the selected unique NCR record can include the date of cancer diagnosis that precedes the date of starting services reported to NHF or follows it.

The method of feeding in data to the database does not force the reporter to fill out all the fields of the form. Due to this fact, information about the cancer stage is not provided in case of some newly recorded cancer cases. If the stage of cancer is not provided in the latest record in NCR, and there is some other record in NCR which is made earlier in the same year and which reveals the cancer stage, then this earlier record describing the revealed cancer stage is taken account of.

Cancer staging

NCR database is the only direct information source about cancer stage. However, there is no possibility to obtain information about all the cases. This variable has a high percentage of data absence. Moreover, there are patients who only appear in the NHF. The information sources used for the purposes of staging procedure has been presented in Table 5.

[77] Application form - http://onkologia.org.pl/wp-content/uploads/KZNZ_2014.pdf (access: 7.05.2015).

Table 5. Sources of information used for staging procedure (own analysis DAiS)

		Is the patient recorded in the NCR database?		
		YES		NO
		Stage		
		KNOWN	UNKNOWN	
Is the patient recorded in the NHF database?	YES	NCR STAGE	Imputation possible	Imputation possible
	NO	NCR STAGE	Imputation impossible	Imputation impossible

Services that are closely related to cancer treatment are listed based on analysis of procedures against ICD-9 or products' classifications (only in case of chemo- and radiotherapy). This approach ensures taking account of all the services used in oncological treatment, also those that have been coded in the NHF database with non-oncological diagnosis or product.

Since there is a big percentage of data absence in NCR concerning stage of cancer and patients who are recorded only in NHF, this variable must be imputed by means of an expert method. Statistical methods are not applicable here because one of the categories is not represented within the set (i.e. stage of cancer = 1).

The staging process is analogous to defining new patients (see point 4 in chapter "Methodology for estimating cancer incidence rate in Poland".) Based on product dictionaries and procedures developed earlier the character of patient's treatment has been determined. Based on the data concerning:

- the fact of providing chemotherapy,
- the fact of providing radiotherapy,
- the most important procedure;
- whether the patient died within a year from being recorded in the system,

it was possible to define the patient's treatment pathway and to conclude whether the patient was alive after 365 days from the malignant neoplasm diagnosis. The patient's pathway served to define the chances of patient to be included in a group of one of four cancer stages. They were defined on the basis of expertise based on foreign decision trees

describing optimal treatment pathways of oncological patients in particular cancer stages, on recommendations of medical associations as well as on knowledge and clinical experience concerning treatment of a given type of cancer.

Due to up-coding and problems with completeness of data in NCR, the patients included in the register with unidentified stage of disease and patients not included in the NCR were analysed separately. In case of the first group of patients, it was assumed that every patient registered in NCR is an oncological patient with a given type of cancer and that there are no mistakes in the database records. It was also assumed, that this group may include the follow-up patients, who received medical services before 2009 and were not registered in the NCR database then. The treatment pathway of such patient include mainly diagnostic procedures or – in certain types of cancer – additionally monotherapy in the form of chemotherapy. The analogous assumption was made for patients who were not registered in NCR, but who received services with malignant neoplasm diagnosis. However for this group of patients an additional assumption was made, that the diagnosis for some of them is registered erroneously. The treatment pathway for such persons included services that were not appropriate for the given type of cancer or which were related only to diagnostic procedures.

Methodology for estimating 5-year oncological prevalence

The complete analysis of the oncological care system needs determining, apart from incidence, the level of prevalence. The number of currently living oncological patients translates into demand for medical services and into the need to adjust availability of resources to demand. This information is crucial in health care investment planning, as it enables ensuring efficiency of the allocated means and allows better adjustment to the health care needs of the population. Additionally this statistic is important for further epidemiological analyses.

The register potentially containing information on prevalence in Poland is the National Cancer Registry – it should include registration of both cancer diagnosis and patient's death. Nevertheless, considering the data gaps in reports to NCR, which were found during the analyses, the use of different, additionally available information should be considered. Not every oncological patient appears each year in the public health care system (NHF data base)

– part of them will undergo check-up[78], however not every patient uses this option in the public system. Therefore, it is not possible to define prevalence with the use of method based on register.

Prevalence can be estimated on the basis of the information about the incidence. A number of living patients who appeared in the system before a YEAR^* need to be added to a number of new cases diagnosed in the analysed YEAR^*. In such a case prevalence in the beginning of the YEAR^* is expressed with the following formula

$$PREV_{YEAR^*} = z_{YEAR^*} + \sum_{i=1}^{\infty} z_{YEAR^*-i}\, p_i$$

where:

p_i –survival rate for *i* years, i.e. a chance, that a patient will live for *i* years; defined on the basis of theoretical or empirical data,

z_{YEAR^*} –incidence in a YEAR^*.

As the calculation with the use of non-finite sums is difficult, the assumption limiting this number is often made. One possible limitation consists in assuming such *j*, that:

$$\bigwedge_{i>j} p_i = 0$$

that is defining such a year, for which it is assumed, that patients recorded in the system in this year still live in a YEAR^*. Alternatively, a relevant set may be limited. In case of cancer it may concentrate on 5-year prevalence – patients who were diagnosed within last 5 years. In many cases it reflects the time of treatment and of intensive monitoring of the results of treatment – those patients require regular control visits with specialised physicians. Therefore the final formula is the following:

$$PREV_{5:K} = z_K + \sum_{i=1}^{4} z_{K-i}\, p_i$$

Therefore, to calculate 5-year prevalence, it is necessary to determine incidence $(z_{YEAR^*}, \dots, z_{YEAR^*-4})$ and survival $(p_1, \dots, p_4)$. Incidence per year YEAR^* may be estimated on the basis of empirical incidence referred to the projected one in the year YEAR^* of the

[78] So called hospitalised prevalence.

population. Additionally this incidence may be adjusted by the age structure to include projected changes in the demographic structure (population ageing). The abovementioned mechanism allow determining incidence $(z_{YEAR^*}, \dots, z_{YEAR^*-4})$ on the basis of the Central Statistical Office (CSO) projections concerning demographic structure for years $\mathrm{YEAR}^* - 4$, ...,YEAR^*.

$$z_{YEAR^*} = \sum_{i \in I} W_z^i \, L_{YEAR^*}^i$$

where I is a set of age groups, W_z^i is an incidence ratio in a given age group and $L_{YEAR^*}^i$ is a population in a given age group and in a year YEAR* (for remaining years in an analogous way).

Then, with the use of chosen methods, the survival rate for one, two, ..., five years need to be determined. Relevant publicly available statistics may be used (keeping in mind possibility of errors they comprise), as well as expertise and empirical data. Those survivals can also be determined precisely according to age groups, which allows better inclusion of changes in demographic analyses. After determining the abovementioned survivals, the calculation of 5-year prevalence consists in calculating the appropriate sum of products. Therefore, by applying formula:

$$PREV_{5:YEAR^*} = \sum_{i \in I} W_z^i \, L_{YEAR^*}^i + \sum_{j=1}^{4} \left(\sum_{i \in I} W_z^i \, L_{YEAR^*}^i \right) p_j$$

the value of five-year prevalence without dividing survival rate into age groups will be calculated, while by applying the formula:

$$PREV_{5:YEAR^*} = \sum_{i \in I} W_z^i \, L_{YEAR^*}^i + \sum_{j=1}^{4} \left(\sum_{i \in I} W_z^i \, L_{YEAR^*}^i p_j^i \right)$$

where:

p_j^i – j-year survival rate in an age group i

enables calculating this value with the use of survival rate differentiation among age groups.

In order to determine five-year oncological prevalence using the abovementioned methods, it was necessary to define incidence ratio and survival rate ratio for the given age groups. For this purpose, the discretization of patients' age into the following age groups was performed

(set): 0–44, 45–54, 55–64, 65–74, 75–84, 85+. The reason for choosing such a division was to include the relationship between the incidence and the age, to retain compliance with the age grouping in CSO projections and so that the sample size in all the resulting groups enabled statistical inference.

For every cancer group, every stage and every defined age group, the incidence ratio was determined on the basis of empirical data from the years 2010–2012 as:

$$\frac{number\ of\ cases\ in\ years\ 2010\text{–}2012}{population\ in\ years\ 2010\text{–}2012\ (sum\ of\ population\ in\ a\ year)}.$$

This method of case grouping enabled within 3 years to increase the sample, which resulted in decrease of errors resulting from random factors. The values W_z^i received in this way, together with CSO projections $L_{YEAR^*}^i$ allow projecting the number of cancer cases in years 2013–2025. For the prevalence projections these values need to be adjusted by the information concerning survival rate. This information was received on the basis of empirical data on new patients in the years 2010–2012 and of information about deaths among these patients until 2014. With the use of Kaplan–Meier estimator[79] the survival rate curve was estimated for the analysed population, using information for all cohorts available and values of ratios p_j^i.

The approach presented above enabled forming a 5-year prevalence projection for years 2015–2025. Where possible, for the projections for years 2015-2017 the empirical data on incidence were used.

The created model provides possibilities for a scenario analysis. As it is based on i.a. incidence ratio for a given cancer, in a given stage and in a given age group, a simple adjustment enables expressing this variable as: (1) incidence ratio for a given cancer, (2) age structure of the incidence ratio for a given cancer, (3) structure of cancer stages during diagnosis. Points (1) and (3) are especially important for scenario analysis, as they enable answering the question such as what influence will epidemiological changes have (risk factors increase) or the impact of quality of introduced screening programmes (change of structure towards earlier stages) on prevalence. The second key variable determining the type of constructed model is survival rate, where it is possible to illustrate in the sensitivity analysis the influence of introducing

[79] It is a statistical method to estimate with the use of censored observations – the lack of data from a given point in time dependent on the object.

new therapies or improving quality of care – these changes are reflected in the improvement of survival ratios.

Summary

The above paper presents the approach to analysis of oncological epidemiology in Poland on the basis of two data sources (National Cancer Registry database and National Health Fund database), the aim of which was to estimate incidence and prevalence for particular cancer types in Poland, using division on age groups and on stages. NCR database is the only information source about cancer stage in Poland, though it is characterised with significant percentage of data gaps. In order to make conclusions solely on the basis of this data, the assumption about the randomness of process generating data gaps (i.a. independently of the stage) or precise knowledge of this process would be needed. None of the assumptions above were fulfilled[80]. The purpose of creating and keeping NHF data base (i.e. settlement of services by service providers) does not enable treating its data uncritically as the only basis of information concerning oncological diseases (up-coding and wrong coding). Therefore the indirect approach was adopted, linking information from two databases, based on reliable analysis of patient's pathways, using expertise and Polish and international treatment standards. Thanks to such an approach it was possible to calculate values of variables necessary to estimate incidence of particular cancer groups and dividing them according to key variables from the epidemiological perspective (age and diagnosis stage) and consequently – to create incidence projections and five-year prevalence for years 2015–2025. The projection of these variables constitutes key information from the perspective of service planning in health care system – their values may be used to prepare projection of demand for particular services.

Bibliography

European Observatory on Health Systems and Policies Series: Diagnosis-Related Groups in Europe (2011).

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013), *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11* [Internet], Lyon: International Agency for Research on Cancer. Access: http://globocan.iarc.fr, download date: 2.04.2015.

National Cancer Registry. Access: http://onkologia.org.pl/, download date: 15.05.2015

Silverman E., Skinner J. (2004) Medicare upcoding and hospital ownership, *Journal of Health Economics*, 23.

[80] For diverse completeness of data dependent on the stage – see chapter ...

Treatment pathway model in lung cancer

Iwona Włodarska-Polińska, Beata Koń, Barbara Więckowska

Introduction

Lung cancer is the most frequently occurring type of malignant neoplasm in humans. It is characterised by bad prognosis and it is ranked as fifth among cancers with the worst prognosis (Wojciechowska et al. 2014). The main reason of its bad prognosis is late diagnosis resulting from the fact that symptoms often appear when the tumour mass is very large and when distant metastases occur. The most frequent symptoms of lung cancer – i.e. cough, breathlessness, pain in the chest and weight loss – are the same as those of chronic obstructive pulmonary disease, which makes an early lung cancer diagnosis much more difficult.

Lung cancer belongs to the group of cancers that develop due to exposure to tobacco smoke, i.e. those, where the strong correlation between the tobacco smoking addiction and the risk of developing cancer is present. Not only active smoking, but also passive smoking increases the risk of developing lung cancer. This is why the key element of combating lung cancer is education of society in the scope of health behaviours (NCCN 2015). In spite of unsatisfactory treatment results, latest decades have witnessed progress in treatment for tumour of the lung. The minimal invasive screening methods were introduced in the form of low-dose computerised tomography enabling diagnosis in the early stages with relatively good prognosis. Introduction of modern stereotactic radiotherapy technique has provided an alternative treatment for patients with small tumour and non-oncological contraindication to surgery, providing serious chance of local control of cancer. The progress has been observed also in the field of systemic treatment – tests on molecular level provoked the clinical use of targeted treatment against defined receptors specific for a cancer cell. Additionally, introduction of targeted therapies into systemic treatment improved its efficiency and tolerance (Horn 2014).

The aim of this article is to present structural model of lung cancer treatment in Poland. In the first part of this work the medical aspects concerning lung cancer, i.e. epidemiology and ethiopathogenesis are presented, as well as economic analysis of oncological diagnosis. The

following section presents foreign decision-making models describing lung cancer treatment and theoretical model developed for Poland. The third part includes contents related to analytical work results showing estimated incidence of lung cancer in Poland and results of empirical model of treatment pathway for this cancer group.

Epidemiology

In 2012 lung cancer was the most frequently diagnosed cancer in the world. It was diagnosed in approximately 1.825 million cases, which constituted about 13% of all developed cancers in this period. It was also the most frequently occurring type of malignant neoplasm in men. It constituted also more than a half of 8.2 million deaths caused by cancers in 2012 and it resulted in losing 24.483 million years of life measured with the DALY indicator (disability adjusted life-years) (WHO 2014).

According to Globocan data[81], lung cancer incidence in Poland was one of the highest in the region (cf. Figure 1). This value was higher than in highly developed countries (the difference between Poland and Germany, Great Britain is significant, the value is slightly lower for France) and it exceeded incidence values in the countries with similar level of social and economic development (Czech Republic, Slovakia, Latvia). Similar relationships may be observed in case of 5-year prevalence, i.e. number of persons living in a given year, who were diagnosed with lung cancer within last 5 years, per 100 thousand citizens – in this case values for Poland are also high compared to other countries in the region. One exception is France, where the prevalence is one of the highest in the region. However, the interpretation of the degree of prevalence calls for special attention. Prevalence combines information about incidence and survival outcome, so it is necessary to identify a factor (of negatively correlated survival outcome or positively correlated incidence) that is going to determine a high prevalence value.

Considering the structure of deaths due to malignant neoplasm in Poland, according to Globocan data, lung cancer accounts for over 30% of deaths caused by malignant cancers

[81] It is also worth mentioning the GLOBOCAN methodology - values for Poland were obtained based on three regional registers (Cracow, Kielce and Lower Silesia), which cover 13% of the population - it is disputable whether a sample made up in such a way is representative from the point of view of making inferences about the population of the whole Poland.

and the value is by nearly 10 percentage points higher than the world value (compare with Figure 1). It is also higher than in the neighbouring countries and may result from two factors, i.e. high (comparing to other countries) lung cancer incidence or low survival outcome. It is worth noticing that Denmark is a country with highly similar incidence, 5-year prevalence and percentage of deaths as a result of lung cancer.

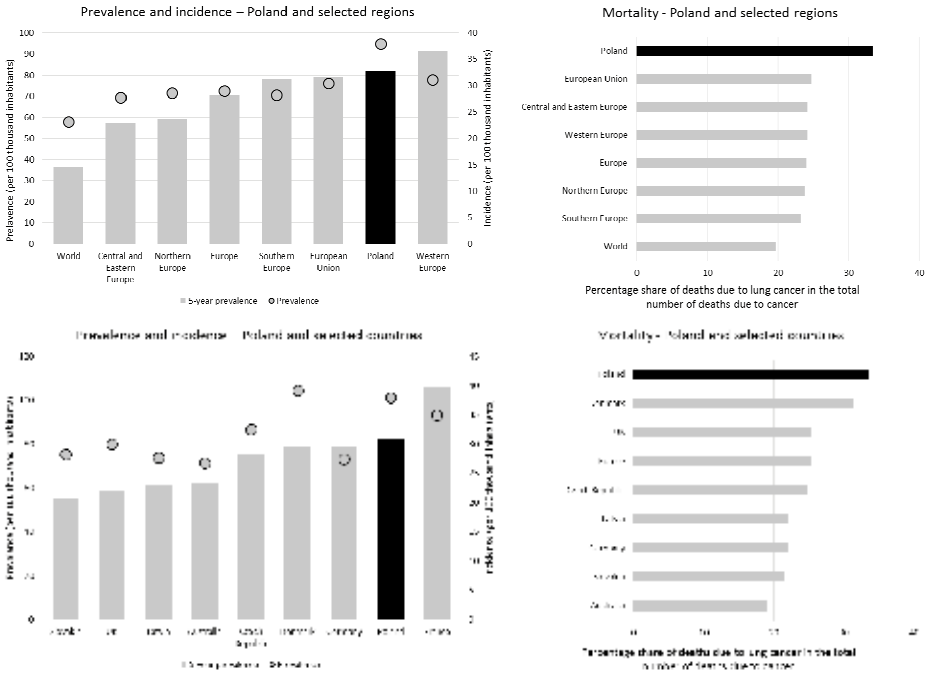


Figure 1. Basic statistics concerning the epidemiology of lung cancer for Poland and selected regions (source: own analysis based on GLOBOCAN 2012

As it has already been mentioned, lung cancer features especially high degree of malignancy. According to Eurocare figures, a probability of surviving one year after the diagnosis for the European countries is 38%. According to international statistics, in case of Poland, the values of five-year survival outcomes are highly similar to the European average. In comparison to other post-communist states of Central Europe, such as the Czech Republic, Slovakia and Latvia, Poland achieves slightly higher values of 5-year survival outcomes - this is a difference of 2 percentage points in case of Latvia and the Czech Republic and 4 percentage points in case of Slovakia. This means that Poland does not deviate from the average treatment

results achieved in the European countries. The highest values of the five-year survival rates for patients suffering from lung cancer are achieved in the Central Europe (De Angelis 2013, Eurocare 5). On the other hand, conditional survivals[82] show that after the survival of one year from the date of diagnosis, the probability of surviving another year increases significantly (cf. Figure 2). Thus, a high share of deaths caused by lung cancer in Poland and a high values of 5-year prevalence do not result from low survival outcomes, but from significantly higher incidence.

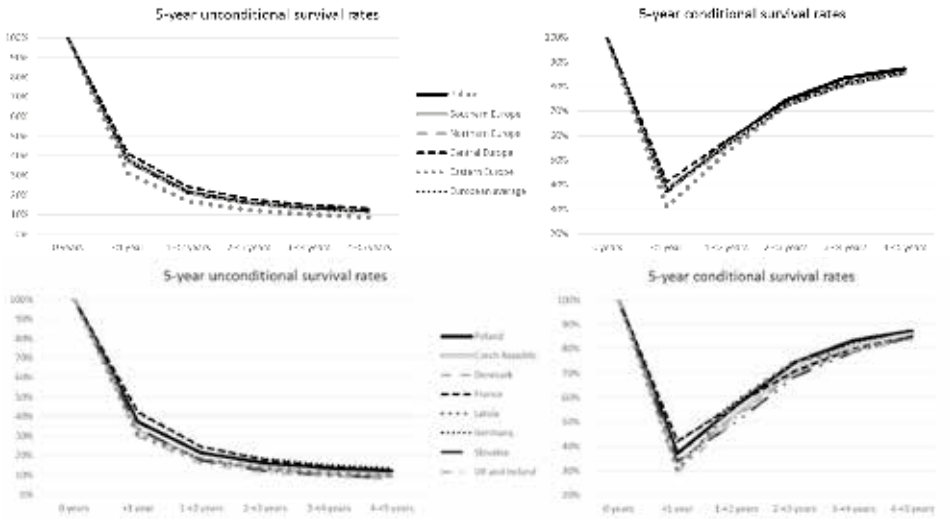


Figure 2. Five-year survival outcomes for patients suffering from lung cancer in Poland and selected regions(source: own analysis based on GLOBOCAN 2012)

In addition, the risk of developing lung cancer increases with age: 95-96% diseases develop after 50 years of age, and over a half - after 65 year of age. Until the end of the 20 century a standing increase of incidence as far as this type of cancer was observed, but despite the process of population aging, in the last years of the 20 century a slow decrease in incidence began as a result of dropping rate of smokers in the Polish society. Unfortunately, this process can be observed only among male population (NCR).

[82] against the survival of the previous year.

Prognosis for lung cancer is rather negative, but certain progress can be observed in treating also that type of cancer. 5-year survival outcomes among male patients suffering from that type of cancer increased from 10.6% to 11.9% during the first decade of the 21 century. In case of women the increase was from 15.7% to 16.9%. Despite that, mortality rates for Poland are still unsatisfactory. Moreover, mortality rate due to lung cancer among women exceeds mortality ratio due to breast cancer ,which is the most frequently occurring type of cancer in women (NCR).

85-90% of lung cancer cases are thought to be related to smoking tobacco. Smokers are in higher risk of developing lung cancer as well as a whole group of tobacco-dependent oncological conditions (cancers of head and neck, oesophagus, stomach, pancreas, colon, cervix and ovary, kidney and bladder), where there is a strong relationship between smoking addiction and smoker's death. Carcinogens present in tobacco smoke, include mainly nitrosoamine and benzopyrene. The risk of developing lung cancer increases with the number of cigarette packages smoked, this is why a notion of pack-years is used for the purpose of assessing lung cancer development risk. Also, a relationship between passive smoking and a risk of developing the disease was proven (Taylor 2007). Among the forms of nicotine addiction, which play a role in lung cancer development, there is also pipe and cigar smoking, as well as the smoking of marihuana (Hashibe et al. 2006).

Among other lung cancer predisposing factors there is also a chronic obstructive lung disease, family history of cancers (including lung cancer itself) as well as exposure to other carcinogenic compounds. Factors that induce lung cancer carcinogenic process include asbestos, arsenic compounds, radon, nickel, beryllium and cadmium compounds, pneumoconiosis and diesel fumes (Driscoll 2005, 2011). Asbestos is a well-known main factor, which induces pleural mesothelioma. Exposure to that factor is estimated to account for 3-4% of lung cancer cases. A synergic effect of tobacco smoking and exposure to asbestos has also been proven. On the other hand, radon is a radioactive gas produced in the chain of radioactive decay of radium 226 and it was proven that it also impacts lung cancer incidence. It occurs in natural conditions in the Earth crust, in higher concentration in some regions of the world, including in Poland - in the Sudetes and in Przedgórze Sudeckie. In addition, the role of air pollution in lung cancer development is underlined (NCCN 2015).

Economic analysis of cancer diagnostics

Prevention

High mortality rate among lung cancer patients made scientists and medical practitioners develop interest in the cancer prevention. The most effective form of primary lung cancer prevention is educating society about harmful effects of smoking. This is to influence the reduction of the percentage of smokers in the society. Among the main recipients of education schemes there is youth and young adults, i.e. people who can be prevented from developing that harmful addiction or who can be persuaded to give up smoking before serious health consequences follow. Long-time smokers remain in the group featuring a higher risk of lung cancer development, even many years after giving up smoking. Pharmacological support to people determined to give up smoking involves the use of preparations including nicotine in the first period of breaking up with addiction (Parsons et al. 2010).

On the other hand, secondary prevention involves early identification of the disease at a sub-clinical stage. If a tumour is small it can be eliminated by surgery, a prognosis is far better - a percentage of people surviving the period of 5 years exceeds 70% in case of the first stage (NCCN 2015; Orłowski et al. 2014).

Screening

A number of prospective randomised tests to assess the effectiveness of screening actions were done. In 1970s it was determined that by means of screening conducted based on chest X-ray and the Pap test of sputum it is possible to identify stage I or II. One of the ways to make an early diagnosis included low-dose high resolution CT scan performed in patients from a high risk group (long-term intensive smokers). The US National Lung Cancer Prevention Programme revealed in 2010 that low-dose CT scan performed in the high-risk group may reduce mortality rate by 20%. A high-risk group is defined as a group of people aged between 55-74 who do not reveal any lung cancer symptoms, who have been smoking for at least 30 pack-years, who have been smoking or quit smoking up to 15 years before the period of screening. Due to this fact low-dose CT scan is currently a recommended method of screening of the high-risk group (NLSTRT 2011).

Lung cancer diagnostics

Lung cancer may develop in the lumen of large bronchi (hilum type) or peripherally (typical for adenocarcinoma of the lung). The process is identified in 1/3 patients in early development stages, in further 1/3 patients in advanced locoregional stage, and in the remaining 1/3 patients - in a hematogenous spread stage (metastases to brain, bones, liver, the other lung). Lung tumour is suspected based on an interview and physical examination and chest X-ray taken in 2 projections. The most frequent radiological symptoms of lung tumour include: round shadowing, enlarged hilum or outline of mediastinum, abnormal pulmonary aeration, fluid in pleural cavity. In case of abnormalities, the next basic test includes bronchofiberoscopy, with possible histopathology of material taken from visible tumour lesions, bronchial brushing or bronchoalveolar lavage. Bronchoscopy enables identification of approx. 90% of centrally located tumours. In case of patients in worse general condition a simple Pap test of sputum can enable identifying lung cancer. Patients with peripherally located tumour require the tumour biopsy to be made through a chest wall with the control of X-ray image or CT. Material for histopathology or Pap test can also be obtained by means of a biopsy under control of ultrasound image through tracheal wall (EBUS - *Endobronchial ultrasound*) or oesophagus (EUS - *Endoscopic ultrasound).* In case of patients for whom those methods of testing failed, such other methods are considered as thoracentesis, mediastinoscopy with biopsy (also prior to qualifying for surgery), and finally - thoracotomy or thoracoscopy. In case of patients with metastasis to lymph nodes or distant organs, histological verification can involve taking a biopsy from a focus outside chest (PTOK 2013).

The second stage of diagnostic procedure includes evaluation of cancer process development by means of CT images of chest and upper abdominal cavity (evaluation of liver, adrenal glands which are frequent location of distant metastasis). In patients with chest wall infiltration, MRI test can evaluate the stage of disease and possibilities of surgery. PET-CT is a very useful and modern test which allows staging and which can differentiate between active foci and unrelated lesions. A presence of a single lung tumour of an unclear character is a frequent indication for performing the procedure. The usefulness of PET-CT scan cannot be overestimated in patients for whom radical treatment is planned. The image of lung cancer foci marked with Fluor-Deoxy-Glucose is more sensitive in relation to the invaded lymph nodes of mediastinum and distant metastases. Exclusion of distant metastases to brain and bones

is indicated in patients with symptoms suggesting metastatic changes as well as in patients with significant locoretional staging. In case of evaluating focal lesions of brain, MRI of head is preferred, while for evaluation of lesions in bones - skeletal scintigraphy is performed. In case of patients suffering from small cell lung cancer, routine diagnostic procedure before starting treatment includes brain CT or MRI scan or bone marrow evaluation . In this group of patients, even in the absence of clinical symptoms, cancer foci can be present in distant organs (PTOK 2013). Lung cancer staging is defined according to TNM classification, 7th edition (conf. Table 1.

Table 1. TNM classification of lung cancers (source: own analysis based on Goldstraw (2007)

Symbol	Meaning
Primary tumour (T)	
T_x	Primary tumour cannot be assessed, or the tumour is proven by the presence of malignant cells in sputum or bronchial washing but is not visualised by imaging or bronchoscopy.
T_0	No evidence of primary tumour
T_{is}	Carcinoma in situ
T_1	Tumour up to 3 cm in greatest dimension, surrounded by lung or visceral pleura, no bronchoscopic evidence of invasion more proximal than the lobar bronchus (not in the main bronchus)
T_{1a}	Tumour up to 2 cm in the greatest dimension
T_{1b}	Tumour >2cm but < 3 cm
T_2	Tumour > 3 cm, but <7 cm with any of the following (tumours < 5 cm with those features are classified as T2a) - invades the main bronchus above 2 cm distal to the carina - invades visceral pleura - associated with atelectasis/obstructive pneumonitis extending to hilar region but not involving the entire lung
T_{2a}	Tumour > 3 cm but < 5 cm in the greatest dimension
T_{2b}	Tumour> 5 cm, but < 7 cm in the greatest dimension
T_3	Tumour > 7 cm or one that directly invades any of the following: - chest wall (including superior sulcus tumours), diaphragm, phrenic nerve, mediastinal pleura, or parietal pericardium - tumour in the main bronchus < 2 cm, distal to the carina but without involvement of the carina - associated atelectasis/obstructive pneumonitis of the entire lung - or separate tumour nodule(s) in the same lobe
T_4	Tumour of any size that invades any of the following: - mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, or carina or - separate tumour nodule(s) in a different ipsilateral lobe
Regional lymph nodes (N)	
N_x	Regional lymph nodes cannot be assessed.
N_0	No regional node metastasis

N_1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N_2	Metastasis in the ipsilateral mediastinal and/or subcarinal lymph node(s)
N_3	Metastasis in the contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes
Distant metastasis (M)	
M_x	Distant metastasis cannot be assessed.
M_0	No distant metastasis
M_1	Distant metastasis
M_{1a}	Separate tumour nodule(s) in a contralateral lobe
M_{1b}	Tumour with pleural nodules or malignant pleural (or pericardial) effusion

Decision-making models in lung cancer treatment

World Health Organization (WHO), taking account separate biology, which results in separate treatment pathways, divides lung cancer into two groups: non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). SCLC takes more aggressive course, with quick tendency to hematogenous spread, greater chemo- and radiosensitivity. NSCLC can be divided into two groups: i) planoepithelial carcinoma and ii) non-planoepithelial carcinoma (adenocarcinoma, etc.) Major prognosis factors in patients with lung tumour include: early staging, good overall performance of a patient (ECOG 0-1), no more than 5% weight loss and histological type of carcinoma. In case of women - the prognosis is better (NCCN 2015; PTOK 2013). The molecular prognostic factors include the overexpression of Epidermal Growth Factor Receptor (EGFR) gene mutation among the patients in advanced NSCLC stage and high level of lactate dehydrogenase among the SCLC patients. Both of them are connected with a worse prognosis (PTOK 2013).

In the international models of lung cancer treatment approx. 85% of the cases are NSCLC cases and approx. 15% SCLC cases (cf. NHS Scotland 2005; Jacob et al. 2009; Barton et al. 2013). The SCLC depending on the extent and the adopted treatment can be divided into cases limited to the half of chest (limited disease – LD) and cases diagnosed in the spread stage (extensive disease – ED). Recently the TNM classification has been applied also in relation to the small cell lung cancer, in case of which the size of tumour, the condition of lymph nodes and the presence of distant metastases are evaluated separately (NCCN 2015).

In the Scottish model describing the application of radiotherapy in the lung cancer treatment the advanced locoregional SCLC cases constitute 48%. Approximately 67% patients

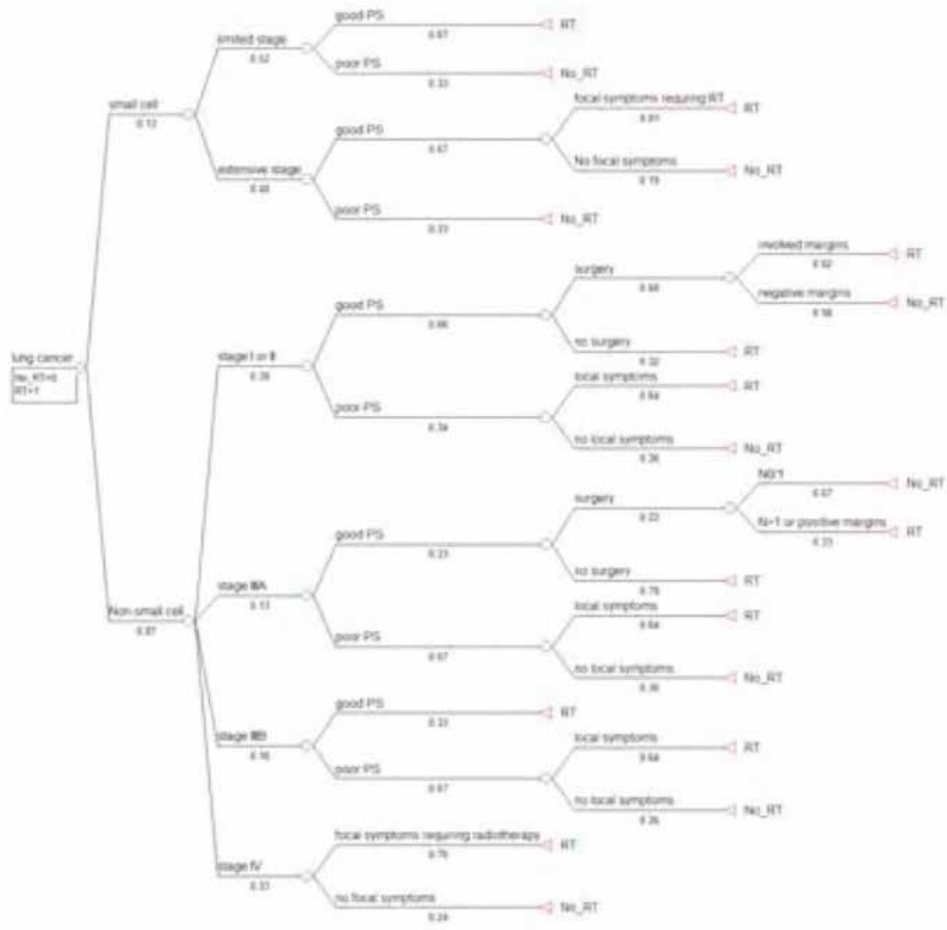
of this group are people in good general condition, who apart from systemic treatment are treated with radiotherapy of residual cancer. Remaining 33% patients in bad general condition do not qualify for radical treatment, including radical radiotherapy (NHS Scotland 2005).

In the group of NSCLC patients the choice of treatment strategy depends both on the stage of cancer development and the patient's condition. The patients with an early development stage of lung cancer with the greatest chances for recovery compose in the Scottish model approx. 40% of all NSCLC cases, of which 45% undergo surgery and in case of non-radical resection (neoplastic cells present in the excisional margins) the patient is also treated with complementary radiotherapy. The remaining group of patients in stage I and II is treated with radiotherapy alone. The group of patients in stage IIIA of cancer development constitutes in this model approx. 11% of all NSCLC cases and depending on the general condition may be treated with surgery and in case of non-radical treatment or affected mediastinal lymph nodes receive complementary radiotherapy. Patients in stage IIIA of cancer development may receive conservative treatment, radiotherapy or chemotherapy. However patients in stage IIIA of cancer development and in bad general condition qualify for the treatment only in case of clinical symptoms of the disease, usually they receive palliative radiotherapy or systemic treatment (NHS Scotland 2005).

In addition, the Scottish model presenting the optimal treatment based on radiotherapy indicates that cases in stage IIIB constitute approx. 20% of all NSCLC cases. The patients qualify for treatment in case of good general condition and treatment includes separate radiotherapy or more effective method of combining chemotherapy and radiotherapy. The patients in this stage of cancer development with compromised general health condition receive treatment in case of severe clinical symptoms of the disease (radiotherapy). The Scottish model, similarly to publications from other countries, indicates that over 30% of NSCLC patients are diagnosed in the metastatic stage. Due to incurable stage of the disease and presence cancer foci outside chest in this model approx. 80% patients require palliative radiotherapy aimed primarily at decreasing the intensity of clinical symptoms resulting from the advanced locoregional stage (cf. Figure 1).

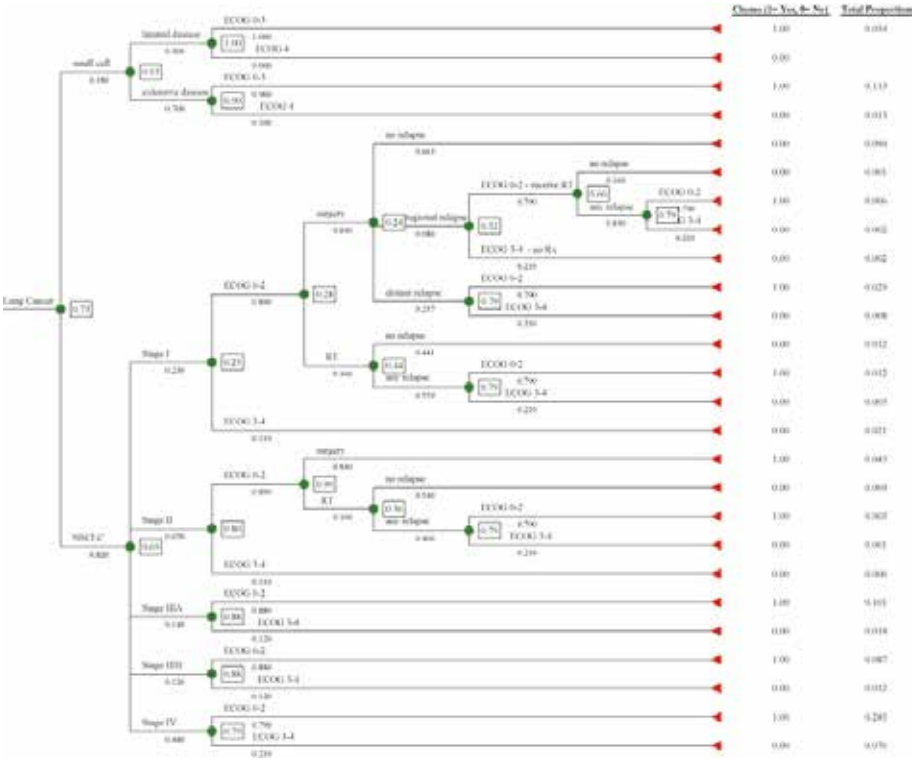
In the Australian model relating to the application of chemotherapy, the NSCLC cases constitute approx. 80% of all diagnosed cases of lung cancer. The patients in stage I and II (early

stages) comprise 1/3 of NSCLC cases. In this group over 80% patients in good general condition receive surgical treatment with potential complementary radiotherapy, similarly as in the Scottish model. The patients in bad general condition in early stage of cancer development receive oncological treatment only in case of clinical symptoms of the disease. The patients in stage IIIA constitute approx. 15% of Australian patients. Similarly as in the Scottish model patients in this stage of cancer development receive surgical treatment (20% of stage IIIA cases) with potential adjuvant chemotherapy or radiotherapy. However over 70% of patients in stage IIIA receive conservative treatment, radiotherapy or chemotherapy. The patients in stage IIIB constituting approx. 15% of all NSCLC patients receive only conservative treatment with the radical approach (in case of good general condition – over 80%) or palliative approach in case of clinical symptoms and bad general condition. Another 1/3 of NSCLC patients are patients in stage IV of cancer development, of which approx. 70% with clinical symptoms of the disease requires palliative treatment due to symptoms caused by chest lesions or distant metastasis (40% metastasis to CNS, 15% to bones) (cf. Figure 2).



Flowchart 1. The decision tree for the application of radiotherapy in Scotland (source: NHS Scotland 2005)[83]

[83] NSCLC – *non-small cell lung cancer*, SCLC – *small cell lung cancer*.



Flowchart 2. The decision tree for the application of chemotherapy in Australia (source: Barton et al. 2013)[84]

Decision-making models in lung cancer treatment in Poland

In Poland the recommendations concerning lung cancer treatment are developed by Polish Society of Clinical Oncology (PTOK 2013). They include diagnostic and therapeutic standards in case of this type of neoplasm. On their basis, as well as using expertise and international recommendations, a theoretical decision-making model of diagnosed lung cancer treatment was developed (cf. Flowchart 3). It does not take into account the division of lung cancer into NSCLC and SCLC due to the lack of such division in ICD-10 classification.

[84] ECOG – Scale of Performance Status of Eastern Cooperative Oncology Group.

According to the lung cancer treatment principles applicable in Poland generally the sequence of individual therapeutic methods is similar to treatment strategies applied in other countries. The treatment of SCLC consist primarily in systemic treatment, including chemotherapy, hormone therapy and biological treatment. In case of a limited disease and patients in good general condition (ECOG 0–1) the ionising radiation treatment of residual cancer is used. The basic chemotherapy treatment regimen is cisplatin with etoposide (PE), less often cyclophosphamide, doxorubicin and vincristine (CAV, CAE). Doxorubicin is contra-indicated in cases of parallel radiotherapy, and cisplatin in patients with renal impairment. In case of the sequential treatment usually 4–6 cycles of chemotherapy with subsequent ionising radiation treatment are applied. The simultaneous treatment with radiochemotherapy from the second cycle of chemotherapy brings better treatment results. In such case patients are administered 45 Gy twice a day, 1.5 Gy fraction for 3 weeks. Such intensive treatment regimen can be used only in patients in very good general condition, without massive lesions in chest, lesions in pleural cavity or supraclavicular lymph nodes (PTOK 2013; NCCN 2015).

Radiotherapy plays an important role in preventing or treating metastasis to CNS, which often cause of systemic treatment failures. Metastasis to brain is a symptom of impeded penetration of cytostatic medicines through the blood-brain barrier. The patients with metastases in a good general condition are treated with chemotherapy and prophylactic irradiation of brain (PCI) in a dose 25 Gy in 10 fractions 2–5 weeks after completion of systemic treatment. The patients with metastases in a bad general condition are administered only symptomatic treatment or palliative chemotherapy (PTOK 2013).

The NSCLC treatment principles are similar to strategies applied in other countries, which results from creating treatment regimens on the basis of results of large and reliable clinical trials. In early cases (stage I and II) and good general patient's condition the alternative cardiothoracic surgery or stereotactic ablative radiotherapy (SABR) is used. Many lung cancer patients do not receive surgical treatment due to coexisting diseases and old age. It is difficult to obtain the histological confirmation before starting the basic treatment of lung tumours diagnosed during screening, especially if the tumour' s diameter is up to 2 cm (PTOK 2013).

The surgical treatment of lung cancer consist in performing a lobectomy with lymphadenectomy of hilar and mediastinal lymph nodes with the minimal number of 6 lymph

nodes. Pneumonectomy (total or partial lung resection) is performed in rare cases, if lobectomy does not guarantee the radical resection in case of the invasion of main bronchus. The less extensive resections, such as segmentectomy or wide, wedge-shaped resection of lesion can be considered in case of small tumours or in patients with impaired respiratory function. In case of patients with lesions up to 2 cm diagnosed in PET scan without lesions in the lymph nodes the lymphadenectomy is not obligatory. In patients with medical contraindications to the surgery or in case of lack of consent for this type of treatment, an alternative treatment is the stereotactic ablative radiotherapy (SARB) is used. In every case of planned surgical procedure it is necessary to accurately evaluate the cardiac state and respiratory efficiency in order to estimate the perioperative mortality risk (ESMO). The cardiac state is evaluated according to Revised Cardiac Risk Index (RCRI) and the respiratory efficiency on the basis of FEV1 and DLCO indicators (minimum level of 80%). Similar criteria of the respiratory efficiency evaluation concern the radical radiotherapy (PTOK 2013).

In case of lung cancer the radical radiotherapy is performed using conformal technique or IMRT, which consists in the administration of 66–76 Gy dose in 33–37 fractions. In order to conduct the therapy good general condition and good respiratory efficiency are necessary. In case of patients with a small tumour without lesions in lymph nodes in PET-CT scan the stereotactic ablative radiotherapy in high doses (biologically equivalent dose 90–110 Gy) can be used. Using the stereotactic radiotherapy in case of tumours situated close to the hilar requires further clinical trials (PTOK 2013).

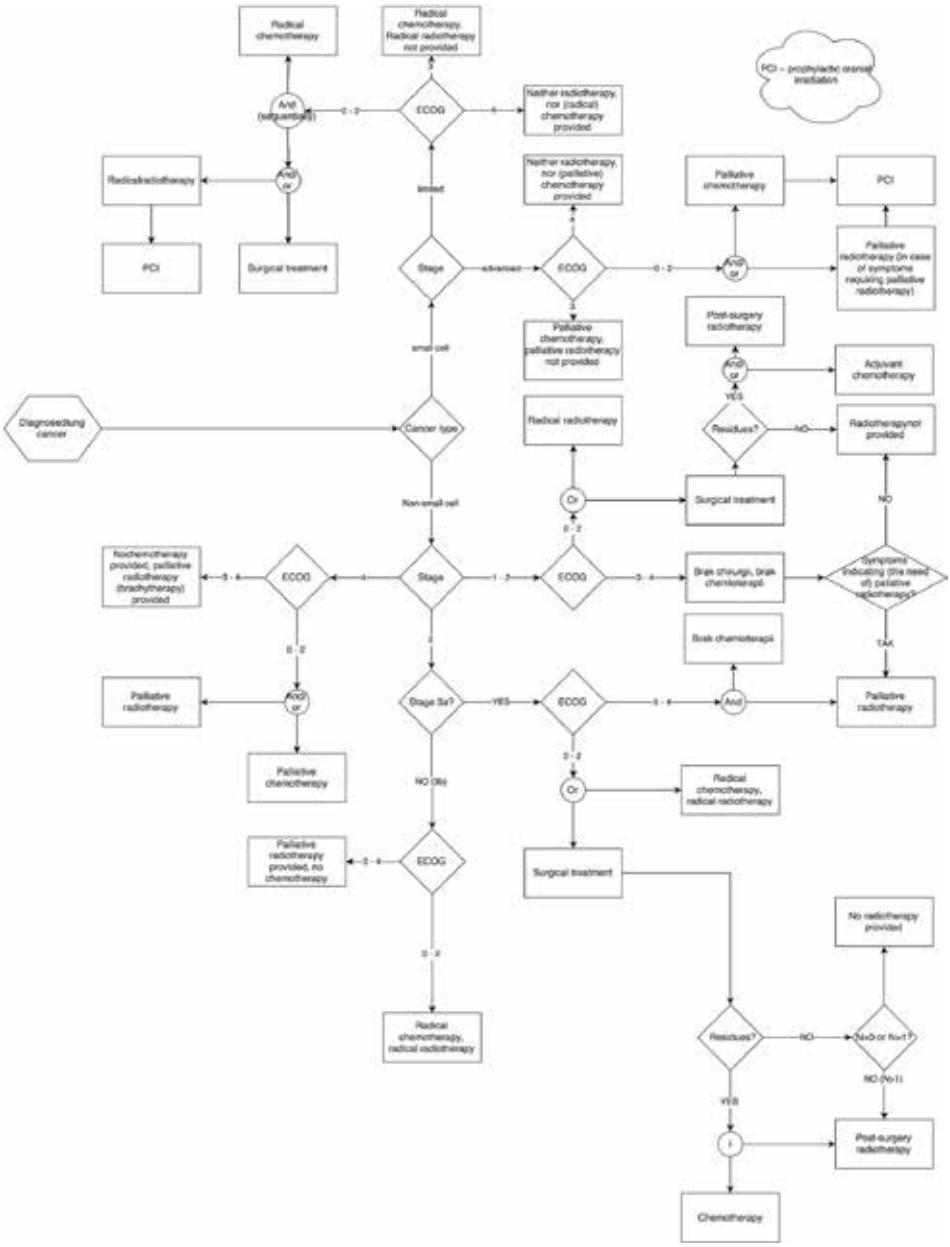
In case of unfavourable prognosis factors identified in the post-surgery examination the complementary treatment is also applied. The complementary radiotherapy (PORT) is indicated in patients with no radicalness along the surgical incision or N2 feature (metastasis to mediastinal lymph node in histopathology). The dose administered in such case is 55–65 Gy in 1.8–2 Gy per fraction. The post-surgery treatment should begin up to 6 weeks after the surgery date. The complementary chemotherapy is considered among patients in stages II and higher in good general condition and without severe coexisting illnesses. It usually consists in administering 3–4 cycles of two-drug chemotherapy based on cisplatin (most often cisplatin and vinorelbine every 3 weeks in dose of 80–100 mg/m2 and 25–30 mg/m2 respectively). In case of the necessity to administer complementary radiotherapy and chemotherapy, the sequential treatment is applied (chemotherapy followed by radiotherapy). In case of certain,

small group of patients the treatment in pre-surgical stage can be taken into consideration – both systemic and radiotherapy. Patients in stage IIIA with the positive N2 feature receive 2–3 cycles of two-drug chemotherapy based on cisplatin. The cardiothoracic surgery is performed up to 3 weeks since the last chemotherapy cycle only in case of possible radical resection. It is also indicated that the neoadjuvant (pre-surgical) chemotherapy improves total 5-year survival rates by 5% (NCCN 2015). The positive impact of pre-surgical radiotherapy in patients with superior sulcus tumour has been proven and it consists in administering a dose of 50–60 Gy optimally together with 2 chemotherapy cycles followed by resection during 4–6 weeks (PTOK 2013).

Additionally in case of small group of patients in stage IIIA the surgery can be taken into account, but it occurs very rarely. The group consists of patients in stage T4N0M0 and T4N1M0. The metastasis to mediastinal lymph nodes on one or both sides, as well as supraclavicular lymph nodes disqualifies patient from the surgery. The standard treatment in inoperable stages IIIA and IIIB is radiochemotherapy (RCTH) or radiotherapy alone (RTH) in patients with contraindications to systemic treatment. According to the results of clinical trials the optimal method of treating is the simultaneous radiochemotherapy. Patients in very good general condition without massive lesions in chest are qualified for this method. The simultaneous combined treatment presents a higher risk of severe oesophagus reactions and to a lesser extent pneumotoxicity and myelotoxicity. The most frequently applied form of treatment in this group of patients is sequential CRTH. After administration of 2–3 systemic treatment cycles, the radical radiotherapy is conducted. The radical ionising radiation treatment consists in the administration of 66–72 Gy targeted at macroscopic lesions present before starting treatment, including chemotherapy. Using the selective irradiation of nodal groups without lesions is currently not recommended. The dose escalation to the tumour area is expected to improve the effectiveness of radiotherapy. In the simultaneous combined treatment the chemotherapy based on cisplatin in a dose of 75–100 mg/m2 in the form of an infusion on 1 day or 15–30 mg/m2 on 1,2,3 days in combination with vinorelbine (25–30 mg/m2) or etoposide (100–120 mg/m2) is applied. In case of the sequential treatment the basis for chemotherapy regimens is cisplatin or carboplatin with fewer side effects in combination with vinorelbine, etoposid, as well as gemcitabine, paclitaxel (PTOK 2013).

In patients with contraindications to CRTH the radiotherapy alone can be considered. In case of patients in bad general condition (ECOG 2 or higher) with weight loss of over 10% during 3 months since diagnosis, with coexisting severe diseases (renal failure, circulatory and respiratory failure, recent myocardial infarction or stroke), despite the lack of metastasis, an attempt to use palliative radiotherapy or chemotherapy is made. In most cases, however, the symptomatic treatment is administered (PTOK 2013).

1/3 of diagnosed lung cancer cases have metastases, which means there are no chances for recovery. The exception are patients with a single operable distant metastasis. After resection of metastatic change patient should receive treatment adequate to the stage of disease in chest. In this group there are patients with a single metastatic focus in the brain, adrenal gland or second lung. In case of multiple metastatic foci the possible treatment method is systemic therapy, if the patient's general condition is good. Apart from chemotherapy, in case of adenocarcinomas with EGFR mutation or EML4–ALK fusion the much better tolerated tyrosine kinase inhibitors (gefitinib, erlotinib) are indicated. The patients in stage IV also receive monoclonal antibodies against vascular endothelial growth factor (VEGF) – bevacizumab. The contraindications to bevacizumab are the structure of a squamous cell carcinoma, clinical signs of haemoptysis, coagulation disorder or metastasis to brain. Using this medication has many side effects. The careful approach to the combination of cetuximab and chemotherapy as the first-line therapy is recommended. If there are clinical symptoms originating from lung tumour or distant metastases (most often to brain and bones) then palliative radiotherapy is used. The total dose and length of treatment depend on the patient's condition and on the advancement of carcinogenesis - from 1 8 Gy fraction per symptomatic metastasis foci in bones to 30 Gy in 10 fractions. Patients in bad overall condition are usually administered symptomatic treatment (PTOK 2013)



Flowchart 3. Oncotherapy model in Poland (source: own analysis)

Empirical model of lung cancer treatment

When analysing cancer care system, one must first of all define precisely how many patients were diagnosed with cancer in a given calendar year. Information on patients suffering from cancer is provided by the National Cancer Registry.

According to epidemiological statistics, lung cancer is the most frequently diagnosed type of carcinoma. According to the database provided by NCR, 21,272 new cases of lung cancer were recorded in 2012 (conf. Table 2). Those are patients who in 2012 were diagnosed with C33 or C34 according to the International Classification of Diseases ICD-10 and who have not appeared in NHF records with that diagnosis since 2009. Cancer stage was defined in respect of 73% patients recorded in NCR, which means that in 2012 cancer stage was not defined for 5,826 patients. Patients with stage IV dominated the group of new patients making up 50% of the group (conf. Table 3). Moreover, an insignificant number of patients diagnosed with early cancer stages (I, II) is reported in NCR. In 2012 they accounted for 18% of patients for which stage was defined. Moreover, information on patients with cancer stage I was not recorded in NCR database - between 2010-2012 only one person was recorded in 2011 with a defined stage I.

Table 2. Distribution of information on cancer stage in NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	0	0%	0%	0%
II	2,762	2,608	2,714	13%	13%	13%
III	5,509	5,316	4,981	26%	25%	23%
IV	7,295	7,566	7,751	35%	36%	36%
Stage not recorded in NCR	5,313	5,360	5,826	25%	26%	27%
Total	20,879	20,851	21,272	100%	100%	100%

Table 3. Distribution of information on cancer stage in NCR database for new patients whose cancer stage was defined (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	0	0%	0%	0%
II	2,762	2,608	2,714	18%	17%	18%
III	5,509	5,316	4,981	35%	34%	32%
IV	7,295	7,566	7,751	47%	49%	50%
Total	15,566	15,491	15,446	100%	100%	100%

A small number of patients with early stage of cancer may point to a very late detection of lung cancer, which is a consequence of low cancer awareness of Poles or significant problems with the processes within of the health-care system that do not provide patients with appropriate diagnostics and screening tests. In order to verify that hypothesis an empirical model of lung cancer treatment in Poland has been developed. It is based on data from NCR and information about services provided to patients with C33 or C34 diagnoses, which was fed into the NCR. The analysis takes into account all services that were provided to patients during 365 days of their first appearance in the system (defined as the provision of the first service to a patient with C33 or C34 diagnosis or the first record of the patient in NCR with that diagnosis).

In the first stage, the analysis was focused on those patients recorded in NCR, whose cancer stage was not defined in the database. To this end foreign decision-making models were used, which defined an optimum care pathway for a patient diagnosed with lung cancer, as well as information about services provided to those patients, which were defined according to ICD-9. This enabled the analysts to see which patients were provided such treatment as i.a. surgical treatment, radiotherapy or chemotherapy. Thanks to that, as well as thanks to international experience and Polish recommendations for lung cancer treatment, it was possible to define cancer stage in that group of patients[85]. At this stage of analysis it was also assumed that patients recorded in NCR do suffer from a given type of cancer. One might, however, allow for

[85] The analysis takes account of 99% of patients whose cancer stage is not defined in NCR. For the remaining 1% of patients the analysis was impossible because there were no services recorded in NCR which were settled by NHF.

a possibility that a patient who was recorded in NCR in a given year might not be diagnosed in that year. The reason behind is that, during a year of being recorded in NCR, such a patient was provided with main diagnostic procedures that are appropriate for *follow-up* patients (conf. Table 4)[86].

Based on such a methodology it was possible to define lung cancer stage. It was established that 10% of patients recorded in NCR were *follow-up* patients. Approx. 50% were stage IV patients, and 14% suffered from cancer in early stage (I, II).

Table 4. Cancer stage categorization of new patients whose cancer stage was not defined in NCR (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	426	480	565	8%	9%	10%
II	180	209	228	3%	4%	4%
III	1,371	1,357	1,451	26%	25%	25%
IV	2,723	2,771	2,944	52%	52%	51%
Follow-up patients	559	507	596	11%	10%	10%
Total	5,259	5,324	5,784	100%	100%	100%

The above figures take into account only patients recorded in NCR database. They therefore define an assumption that NCR database is complete and information about all cancer patients is fed into it. However, according to an NCR publication, the information about incidence might be biased due to incomplete information that is entered in the NCR (Wojciechowska et al. 2012). This is why, in the second stage of analysis, NHF data of patients with C33 and C34 diagnoses was also taken into account. Since those patients were not recorded in NCR, there is no information about cancer stage and thus one should take an approach which is analogous to that taken in case of patients recorded in NCR without information about cancer stage. However, in this case it was assumed that a patient, who was provided a service according to NHF, might not necessarily suffer from cancer. This most probably results from errors in service reporting.

[86] See: *Sources and Quality of Cancer Epidemiological Data in Poland - Data Analysis Methodology*

According to NHS data, in 2012 there were 10,613 patients with C33 and C34 diagnoses in Poland, who were not recorded as such in the NCR database since 2000 and since 2009 they did not receive any treatment services resulting from lung cancer diagnoses either in ambulatory specialized care system or in a hospital (conf. Table 5). However, according to the methodology adopted, 50% of those patients were classified to a group of patients who were wrongly diagnosed with lung cancer. This means that the completeness of NCR data concerning incidence in 2010-2012 amounted to 86%, 82% and 83%, respectively. However, if we consider information about patients whose cancer stage was defined in the database, then in the years 2010-2012 for respectively 64%, 61% and 60% of new patients it was information recorded in NCR.

Table 5. Cancer stage categorization of new patients who were not recorded in NCR database, but who received oncological services according to NHF database (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	89	714	825	1%	7%	8%
II	143	207	222	1%	2%	2%
III	868	962	979	8%	9%	9%
IV	3,118	3,065	3,023	28%	29%	28%
other diagnosis	6,747	5,601	5,564	62%	53%	52%
Total	10,965	10,549	10,613	100%	100%	100%

Based on the above described 3 groups of patients, i.e. patients recorded in NCR with cancer stage recorded, patients recorded in NCR with cancer stage unknown and patients not recorded in NCR, a cumulative distribution of lung cancer stage for new patients in 2010-2012 was defined (conf. Table 6). In case of a small percentage of patients it was impossible to define cancer stage due to no record of services paid by NHF being provided to those patients.

Table 6. Cumulative distribution of incidence against cancer stage for years 2010-2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
1	1,139	1,214	1,422	4%	5%	6%
2	3,188	3,025	3,165	12%	12%	12%
3	7,935	7,635	7,410	31%	30%	29%
4	13,234	13,403	13,720	52%	53%	53%
impossible to define	54	36	42	0%	0%	0%
Total	25,550	25,313	25,759	100%	100%	100%

The following stage of constructing an empirical model of lung cancer treatment involved a detailed analysis of the structure of services provided to patients diagnosed with lung cancer in 2012. The analysis included the structure of services provided within 365 days of a record of patient with diagnosis being made in the database.

In case of lung cancer, only 17.8% of patients were provided with surgical treatment appropriate for that type of cancer. This results from the fact that in case of that type of cancer surgical treatment is indicated only in the early stage of cancer (93% of patients with stage I underwent surgical treatment). The more advanced cancer stage, the smaller percentage of patients provided with such therapy (only 6.2% of patients with stage IV underwent surgical operations). Nearly half of patients with lung cancer diagnosed in 2012 received chemotherapy. It was most often the case of patients with stage III (nearly 60% cases). A significant percentage of patients with stage II and IV received chemotherapy (42% and 50%, respectively). Very few patients with stage I cancer were administered chemotherapy. Radiotherapy was not very often used for treating lung cancer - it was administered to 21.6% of patients, especially those with stage II and III cancer (conf. Table 7 and 8).

Table 7. Empirical model of lung cancer treatment in Poland part 1 (source: own analysis)

Type of therapy	patients who underwent the therapy
surgical treatment	17.8%
chemotherapy	49.1%
radiotherapy	21.6%

Table 8. Empirical model of lung cancer treatment in Poland part 2 - patients who underwent a given therapy depending on cancer stage (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
surgical treatment	93.3%	41.8%	14.8%	6.2%
chemotherapy	4.2%	42.1%	59.3%	49.9%
radiotherapy	10.4%	36.6%	31.4%	14.0%

In case of combined treatment methods, the biggest group of patients are patients who did not receive (approx. 34%) either radiotherapy or chemotherapy or did not have surgical treatment. This results most probably from advanced stage of cancer. The second biggest group includes patients who did not have a surgical treatment but received chemotherapy, and did not receive radiotherapy. In addition, the majority of patients who had surgical treatment did not receive chemotherapy or radiotherapy. A precise distribution of the combinations of the three types of treatment is presented in Table 9. Additional extension of the empirical model, which takes also account of other information concerning the care pathway, is presented in Flowcharts 4 and 5. It includes additional information concerning patient's death within 365 days of diagnosis, as well as information concerning palliative treatment (including palliative radiotherapy).

Table 9. Empirical model of lung cancer treatment in Poland part 3 (source: own analysis)

Was surgical treatment provided?					
NO - 82.16%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	33.77%	6.26%	40.03%
		YES	29.55%	12.58%	42.13%
	Total		63.31%	18.85%	82.16%
YES - 17.84%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	9.94%	0.90%	10.84%
		YES	5.17%	1.82%	7.00%
	Total		15.11%	2.73%	17.84%

Stage					Including surgical treatment					Including chemotherapy					Including radiotherapy					Including paliative treatment				
Stadium	Number of cases	Share	Number of deaths	Percentage of	NO/YES	Number of cases	Share	Number of deaths	Percentage of	NO/YES	Number of cases	Share	Number of deaths	Percentage of	NO/YES	Number of cases	Share	Number of deaths	Percentage of	NO/YES	Number of cases	Share	Number of deaths	Percentage of
STAGE1	1422	5.5%	0	0.0%	NO	96	6.7%	0	0.0%	NO	48	50.3%	0	0.0%										
										YES	48	49.7%	0	0.0%										
					YES	1327	93.3%	0	0.0%	NO	1316	99.1%	0	0.0%	NO	1274	96.8%	0	0.0%	NO	1274	100.0%	0	0.0%
															YES	42	3.2%	0	0.0%					
										YES	12	0.9%	0	0.0%										
STAGE2	3164	12.3%	839	26.5%	NO	1842	58.2%	705	38.3%	NO	932	50.6%	396	42.5%	NO	607	65.2%	346	57.0%	NO	494	81.4%	265	53.6%
																				YES	113	18.6%	81	71.7%
															YES	324	34.8%	50	15.4%	NO	291	89.7%	36	12.4%
																				YES	34	10.3%	14	41.8%
										YES	911	49.4%	309	33.9%	NO	361	39.6%	218	60.4%	NO	204	56.5%	139	68.1%
																				YES	157	43.5%	79	50.3%
															YES	550	60.4%	91	16.6%	NO	471	85.8%	63	13.4%
																				YES	78	14.2%	28	35.8%
					YES	1322	41.8%	134	10.1%	NO	900	68.0%	82	9.1%	NO	777	86.4%	71	9.1%	NO	761	97.9%	64	8.4%
																				YES	16	2.1%	7	43.8%
															YES	122	13.6%	11	9.0%	NO	116	95.1%	7	6.0%
																				YES	6	4.9%	4	66.7%
										YES	423	32.0%	52	12.3%	NO	261	61.7%	40	15.3%	NO	237	90.8%	33	13.9%
																				YES	24	9.2%	7	29.2%
															YES	162	38.3%	12	7.4%	NO	152	93.8%	6	4.0%
																				YES	10	6.2%	6	60.0%

Flowchart 4. Empirical model of lung cancer treatment in Poland part 4a (source: own analysis)

Flowchart 5. Empirical model of lung cancer treatment in Poland part 4b
(source: own analysis)

Summary

The analysis of lung cancer therapy regimens in various countries shows their overall coherence. This is because national decision-making models are based on international clinical trials involving a large number of subjects, as well as on medical recommendations developed based on evidence-based medicine. Insignificant differences include availability of targeted

treatment and records thereof in particular countries. the use of new expensive system-based therapies depends on different level of health-care funding in particular countries. Despite quite uniform indications for radiotherapy treatment, there are differences among the European countries in its availability in qualitative and quantitative terms.

The developed model of lung cancer treatment indicates that the cancer register (NCR) does not account for all the cancer cases and includes over 80% cases. If, however, one takes account of lack of information in the register about cancer stage, then the NCR completeness ratio is approx. 60%. Patient treatment analysis shows low number of patients who were subject to surgical treatment. It was administered mainly to patients in early cancer stages. Moreover, among the newly diagnosed patients there is a group of patients with advanced cancer stage, who did not receive any services such as surgical treatment, chemotherapy or radiotherapy. One also has to point out that radiotherapy was a relatively rarely used method of treatment in case of lung cancer.

When analysing treatment results, as well as etiology and pathogenesis of the disease it seems that there are two basic methods for improving prognosis of patients with lung cancer. The first one involves improving the effectiveness of primary prevention schemes, which are based on broadly ranged educational programmes, targeted especially at youth. Disseminating information about dangers related with tobacco smoking to young people before the addiction is well-developed in adult age, after only a short period of exposure to carcinogens from nicotine, may effectively prevent the target group from developing lung cancer.

The second one involves actions aiming to introduce population based screening schemes which enable diagnosing the disease in subclinical stage, which may contribute to improved results of treatment. Currently there is no national lung cancer screening scheme introduced in Poland, which would be similar to breast cancer or cervical cancer screening programmes which are in operation. Mortality rate due to lung cancer is incomparably higher than in case of the above mentioned other types of cancer. On the initiative of cardiothoracic surgery centres in Pomerania and Western Pomerania, screening tests were performed using low-dose CT scans, the results of which are similar to the results achieved in Europe and the US (Orłowski 2014). The proportion of cases that underwent surgical treatment in regions covered with

screening reached 80% in stage I and II, which undoubtedly impacts the improvement of the 5-year survival rates. Thanks to the initiative of professor Tadeusz Orłowski, an early lung cancer intervention scheme was launched, funded from the National Programme for Combating Oncological Diseases. The scheme was introduced in Mazovia, Warmia and Mazuria, Lesser Poland, Silesia and Opole voivodeships. The scheme increased the effectiveness of surgical treatment - there are more patients who undergo surgical treatment in early stages of cancer, and the percentage of patients with higher cancer stage who underwent surgery has dropped. At the same time, the number of patients operated on every year has not changed or even increased slightly (Orłowski 2014).

Bibliography

Barton M., Jacob S., Shafiq J., Hsin Wen Wong K., Thompson S., Delaney G., Hanna T. (2013). *Review of optimal radiotherapy utilization rates*.

De Angelis, R., Sant M., Coleman, M.P., Francisci, S., Paolo Baili, Pierannunzio, D., Trama, A., Otto, V., Brenner, H., Ardanaz, E., Bielska-Lasota, M., Engholm, G., Nennecke, A., Siesling, S., Berrino, F., Capocaccia, R., EUROCARE-5 Working Group (2014) Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5 – a population-based study. *The Lancet Oncology*, 15 (1), pp. 23–24.

Driscoll, T., Nelson, DI., Steenland, K., Leigh, J., Concha-Barrientos, M., Fingerhut, M., Pruss- Ustun, A. (2005) The global burden of disease due to occupational carcinogens. *American Journal of Industrial Medicine*, 48 (6), pp. 419–431.

EUROCARE-5 Database, Access: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx, date downloaded: 2.04.2015 r.

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013), *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet], Lyon: International Agency for Research on Cancer. Access: http://globocan.iarc.fr, date dowloaded: 2.04.2015 r.

Goldstraw, P., Crowley, J., Chansky, K., Giroux, D.J., Groome, P.A., Rami-Porta, R., Postmus, P.E., Rusch, V., Sobin, L., International Association for the Study of Lung Cancer International Staging Committee, Participating Institutions. (2007) The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant neoplasms.*Journal of Thoracic Oncology*, 2 (8), pp. 706–714.

Hashibe, M., Morgenstern, H., Cui, Y., Tashkin, D.P., Zhang, Z.F., Cozen, W., Mack, T.M., Greenland, S. (2006) Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. *Cancer Epidemiology, Biomarkers & Prevention*, 15 (10), pp. 1829–1834.

Horn, L. (2014) Advances in the treatment of non-small cell lung cancer.*Journal of the National Comprehensive Cancer Network*, 12, pp. 764–767.

Jacob, S., Hovey, E., Ng, W., Vinod, S., Delaney, G.P., Barton, M. (2010) Estimation of an optimal chemotherapy utilisation rate for lung cancer: An evidence-based benchmark for cancer care. *Lung Cancer*, 69, pp. 307–314.

National Cancer Registry, *Nowotwory złośliwe opłucnej i płuca (C33–34)*, Access: http://onkologia.org.pl/nowotwory-zlosliwe-oplucnej-pluca-c33-34/, date downloaded: 09.04.2015.

National Lung Screening Trial Research Team (2011) Reduced lung-cancer mortality with low-dose computed tomographic screening. *The New England Journal of Medicine*, 365 (5), pp. 395–409.

NCCN Guidelines Version 4.2015, Non-Small Lung Cancer. http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

NHS Scotland (2005), *Cancer In Scotland Radiotherapy Activity Planning For Scotland 2011–2015*.

Orłowski, T. (2014) Early lung cancer diagnosis – role of tests.*Pneumonologia i Alergologia Polska*, 81, pp. 1–2.

Parsons, A., Daley, A., Begh, R., Aveyard, P. (2010) Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: Systematic review of observational studies with meta-analysis. *BMJ*, 340; Access:http://www.bmj.com/content/340/bmj.b5569, date downloaded: 20.04.2015.

Polish Society for Clinical Oncology, Krzakowski M., Jassem J. at al. (2013) *Nowotwory płuca iopłucnej oraz śródpiersia, 2013,* Access: http://www.onkologia.zalecenia.med.pl/pdf/PTOK_2013_03_Nowotwory%20pluca%20i%20oplucnej.pdf, date downloaded: 9.04.2015 r.

Taylor, R., Najafi, F., Dobson, A. (2007) Meta-analysis of studies of passive smoking and lung cancer: effects of study type and continent. *International Journal of Epidemiology*, 36 (5), pp. 1048–1059.

Vansteenkiste, J., Crino, L., Dooms, C., Douillard, J.Y., Faivre-Finn, C., Lim, E., Rocco, G., Senan, S., Van Schil, P., Veronesi, G., Stahel, R., Peters, S., Felip, E., Panel Members (2014) 2nd ESMO Consensus Conference on Lung Cancer: early-stage non-small-cell lung cancer consensus on diagnosis, treatment and follow-up.*Annals of Oncology*, 25 (8), pp. 1462–1474.

Wojciechowska, U., Didkowska, J., Zatoński, W. (2014) *Nowotwory Złośliwe w Polsce w 2012 roku*, National Cancer Registry, Oncology Centre – Maria Skłodowska-Curie Memorial Institute.

World Health Organization, Cancer Research UK, World Cancer Factsheet (2014), Access: http://publications.cancerresearchuk.org/downloads/Product/CS_REPORT_WORLD.pdf, date downloaded: 8.04.2015 r.

Treatment pathway model in breast cancer

Beata Freier, Filip Urbański, Barbara Więckowska

Introduction

Breast cancer is one of the most serious oncological conditions. It is the second most frequently diagnosed type of cancer in the world following lung cancer (it accounts for 11.9% of all cancers). It is the fifth cause of death as a result of cancer and it is the most frequent or the second most frequent cause of death in women, depending on a geographical and economic region (Ferlay et al. 2013).

The high incidence, the cost of therapy and the degree of therapy failures resulting in mortality rate present a huge social and medical challenge. Breast cancer is the major and by far the only oncological disease affecting breasts. Unfortunately, it features a high degree of heterogeneity, both in terms of phenotype as well as genotype.

Learning about broadly understood morphology of that type of cancer translates into its treatment and finally - into prognosis. In recent years a few subtypes of breast cancer have been identified. They feature similar response to treatment, which results from similar biological characteristics of the cancer.

Standard therapy for breasts cancer consists of combined multi-discipline treatment. The aim of such treatment is to adjust an optimum treatment for patient and to provide them with medical, psychological as well as social support. As in the case of other cancers, all medical treatments focus on arriving at the best possible therapeutic effect with the least possible side effects.

In recent years a number of changes in breast cancer treatment have been observed. New surgical procedures have been introduced which allow for breast preservation. Currently quadrantectomy, i.e. segmental mastectomy, has replaced mastectomy. Sentinel lymph node biopsy has reduced the number of axillary lymphadenectomy procedures, which frequently resulted in disability. Women who had mastectomy (removal of breast) are offered reconstruction procedures. Radiotherapy procedures have improved so that the area exposed to irradiation has been very much limited, which contributes to fewer complications.

And in terms of systemic approach to cancer therapy, better knowledge about the cancer biology resulted in the introduction of new drugs while helping reduce a group of patients administered cytostatic drugs. Targeted cancer therapy has improved the results of cancer treatment.

Screening programmes for breast cancer are available worldwide, including Poland. It is of major importance for curbing mortality due to breast cancer.

The changes described have contributed to improvement of therapy results and to reverse the mortality curve. For the majority of patients, breast cancer has become a chronic disease. This also results from the length of therapy (lasting even more than 5 years) and the convalescence time.

Epidemiology

Breast cancer is the most frequently occurring type of carcinoma in women. It is the most frequent cause of death as a result of cancer. Breast cancer is estimated to be diagnosed in over 1.7 million people, 0.5 million of whom die in the end. 50% of all cases of breast cancer occur in developed countries, and the majority of deaths occur in less developed ones (60%) (Wojciechowska, Didkowska 2011).

For Poland, as for the other countries of the region, the values of basic destimulating variables in oncological epidemiology, i.e. 5-year prevalence (for adult cohort) and incidence and mortality, expressed as a share of deaths due to breast cancer in the total number of deaths due to cancer[87], are lower than in the highly developed countries where oncological care is well developed, such as Australia or France (mortality rate observed in Latvia is an exception, conf. Figure 1). It must thus be assumed that the observed correlations result from non-epidemiological reasons such as e.g. a different quality of cancer records kept in those countries[88]. Alternatively, a lower value of those statistics may result from the quality of medical care in other domains (death is caused by other disease than cancer, which had

[87] Variables standardised against age per 100 thousand inhabitants.

[88] It is also worth mentioning the GLOBOCAN methodology - values for Poland were obtained based on three regional registers (Cracow, Kielce and Lower Silesia), which cover 13% of the population - it is disputable whether a sample made up in such a way is representative from the point of view of making inferences about the population of the whole Poland.

developed earlier than cancer), or from the whole health-care system (patients diagnosed with cancer do not enter the health-care system, and are not recorded as a result). Thus, the following comparison with highly developed countries should be treated as a kind of forecast that may indicate the position of Poland in the future. One should not, however, make any optimistic conclusions about breast cancer epidemiology in Poland. The values of unconditional as well as conditional five-year survivals in Poland (in relation to surviving the previous year) are the lowest (next to Latvia) for the countries taken into account for the analysis (Figure 2). One should expect that leading to a situation where breast cancer could be diagnosed and treated at earlier clinical stage would level the differences observed.

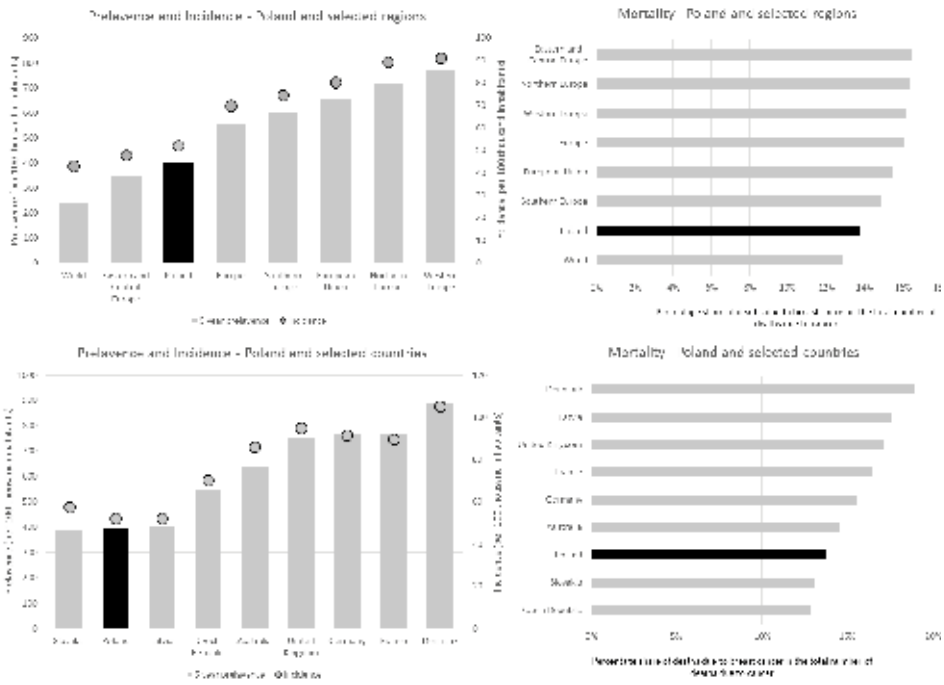


Figure 1. Basic statistics concerning the epidemiology of breast cancer for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

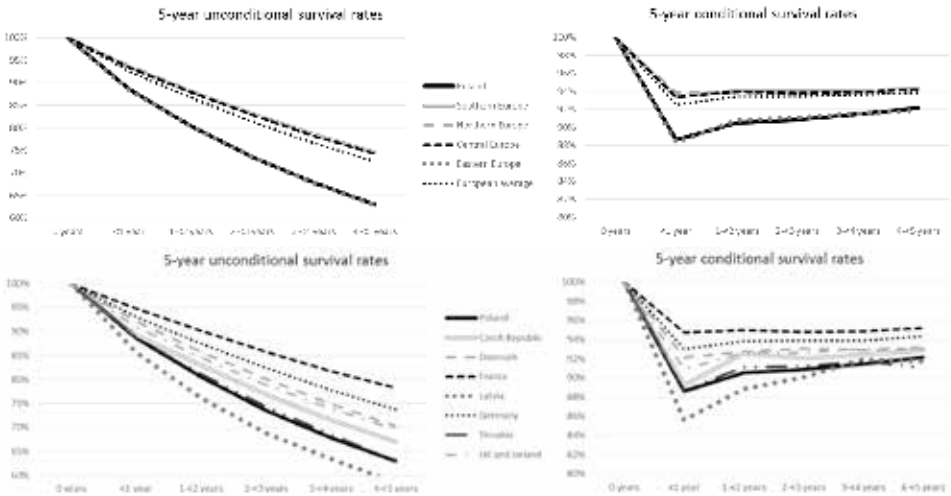


Figure 2. Five-year survival outcomes for patients suffering from breast cancer in Poland and selected regions (source: own analysis based on EUROCARE - 5)

In the majority of breast cancer cases it is impossible to determine the cause of the disease. Breast cancer is determined mainly by sex. Women develop breast cancer over 100 times more often than men. Research into breast cancer incidence in immigrant females shows that the impact of environmental factors on the development of the disease is greater than the impact of genetic predispositions (Kornafel 2011). The greatest number of cases is recorded in highly developed countries such as Belgium, Denmark and the Netherlands. The smallest number of women suffer from breast cancer in Africa and South-Eastern Asia (Ferlayet et al. 2013). It can be related to lifestyle (including diet), consumption of stimulants, social changes in terms of reproduction, etc.

Genetic factor increases the risk of breast cancer development. According to various sources, it does not, however, exceed the value of 10%. The average of 4-8% of the total number of cases is related with a presence of mutation in BRCA1 or BRCA2 gene, or with very rare genetic syndromes, e.g. Cowden and Li-Fraumeni syndromes. BRCA1 mutation increases the risk of breast cancer development by 56-85% (Matkowski 2008). In this group, breast cancer will develop earlier than in the remaining population.

Breast cancer incidence is also strongly determined by age. This type of cancer is most frequently diagnosed in women in post-menopausal age, between 50-70 years of age - in the Polish population of female patients - over 80% of them are 50+. Breast cancer is most infrequent in women before 20. In the recent decades more and more younger women developing breast cancer have been observed. The number of patients aged 20-49 increased twice in the last 30 years. At the same time one can observe that the number of cases in each decade of life up to menopause has been doubling. After the menopause the risk achieves a stable level that it is maintained until 70 years of age, then the risk drops (National Cancer Registry).

Another factor that increases the probability of developing the disease is a family history of breast, ovary, colon and prostate cancer. The risk of developing breast cancer increases in women whose female relatives in first degree of consanguinity also had the disease, especially in their young ages. Also, the number of relatives who developed the disease strongly determines the risk of breast cancer - breast cancer developed by two relatives increases the risk 3-6 times (Jassem, Krzakowski 2014).

Another determining factor is physiological function of endocrine system and reproductive activity. An extended reproductive period related to early menarche (before the age of 12) or late menopause (after the age of 55) is a well-proven risk factor (Collaborative Group on Hormonal Factors in Breast Cancer 2002). The same relates to childlessness or having the first baby at a late age. Maternity before 25, bearing many children and active lactation (over 6 months) reduce the risk of breast cancer.

Factors having adverse effect on breast cancer risk also include pharmacological hormonal treatment. Hormone replacement therapy (HRT) received for more than 5-7 years increases relative risk to 1.6. Each year of HRT increases the risk by 2.7% (Collaborative Group on Hormonal Factors in Breast Cancer 2002). There is data, according to which long-term hormonal contraception causes insignificant increase of relative risk, the risk dropping every year following the therapy termination.

A major factor that increases the risk includes a past episode of breast cancer, as well as benign lesions with proliferation, e.g. atypical ductal hyperplasia. If the condition is diagnosed and if cancer is diagnosed in a close relative, both factors are aggregated and the risk increases nine times.

Among the other factors affecting the risk of breast cancer one must mention obesity in women before menopause as well as their lifestyle (diet rich in fats of animal origin, drinking alcohol, smoking tobacco during pregnancy) and exposure to ionising radiation.

One has to underline that groups featuring genetic risk of breast cancer can make use of primary prevention[89]. However, there is no primary prevention in case of breast cancer which is not genetically conditioned. Nevertheless, healthy lifestyle meaning: physical activity, appropriate body mass index (BMI), balanced diet, limited consumption of stimulants and rational use of hormone therapies - these are recommendations which can lower the risk of developing the disease. The most important is, however, secondary prevention, namely participation in screening, as early detection of cancer gives a chance for full recovery.

Economic analysis of cancer diagnostics

Screening

Breast cancer diagnostics is based on an interview as well as physical examination (using eyes and hands - palpation)[90] and radiological imaging. Radiology imaging enables the determination of subclinical lesions, i.e. lesions that cannot be detected by palpation by a woman or by trained medical staff.

A large number of cured cases of early stage breast cancer resulted in worldwide screening schemes with the use of mammography - medical imaging of breasts. The screening is of major importance for curbing mortality due to breast cancer. Screening schemes implemented in different countries can assume various modalities, but usually for women in particular age groups[91] it involves palpation of breasts and mammography scan. The examination involves age groups which are most at risk of developing breast cancer.

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[89] Breast cancer prevention procedures have still been unsatisfactory in Poland. Significantly small group of patients receive appropriate genetic advice and are covered with proper care. In terms of recommendations concerning preventive surgery there are no differences of procedures between Poland and the rest of the world. From the point of view of systemic solutions, pharmacological prevention is not refunded in Poland (as it is in the USA and a selected group of developed countries).

[90] Many years ago self-examination started to be promoted, involving regular monthly examination of breasts by a woman, including palpation. In big cohort research this method has not been acknowledged as effective in terms of lowering mortality rates, but it remains an important element of pro-health education. Examination by trained medical staff yields better results.

[91] The European Commission recommends screening for women aged 50-69 to be done every 2-3 years, in the US

In Poland screening is free. Women aged 50-69 receive a letter with an invitation; additionally, information campaigns are conducted, to disseminate information about screening access and venue. The first stage includes filling out a questionnaire and taking a mammography test. If the test result is normal, the test is repeated every 2 years in case of women without risk factors, or every year for women at risk. If the test result is abnormal, a woman is directed to a doctor, another mammography test is done, or breast ultrasound or a biopsy (fine-needle aspiration biopsy or core needle biopsy depending on type of lesions).

Each diagnostic method has its degree of sensitivity (true positive rate) and specificity (true negative rate). Mammography is not free from errors. In some patients who have cancer the result will be negative, and even greater percentage of patients will undergo further diagnostic procedures which will not confirm cancer. Despite this, none of the countries decided to give up their screening schemes. However, certain serious restrictions have been introduced, and impact has been put on quality increase and maintenance of high standards of tests in order to reduce the incidence of cancer overdiagnosis and the number of falsely negative results. In addition, attention is paid to the need of extending the screening to cover other age groups, considering currently existing risk factors. Other types of radiology imaging are also being introduced, e.g. breast MRI for carriers of BRCA1 and BRCA2 mutations.

Social education and 70% response to an invitation to screening are estimated to reduce mortality due to breast cancer by as much as 40%. Current response to screening in Poland does not exceed 45% of the population covered with the test (conf: Program screening, further: PBP).

Breast cancer diagnostics

Breast cancer diagnostics includes a clinical examination during which attention is focused on observing mammary glands and the surrounding axillary lymph nodes. The examination focuses on the size of a breast lump, its mobility and possible skin and nipple lesions caused by lump growth. In addition, the doctor examines also the surrounding lymph nodes in search of metastasis. These include axillary nodes as well as supraclavicular and subclavicular nodes, the enlargement and mobility of which are the bases for determining cancer stage. The medical

all women aged 50-74 should undergo screening every 2 years (Jassem, Krzakowski 2014).

examination is completed by radiological imaging, including mammography, described above. Its effectiveness increases with age, due to physiological involution of glandular tissue into fatty tissue. Lesions visible in younger women whose breast is more glandular, are better visible in ultrasonography. Ultrasound is less sensitive and relatively more specific, that is why it is used for differential diagnosis and for making the majority of targeted biopsies. Both tests are mutually complementary. Radiologically, in order to harmonise the system of describing breast and visible lesions, BI-RADS (Breast Imaging Reporting Data System) scale was introduced. It enables categorising visible abnormalities by determining whether they are benign or may be malignant. The role of magnetic resonance imaging (MRI) has been increasing. Due to high degree of sensitivity, the MRI test may be useful in detecting small lesions. Moreover, it is performed in certain groups of patients, e.g. pregnant women, BRCA mutation carriers and in women already treated for cancer.

Medical examination and radiological imaging are the basis for suspecting the disease, and this suspicion is verified by means of histopathology. Histopathological examination is conducted based on material obtained during biopsies which are made under control of ultrasonography or mammography machine. Biopsies can take a form of fine-needle aspiration biopsy FNAB, core needle biopsy (CNB) or vacuum assisted biopsy (VAC). In case of evident enlargement of lymph nodes there is a need to verify the presence of metastasis by means of an ultrasound controlled biopsy.

If the result of histopathological examination shows cancer cells, a description of cancer stage is done based on the above mentioned tests (complemented by radiology images of body organs exhibiting metastases). This is done by means of an international TNM classification. According to the adopted criteria the following is described: T (Tumour), lymph node : N (Node) and visible metastases: M (Metastases) (conf. Table 1).

Table 1. TNM classification of breast cancer according to 7th edition of UICC classification (source: own analysis based on 7th edition of UICC classification

Symbol	Meaning
Primary tumour (T)	
T_x	Primary tumour size cannot be assessed.
T_0	No evidence of primary tumour
T_{is}	Carcinoma in situ: ductal carcinoma (DCIS), lobular carcinoma (LCIS), Paget disease of the breast
T_1	Tumour up to 2 cm in the greatest dimension
T_{1a}	Tumour below 0.5 cm in the greatest dimension
T_{1b}	Tumour >0.5 cm but < 1.00 cm
T_{1c}	Tumour >2.0 cm but < 0.5 cm
T_2	Tumour >2.0 cm but < 5.0 cm
T_3	Tumour > 5.0 cm
T_4	Tumour of any size invades chest wall or skin
T_{4a}	Tumour invades chest wall (ribs, muscles between the ribs)
T_{4b}	Tumour invades skin (oedema - including peau'd orange, ulceration, satellite skin nodules confirmed in the same breast. The following is not considered invasion: dimpling of the skin, nipple retraction, or other skin changes not listed as invasion) those changes may occur in T1, T2, T3)
T_{4c}	T_{4a} and T_{4b} at the same time
T_{4d}	inflammatory carcinoma (carcinoma inflamatorium)
Regional lymph nodes (N)	
N_X	Regional lymph nodes cannot be assessed.
N_0	No regional lymph node metastases (after examination of at least 10 lymph nodes which have been removed)
N_1	Metastases to movable ipsilateral level I, II axillary lymph node(s)
N_{1a}	Micrometastases below 0.2 cm in the greatest dimension
N_{1b}	Macrometastases > 0.2 cm
N_{1bi}	Macrometastases in 1-3 axillary lymph nodes
N_{1bi}	Macrometastases in 4 and more axillary lymph nodes
N_{1bi}	Invasion of lymph node capsule
N_{1bi}	Macrometastases > 2 cm
N_2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted
N_3	Metastases in ipsilateral infraclavicular axillary lymph nodes
Distant metastasis (M)	
M_X	Distant metastasis cannot be assessed.
M_0	No distant metastasis
M_1	Distant metastasis

Based on TNM, considering prognosis and further therapy, breast cancer stages have been defined as presented in the following Table 2.

Table 2. Anatomic stage of breast cancer based on TNM staging
(source: own analysis based on TNM UICC)

Anatomic stage based on TNM			
Stage	**Primary tumour (T)**	**Regional lymph nodes (N)**	**Distant metastasis (M)**
0	T_{is}	N_0	M_0
I	T_1	N_0	M_0
IIA	T_0 T_1 T_2	N_1 N_1 N_0	M_0 M_0 M_0
IIIB	T_2 T_3	N_1 N_0	M_0 M_0
IIIA	T_0 T_1 T_2 T_3 T_3	N_2 N_2 N_2 N_1 N_2	M_0 M_0 M_0 M_0 M_0
IIIB	T_4 T_4 T_4	N_0 N_1 N_2	M_0 M_0 M_0
IIIC	every T	N_3	M_0
IV	every T	every N	M_1

Diagnostic procedures in Poland (conf. Table 3) and in the majority of other countries are similar. Possible differences result from the fact that certain tests may be accessible of subject to refund, however the diagnostic regime remains the same.

Table 3. Diagnostic tests in breast cancer patients
(source: own analysis based on Jassem, Krzakowski 2013)

	Stage	Scope of testing	Additional tests depending on clinical indications
Primarily operable cancer	0 I IIA IIIB	Interview and physical examination Blood tests: - complete blood count with blood film - basic metabolic panel Breast imaging procedures - bilateral screening mammogram, accompanied with ultrasound or MRI depending on indications Histopathology: - fine needle aspiration biopsy (FNAB) - core needle biopsy (CNB) - open biopsy Chest X-ray	- bone scan: ostealgia or elevated alkaline phosphatase or calcium - ultrasound or CT scan of abdomen and/or small pelvis: abdominal or pelvic pain, abnormalities in physical examination or elevated liver enzymes - Chest X-ray or CT scan: symptoms related with respiratory system - PET or CT scan: metastases to axillary lymph nodes from a focus of unknown origin Consultation with genetic specialist in case of patients with eventful family history of disease
	IIIA T3, N1, M0	The above as well as: - bone scan - ultrasound or CT scan of abdomen and/or small pelvis	
Locally advanced cancer with	IIIA T0, N2, M0 T1, N2, M0 T2, N2, M0 T3, N2, M0 IIIB IIIC	Interview and physical examination Blood tests: - complete blood count with blood film - basic metabolic panel Breast imaging procedures - bilateral screening mammogram, accompanied with ultrasound or MRI depending on indications Histopathology: - core needle biopsy (preferred) - open biopsy Chest X-ray Additionally recommended: - bone scan - ultrasound or CT scan of abdomen and/or small pelvis	
	IV	Interview and physical examination Blood tests: - complete blood count with blood film - basic metabolic panel Histopathology: Breast imaging procedures: Breast imaging procedures - bilateral screening mammogram, accompanied with ultrasound or MRI depending on indications - Chest X-ray or CT scan - ultrasound or CT (preferred) or MRI scan of abdomen and/or small pelvis - bone scan and X-ray, CT or MRI scan in order to confirm exact diagnosis concerning the character and scope of bone lesions - PET or CT scan - other imaging procedures depending on clinical indications	

Breast cancer treatment

Therapeutic procedure in case of breast cancer depends first of all on the evaluation of clinical stage (cTNM), which determines the treatment regimen to a great extent. Breast cancer treatment involves various combinations of surgery, radiotherapy and systemic therapy such as chemotherapy, hormone therapy as well as targeted therapy. Surgical treatment involving breast and regional lymph nodes remains the mainstay of the therapy. The sequence order and scope of treatment is determined by patient's consent and individual medical indications and contraindications, including a possibility of induction therapy.

The following surgical operations can be made in case of breast cancer:

- in the scope of breast:
  - conservative surgical options,
  - amputations,
- in the scope of regional lymph nodes:
  - axillary lymphadenectomy
  - sentinel lymph node biopsy

Breast conserving therapy - BCT - involves a dissection of tumour together with an appropriately wide margin of healthy tissues. The type of surgery depends on tumour size and location. The objective of such a procedure is to preserve the breast, bearing in mind aesthetic concerns. This approach obviously improves the quality of live of patients without a negative impact on the therapy. BCT requires additional treatment in the form of breast radiotherapy. Because of this the therapy is extended and direct cost of therapy increases. Currently studies are conducted in view of reducing the amount of radiotherapy sessions, however, BCT standard still involves surgery followed by radiotherapy.

There are different approaches to mastectomy: simple mastectomy, subcutaneous (simple skin-sparing mastectomy) and modified (Patey, Modden and Halsted method). They are applied in case of contraindications to conservative treatment due to advanced stage or due to individual contraindications, including when a patient does not agree to conservative therapy.

Breast reconstruction surgery currently forms a part of oncological therapy also in case of breast cancer. Reconstructions may be conducted simultaneously with mastectomy or may follow it at a later time.

Surgeries involving lymph nodes depend on clinical assessment of metastases. Suspected metastases result in axillary lymphadenectomy, which may cause a number of complications, including permanent lymphatic oedema of an extremity. If no metastasis has been clinically confirmed, a standard procedure involves a biopsy of sentinel lymph node. The biopsy involves injecting a tracer material (dyes or radioisotope) in order to see the way lymph is drained from breast and to locate nodes which are the first “obstacle” to the lymph. It is established that if lymph nodes are invaded, another treatment stage involves axillary lymphadenectomy. In the remaining cases axillary lymphadenectomy is not done.

A decision concerning complementary therapy is made based on the type of surgery, assessment of cancer stage (pTNM) and tumour cell morphology. Advanced stages of cancer or special clinical cases are treated by induction therapy as the first step. All methods of systemic treatment are used, chemotherapy being the most frequent. Hormone therapy may be administered only to selected groups of patients, i.e. if hormone receptors are present in the tumour, when the disease progresses slowly or when there are contraindications to administer cytostatic drugs. In contrast to other countries, targeted therapy in pre-surgical stage is not refunded in Poland, although it is medically justified.

Radiotherapy is an integral part of conservative therapy. It reduces the risk of cancer reappearance in the remaining part of breast. Irradiation, depending on a method, includes 25 fractions of irradiation up to 50 Gy administered within 5 weeks of exposure or 15 fractions up to 45 Gy. The whole breast is subject to irradiation. Additional boost dose is targeted at the primary tumour bed. Radiotherapy is also conducted regardless of the type of surgical procedure, if the tumour exceeds a certain size (currently T3=5 cm) or surgical margin is insufficient. Radiotherapy of lymph nodes follows if at least 4 lymph nodes have been invaded. Individually it may also be considered if smaller number of nodes (1-3) are invaded. If there is a need to administer cytostatic drugs as complementary therapy, radiotherapy starts when chemotherapy is finished.

Tumour morphology is the main factor which determines systemic therapy. Histologic classification of breast cancer includes to subtypes: i.a. ductal carcinoma and lobular carcinoma. The other histologic sub-types occur infrequently, but they feature slightly better prognosis (tubular, mucinous, etc.). Changes observed in the last decade involve adjusting the therapy not only to cancer stage but first of all to cancer biology. When making assessments, one takes account of the presence of hormonal (ER and PR) receptors and HER2 (receptor which indicates a possibility of applying targeted therapy). Moreover, cancer sub-type is determined by Ki-67 indicator which describes cancer cell proliferation ability. Systematics of breast cancer has been presented in Table 4.

Table 4. Definition of biological sub-types of breast cancer based on histopathology by means of immunohistochemical techniques (Source: Jassem, Krzakowski 2013, p.225)

Breast cancer sub-type	Clinical definition	Comments
Luminal A	ER+ H_{ER2} Ki-67 < 14% PgR≥ 20% Favourable molecular signature1	
Luminal B	Luminal B, HER2– ER/PgR+ HER2– Ki-67 ≥ 14% or PgR< 20%	If Ki-67 determination is impossible, one can rely on the degree of histologic differentiation
	Luminal B, HER2+ ER+ HER2+ Every Ki-67 and PgR	
HER2+ non “luminal”	ER/PgR– HER2+	
Basal-like	“triple negative” without a special type (formerly ductal) ER/PgR– HER2–	Approx. 80% of triple negative cancers overlap with basal-like, but this category also includes types with a low risk of recurrence (medullary carcinoma, adenoid cystic carcinoma)
Special histologic types	ER+ (cribiform, tubular and mucinous) ER– (apocrine, medullary, adenoid cystic, metaplastic)	

There are harmonized principles of applying therapy in case of breast cancer. There are a few

compatible medical procedure guides, developed by huge international scientific associations. In Europe (including Poland) the recommendations are based on a consensus arrived at by specialists in the course of regular conferences held in St. Gallen (for early stage breast cancer) and Lisbon (for metastatic breast cancer).

Table 5. Election of complementary systemic therapy, account taken of biological sub-types of cancer, defined based on IGC histopathologic evaluation according to the 2013 St. Gallen conference (Source: Jassem, Krzakowski 2013, p.239)

Breast cancer sub-type	Treatment	Comments
Luminal A	hormone therapy	Chemotherapy in few cases of massive invasion of lymph nodes or other risk factors
Luminal B, HER2-	hormone therapy ± chemotherapy (the majority of patients)	Application of chemotherapy and its type depending on the expression of hormonal receptors, risk level and patient's preferences
Luminal B, HER2+	chemotherapy + trastuzumab + hormone therapy	No data available on treatment without chemotherapy
HER2+ non "luminal"	chemotherapy + trastuzumab	Trastuzumab recommended from T1b > 5 mm and in patients with pN+
"triple negative" without a special type (formerly ductal)	chemotherapy	
Special histologic types		
ER+	HTH	
ER-	chemotherapy	In case of N0 chemotherapy is optional in case of medullary and adenoid cystic type of cancer

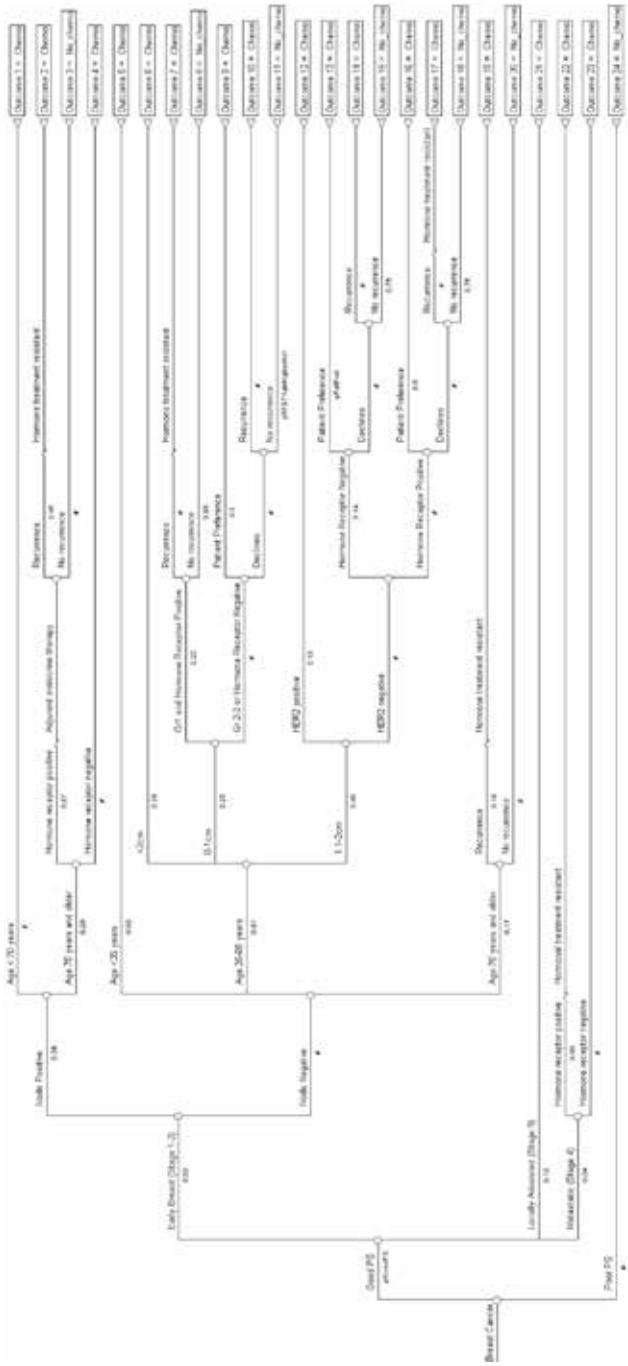
Current differences in early stage cancer therapy are related to drug refunding restrictions, which limit the possibility of applying targeted therapy. In Poland a refund does not include adjuvant treatment with trastuzumab before surgery and in cases with tumour dimension ranging between 0.5 and 1 cm.

Greater disproportions relate to the availability of innovative drugs, including targeted ones, for the treatment of breast cancer with distant metastases. The process of medicinal

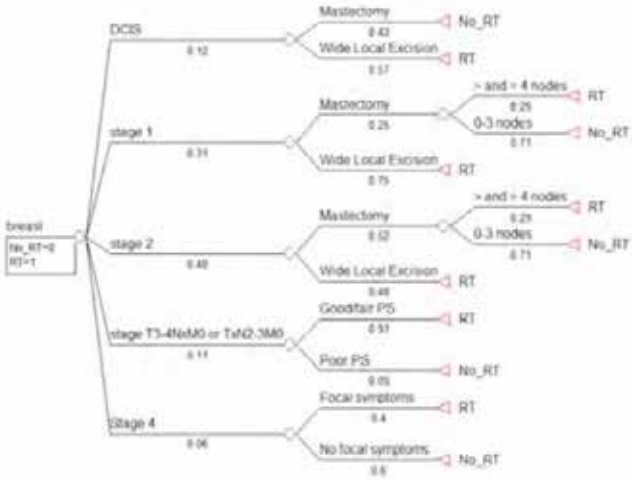
product registration in Poland is a relatively expensive and long-lasting procedure, as is the refund permit obtainment procedure. As a result one can observe limited access to innovative therapies. Disproportions in the access to innovative treatment procedures have been described in detail in an EU report (European Commission 2014).

Decision-making models in breast cancer treatment

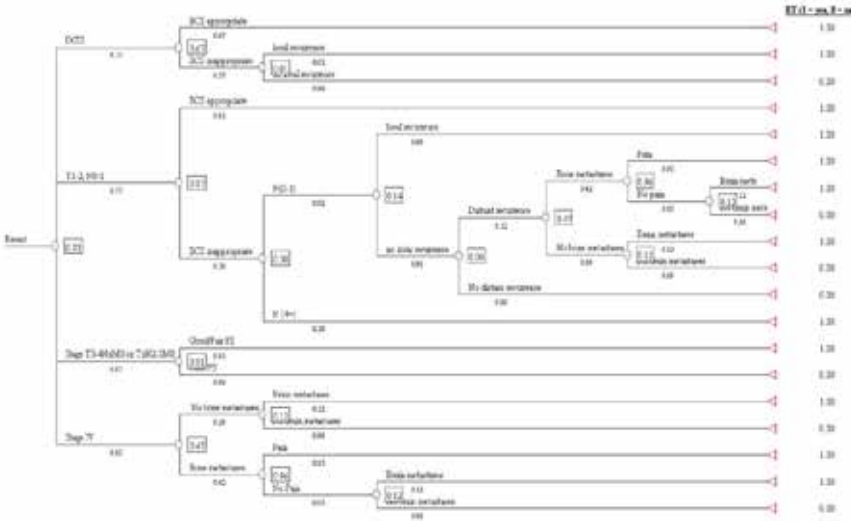
Decision-making models in breast cancer treatment are usually presented in the form of decision trees. Ng et. al (2010) have described a model of chemotherapy for Australia. Chemotherapeutical treatment model for Scotland has been developed by NHS Scotland (2005), and the one for Australia has been published by Barton (2013). Relevant decision trees have been presented in Flowcharts 1-3.



Flowchart 1. Decision tree for the application of chemotherapy in Australia (source: own analysis based on Ng et al. 2010)



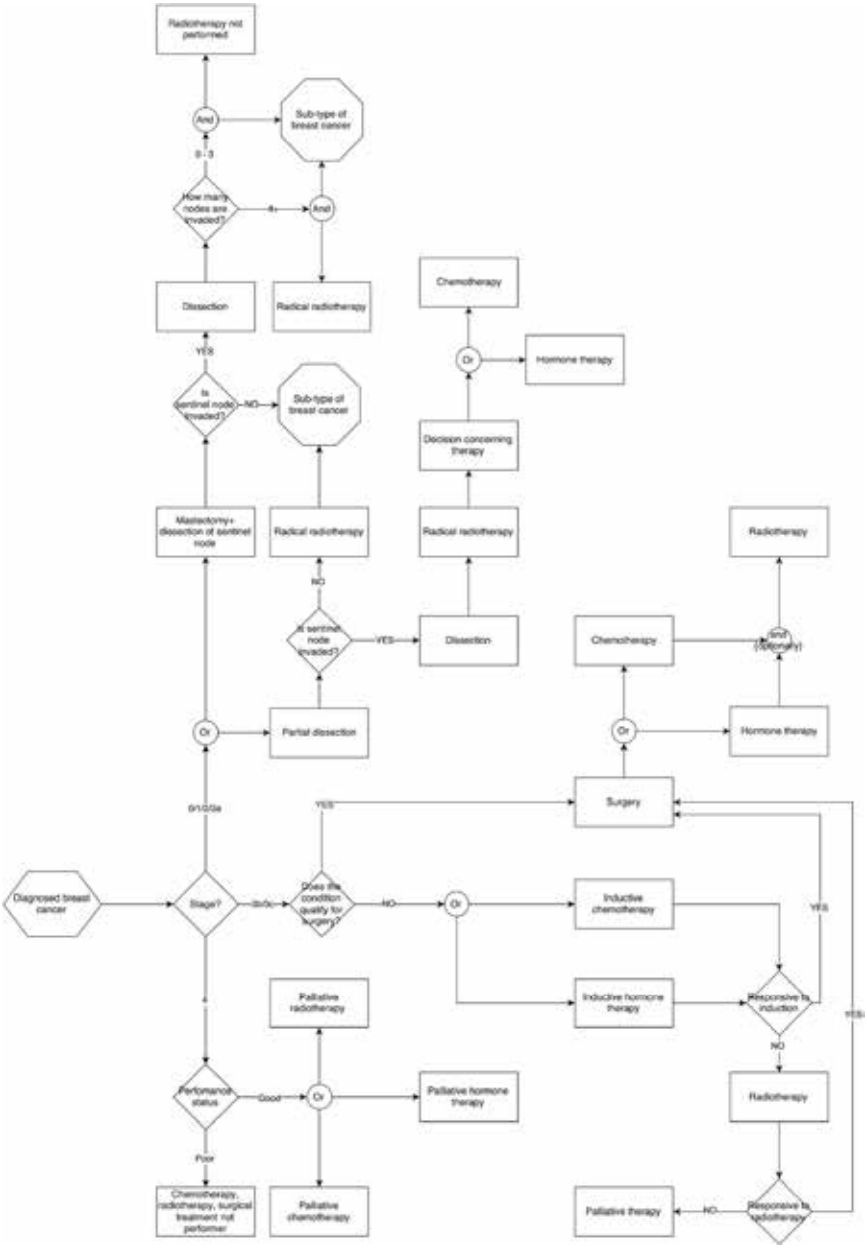
Flowchart 2. Decision tree for the application of radiotherapy in Scotland (source NHS Scotland 2005)



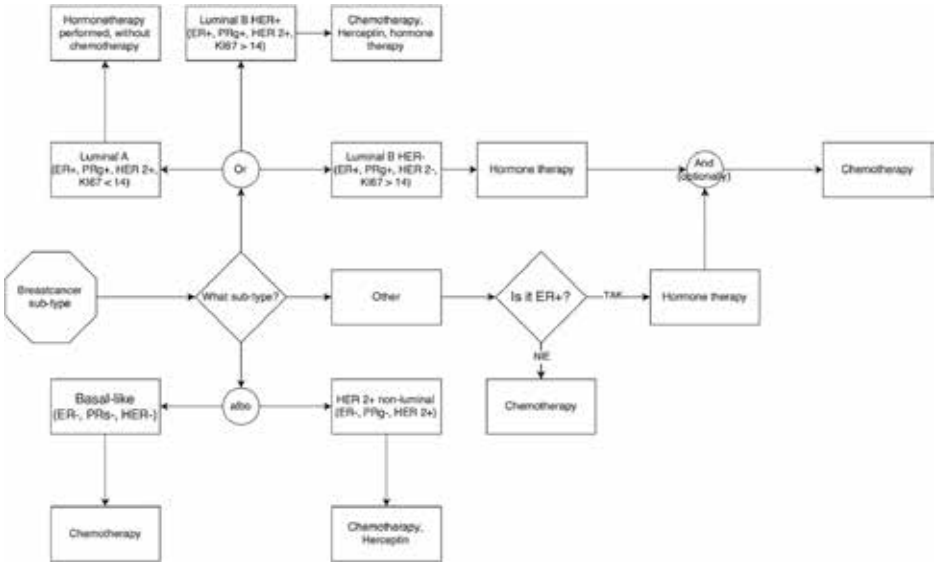
Flowchart 3. Decision tree for the application of radiotherapy in Australia (source: own analysis based on Barton 2013)

A theoretical model of oncological therapy in Poland, including surgical treatment, chemotherapy and radiotherapy, has been presented in Flowcharts 4-5. The model was developed on the basis of analyses of the above mentioned models, adjusted to take account

of standards of oncological treatment which are recommended by academic associations in Poland and expert knowledge concerning practical treatment of cancer in Poland.



Flowchart 4. Oncotherapy model in Poland (source: own analysis)



Flowchart 5. Decision making procedure for square "Breast cancer sub-type" in Flowchart 4 (source: own analysis)

Empirical model of breast cancer treatment in Poland

According to the data provided by the National Cancer Registry (NCR), 16,866 cases of breast cancer in both sexes were[92] recorded in Poland in 2012, including approx. 100 male patient cases. Currently in Poland breast cancer is the most frequent type of cancer occurring in women (22.8%). Every year more and more women are diagnosed with breast cancer and according to NCR, the incidence rate has grown more than twice over the last three decades (Wojciechowska, Didkowska 2011).

Breast cancer is the second (following lung cancer) cause of women mortality due to malignant neoplasms. In 2011 approx. 5.3 thousand women died because of breast cancer, which accounts for 13% of deaths due to cancer. Incidence features growing trend, whereas

[92] The figures presented by NCR have been initially verified based on NHF database. This means that they do not include patients who appeared for the first time in the NCR database in a given year with breast cancer diagnosis and who were recorded with the diagnosis in the NHF database before that year.

mortality trend has been reversed. Improved level of prevention, early stage detection and optimization of therapy have resulted in widening the gap between the incidence and mortality curves.

Construction of a full empirical model of breast cancer treatment based on theoretical model presented in Flowchart 5 would require having access to data on breast cancer stage or subtype. National Cancer Registry database is the only source of information on the cancer stage. Analysis of that database which was carried out with the use of the NHF database has supplied evidence for major information gaps of the NCR database. First, cancer stage has not been recorded in the majority of entries, which is presented in Table 6. The share of records without information about cancer stage ranges between 17-22% depending on year. At the same time, a very low percentage of stage I cases are recorded.

Table 6. Distribution of information on cancer stage in NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	707	758	758	4%	4%	4%
II	7,342	7,552	7,165	45%	44%	42%
III	4,521	4,563	4,299	28%	26%	25%
IV	1,026	1,075	955	6%	6%	6%
Stage not recorded in NCR	2,782	3,358	3,689	17%	19%	22%
Total	16,378	17,306	16,866	100%	100%	100%

Apart from lack of information about the cancer stage it has been noticed that many patients who are recorded in NHF are not recorded in NCR database at the same time. Based on the analysis of services provided to them[93], some of those patients were classified as follow-up patients or patients who were treated at a given moment for a different disease than cancer (despite the ICD-10 indicated breast cancer). The analysis of services for patients who were provided hospital or ambulatory treatment and who have not been recorded in the NCR database was the basis for a conclusion that every year approx. 2.9 thousand patients

[93] On more information on the methodology for estimating cancer incidence in Poland see: Sources and Quality of Cancer Epidemiological Data in Poland - Data Analysis Methodology

are not recorded in that database. Patient categorization based on services provided has been presented in Table 7.

Table 7. Cancer stage categorization of new patients who have not been recorded in NCR (source: own analysis)

Cancer stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	812	776	838	8%	10%	11%
II	257	276	389	3%	3%	5%
III	289	324	465	3%	4%	6%
IV	1,582	1,464	1,398	16%	18%	19%
other cause	3,487	2,551	2,170	35%	32%	29%
follow-up	3,566	2,616	2,192	36%	33%	29%
Total	9,993	8,007	7,452	100%	100%	100%

Finally, based on information from NCR database and on the analysis of patients recorded in the NHF database, as well as based on the analysis of services provided to those patients, breast cancer incidence in 2010-2012 was established to be characterised by distribution against the stage as presented in Table 8. A comparison of Tables 6-8 results in a conclusion that, following the adjustments based on NHF database, the number of new diagnoses of breast cancer in the period under consideration increased on average by approx. 16% per annum. The statistics in terms of cancer stage also changed significantly, e.g. the share of patients with breast cancer stage I increased to 12% in 2012 (i.e.3 times), and the share of patients with the highest stage increased to 14% (more than twice).

Table 8. Distribution of incidence against cancer stage for the period 2010–2012 (source: own analysis)

Cancer stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	2,123	2,272	2,394	11%	11%	12%
II	8,454	8,902	8,721	44%	45%	44%
III	5,494	5,739	5,697	29%	29%	29%
IV	2,979	2,952	2,783	16%	15%	14%
impossible to define	30	14	19	0%	0%	0%
Total	19,080	19,879	19,614	100%	100%	100%

During the following stage of constructing the empirical model, analysis was focused on services provided to patients during one year of starting the therapy. Based on the reporting procedures according to International Classification of Medical Procedures ICD-9 and Homogenous Patient Groups, four variables were defined which carried information whether a patient (1) underwent breast surgery (ICD-9 procedure glossary was developed), (2) received chemotherapy[94], (3) received radiotherapy and (4) received palliative treatment. This approach made it possible to present analysis results in the form of four binary trees (for each cancer stage), which presented the size of a group obtained as a result of subsequent divisions, the size of the group in relation to the previous division and in relation to the whole cohort of new patients suffering from breast cancer (regardless of stage). For groups smaller than 50 patients no further divisions were made. Moreover, information was provided about recorded death cases which occurred during 365 days of the first appearance in the system as a patient classified to a given group[95]. Information presented pertains to patients who entered the system in 2012 (conf. Flowchart 6).

The empirical model confirms that in general, surgical treatment is the most frequent method of treating breast cancer (80.6% of cases) (conf. Table 9). Almost 100% of patients with stage I breast cancer survive the first year since the start of treatment. These statistics decline with the advancement of cancer stage and amount to respectively 98,5% in case of stage II, 94.2% in case of stage III and 53.5% in case of stage IV (conf. Flowchart 6).

Table 9. Empirical model of breast cancer treatment in Poland part 1 (source: own analysis)

Type of therapy	patients who underwent the therapy
surgical treatment	80.6%
chemotherapy	51.7%
radiotherapy	53.0%

[94] including: whether the patient received targeted therapy or hormone therapy within the framework of drug schemes or therapy regimens. Hormone therapy based on drugs bought by a patient in a pharmacy was not taken account of.

[95] Due to data availability the causes of deaths were not differentiated.

Table 10. Empirical model of breast cancer treatment in Poland part 2 - patients who underwent a given therapy depending on cancer stage (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
surgical treatment	97.1%	93.6%	88.3%	9.8%
chemotherapy	23.8%	44.9%	70.1%	58.8%
radiotherapy	36.6%	60.2%	64.0%	21.8%

In case of stages I-III, breast surgery is the most frequently applied treatment, and patients with stage IV most often receive chemotherapy. However, radiotherapy is (relatively) most commonly applied in case of stage III and II (cf. Table 10).

Analysis of Table 11 shows that, without differentiating the analysed population of patients based on the disease stage, the most common treatment scheme is simultaneous[96] surgery, chemotherapy and radiotherapy, applied in 28.41% of cases. The least commonly applied method is radiotherapy only (2.00%) and the combination of radiotherapy and chemotherapy (2.32%).

Table 11. Empirical model of breast cancer treatment in Poland part 3 (source: own analysis)

Was surgical treatment provided?			radiotherapy		Total
			NO	YES	
NO - 19%	chemotherapy	NO	7.37%	2.00%	9.37%
		YES	7.71%	2.32%	10.03%
	Total		15.09%	4.32%	19.41%
YES - 81%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	18.71%	20.26%	38.97%
		YES	13.22%	28.41%	41.62%
	Total		31.93%	48.66%	80.59%

[96] The use of the term *simultaneous* in relation to surgery/chemotherapy/radiotherapy is intended to emphasise the fact that these two/three types of therapy are used in the treatment of one patient, up the most within one year of the commencement of treatment. This term is used in the same context later in this publication.

The most common method of treating stage I breast cancer is breast surgery only, which is applied in almost 52% of cases. 22% of patients were simultaneously treated with breast surgery and radiotherapy, and less than 14% of patients were simultaneously treated with surgery, chemotherapy and radiotherapy. Almost every tenth patient has undergone breast surgery and chemotherapy.

In the case of stage II breast cancer, the most commonly used treatment is simultaneous breast surgery and radiotherapy (over 30% of cases) and simultaneous breast surgery, chemotherapy and radiotherapy (over 28% of cases). Every fifth patient in the analysed disease stage undergoes surgery only, and in 15% of cases the combination of surgery and chemotherapy is applied. What is interesting, 324 patients that were assigned stage II in the NCR database have not received any of the analysed therapies, of which 12% did not survive the first year.

Patients with stage III breast cancer are most frequently treated with simultaneous surgery, chemotherapy and radiotherapy (48% of cases). In more than 16% of cases surgery and chemotherapy were used simultaneously, in 13% of cases patients were treated with surgery and radiotherapy, and in 11% – surgery only. What is more, almost 3% of patients received palliative care.

The most commonly used treatment regimen in the case of patients in the most advanced disease stage is chemotherapy only (almost 44%). More than 782 patients (28%) were not treated with surgery, radiotherapy or chemotherapy, and 28% of these patients received palliative care. 9% of patients simultaneously received chemotherapy and radiotherapy. The same percentage of patients has undergone radiotherapy only. 27% of patients in the IV disease stage received palliative care.

Stadium zaawansowania					Including surgical treatment					Including chemotherapy					Including radiotherapy					Including paliative treatment				
Stadium	Number of cases	Share	Number of deaths	Percentage of deaths	NO/YES	Number of cases	Share	Number of deaths	Percentage of deaths	NO/YES	Number of cases	Share	Number of deaths	Percentage of deaths	NO/YES	Number of cases	Share	Number of deaths	Percentage of deaths	NO/YES	Number of cases	Share	Number of deaths	Percentage of deaths
1	2394	12.2%	2	0.1%	NO	69	2.9%	1	1.4%	NO	62	88.7%	1	1.6%	NO	44	71.5%	1	2.3%					
															YES	18	28.5%	0	0.0%					
										YES	8	11.3%	0	0.0%										
					YES	2325	97.1%	1	0.0%	NO	1762	75.8%	1	0.1%	NO	1237	70.2%	1	0.1%	NO	1237	100.0%	1	0.1%
															YES	525	29.8%	0	0.0%	NO	524	99.8%	0	0.0%
																				YES	1	0.2%	0	0.0%
										YES	563	24.2%	0	0.0%	NO	233	41.4%	0	0.0%	NO	233	100.0%	0	0.0%
															YES	330	58.6%	0	0.0%	NO	329	99.7%	0	0.0%
																				YES	1	0.3%	0	0.0%
2	8721	44.5%	131	1.5%	NO	555	6.4%	62	11.2%	NO	402	72.5%	44	11.0%	NO	323	80.4%	39	12.1%	NO	312	96.6%	34	10.9%
																				YES	11	3.4%	5	45.4%
															YES	79	19.6%	5	6.3%	NO	76	96.2%	5	6.6%
																				YES	3	3.8%	0	0.0%
										YES	153	27.5%	18	11.8%	NO	87	56.9%	15	17.3%	NO	70	80.4%	11	15.8%
																				YES	17	19.6%	4	23.5%
															YES	66	43.1%	3	4.6%	NO	63	95.4%	2	3.2%
																				YES	3	4.6%	1	33.3%
					YES	8166	93.6%	69	0.8%	NO	4401	53.9%	36	0.8%	NO	1724	39.2%	29	1.7%	NO	1718	99.6%	28	1.6%
																				YES	6	0.4%	1	16.7%
															YES	2677	60.8%	7	0.3%	NO	2672	99.8%	6	0.2%
																				YES	5	0.2%	1	20.0%
										YES	3765	46.1%	33	0.9%	NO	1336	35.5%	24	1.8%	NO	1323	99.0%	20	1.5%
																				YES	13	1.0%	4	30.8%
															YES	2429	64.5%	9	0.4%	NO	2422	99.7%	8	0.3%
																				YES	7	0.3%	1	14.3%
3	5697	29.1%	334	5.8%	NO	668	11.7%	156	23.4%	NO	330	49.4%	86	26.1%	NO	296	89.6%	81	27.4%	NO	262	88.8%	65	24.8%
																				YES	33	11.2%	16	48.5%
															YES	34	10.4%	5	14.5%					
										YES	338	50.6%	70	20.7%	NO	209	61.8%	60	28.7%	NO	172	82.3%	53	30.9%
																				YES	37	17.7%	7	18.9%
															YES	129	38.2%	10	7.7%	NO	111	86.1%	8	7.2%
																				YES	18	13.9%	2	11.1%
					YES	5029	88.3%	178	3.5%	NO	1371	27.3%	68	5.0%	NO	615	44.9%	59	9.6%	NO	608	98.9%	56	9.2%
																				YES	7	1.1%	3	42.9%
															YES	755	55.1%	9	1.2%	NO	750	99.3%	9	1.2%
																				YES	5	0.7%	0	0.0%
										YES	3658	72.7%	110	3.0%	NO	930	25.4%	81	8.7%	NO	894	96.1%	70	7.8%
																				YES	36	3.9%	11	30.6%
															YES	2728	74.6%	28	1.0%	NO	2709	99.3%	20	0.8%
																				YES	19	0.7%	8	42.1%
4	2783	14.2%	1294	46.5%	NO	2511	90.2%	1207	48.1%	NO	1044	41.6%	688	65.9%	NO	782	75.0%	614	78.5%	NO	560	71.6%	497	88.7%
																				YES	222	28.4%	117	52.7%
															YES	261	25.0%	74	28.3%	NO	225	86.2%	51	22.7%
																				YES	36	13.8%	23	63.9%
										YES	1467	58.4%	519	35.4%	NO	1211	82.6%	436	36.0%	NO	885	73.1%	295	33.3%
																				YES	326	26.9%	141	43.2%
															YES	256	17.4%	83	32.4%	NO	176	68.8%	42	23.9%
																				YES	80	31.2%	41	51.2%
					YES	272	9.8%	88	32.1%	NO	102	37.4%	56	54.9%	NO	90	88.2%	54	60.0%	NO	75	83.3%	47	62.7%
																				YES	15	16.7%	7	46.7%
															YES	12	11.8%	2	16.7%					
										YES	170	62.6%	32	18.5%	NO	92	54.0%	24	26.1%	NO	48	52.2%	11	22.9%
																				YES	44	47.8%	13	29.6%
															YES	78	46.0%	8	9.6%	NO	54	68.2%	4	8.4%
																				YES	25	31.8%	3	12.0%

Flowchart 6. Empirical model of breast cancer treatment in Poland part 4 (source: own analysis)

Summary

Compared with other European countries, the epidemiological situation in Poland is unfavourable. There are large disparities in the outcomes of medical treatment between Poland and the countries of Western Europe, as evidenced by differences in the 5-year survival ratios. The situation described above indicates the need for changes in the field of diagnosis and therapy for the improvement of treatment results. Education and increasing uptake of screening programmes remain the two fundamental measures, as these two factors significantly influence the improvement of the five-year survival ratios. Early diagnosis gives the possibility to apply tissue sparing surgical techniques and primarily increases the chances for full recovery. It is necessary to implement the standard of multidisciplinary approach towards therapy and make the treatment outcomes of individual centres available to the public. Systemic changes were initiated, but they require quality assessment.

The empirical model presented in this article describes in detail treatment regimens for patients with breast cancer. The model was developed based on the analysis of therapies provided to patients within the first year in which they were diagnosed in the system with cancer. By means of this model it was established that the most common regimen for treating breast cancer in Poland is simultaneous surgery, chemotherapy and radiotherapy. The least commonly applied method is radiotherapy only as well as the combination of radiotherapy and chemotherapy. Moreover, while building the model, data gaps were filled regarding cancer stages that were present in the National Cancer Registry and it was indicated that statistical data concerning incidence and prevalence developed based on this registry were underestimated.

The results obtained in the process of developing the model allow for constructing precise forecasts concerning the cost of breast cancer treatment from the payer perspective.

Bibliography

Barton, M., Jacob, S., Shafiq, J., Hsin Wen Wong, K., Thompson, S., Delaney, G., Hanna, T. (2013) *Review of optimal radiotherapy utilization rates*.

Collaborative Group on Hormonal Factors in Breast Cancer (2002) Breast cancer and breastfeeding; collaborative re-analysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet*, 360, pp. 187–195.

EUROCARE-5 Database, access: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx, date downloaded: 2.04.2015.

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013), *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet], Lyon: International Agency for Research on Cancer. Access: http://globocan.iarc.fr, download date: 2.04.2015.

Jasem, J., Krzakowski, M. (2014) *Rak piersi – praktyczny przewodnik dla lekarzy*. Gdańsk: Via Medica.

European Commission (2014) *Research and Innovation performance in Poland. Country Profile 2014,* Luxembourg: Publications Office of the European Union.

Kornafel, J. (2011) *Wprowadzenie do specjalizacji z ginekologii onkologicznej. Podstawy radioterapii nowotworów.* Warszawa: Centrum Medyczne Kształcenia Podyplomowego.

National Cancer Registry, Nowotwory piersi u kobiet (C33–34), Access: http://onkologia.org.pl/nowotwory-piersi-kobiet/, date downloaded: 2.04.2015.

Matkowski, R. (2008) *Epidemiologia raka piersi*. Access: http://www.wok.wroclaw.pl/upfiles/szkolenia/07/puo/Matkowski.pdf, date downloaded: 2.04.2015.

NHS Scotland (2005)*Cancer In Scotland Radiotherapy Activity Planning For Scotland 2011–2015*.

Ng, W., Delaney, G., Jacob, S., Barton, M. (2010) Estimation of an optimal chemotherapy utilisation rate for breast cancer: Setting an evidence-based benchmark for the best-quality cancer care. *European Journal of Cancer*.

Pieńkowski, T. et al. (2011) *Rak piersi. Leczenie ogólnoustrojowe*, Warszawa: Medmedia.

Polskie Towarzystwo Onkologii Klinicznej, Krzakowski, M., Jassem, J. (red.) (2013) *Rak piersi.* Access: http://www.onkologia.zalecenia.med.pl/pdf/PTOK_2013_05_Rak%20piersii.pdf, date downloaded: 2.04.2015.

Program Badań Przesiewowych. Access: http://pbp.org.pl.

Smaga, A., Mikułowska, M., Komorowska, A., Falkiewicz, B., Gryglewicz, J. (2014) *Rak piersi w Polsce – leczenie to inwestycja*. Warszawa: Sequence HC Partners Sp. z o.o.

Wojciechowska, U., Didkowska, J. *Zachorowania i zgony na nowotwory złośliwe w Polsce 2011.* National Cancer Registry, Maria Skłodowska-Curie Institute of Oncology. Access: http://*onkologia*.org.pl.

Treatment pathway model in malignancies of the female reproductive system

Iwona Włodarska-Polińska, Filip Urbański

Introduction

The cancer of the female reproductive system (Gynaecologic Cancer) is one of the most frequent oncological conditions in women – according to data presented by the National Cancer Registry, in the years 2010–2012 this type of cancer amounted to more than 16% of all cases of female oncological diseases and was the cause of ca. 14% of cancer-related deaths. The most common gynaecologic cancer types include endometrial cancer, ovarian cancer and cervical cancer[97]. Hence, this paper will analyse these three most common types of gynaecologic cancer. The common feature of this group of diseases is their occurrence in the small pelvis, while the factors differentiating individual cancer types are their biological nature and the direction of spread.

Cervical cancer is a type of cancer that spreads locally, invading the closest tissues and metastasising first through lymphatic ducts to regional lymph nodes. This type of cancer has the structure of a squamous cell carcinoma and is characterised by varying grades of malignancy. Endometrial cancer in turn has the structure of an adenocarcinoma, which shows early clinical symptoms and in the majority of cases is diagnosed in the first stage. In advanced cases this cancer spreads both through lymphatic ducts and blood vessels, resulting in distant metastasis. Ovarian cancer is the female reproductive organ cancer with the worst prognosis for recovery. This type of cancer develops slowly in the abdominal cavity without showing any symptoms and is characterised by a significant tendency to spread on the peritoneum surface and around the entire reproductive organ, including in the area of the second gonad and lymph nodes in the abdominal cavity. In relation to the different biological nature of individual female genital cancer types a different treatment philosophy applies.

[97] The criterion is the strict incidence ratio (onkologia.org.pl).

Epidemiology

In most cases of cervical cancer patients are diagnosed with an HPV infection (*human papilloma virus*). Infection with this virus is considered to play a significant role in the etiology of cervical cancer. The most oncogenic HPV types are type 16 and 18, which are responsible for 53% and 15% of cases, as appropriate (Villa et al. 2005). Women suffering from cervical cancer are mainly those who start being sexually active at an early age, have many sexual partners, gave many births, as well as those with low social status and smokers. Other risk factors for this type of cancer include HIV infections and other conditions lowering immunity, infections with sexually transmitted pathogens, inappropriate diet and the use of hormonal contraceptives over many years (Kornafel et al. 2013; NCCN). In developed countries, the decline in the number of people diagnosed with this type of cancer is the result of the implementation of primary prevention (i.e. the introduction of HPV vaccinations) and secondary prevention programmes (i.e. screening tests) (Castellsagué et al. 2006; Kornafel et al. 2013). These measures led to the reduction in mortality due to cervical cancer (Didkowska et al. 2011, NCCN).

Poland, as other countries of the region (Czech Republic, Slovakia, Latvia), report higher values of three basic variables in the epidemiology of cervical cancer (i.e. 5-year prevalence, incidence and mortality) than in countries with more developed oncological care (cf. Figure 1).

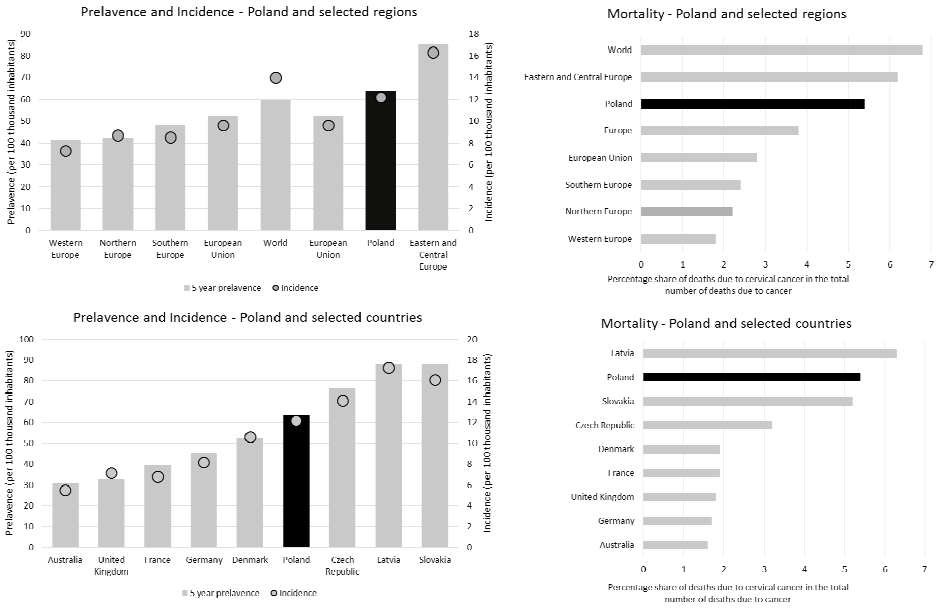


Figure 1. Basic statistics concerning the epidemiology of cervical cancer for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

The incidence of cervical cancer in Poland remains on an average level compared to the number of instances in Europe. Among the analysed countries only Latvia reported lower statistic values regarding 5-year survival rates than in Poland (cf. Figure 2). This observation may be indicative of worse outcomes of oncological treatment of this cancer type or of a worse condition of the entire healthcare system (e.g. delays in starting the therapy). Unambiguous statement of the reasons for the differences in the 5-year survival rate would require taking into account the information on the stage structure of individual cancer types, which, due to the lack of appropriate data, was not possible to date[98].

[98] As it will be demonstrated further in this publication, the data collected by the National Cancer Registry are characterised by an excessively high percentage of missing data in the variable concerning cancer stages, which prevents from formulating any conclusions based on this variable.

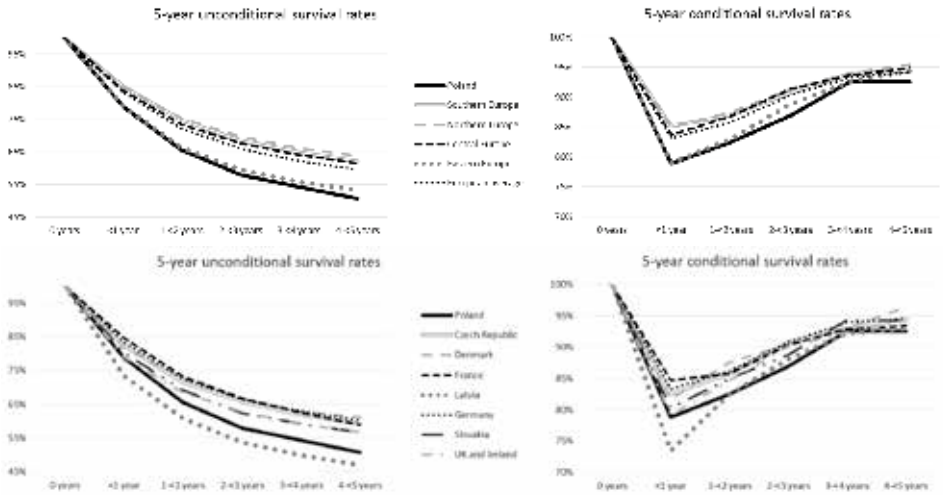


Figure 2. Five-year survival outcomes for patients suffering from cervical cancer in Poland and selected regions (source: own analysis based on EUROCARE - 5)

Endometrial cancer is most common in women aged 50+. The other risk factors for endometrial cancer include: low fertility, excessive oestrogen stimulation (obesity, hormonally active ovarian tumours, long period of menstruation, the use of Tamoxifen), diabetes, hypertension, as well as the genetically conditioned Lynch syndrome. For people who are carriers of the gene responsible for the Lynch syndrome the risk of developing endometrial cancer is 30–60% (Kornafel et al. 2013). Two-component hormonal products are considered to constitute a protective factor (NCCN).

As already stated, endometrial cancer is the most common female genital cancer both in Poland and in the majority of European countries. As in the case of cervical cancer, in Poland and in other countries in the region, the values of statistics concerning the incidence, prevalence and mortality are higher than in more developed countries (cf. Figure 3).

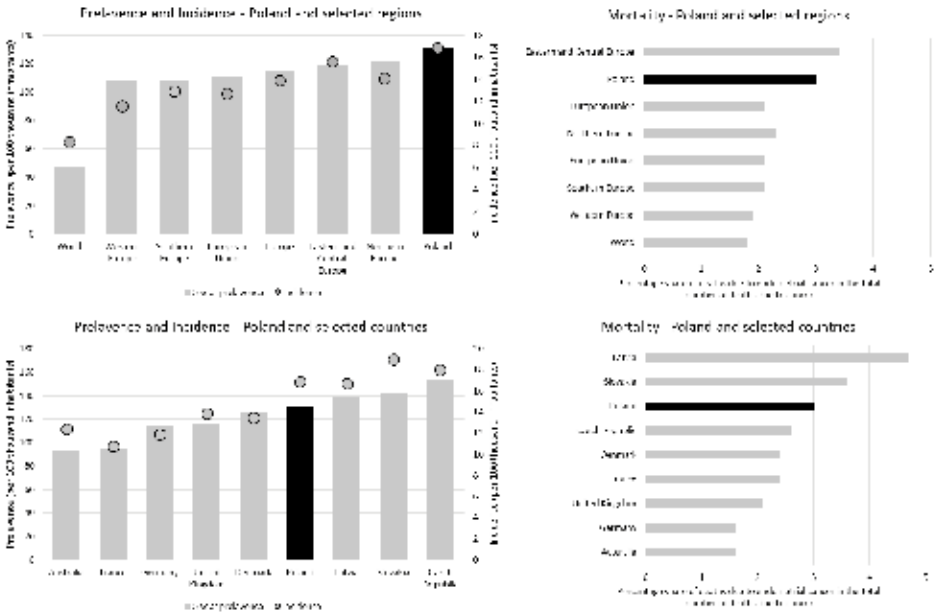


Figure 3. Basic statistics concerning the epidemiology of endometrial cancer for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

Among the cancer types included in this analysis, endometrial cancer is characterised by the best prognosis for recovery. According to EUROCARE, the 5-year survival rate – depending on the country – ranges from 60% (Latvia) to more than 72% (Germany). According to this source this rate is equal to 63.42% in Poland (cf. Figure 4).

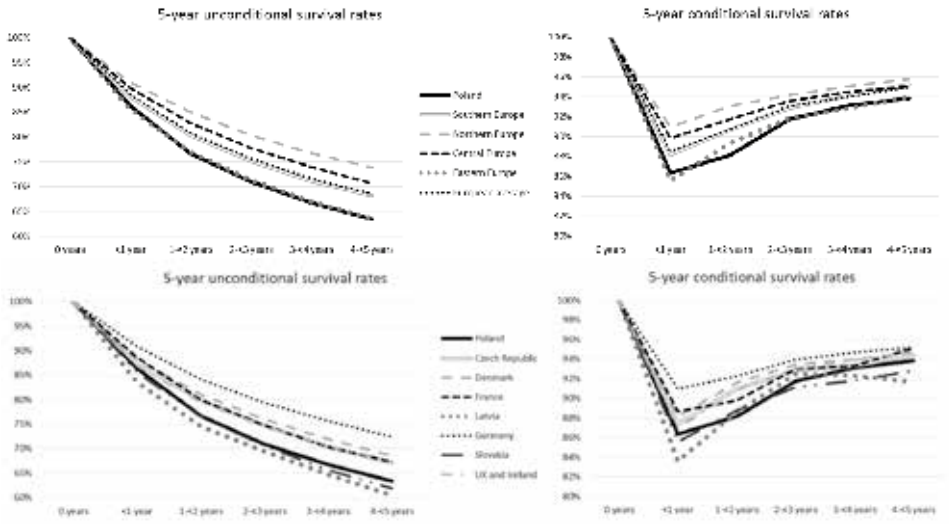


Figure 4. Five-year survival outcomes for patients suffering from endometrial cancer in Poland and selected regions (source: own analysis based on EUROCARE - 5)

95% of ovarian cancer cases are of epithelial origin. 13% of cases of ovarian tumours are cancers of genetic background, conditioned by the presence of BRCA 1 or BRCA2 mutations, as well as other mutations responsible for the co-existence of ovarian and breast cancer. People facing such risk factors are recommended to undergo preventive removal of the reproductive organ with ovaries upon the end of the reproductive period. People with Lynch syndrome are facing a significantly higher risk of ovarian cancer (colorectal cancer, endometrial cancer, upper gastrointestinal tract cancer and urothelial ureter cancer). The factors decreasing the risk of this cancer include hormonal contraception, ovarian occlusion, uterus removal, breastfeeding and giving first birth at a young age (under 25). An increase in the risk of this type of cancer may be caused by the use of oral hormone therapy, pelvic inflammations and stimulating ovulation as a preparation for in vitro fertilisation (NCCN, Kornafel et al. 2013).

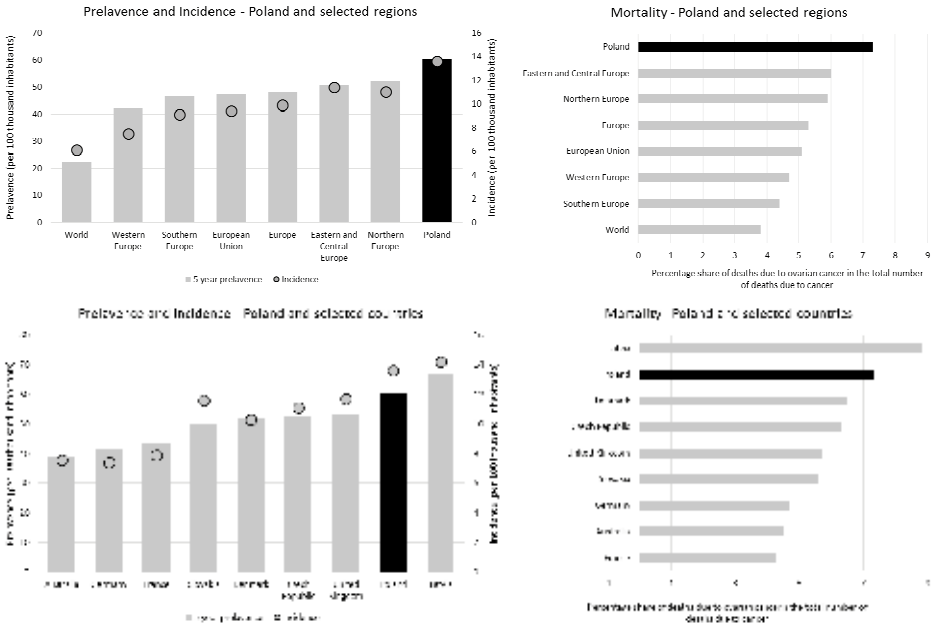


Figure 5. Basic statistics concerning the epidemiology of ovarian cancer for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

In 2011 ovarian cancer was the 6th most common type of cancer in women with regard to incidence and 5th with regard to the number of deaths. For over a decade a slight increase has been observed in the incidence rate and the number of deaths related to ovarian cancer, which is due to the process of population ageing. Poland is characterised by the highest, next to Latvia, statistics concerning the incidence, prevalence and mortality related to ovarian cancer (cf. Figure 5).

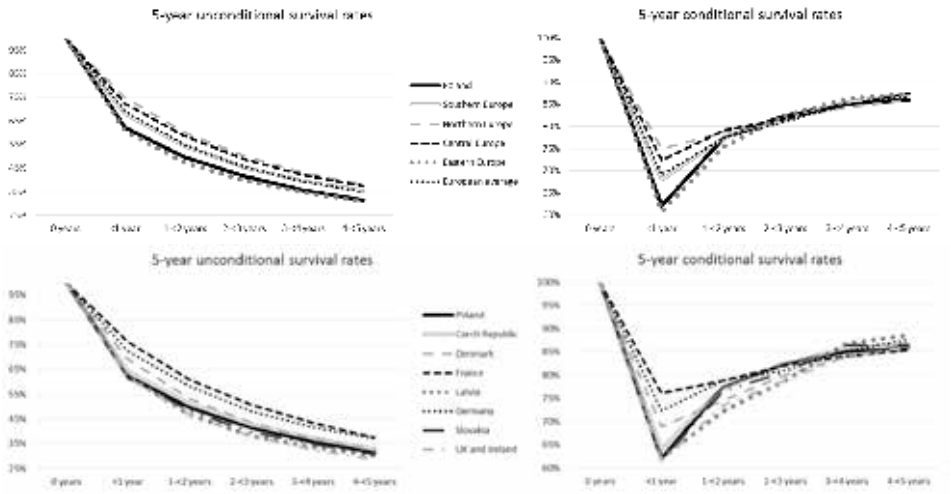


Figure 6. Five-year survival outcomes for patients suffering from ovarian cancer in Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

Ovarian cancer is the type of cancer with the worst prognosis for recovery in the analysed group. Depending on the country, the 5-year survival rate ranges from 30% to 36% (cf. Figure 6).

To sum up, the assessment of the epidemiological situation of female genital cancers in Poland, compared to the other countries included in the analysis, differs depending on the place of occurrence of a given cancer type. In case of cervical cancer, incidence and prevalence levels are similar to the European levels and they are lower than in the remaining countries of the region (the Czech Republic, Slovakia and Latvia). This is also the case with endometrial cancer, except that in Latvia the incidence is slightly lower. When compared to the other countries, the least favourable statistics have been observed in case of ovarian cancer - higher prevalence and incidence have been recorded only in Latvia. A comparative analysis of 5-year survival outcomes concerning each of the above mentioned types of cancer enables a conclusion that also in this respect Poland is in the group of European countries featuring the lowest values of that variable.

Economic analysis of cancer diagnostics

Despite the fact that they occur in the same location, namely the small pelvis, female reproductive system cancers feature a variable clinical picture. As a consequence, each one requires a different diagnostic approach.

Cervical cancer most often is a squamous cell carcinoma (80%), less often adenocarcinoma (approx. 10 % cases) or mixed squamous and adenocarcinomas. Still less frequent are neuroendocrine tumours, small cell tumours and sarcomas. In Poland, thanks to the National Screening Programme for Active Cervical Cancer Prevention, this type of cancer can be diagnosed at an early stage: precancerous changes (CIN2-3) and preinvasive cancer stages (cervical intraepithelial neoplasia). The screening is based on regular Pap tests of material collected from cervical canal and vaginal portion of the cervix every 3 years. If the Pap test result is abnormal, colposcopy is done, followed by collecting material for histopathology. In case of clinical change, the first stage of procedure involves histological verification of the change. In order to define cancer stage, information collected in the process of physical examination and an interview is used, particular attention being paid to lymph nodes. Performing bimanual vaginal abdominal examination and rectovaginal examination gives detailed information on the size of tumour in pelvis. In case of obese and suffering women, the examination is conducted under general anaesthesia. Complementary diagnostic tests are done by checking full blood count and urinalysis, including chest X-ray (to exclude metastasis to lungs) as well as transvaginal and abdominal ultrasound. In order to diagnose early stages of cervical cancer, in order to assess the depth of tumour invasion, it is necessary to perform cervical conization. In advanced cancer stages, if a doctor suspects that the neighbouring organs are invaded, cystoscopy or proctosigmoidoscopy. Such a scope of testing is recommended by International Federation of Gynaecology and Obstetrics (FIGO) in order to determine cancer stage (conf. Table 1). Currently recommended diagnostic imaging includes: CT, PET-CT and MRI scans.

A clinical picture of early cancer stages is dominated by: watery discharge from the vagina, bleeding after sex or bleeding or spotting between periods. Routine diagnostic procedure includes a HIV test.

Table 1. Staging of cervical carcinomas according to FIGO (source: own analysis based on FIGO Committee on Gynaecologic Oncology, 7th edition)

Stage	Description
I	Carcinoma strictly confined to the cervix
IA	Invasive cancer identified only microscopically.
I_{A1}	Measured invasion of the stroma no greater than 3 mm in depth and no wider than 7 mm in diameter.
I_{A2}	Measured invasion of the stroma no greater than 5 mm in depth and no wider than 7 mm in diameter.
IB	Tumours greater than 7 mm in size clinically visible or not
I_{B1}	Tumour no greater than 4 cm in size
I_{B2}	Tumour greater than 4 cm in size
II	Carcinoma extends beyond the cervix, but it does not extend into the pelvic wall. The carcinoma invades vagina but not as far as the lower third.
IIA	No obvious parametrial involvement, involvement of up to the upper two-thirds of the vagina.
I_{IA1}	Tumour no greater than 4 cm in size
I_{IA2}	Tumour greater than 4 cm in size
IIIB	Obvious parametrial involvement, but not into the pelvic sidewall
III	Carcinoma has extended into the pelvic sidewall, and the lower third of the vagina, causes hydronephrosis or a non-functioning kidney/s.
IIIA	No extension into the pelvic sidewall but involvement of the lower third of the vagina
IIIB	Extension into the pelvic sidewall or hydroneprosis or non-functioning kidney.
IV	Carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.
IVA	Spread of the tumour into adjacent pelvic organs
IVB	Distant metastasis

Endometrial cancer can be divided into two groups in terms of histology and prognosis: type I and II. Type I includes carcinomas which feature good prognosis, are hormone-dependent, account for 80% of cases, including PTEN, PIK3CA and iKRAS microsatellite mutations, which in terms of histology corresponds to high grade adenocarcinoma G1/2. Type II includes poorly differentiated G3 endometrial carcinomas, mucinous, mesonephroma, serous carcinoma, clear cell carcinoma and squamous cell carcinoma. They are characterised by chromosome instability and frequent occurrence of TP53 mutation.

Vaginal bleeding is an early symptom of endometrial cancer. Anatomopathologic diagnosis is made based on endometrial biopsy, a biopsy performed during hysteroscopy or during classical diagnostic curettage of the uterus in case of the occurrence of mucous membrane thickening in the ultrasound image. The most important information includes the determination of cancer type, visible invasion of cervical canal and tumour grading. The scope of examination to assess the stage is similar to the examination performed in case of cervical cancer. Particular attention should be paid to assessing the size of uterine body by means of ultrasound performed before surgery and to assessing the condition of pelvic as well as paraaortic lymph nodes, by means of imaging and histopathology. Endometrial cancer grading according to FIGO has been presented in Table 2.

Table 2. Endometrial cancer grading according to FIGO of cases not treated by surgery (source: own analysis based on FIGO Committee on Gynaecologic Oncology, 7th edition)

Stage	Description
0	Carcinoma in situ (endometrial hyperplasia with atypia)
I	Carcinoma confined to corpus uteri, including isthmus uteri
IA	Carcinoma confined to corpus uteri, more than 8 cm in length
IIIB	Carcinoma confined to corpus uteri, more than 8 cm in length
II	Tumour invades corpus uteri and cervix
III	Tumour extends beyond uterus, but not extending beyond pelvis
IV	Tumour extends beyond pelvis and/or adjacent organs (bladder, rectum)
IVA	Tumour invades adjacent organs - bladder, rectum, pelvic colon and small intestine
IVB	Distant metastasis

Among all malignant tumours of the ovary, epithelial carcinomas account for 95% of all cases. As far as the etiology of that type of cancer, a huge role is played by genetic predisposition, namely BRCA1 or BRCA2 mutation carrier state, which is the cause of 13% of cases, as well as genetically conditioned ovarian cancer and breast cancer and Lynch syndrome (colon and endometrium cancers, upper gastrointestinal cancers and urothelial cancer of ureter). Screening tests are conducted in a sub-cohort of patients featuring a high risk of the disease who are BRCA mutation carriers. 20-30% of cases are detected in early stage, and approx. 70% in stages III and IV (Kornafel at al. 2013). Recommendation for high risk patients includes a removal of uterine appendages, at the beginning of the 5th decade of life at the

latest, following the termination of child bearing period. In early stages non-characteristic symptoms occur, such as dyspepsia or enlarged ovary. Advanced clinical stages include ascites and pleural effusion. 70% cases feature elevated Ca125. It can happen that primary ovarian tumour with metastases to peritoneal cavity does not grow big in size. Prospective tests which evaluate the effectiveness of ovarian cancer screening which involves vaginal ultrasound and Ca125 evaluation, do not demonstrate in an unequivocal way that the screening impacts prognosis (NCCN).

A basic diagnostic test involves combined pelvic examination (bimanual vaginal abdominal examination, rectovaginal examination and examination with speculum) complemented by transvaginal and abdominal ultrasound. Patients with ovarian cancer must do blood and urine tests, including CA125, CEA and Ca 15.3 tests, X-ray or CT scan of chest, abdominal cavity and pelvis. In justified cases this is followed by MGF, colonoscopy and gastroscopy. Histological examination is made based on material removed during a surgery. Rarely is it possible to verify the diagnosis based on material collected from a metastatic focus in the liver, lymph nodes and based on examining peritoneal or pleural cavity fluid. Histologically ovarian cancers assume the form of serous, mucinous, endometrial, clear cell carcinomas, Brenner tumour or mixed and non-differentiated forms. During histopathologic examination, apart from the form of cancer also its malignancy is defined in a 2- or 3-grade scale. Staging is done based on information from surgery and anatomopathologic examination according to FIGO (conf. Table 3).

Table 3. Ovarian cancer grading according to FIGO of cases not treated by surgery (source: own analysis based on *AJCC 7th edition*)

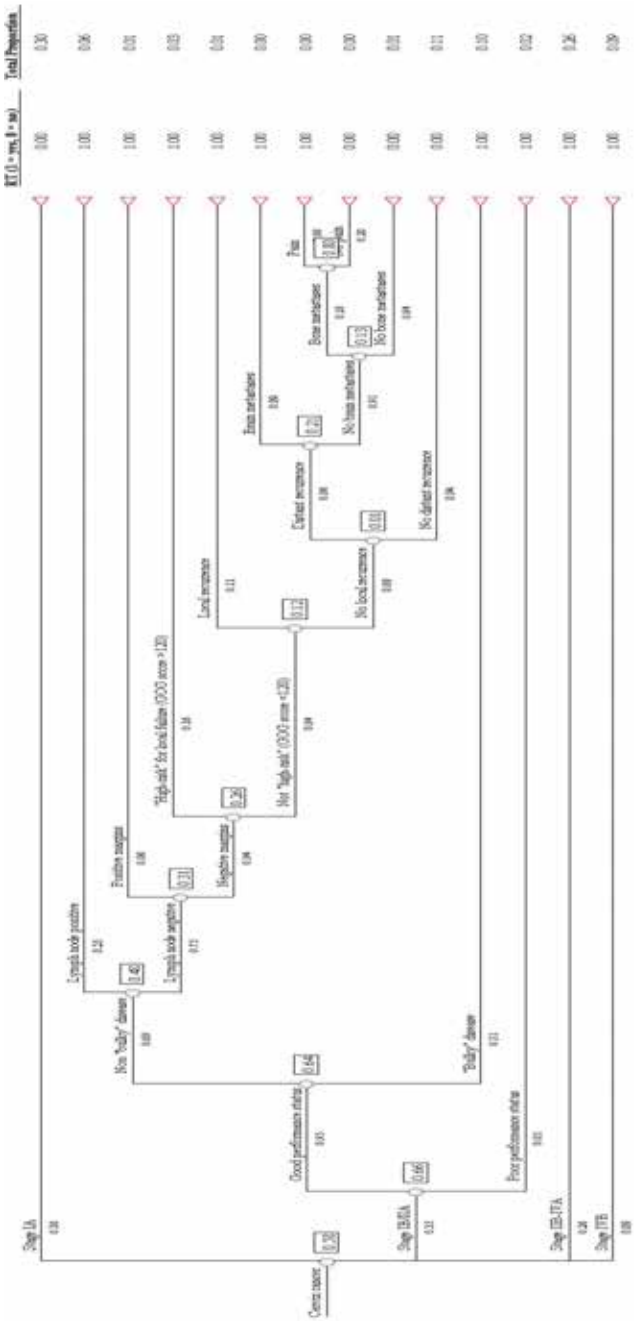
Stage	Description
I	Tumour confined to one ovary/both ovaries
IA	Tumour limited to 1 ovary, capsule intact, negative peritoneal washings
IB	Tumour involves both ovaries, capsule intact, negative peritoneal washings
IC	Capsule involved or ruptured, ascites and/or positive peritoneal washings
II	Tumour involves one or both ovaries with pelvic extension
IIA	Invasion on uterus and/on Fallopian tubes
IIB	Invasion on other pelvic organs (bladder, rectum, vagina)
IIC	Invasion on pelvic organs and positive washings
III	Tumour invades peritoneum and retroperitoneal or femoral lymph nodes
IIIA	Microscopic metastasis beyond pelvis
IIIB	Extrapelvic metastases up to 2 cm in greatest dimension
IIIC	Extrapelvic metastases bigger than 2 cm in greatest dimension and/or metastasis to retroperitoneal or femoral lymph nodes
IV	Distant metastasis
IVA	Metastasis to liver
IVB	Metastasis to other distant organs

Decision-making models in female reproductive system cancers

Decision-making trees are a convenient and frequently applied form of decision making models in treating cancers, including female genital cancers. The following is a radiotherapeutical treatment model for Scotland which was developed by NHS Scotland (2005), and the one for Australia (Barton 2013).

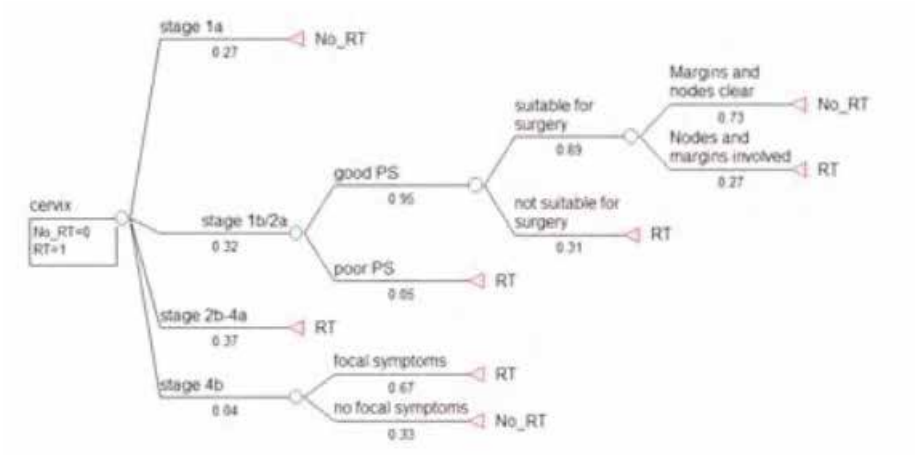
In the Australian model of cervical cancer treatment (Barton 2013) as well as in the other treatment models, therapeutic methods depend on the cancer stage. In cancer stage IA1, which accounts of 30% of cervical cancer stages, surgical treatment is the treatment by choice. In case of stage IA2–IIA (approx. 35% cases), patients in good general condition without massive changes (69%) undergo a surgery. In post-surgery patients with positive lymph nodes, who feature no microscopic radicalness and unfavourable prognosis made after post-surgery histopathology, radiotherapy is administered as complementary therapy. Radiotherapy is

applied in that group of patients also in case of locoregional recurrence (11%) or metastasis to brain and/or bones (6%). The group of 31% of patients with stage IB-IIA cancer with a massive invasion or patients in worse general condition receive radiotherapy. Patients with stage IIB-IVA cancer (approx. 26%), receive radiotherapy and possibly chemotherapy. Patients with metastases to distant organs (9%) are treated by means of palliative radiotherapy (conf. Flowchart 1).



Flowchart 1. Model of radiotherapeutic treatment of cervical cancer for Australia (source: NHS Scotland 2005)

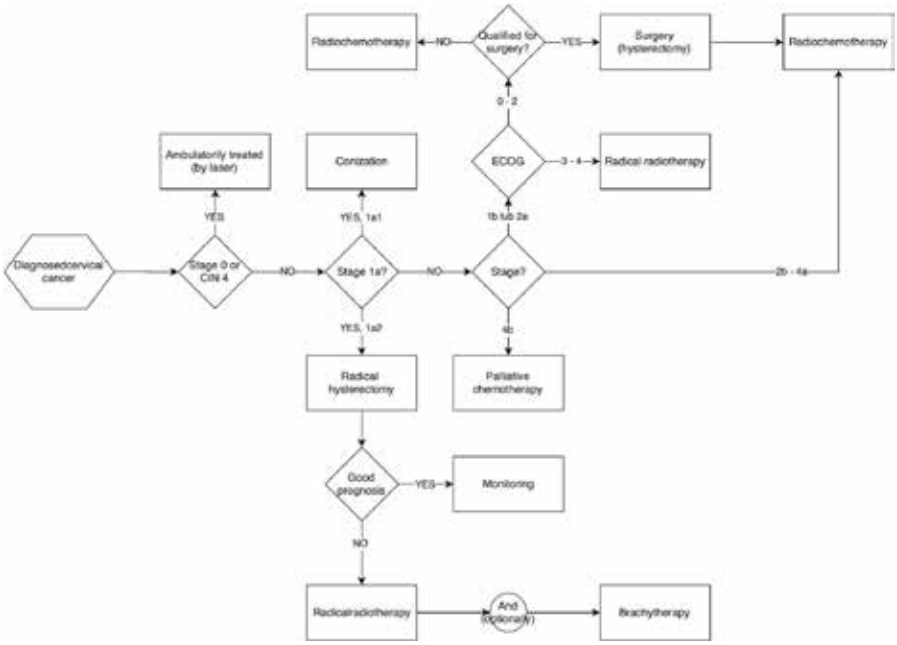
In the Scottish model of cervical cancer treatment, patients with stage IA cancer (27%) are subject to surgical treatment (NHS 2005). Patients with stage IB/IIA cancer (32%) who are in good general condition undergo a surgery which in 27% of patients is complemented by radiotherapy. Patients with a massive tumour who are in bad general condition also receive radiotherapy. A group of patients with advanced stage IIB-IVA cancer (37%) receive conservative treatment with ionizing radiation, and patients with metastases (4%) and primary tumour symptoms receive radiotherapy (67% in that group of patients) (conf. Flowchart 2).



Flowchart 2. Model of radiotherapeutic treatment of cervical cancer for Scotland (source: NHS Scotland 2005)

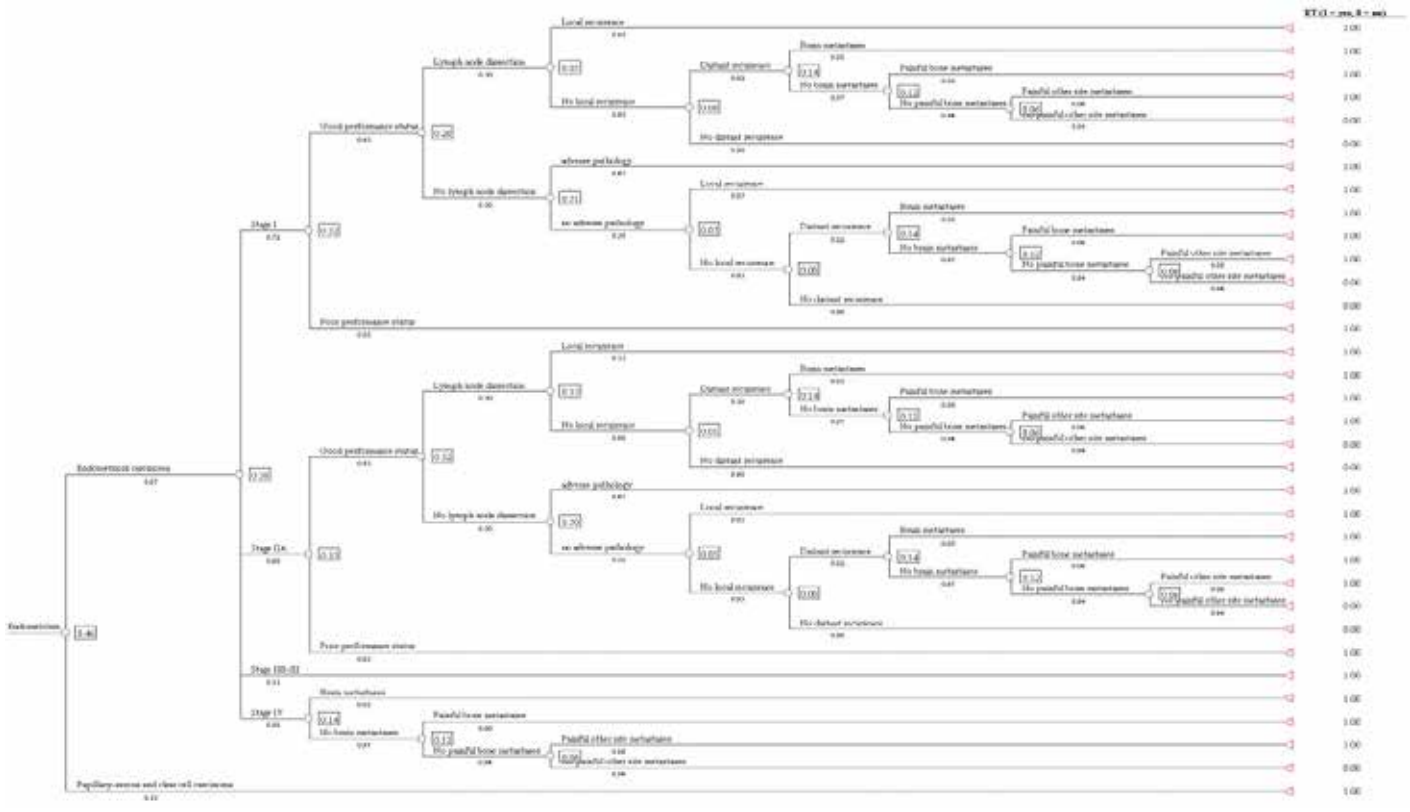
According to Polish recommendations, in pre-cancer stage and in case of cervical intraepithelial neoplasia the treatment involves local removal of lesions. In early IA stage lesions present in young women who plan to have a baby, BCT can be considered, including cervical conization with evaluation of microscopic radicalness. In other cases radical hysterectomy is performed, as in stage IB. Such patients receive complementary radiotherapy if their prognosis is unfavourable. Starting from stage IB through IVA - patients in good general condition receive radiochemotherapy, and patients with contraindications to systemic treatment receive radiotherapy alone. Patients with metastases are treated with chemotherapy and - if there are clinical symptoms originating from metastatic foci or primary tumour - they receive palliative radiotherapy. A simplified theoretical model of cervical cancer treatment in Poland, account taken of surgical treatment, chemotherapy and radiotherapy, has been presented

in Flowchart 3. The model is based on the analyses of the above presented models, which were adjusted to take account of guidelines concerning oncological treatment, elaborated by Polish scientific associations and to take account of the knowledge of oncologists concerning practical treatment of cervical cancer in Poland.



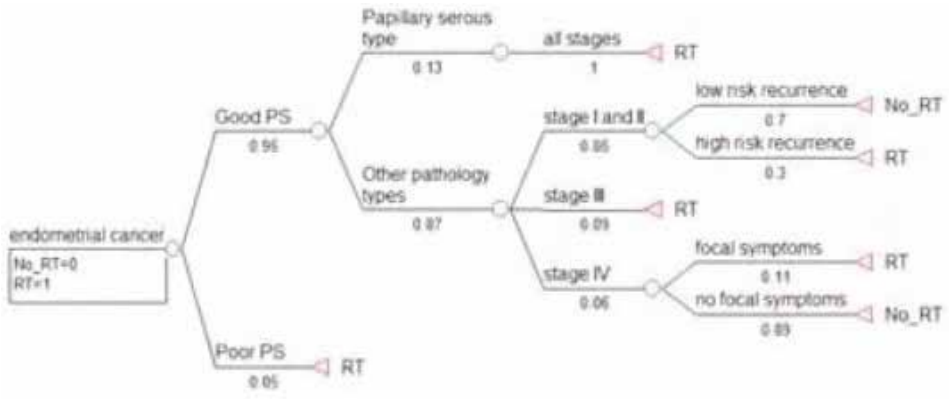
Flowchart 3. Model of cervical cancer treatment in Poland (source: own analysis)

In the Australian model, endometrial cancer is most often detected in stage I (72% of cases). Patients who underwent hysterectomy without the regional lymphadenectomy always receive complementary radiotherapy, and patients with radical hysterectomy receive radiotherapy only in case of unfavourable prognosis or in case of recurrence or metastasis. In stage I in 5% cases resection is impossible due to a bad general condition of the patient. Then, the only therapy possible is radiotherapy. In case of patients with stage IIA cancer (approx. 8%), treatment regimen is similar to treatment in stage I. Patients with stages IIB-III (11%) receive radiotherapy). In case of stage IV cancer (9% of cases), radiotherapy is indicated if metastases to brain and painful metastases to bones have been identified (conf. Flowchart 4).



Flowchart 4. Model of radiotherapeutic treatment of endometrial cancer for Australia (source: Barton 2013)

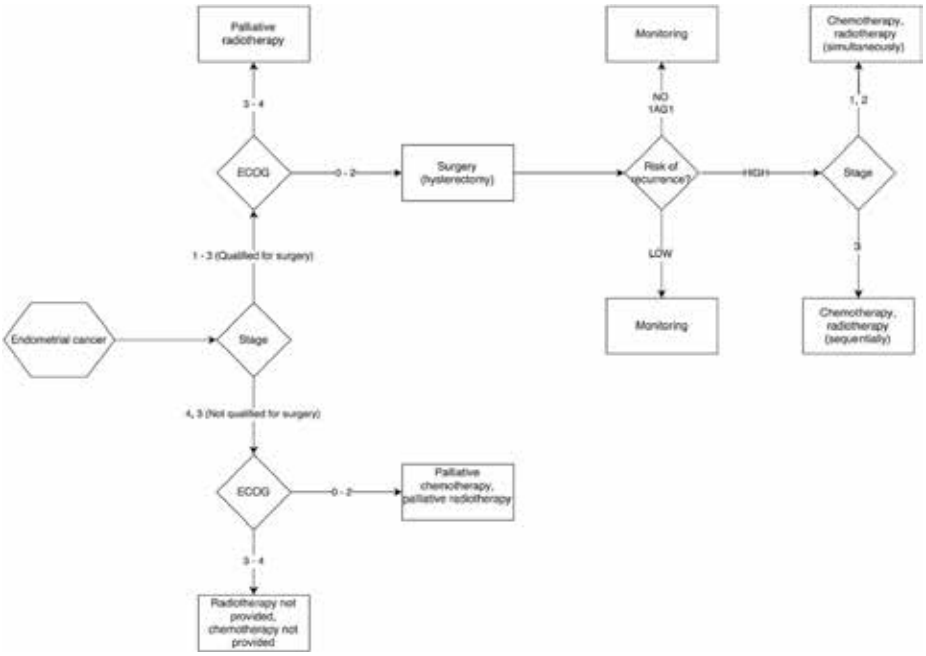
In the Scottish model of endometrial cancer treatment, apart from stages I and II without certain unfavourable prognosis in post-surgery histopathology (70% patients in stage I-II) in case of metastases without clinical tumour symptoms, radiotherapy is one of the treatment methods (89% of patients with stage IV cancer). In all other clinical situations, including in particular in cases of papillary serous carcinoma (13% of all endometrial cancers in good condition) and patients in bad overall condition (5% of patients with endometrial cancer), radiotherapy is always provided as treatment (conf. Flowchart 5).



Flowchart 5. Model of radiotherapeutic treatment of endometrial cancer for Scotland (source: NHS Scotland 2005)

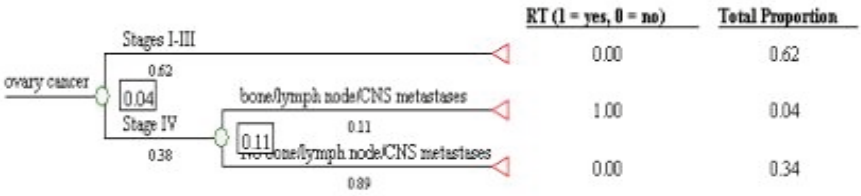
According to the decision making tree applicable in Poland, in stage I cases qualified for surgery, when the overall condition is good and there is no unfavourable prognosis (stage IA1 G1), following the surgery a patient is subject to observation. However, in stage I with unfavourable prognosis and in stages II-III, radical hysterectomy is always followed by complementary radiotherapy or chemotherapy. First-line therapy of patients with stages I-III suffering from coexisting conditions which worsen the overall condition includes radiotherapy. Patients with stage III-IV cancer whose tumour is not qualified for a surgery but whose overall condition is good, can be provided with systemic therapy and/or radiotherapy. Patients with advanced stage cancer accompanied by coexisting illnesses most often receive symptomatic treatment. A theoretical model of endometrial cancer treatment in Poland, account taken of surgical treatment, chemotherapy and radiotherapy, has been presented in Flowchart 6. Scottish and Australian models, presented above, were used for its development along with

the guidelines of Polish scientific societies and practical knowledge of oncologists concerning endometrial cancer treatment in Poland.



Flowchart 6. Model of endometrial cancer treatment in Poland (source: own analysis)

Australian model of treating ovarian cancer provides for systemic treatment and surgical treatment of stages I-III (62% of all the cases), without radiotherapy. Stage IV (38%) with metastases to bones, lymph nodes or brain (4%) is the only indication for radiotherapy (conf. Flowchart 7).



Flowchart 7. Model of radiotherapeutic treatment of ovarian cancer for Australia (source: Barton 2013)

According to ovarian cancer treatment principles applicable in Poland, first-line treatment of patients without distant metastases involves maximum possible radical treatment, namely hysterectomy including resection of all macroscopic foci, appendectomy, myomectomy and collecting peritoneal cavity fluid for testing. Almost all post-surgical patients are treated with adjuvant chemotherapy with possible removal of previously left foci. Only in case of patients with early stage ovarian cancer featuring small level of malignancy (IA G1) surgery is the only stage of treatment. For patients with metastases, the only treatment includes systemic one with possible palliative radiotherapy to treat changes in central nervous system or bones. A simplified decision-making model of treating ovarian cancer in Poland, account taken of surgical treatment, chemotherapy and radiotherapy, has been presented in Flowchart 8.

Flowchart 8. Model of ovarian cancer treatment in Poland (source: own analysis)

Empirical model in treating female reproductive system cancers

According to the NCR figures, 2,684 cases of cervical cancer were recorded in Poland in 2012[99]. In comparison to 2011, the incidence dropped by over 10%[100] (conf. Table 4). This cancer causes approx. 4% of all deaths of women due to cancer.

Information about staging is the most important one for a parametrization of the theoretical model which was presented in the previous sub-chapter. National Cancer Registry

[99] The figures presented by NCR have been initially verified based on NHF database. This means that they do not include patients who appeared for the first time in the NCR database in a given year with breast cancer diagnosis and who were recorded with the diagnosis in the NHF database before that year.
[100] Figures presented by NCR on the portal http://onkologia.org.pl/raporty/ point to a 6% drop in the incidence.

database is the only source of information on the cervical cancer stage, however, the analysis of the data included therein showed a high degree of data incompleteness: a major part of records do not provide staging information (17-23%). Moreover, only single cases of cancer stage I have been recorded.

Table 4. Distribution of information on cervical cancer stage in NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	2	4	0%	0%	0%
II	1,432	1,293	1,121	46%	43%	42%
III	840	777	688	27%	26%	26%
IV	299	304	263	10%	10%	10%
No stage provided in NCR	520	617	608	17%	21%	23%
Total	3,091	2,993	2,684	100%	100%	100%

Apart from figures concerning staging, NCR database was found to feature underreporting of 25-30%[101]. Based on the analysis of the hospital or ambulatory services, it was established that every year 2.7 thousand - 3 thousand patients are not recorded in NCR. Patient categorization based on services provided has been presented in Table 5.

Table 5. Cancer stage categorization of new patients who have not been recorded in NCR (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	381	407	414	13%	15%	14%
II	54	58	100	2%	2%	3%
III	142	150	207	5%	6%	7%
IV	479	502	565	16%	19%	19%
other diagnosis	1,916	1,589	1,758	64%	59%	58%
follow-up	0	0	0	0%	0%	0%
Total	2,972	2,706	3,044	100%	100%	100%

[101] For more information on the methodology for estimating cancer incidence in Poland see: *Sources and Quality of Cancer Epidemiological Data in Poland - Data Analysis Methodology*

Finally, after the adjustment of data reported to NCR it was established that cervical cancer incidence in the period 2010-2012 was distributed (against stage) as shown in Table 6. Based on the analysis of figures presented in Tables 4-6 it was established that, apart from the increase in the number of new cases in each of the years analysed, the stage structure also changed, i.e. the share of patients with the least advanced cervical cancer stage increased from 0% to 14% and the share of patients with cancer stage IV increased from 10% to 24% in 2012.

Table 6. Distribution of incidence against cancer stage for the period 2010–2012 (source: own analysis)

	Absolute value			%		
Stage	2010	2011	2012	2010	2011	2012
I	531	573	563	13%	14%	14%
II	1,602	1,487	1,360	39%	37%	35%
III	1,114	1,087	1,060	27%	27%	27%
IV	861	914	944	21%	22%	24%
impossible to define	5	4	5	0%	0%	0%
Total	4,113	4,065	3,932	100%	100%	100%

The next stage of developing empirical model of cervical cancer treatment (and the treatment of the other cancers of female reproductive organs, which has been presented further) involved an analysis of data concerning services[102] provided to patients within a year of starting treatment. On such a basis four variables were formulated, which carried information on whether the patient: (1) underwent a surgical procedure (glossary of ICD-9 procedures for appropriate surgical treatment was defined), (2) received chemotherapy, (3) received radiotherapy and (4) received palliative treatment. This approach made it possible to present analysis results in the form of four binary trees (for each cancer stage), which presented the size of a group singled out as a result of subsequent divisions, the size of the group in relation to the previous division and in relation to the whole cohort of new patients suffering from breast cancer (regardless of stage). The division of the singled out group was continued if it was composed of at least 50 units. Information concerning death within one

[102] Based on International Classification of Procedures in Medicine ICD-9 and Homogenous Patient Groups

year of the onset of treatment was also taken account of[103]. The model constructed pertains to the year 2012. The analysis has shown that in general, radiotherapy treatment was the most frequent method of treating cervical cancer (applied in 63% cases) (conf. Table 7).

Table 7. Empirical model of cervical cancer treatment in Poland part 1 (source: own analysis)

Type of therapy	patients who underwent the therapy
surgical treatment	37%
chemotherapy	44%
radiotherapy	63%

It was observed that for patients with cervical cancer stage I one-year survival outcome exceeds 98%. These statistics decline with the advancement of cancer stage and amount to respectively 91,5% in case of stage II, 76.4% in case of stage III and 45% in case of stage IV (conf. Flowchart 9).

The analysis has shown that surgical treatment is the most frequent method of treating cervical cancer stage I (applied in 82% cases). At that stage chemotherapy is not applied, and radiotherapy is applied to almost every third patient. Stages II and III cervical cancer are in most cases treated by means of radiotherapy. Patients with stage IV cancer are subject to chemotherapy (48%), less often radiotherapy (35.9%) and surgical treatment (11.3%) conf. Table 8).

Table 8. Empirical model of cervical cancer treatment in Poland part 2 (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
surgical treatment	82%	44.6%	24.7%	11.3%
chemotherapy	0%	46.8%	60.1%	48.0%
radiotherapy	32%	79.5%	83.8%	35.9%

Analysis of Table 9 shows that, in general (i.e. not considering the stage) , the most common treatment regimen includes simultaneous[104] chemotherapy and radiotherapy

[103] Due to data availability, death causes were not discriminated.
[104] The use of the term *simultaneous* in relation to surgery/chemotherapy/radiotherapy is intended to emphasise the fact that these two/three types of therapy are used for treating one patient within no longer than one year of the onset of treatment. Further in this paper the similar approach to treatment regimen description will be applied.

applied in 25.63% of cases. The least commonly applied method includes simultaneous surgical treatment and chemotherapy (2.06%).

Table 9. Empirical model of cervical cancer treatment in Poland part 3 (source: own analysis)

Was surgical treatment provided?			radiotherapy		Total
			NO	YES	
NO - 63%	chemotherapy	NO	14.65%	15.82%	30.47%
		YES	7.29%	25.63%	32.92%
	Total		21.94%	41.45%	63.39%
YES - 37%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	12.69%	12.89%	25.58%
		YES	2.06%	8.97%	11.03%
	Total		14.75%	21.86%	36.61%

Surgical treatment alone is the most frequent method of treating stage I cervical cancer (applied in 57% cases). Every fourth patient undergoes surgical treatment followed by radiotherapy. In case of 11% patients no chemotherapy, surgery or radiotherapy has been recorded. Those patients might have been treated beyond the national health-care system or the tumour might have been removed at the diagnostic stage (biopsy).

In stage II cervical cancer the most frequent treatment regimen includes simultaneous radiotherapy and chemotherapy (31%). In 31% of cases patients in this group receive palliative treatment. Every fifth patient with this cancer stage receives surgical treatment followed by radiotherapy. 15% of patients receive radiotherapy alone, and almost 43% were additionally offered palliative treatment. Simultaneous surgical treatment, chemotherapy and radiotherapy occur in 14% of cases.

Patients with stage III cancer are mostly subject to simultaneous chemotherapy and radiotherapy (43%). Every third patient in that group receives additional palliative treatment. Almost every firth patient receives radiotherapy alone, and 58% are additionally subject to palliative treatment. Simultaneous surgical treatment, chemotherapy and radiotherapy are applied in 14% of cases. 11% of patients do not receive any treatment, of which 82% dies within one year of the onset of treatment.

In stage IV cervical cancer usually none of the analysed treatments are applied (i.e. neither surgical treatment, nor chemotherapy nor radiotherapy). This is the case with 29% of patients. Half of that group receives palliative treatment. More than every fourth (26%) patient receives chemotherapy only. Almost every fifth (19%) patient receives radiotherapy only, of which 95% receive palliative treatment in addition. 14% of patients receive simultaneous chemotherapy and radiotherapy, of which the majority (88%) also receive palliative treatment.

Stage					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	563	14.3%	11	1.9%	NO	101	18.0%	1	1.2%	NO	101	100.0%	1	1.2%	NO	63	62.3%	0	0.0%	NO	57	90.5%	0	0.0%
																				YES	6	9.5%	0	0.0%
															YES	38	37.7%	1	3.1%					
					YES	462	82.0%	10	2.1%	NO	462	100.0%	10	2.1%	NO	322	69.8%	7	2.2%	NO	322	100.0%	7	2.2%
															YES	140	30.2%	2	1.8%	NO	140	100.0%	2	1.8%
2	1360	34.6%	115	8.5%	NO	753	55.4%	99	13.1%	NO	314	41.8%	67	21.3%	NO	115	36.6%	30	26.1%	NO	103	89.6%	21	20.4%
																				YES	12	10.4%	9	75.0%
															YES	199	63.4%	37	18.6%	NO	114	57.4%	8	7.4%
																				YES	85	42.6%	28	33.6%
										YES	438	58.2%	32	7.2%	NO	16	3.6%	7	43.8%					
															YES	422	96.4%	25	5.8%	NO	290	68.6%	4	1.3%
																				YES	133	31.4%	21	15.7%
					YES	607	44.6%	17	2.8%	NO	410	67.5%	10	2.3%	NO	136	33.2%	2	1.5%	NO	136	100.0%	2	1.5%
															YES	274	66.8%	8	2.7%	NO	274	100.0%	8	2.7%
										YES	197	32.5%	7	3.6%	NO	12	6.1%	2	16.7%					
															YES	185	93.9%	5	2.8%	NO	183	98.9%	5	2.8%
																				YES	2	1.1%	0	0.0%
3	1060	27.0%	250	23.6%	NO	797	75.3%	231	29.0%	NO	322	40.3%	169	52.5%	NO	119	37.1%	98	82.4%	NO	75	62.8%	60	80.0%
																				YES	44	37.2%	38	86.5%
															YES	202	62.9%	70	34.8%	NO	84	41.8%	14	16.5%
																				YES	118	58.2%	56	47.9%
										YES	476	59.7%	63	13.2%	NO	21	4.4%	12	57.1%					
															YES	455	95.6%	51	11.2%	NO	300	66.0%	13	4.4%
																				YES	155	34.0%	38	24.2%
					YES	262	24.7%	19	7.2%	NO	101	38.7%	12	12.2%	NO	21	21.1%	7	34.6%					
															YES	80	78.9%	5	6.2%	NO	75	93.8%	3	4.0%
																				YES	5	6.2%	2	40.0%
										YES	161	61.3%	6	4.0%	NO	10	5.9%	1	10.5%					
															YES	151	94.1%	6	3.6%	NO	151	100.0%	6	3.6%
4	943	24.0%	519	55.0%	NO	837	88.7%	474	56.6%	NO	459	54.9%	327	71.2%	NO	278	60.5%	213	76.6%	NO	138	49.7%	130	94.2%
																				YES	140	50.3%	83	59.2%
															YES	182	39.5%	114	63.1%	NO	9	5.0%	8	88.9%
																				YES	172	95.0%	106	61.7%
										YES	378	45.1%	147	38.8%	NO	249	65.9%	86	34.5%	NO	157	63.0%	32	20.1%
																				YES	92	37.0%	54	59.2%
															YES	129	34.1%	61	47.2%	NO	15	11.7%	4	26.7%
																				YES	114	88.3%	57	49.9%
					YES	106	11.3%	45	42.2%	NO	32	29.7%	26	81.0%										
										YES	75	70.3%	19	25.8%	NO	60	79.6%	15	25.2%	NO	60	100.0%	15	25.2%
															YES	15	20.4%	4	28.1%					

Flowchart 9. Empirical model of cervical cancer treatment in Poland part 4 (source: own analysis)

Methodology for developing empirical model for endometrial cancer treatment is analogous to the presented methodology concerning cervical cancer. Again, the analysis of data supplied by NCR and NHR provided basis for a conclusion that the first database is very much incomplete. As it was in case of analysing cervical cancer, a lot of records lack information about staging (17-22%), and only single records include information about stage I cancer.

Table 10. Distribution of information on endometrial cancer stage in NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	3	1	0%	0%	0%
II	3,407	3,384	3,174	66%	64%	60%
III	582	681	658	11%	13%	13%
IV	267	269	254	5%	5%	5%
No stage provided in NCR	902	990	1,165	17%	19%	22%
Total	5,158	5,327	5,252	100%	100%	100%

It was concluded that NCR database features underassessment of 14-17%, depending on year analysed. Based on the analysis of the hospital or ambulatory services, it was established that every year over 1000 patients are not recorded in NCR. Patient categorization based on services provided has been presented in Table 11.

Table 11. Cancer stage categorization of new patients who have not been recorded in NCR (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	438	494	578	49%	50%	50%
II	112	125	150	13%	13%	13%
III	104	118	144	12%	12%	12%
IV	124	132	161	14%	13%	14%
other diagnosis	0	0	0	0%	0%	0%
follow-up	108	116	126	12%	12%	11%
Total	886	985	1,159	100%	100%	100%

Finally, it was established that endometrial cancer incidence in the period under analysis was distributed in relation to cancer stage, as shown in Table 12. Apart from the increase of the number of new cases, the stage structure also changed significantly, i.e. the share of patients with stage I endometrial cancer increased from 0% to 20% and the share of patients with cancer stage IV increased from 5% to 12% in 2012.

Table 12. Distribution of incidence in relation to cancer stage for the period 2010–2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	944	1,105	1,263	16%	17%	20%
II	3,589	3,600	3,443	60%	57%	54%
III	764	894	923	13%	14%	14%
IV	703	738	757	12%	12%	12%
impossible to define	16	5	6	0%	0%	0%
Total	6,016	6,342	6,392	100%	100%	100%

For the group of patients defined in this way an analysis of services was performed. The analysis has shown that, in general, surgery was the most frequent method of treating endometrial cancer – applied in 86% of cases (cf. Table 13).

Table 13. Empirical model of endometrial cancer treatment in Poland, part 1 (source: own analysis)

Type of therapy	Percentage of patients who underwent the therapy
surgical treatment	86%
chemotherapy	17%
radiotherapy	60%

It was observed that for patients with endometrial cancer stage I one-year survival rate was 100% in 2012. These statistics decline with the advancement of cancer stage and amount to about 95% in the case of stage II, 82% in the case of stage III and ca. 53% in the case of stage IV (cf. Fig. 10).

At the first, second and third endometrial cancer stage usually surgery is employed (96%, 90%, and 83% of cases, respectively), At stage III also radiotherapy is frequently applied (78% of cases). Patients with cancer stage IV are usually subject to chemotherapy (62%) and surgical treatment (35.9%) (cf. Table 14).

Table 14. Empirical model of endometrial cancer treatment in Poland, part 2 (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
surgical treatment	96%	90%	83%	57%
chemotherapy	0%	10%	34%	62%
radiotherapy	33%	69%	78%	39%

Not considering diversification due to cancer stage, the most common treatment scheme is simultaneous chemotherapy and radiotherapy applied in 44.33% of cases. The least commonly applied method is chemotherapy only (2.02%) and the combination of radiotherapy and chemotherapy (cf. Table 15).

Table 15. Empirical model of endometrial cancer treatment in Poland, part 3 (source: own analysis)

Was surgical treatment provided?				
NO – 14%		radiotherapy		Total
		NO	YES	
	chemotherapy NO	3.23%	6.12%	9.35%
	chemotherapy YES	2.02%	2.43%	4.45%
	Total	5.25%	8.55%	13.80%
YES – 86%		radiotherapy		Total
		NO	YES	
	chemotherapy NO	28.94%	44.33%	73.27%
	chemotherapy YES	6.17%	6.76%	12.93%
	Total	35.11%	51.10%	86.20%

Stage I endometrial cancer is usually treated with surgery alone. Simultaneous surgical treatment and radiotherapy are applied in 29% of cases.

At stage II simultaneous surgical treatment and radiotherapy dominate (58%). Almost one in four patients is subject to surgery alone. Simultaneous surgical treatment, chemotherapy, and radiotherapy are applied in 5% of cases. Nearly one in two patients with endometrial cancer stage III is subject to surgical treatment and radiotherapy (47%). 18% of patients are treated with surgery, chemotherapy, and radiotherapy, while one in ten treatments is based on surgery and chemotherapy. Surgical treatment alone is applied in 8% of cases. The most diversified structure characterises treatment of the final stage of endometrial cancer. Every one in four patients is subject to a surgical procedure and chemotherapy. Surgical treatment alone is applied in 15% of cases – it is the second most frequent treatment scheme. It is followed by chemotherapy alone (14%), simultaneous surgery, chemotherapy, and radiotherapy (12%), radiotherapy alone (11%), and simultaneous chemotherapy and radiotherapy (11%). The frequency of other schemes individually does not exceed 10%.

Stage					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	1263	19.8%	0	0.0%	NO	50	4.0%	0	0.0%	NO	50	100.0%	0	0.0%	YES	50	100.0%	0	0.0%	NO	45	89.1%	0	0.0%
																				YES	6	10.9%	0	0.0%
					YES	1212	96.0%	0	0.0%	NO	1212	100.0%	0	0.0%	NO	848	69.9%	0	0.0%	NO	848	100.0%	0	0.0%
															YES	364	30.1%	0	0.0%	NO	364	100.0%	0	0.0%
2	3443	53.9%	159	4.6%	NO	348	10.1%	55	15.8%	NO	306	88.0%	46	15.1%	NO	122	39.8%	29	23.8%	NO	115	94.3%	24	20.9%
																				YES	7	5.7%	5	71.4%
															YES	184	60.2%	17	9.3%	NO	145	78.5%	7	4.7%
																				YES	40	21.5%	10	26.2%
										YES	42	12.0%	9	21.5%										
					YES	3095	89.9%	104	3.4%	NO	2806	90.7%	72	2.5%	NO	813	29.0%	32	3.9%	NO	813	100.0%	32	3.9%
															YES	1993	71.0%	40	2.0%	NO	1974	99.0%	33	1.6%
																				YES	19	1.0%	7	36.8%
										YES	288	9.3%	32	11.3%	NO	113	39.2%	17	15.0%	NO	113	100.0%	17	15.0%
															YES	175	60.8%	16	8.8%	NO	165	94.3%	14	8.8%
																				YES	10	5.7%	1	10.0%
3	923	14.5%	110	11.9%	NO	156	16.9%	53	33.6%	NO	103	66.1%	44	42.7%	NO	30	29.0%	20	66.7%					
															YES	73	71.0%	24	32.9%	NO	43	59.2%	9	21.7%
																				YES	30	40.8%	15	49.2%
										YES	53	33.9%	8	16.0%	NO	8	15.1%	1	12.5%					
															YES	45	84.9%	8	16.7%					
					YES	767	83.1%	58	7.5%	NO	509	66.4%	33	6.5%	NO	74	14.5%	19	25.7%	NO	74	100.0%	19	25.7%
															YES	435	85.5%	14	3.3%	NO	430	98.8%	13	3.1%
																				YES	5	1.2%	1	20.0%
										YES	258	33.6%	24	9.5%	NO	90	34.9%	13	14.4%	NO	90	100.0%	13	14.4%
															YES	168	65.1%	11	6.8%	NO	162	96.4%	8	5.2%
																				YES	6	3.6%	3	50.0%
4	757	11.8%	357	47.2%	NO	326	43.1%	178	54.7%	NO	137	42.0%	104	75.9%	NO	54	39.5%	49	90.7%	NO	42	77.8%	38	90.5%
																				YES	12	22.2%	11	91.7%
															YES	83	60.5%	55	66.1%	NO	10	11.8%	6	59.2%
																				YES	73	88.1%	49	67.1%
										YES	189	58.0%	74	39.4%	NO	105	55.5%	40	38.1%	NO	70	67.1%	24	33.3%
																				YES	34	32.9%	16	47.8%
															YES	84	44.5%	34	41.0%	NO	15	17.3%	3	20.5%
																				YES	70	82.7%	32	45.3%
					YES	431	56.9%	179	41.6%	NO	151	35.1%	120	79.5%	NO	113	74.8%	104	92.0%	NO	113	100.0%	104	92.0%
															YES	38	25.2%	16	42.3%					
										YES	280	64.9%	59	21.1%	NO	191	68.3%	42	22.0%	NO	191	100.0%	42	22.0%
															YES	89	31.7%	17	19.3%	NO	64	71.8%	5	8.0%
																				YES	25	28.1%	12	48.0%

Flowchart 10. Empirical model of endometrial cancer treatment in Poland, part 4 (source: own analysis)

The same analysis as in the case of the two above cancers of female reproductive organs has shown that the database provided by the National Cancer Registry is incomplete in 22-

25% when it comes to ovarian cancer stage. Also, only a few cases of first cancer stage were observed (cf. Table 16).

Table 16. Distribution of information on ovarian cancer stage in the NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	2	0	0%	0%	0%
II	893	891	801	25%	25%	24%
III	968	979	872	27%	27%	26%
IV	953	906	862	27%	25%	25%
No stage provided in the NCR	779	825	855	22%	23%	25%
Total	3,593	3,603	3,390	100%	100%	100%

In the case of ovarian cancer it was established that underestimation of the database provided by the NCR is at the level of 24-30%. In addition, analysis of provided services allowed identification of between 2,400 and over 3,300 patients (depending on the year) who were not registered in the NCR in a given year or earlier. Assignment of stages to those patients based on services reported to the National Health Fund is presented in Table 17.

Table 17. Cancer stage categorization of new patients who have not been recorded in NCR (source: own analysis)

	Absolute value			%		
Stage	2010	2011	2012	2010	2011	2012
I	560	486	474	17%	19%	19%
II	146	99	114	4%	4%	5%
III	579	371	400	17%	15%	16%
IV	474	328	332	14%	13%	14%
other diagnosis	1,347	1,044	958	40%	42%	39%
follow-up	225	177	164	7%	7%	7%
Total	3,331	2,505	2,442	100%	100%	100%

The final and adjusted distribution of ovarian cancer incidence in relation to cancer stage is shown in Table 18. The main change in the structure of cancer stage in incidence for the period 2010-2012 turned out an increase in the share of the first stage, similar as in the case of incidence of cervical cancer and endometrial cancer.

Table 18. Distribution of incidence in relation to cancer stage for the period 2010–2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	755	693	711	15%	15%	16%
II	1,213	1,192	1,133	23%	25%	25%
III	1,718	1,564	1,497	33%	33%	33%
IV	1,454	1,273	1,225	28%	27%	27%
impossible to define	25	7	5	0%	0%	0%
Total	5,165	4,729	4,571	100%	100%	100%

Analysis performed during assembly of an empirical model of ovarian cancer treatment confirmed that, in general, surgery was the most frequent method of treating ovarian cancer – applied in 63% of cases (cf. Table 19).

Table 19. Empirical model of cervical cancer treatment in Poland, part 1 (source: own analysis)

Type of therapy	Percentage of patients who underwent the therapy
surgical treatment	77.6%
chemotherapy	68.8%
radiotherapy	6.5%

It was observed that for patients with ovarian cancer stage I one-year survival rate exceeds 98%. These statistics decline with the advancement of cancer stage and amount to respectively 92.8% in case of stage II, 78.2% in case of stage III and 49.3% in case of stage IV (cf. Fig. 11).

Surgical treatment is the most frequent method of treating stages I and II ovarian cancer, applied in 98% and 87% of cases, respectively. In the case of stage II almost one in four patients

is subject to chemotherapy alone. Patients with stages III and IV ovarian cancer are, in the majority of cases, treated with chemotherapy and surgery (cf. Table 20).

Table 20. Empirical model of cervical cancer treatment in Poland, part 2
(source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
surgical treatment	98.0%	87.2%	79.4%	54.8%
chemotherapy	18.1%	74.2%	89.2%	68.5%
radiotherapy	3.9%	4.7%	5.4%	10.8%

The most frequent treatment regimen is simultaneous surgery and chemotherapy, applied in more than half of cases. The rarest is radiotherapy alone (0.66%) and simultaneous surgery and radiotherapy (0.74%) (cf. Table 21).

Table 21. Empirical model of ovarian cancer treatment in Poland, part 3
(source: own analysis)

Was surgical treatment provided?			radiotherapy		Total
			NO	YES	
NO – 22%	chemotherapy	NO	7.05%	0.66%	7.71%
		YES	12.29%	2.37%	14.65%
	Total		19.34%	3.02%	22.36%
YES – 78%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	22.71%	0.74%	23.46%
		YES	51.49%	2.69%	54.18%
	Total		74.20%	3.44%	77.64%

Surgical treatment alone is the most frequent method of treating ovarian cancer stage I, applied in 79% cases, while 15% of patients are subject to simultaneous surgery and chemotherapy.

At stages II, III, and IV the usual treatment is surgery with chemotherapy in 65%, 68%, and 40% of cases, respectively. Almost one in five patients at stage II is subject to surgery alone. At the third and fourth stage, the usual treatment regimen is chemotherapy alone (16% and 20% of cases, respectively). In addition, at the fourth stage treatment is abandoned in 18% of cases (in this group 22% of patients receive palliative care) and 11% undergo surgery alone.

Stage					Including surgical treatment					Including surgical					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	711	15.6%	9	1.2%	NIE	14	2.0%	0	0.0%															
					TAK	697	98.0%	9	1.2%	NIE	583	83.5%	9	1.5%	NIE	564	96.7%	9	1.5%	NIE	564	100.0%	9	1.5%
															TAK	19	3.3%	0	0.0%					
										TAK	115	16.5%	0	0.0%	NIE	110	95.5%	0	0.0%	NIE	110	100.0%	0	0.0%
															TAK	5	4.5%	0	0.0%					
2	1132	24.8%	82	7.2%	NIE	145	12.8%	12	8.3%	NIE	70	48.2%	6	8.6%	NIE	68	97.1%	6	8.8%	NIE	59	86.8%	5	8.5%
																				TAK	9	13.2%	1	11.1%
															TAK	2	2.9%	0	0.0%					
										TAK	75	51.8%	6	8.0%	NIE	62	82.1%	5	8.1%	NIE	36	58.6%	4	11.0%
																				TAK	26	41.4%	1	3.9%
															TAK	14	17.9%	1	7.4%					
					TAK	987	87.2%	70	7.1%	NIE	222	22.5%	34	15.2%	NIE	215	96.8%	34	15.7%	NIE	215	100.0%	34	15.7%
															TAK	7	3.2%	0	0.0%					
										TAK	765	77.5%	36	4.7%	NIE	734	95.9%	31	4.2%	NIE	734	100.0%	31	4.2%
															TAK	31	4.1%	5	16.0%					
3	1497	32.8%	327	21.8%	NIE	308	20.6%	115	37.4%	NIE	41	13.3%	30	73.2%										
										TAK	267	86.7%	85	31.9%	NIE	240	90.1%	79	32.9%	NIE	155	64.4%	42	27.2%
																				TAK	86	35.6%	37	43.2%
															TAK	26	9.9%	6	22.6%					
					TAK	1189	79.4%	212	17.8%	NIE	121	10.2%	82	67.8%	NIE	119	98.4%	81	68.1%	NIE	119	100.0%	81	68.1%
															TAK	2	1.6%	1	50.0%					
										TAK	1068	89.8%	130	12.2%	NIE	1018	95.4%	126	12.4%	NIE	1018	100.0%	126	12.4%
															TAK	49	4.6%	4	7.1%					
4	1226	26.8%	633	51.7%	NIE	554	45.2%	354	63.9%	NIE	241	43.5%	207	85.9%	NIE	216	89.6%	189	87.5%	NIE	168	77.8%	143	85.1%
																				TAK	48	22.2%	46	95.8%
															TAK	25	10.4%	18	72.0%					
										TAK	313	56.5%	147	47.0%	NIE	248	79.4%	112	45.1%	NIE	152	61.0%	63	41.6%
																				TAK	97	39.0%	49	50.5%
															TAK	64	20.6%	35	54.3%	NIE	9	13.6%	4	45.4%
																				TAK	56	86.4%	31	55.7%
					TAK	672	54.8%	279	41.6%	NIE	146	21.7%	128	87.6%	NIE	140	95.9%	124	88.5%	NIE	140	100.0%	124	88.5%
															TAK	6	4.1%	4	66.7%					
										TAK	526	78.3%	152	28.8%	NIE	489	92.9%	140	28.7%	NIE	489	100.0%	140	28.7%
															TAK	37	7.1%	12	30.8%					

Flowchart 11. Empirical model of ovarian cancer treatment in Poland, part 4 (source: own analysis)

Summing up this part of considerations, it should be concluded that analysis provided an opportunity to depict treatment regimens of cervical cancer, endometrial cancer, and ovarian cancer. Also incidence statistics based on the National Cancer Registry database were verified (cf. Table 22 and Fig. 7). It was established that when information from the National Health Fund database was used, total incidence of the three cancer types under analysis increased by 32%, which is tantamount to a conclusion that the NCR database is underestimated by 24%.

Table 22. Summary of incidence distribution in 2012 in relation to cancer stage (source: own analysis)

Stage	Cervical cancer		Endometrial cancer		Ovarian cancer	
	NCR	Supplement	NCR	Supplement	NCR	Supplement
I	4	563	1	1,263	0	711
II	1,121	1,360	3,174	3,443	801	1,133
III	688	1,060	658	923	872	1,497
IV	263	944	254	757	862	1,225
impossible to define	-	5	-	6	-	5
Stage not recorded (NCR)	608	0	1,165		855	
Total	2,684	3,932	5,252	6,392	3,390	4,571

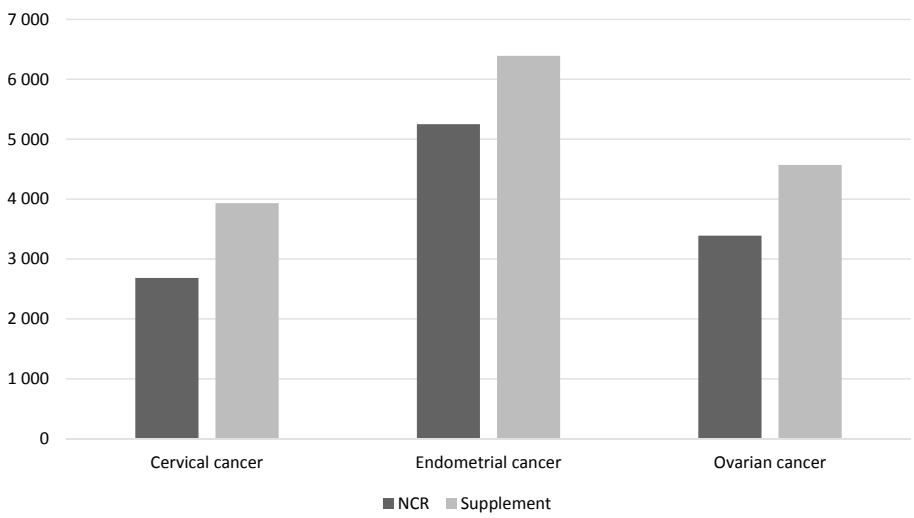


Fig. 7. Comparison of incidence according to the NCR and incidence supplemented with information from the NHF database in 2012 (source: own analysis)

Summary

In the above discussion, analysis concerned the major cancers of female reproductive organs in terms of incidence, i.e. cervical, endometrial and ovarian cancer. Despite common location in the pelvis minor, they differ in terms of epidemiology, diagnostics, treatment, and prognosis.

Firstly, it was established that nearly 4,000 new cases of cervical cancer, close to 6,400 new cases of endometrial cancer, and less than 4,600 new cases of ovarian cancer were diagnosed in 2012 in Poland (respectively 46%, 22%, and 35% more than registered in the NCR database). In the light of the above, it is necessary to conduct an epidemiological comparative analysis with other countries on the basis of adjusted data. Such an analysis would allow verification of conclusions drawn on the basis of GLOBOCAN 2012 and EUROCARE-5 data analysis.

Secondly, it was confirmed using empirical data that there are differences in the therapeutic regimen of these cancer types, for example, without regard to cancer stage, in the case of cervical cancer the rarest treatment is surgery with chemotherapy, while this regimen is applied the most frequently to ovarian cancer. As to the latter cancer, the second rarest regimen is surgery + radiotherapy, while in the case of endometrial cancer it is the most frequent therapy.

Thirdly, a detailed analysis of the treatment pathway was conducted depending on stage of individual cancer types. The empirical model thus obtained constitutes the basis for concluding on future costs of oncological treatment from the payer's point of view.

Bibliography

Armstrong, D.K., Bundy, B., Wenzel, L. et al. (2006) Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *New England Journal of Medicine*, 354, pp. 34–43.

Barton, M., Jacob, S., Shafiq, J., Hsin Wen Wong, K., Thompson, S., Delaney, G., Hanna, T. (2013) *Review of optimal radiotherapy utilization rates*.

Castellsagué, X.,Díaz, M., Sanjosé, S., Muñoz, N., Herrero, R., Franceschi,S., Peeling, R.W., Ashley, R., Smith, J.S.,Snijders, P.J.F., Meijer, Ch.J.L.M., Xavier, F., for the International Agency for Research on Cancer Multicenter Cervical Cancer Study Group (2006) Worldwide Human Papillomavirus Etiology of Cervical Adenocarcinoma and Its Cofactors: Implications for Screening and Prevention. *Journal of the National Cancer Institute*, 98 (5), pp. 303–315.

Didkowska, J., Wojciechowska, U., Zatoński, W. (2011) *Nowotwory złośliwe w Polsce w 2009 roku*. Warsaw: Cancer Centre and Institute of Oncology.

Edge, S.B., Byrd, D.R., Compton, C.C. et al. (2010), *Ovary and primary peritoneal carcinoma AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer, pp. 419–428.

FIGO Committee on Gynecologic Oncology (2014) FIGO staging for carcinoma of the vulva, cervix, and corpus uteri. *International Journal of Gynecology and Obstetrics*, 125 (2), pp. 97–98.

Harter, P., du Bois, A., Hahmann, M. et al. (2006) Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. *Annals of Surgical Oncology*, 12, pp. 1702–1710.

Kornafel, J., Mądry, R., Bidziński, M., Bręborowicz, J., Gawrychowski, K., Łacko, A., Roszak, A., Tacikowska, M. (2013) *Nowotwory kobiecego narządu płciowego. Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych*, PTOK, pp. 278–305.

Lukka, H., Hirte, H., Fyles, A. et al. (2002) Concurrent cisplatin-based chemotherapy plus radiotherapy for cervical cancer – a meta-analysis. *Clinical Oncology*, 14, pp. 203–212.

Monk, B.J., Sill, M.W., Mc Meekin, D.S et al. (2009) Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecological Oncology Group study. *Journal of Clinical Oncology*, 27, pp. 4649–4655.

Maggi, R., Lissoni, A., Spina, F. et al. (2006) Adjuvant chemotherapy vs. radiotherapy in high-risk endometrial carcinoma: results of a randomised trial. *British Journal of Cancer*, 95, pp. 266–271.

Miller, D.S., Filiaci, G., Mannel, R. et al. Randomized Phase III Noninferiority Trial of First Line Chemotherapy for Metastatic or Recurrent Endometrial Carcinoma: A Gynecologic Oncology Group Study. L

Monk, B.J., Tewari, K.S., Koh, W.J. (2007) Multimodality therapy for locally advancedcervicalcarcinoma: state of the art and future directions. *Journal of Clinical Oncology.* http://jco.ascopubs.org.

NCCN guidelines (2015) http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site.

NHS Scotland (2005), *Cancer In Scotland Radiotherapy Activity Planning For Scotland 2011–2015*.

Shepherd, J.H. (1989) Revised FIGO staging for gynaecological cancer. *An International Journal of Obstetrics and Gynaecology*, 96 (8), pp. 889–892.

Tewari, K.S., Monk, B.J.(2009) Recent achievements and future developments in advanced and recurrentcervical cancer: trials of the Gynecologic Oncology Group Seminars in oncology.

Vergote, I., Tropé, C.G., Amant, F. et al. (2010) Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *New England Journal of Medicine*. 363, pp. 943–953.

Villa, L.L., Costa, R.L.R., Petta, C.A., Andrade, R.P., Ault, K.A. (2005) Prophylactic quadrivalent human papillomavirus(types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo, *The Lancet Oncology*, 6, pp. 271–278.

Walker, J.L., Piedmonte, M.R., Spirtos, N.M. et al. (2012) Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *Journal of Clinical Oncology*, 30, pp. 695–700.

Werner, H.M.J., Trovik, J., Marcickiewicz, J. et al. (2011) Revision of FIGO surgical staging in 2009 for endometrial cancer validates to improve risk stratification. *Gynecologic Oncology*, doi:10.1016/j.ygyno.2011.11.008.

Winter, K., Levenback, C., Iyer, R., Gaffney, D. (2007) Extended-field irradiation and intracavitary brachytherapy combined with cisplatin chemotherapy for cervical cancer with positive para-aortic or high common iliac lymph nodes: results of ARM 1 of RTOG 0116. *International Journal of Radiation Oncology, Biology, Physics*, 68 (4), pp. 1081–1087.

Zeppernick, F., Meinhold-Heerlein, I. (2014) The new FIGO staging system for ovarian, fallopian tube, and primary peritoneal cancer. Archives of Gynecology and Obstetrics, 290 (5), pp. 839–842.

Treatment pathway model in colorectal cancers

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Introduction

According to ICD10, colorectal neoplasms have been divided into the following: malignant neoplasm of colon and rectosigmoid junction (C18-19), malignant neoplasm of rectum (C20) and malignant neoplasm of anus and anal canal (C21). Carcinoma is the dominant type of malignant neoplasm of that section of intestine. In most cases, cancers of colon and rectosigmoid junction are adenocarcinomas, while in rectum squamous cell carcinoma is also diagnosed. Etiopathogenesis of rectal and rectosigmoid junction cancers is the same, while the origin of anal cancer is different. Symptoms and treatment of carcinoma of particular sections of intestine differ, but due to similar location (and the resulting problems with the exact location of a neoplasm) the diagnostic procedures are also similar.

Colorectal cancers are the third most frequent type of neoplasm occurring in men (660 thousand cases, i.e. 10%) and the second in women (570 thousand cases, i.e. 9%). Almost 60% of cases occur in developed countries. Inter-population differences as to the frequency of occurrence are immense: the highest frequency is recorded in Australia and New Zealand as well as in Western Europe, and the lowest - in Africa and Central and Southern Asia. Incidence among men is twice as high as among women (NCR). It is similar in terms of mortality rate, which is lower in women than in men. In total, colorectal carcinoma is the cause of 8% deaths due to cancer worldwide (over 600 thousand people a year).

In 3/4 cases colorectal cancer is a sporadic disease, i.e. not hereditary. A clear relationship has been established between the level of industrialization and economic development and the number of people developing the disease. Environmental factors that can impact cancer development have been established, thanks to which social education campaign was started in order to reduce the incidence.

Colorectal carcinoma is a disease of people aged 70+, it is very rare in people before 40. Due to the number of people suffering from the disease, high mortality rate and a long period without symptoms, screening programmes have been introduced in the majority of countries.

Colorectal cancer treatment is harmonized and depends on cancer location and stage. Local surgical treatment has improved thanks to the introduction of new intestinal anastomosis techniques, thanks to which fewer patients are mutilated by creating a stoma. Moreover, in the last two decades a change has been introduced in the treatment regimen for patients with metastases, with increased scope for surgical interventions. In addition, new drugs and targeted therapies have been introduced, with radiotherapy and radiochemotherapy being well-established in treating rectal and anal cancers. All this has had an influence on increased rate of total survival, and colorectal carcinoma, similar to the majority of neoplastic conditions has become a chronic disease.

The aim of this article is to present how colorectal cancers are treated in Poland. The first part of the article presents medical aspects, i.e. epidemiology, diagnostic methods and treatment of colorectal cancer in Poland. The second part is a presentation of the results of an analysis of estimated colorectal cancer incidence in Poland, taking into account an empirical model of patient treatment.

Epidemiology

Colorectal carcinoma (i.e. C18 - colon cancer, C19- carcinoma of rectosigmoid junction, C-20 rectal carcinoma and C21 - anal carcinoma) is one of the most frequently occurring types of malignant neoplasm, in Poland it is the second or third most frequent type of carcinoma in both sexes (men - 12.4%; women - 10.1%), and the incidence has steadily been increasing. In Europe it is one of the most frequent malignant neoplasms (it accounts of almost 14% of all cancer cases) (Screening Programme 2015).

According to NCR data for 2012, almost 11 thousand people were diagnosed with colon cancer (ICD C18-19), and 7.8 thousand people died as a result. Rectal cancer (ICD10 C20) was detected in over 5.6 thousand people, and nearly 3.15 thousand people died of it. On the other hand, in regard of anal cancer (C21) - incidence and mortality oscillate around 100 cases per annum.

In Poland significant dynamics in incidence has been recorded. Between 1980-2010 the incidence rate grew 4 times in case of men and 3 times in case of women. General 5-year prevalence related with colorectal cancer (ICD10 C18-C21) amounted to 46 thousand in

Poland; for the whole Europe this figure exceeds 1.2 million. Globocan figures for Europe show five-year prevalence at the level of 13.3%, whereas for Poland it is 12.8%. For Middle and Eastern Europe the value is 13.5%, and for the Western Europe - 12.8%.

Mortality rate[105]for Europe amounts to 12.2%, including Western Europe - 11.5%, and for Middle and Eastern Europe - 13.2%. For Poland the value is 12% with age-standardized-incidence ASR = 27 (for Europe = 30). Comparison of Poland with the other regions and selected countries has been presented in Figure 1.

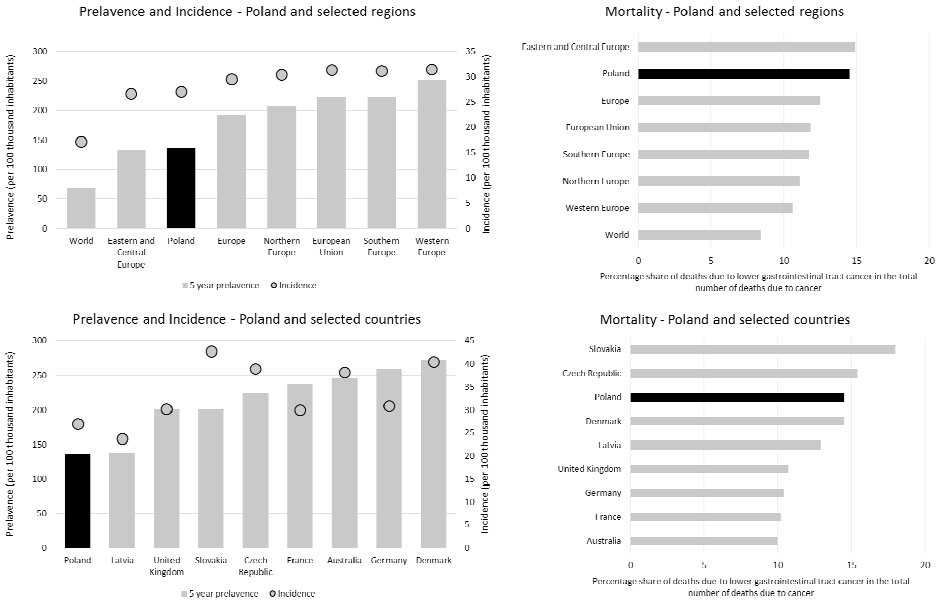


Figure 1. Basic statistics concerning the epidemiology of colorectal cancers for Poland
and selected regions part 1 (source: own analysis based on GLOBOCAN 2012)

Over 94% cases occur in population 50+. The incidence grows with age, with the peak after 70 years of age. The curve for both sexes is shifted because the risk of developing the disease by men is approx. 1.5-2 times higher than in women. Colorectal cancer incidence grew dynamically in the second half of the 20 century. This trend weakened in 1990s in case of women, and in case of men the growth dynamics was reduced in the beginning of the 21st century (National Cancer Registry)

[105] meaning the share of deaths due to colorectal cancer in the total number of deaths due to neoplastic diseases.

5-year survival outcomes published by Eurocare, which are presented in Figure 2, show indirectly that detection of early stages of cancer and the treatment effectiveness is poor. This puts Poland in the group with those Eastern Europe countries for whom rectosigmoid cancer survival outcome (ICD10 C18-19) amounts to 40.4% (Poland 39%), and rectal cancer (ICD10 C20) outcome is 38.8% (Poland - 38.4%). Unfortunately, in relation to the whole of Europe, for which the rate is 49% (in some countries, e.g. in France, 5-year survivals in case of colorectal cancer amount to 52%), the figures are unsatisfactory. This rate points to the need to take concrete actions in order to improve the situation. Mortality - as well as incidence - is correlated with age and increases clearly after 60 years of age. The risk of death due to colorectal cancer is lower in women than in men.

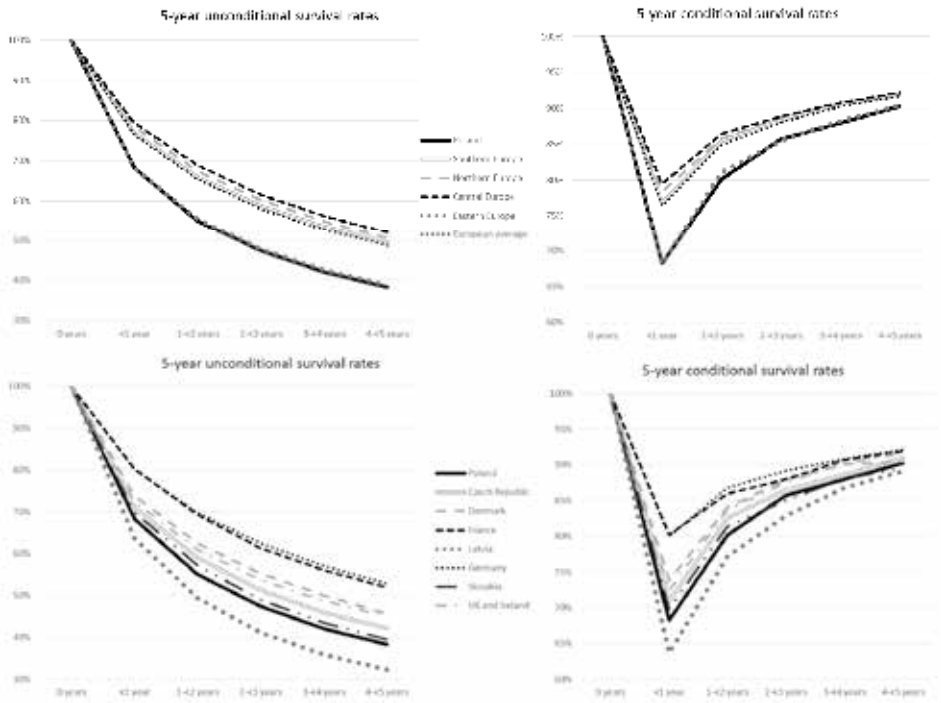


Figure 2. Five-year survival outcomes for patients suffering from breast cancer in Poland and selected regions (source: own analysis based on EUROCARE - 5)[106]

[106]Conditional survivals - against the survival of the previous year.

Etiopathogenesis of colorectal cancer has been well described in literature. At the start it should be recalled that 25% of cancer cases occur because of hereditary genetic mutations, and the remainder are sporadic neoplasms developed mostly as colorectal adenomas, however some of them develop in the unchanged glandular epithelium.

Increased risk factors for rectosigmoid junction and rectal carcinoma have been divided into four groups: epidemiological, intestine-related, diet-related and mixed. Among epidemiological factors, apart from age other factors have been indicated. They are conditioned by: race (higher incidence in case of caucasians), geography (higher incidence in Northern Europe), environment (obesity combined with rare physical activity increases the risk) as well as smoking (the risk for smoking women is by 40% higher than for non-smoking, in case of men the risk increases by 30% in case of smoking). Intestine-related risk factors include those factors which are not hereditary and stimuli in the form of defined genetic syndromes. Those factors include e.g. the history of colorectal cancer, cases of colorectal cancer among 1st degree relatives (where there is no hereditary syndrome), familial adenomatous polyposis, inflammatory bowel disease (ulcerative colitis and Crohn's syndrome) as well as a history of adenomatous polyps. There is a relationship between the size of polyps and increased risk of cancer development. Unfavourable dietary factors include excessive amount of animal fat and red meat (especially fried) and low level of fruit and vegetables consumption. Mixed risks include past radiotherapy, cholecystectomy or intestinal pouch, which significantly (by approx. 400 times) increases the risk of colorectal cancer.

In case of anal carcinoma, a relationship has been established between viral infections (HIV and HPV) and increased incidence risk. Infection with HPV accompanies the cancer in approx. 84% of cases. The risk of developing cancer grows also in case of practicing anal intercourse and after treated cervical cancer.

The analysis of risk factors and 5-year survival outcomes indicates a need to educate and promote healthy lifestyle, to encourage HPV vaccinations and - which is the most important - to encourage the screening. It is also necessary to encourage selected families to attend a genetic consultation.

Diagnostics

Colorectal cancer symptoms are unspecific and occur quite late, they depend on cancer location and staging. External or internal bleeding, abdominal pain, change in the frequency of bowel movements are symptoms occurring in over 50% patients. Over 30% patients lose weight and suffer from anaemia. Less frequent symptoms include: palpable tumour, swollen abdomen, anorexia, fever. Intestinal obstruction, which occurs in advanced stages of cancer is always a bad prognosis factor; it occurs in 6% of cases.

Diagnosis is made based on a medical examination complemented with a digital rectal examination and endoscopy. First-line endoscopic method includes colonoscopy, rectoscopy is performed much less frequently. A biopsy of tumour located during the examination and histopathologic confirmation of cancer cells enables proper diagnosis. The next step is determining cancer stage. To this end a CT scan is made of abdominal cavity and small pelvis, as well as a chest X-ray to verify metastases (if the stage is very low an X-ray test should be enough).

Rectal cancer assessment is made by means of transrectal ultrasound, as well as by means of MRI scan. Those tests assess the depth of cancer invasion in the intestinal wall and provide information about lymph glands. Prior to the onset of the therapy it is also necessary to make a CEA (carcinoembryonic antigen) blood test. CEA level is useful for monitoring therapy and for observation of patients after the therapy is finished.

PET scan is made in order to diagnose colorectal cancer recurrence or in order to verify metastatic changes, but it is not recommended as a primary diagnostic procedure in this respect. The tests provide the basis for final diagnosis and staging.

In case of early stage cancer (stage I), a diagnosing treatment during which colon polyps are removed is also a therapeutic treatment.

Polish Ministry of Health has been coordinating colorectal cancer screening programme for many years. The screening involves colonoscopy, which follows a questionnaire. Until the end of 2011 the screening programme was opportunistic. It meant that volunteers reported to selected medical providers on their own or were referred there by their physician. Screening was targeted at people aged 60-65 and at people aged 40-65 with colorectal cancer history

in the family. Since 2012, due to bad epidemiological indicators and according to the EU suggestions, a screening programme targeted at a certain population was started. Named invitations are mailed to age group 55-64. The programme is intended to detect early lesions and qualify patients for potential removal of adenomas (polyps), or lesions that can undergo neoplasia. In the age group designated for screening, about 25% of people have polyps and as many as 5% are at risk of developing cancer. Removal of lesions reduced cancer risk by 60-90%. For individual genetic conditions and intestinal inflammations follow-up endoscopic examinations were standardised in specific time ranges. On-going screening in a decade is expected to reduce incidence by 10-18% and mortality by 15-20% (PBP 2015).

In the second half of the 20th century there were various intestine cancer classifications describing the stage. Introduction of a unified stage classification by UICC based in TNM, i.e. tumour (T), lymph nodes (N), and metastasis (M), and its popularisation resulted in the scale replacing the other intestine cancer classification systems and becoming the only scale used. The scale is presented in Table 1.

Table 1. Stage according to TNM staging system – IUCC, version 7, 2010
(source: own analysis on the basis of 7th edition of UICC classification)

Clinical stage based on TNM			
Stage	**Primary tumour (T)**	**Regional lymph nodes (N)**	**Distant metastasis (M)**
0	Tis	N0	M0
I	T1–2	N0	M0
IIA	T3	N0	M0
IIIB	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1–2	N1a–c	M0
	T1	N2a	M0
IIIB	T3-4	N1a-c	M0
	T2-3	N2a	M0
	T1	N2b	M0
IVA	Every T	Every N	M1a
IVB	Every T	Every N	M1b

Treatment

The basic therapeutic method in large intestine cancer is a surgery. Stage, location, and vascularisation of a neoplastic tumour affect the extent of the resection. The procedure consists in resection of an intestine section with a mesentery and neighbouring lymph nodes (at least 12 lymph nodes). The procedure of resection of an intestine section with a mesentery and its axial vessels, conducted in anatomical compartments, is called complete mesocolic excision and is a standard oncological surgical procedure. In the case of high stage or unfavourable location, it is not always possible to restore continuity of the digestive tract (mainly in the case of rectal carcinoma). In such case, it is necessary to create an artificial anus (stoma), or to lead intestines out of abdominal integument. A stoma can be temporary (closed after treatment ends) or permanent. In the case of metastasis to other organs, their number and resection plausibility must be evaluated. Metastasectomy procedures can be conducted simultaneously with a topical procedure or after the procedure.

In advanced stage rectal carcinoma, induction therapy is necessary before a surgery. There are two methods. One is independent radiotherapy during which patients receive 25 Gy (5 radiation fractions 5 Gy each) and after which a surgery is conducted, up to 14 days after radiation completion (optimally between the 5th and 7th day after radiotherapy). The second method is chemoradiotherapy. Patients undergo several weeks of exposure to low doses of radiation, accompanied by administration of cytostatics in specific days of planned therapy. Surgical treatment follows after about a month from radiation completion.

In the case of adverse factors, after a surgical procedure patients with colon cancer are subject to adjuvant therapy in the form of a 6-month chemotherapy based on 5-Fluorouracil. Patients with rectal carcinoma who have not undergone t pre-operative treatment are also offered adjuvant treatment. Indication for adjuvant therapy is presence of metastatic lymph nodes or inadequate surgical margins. Depending on tumour location, patients are qualified for complementary radiotherapy or chemoradiotherapy.

In patients at the dissemination stage (stage IV according to UICC classification), therapeutic options depend on the location and number of metastases and the possibility of their radical resection. An optimal therapy that brings about a superior outcome in the form of increased total survival, is combined chemotherapy and surgery. Usually after a few

rounds of chemotherapy a metastasectomy is performed and treatment with cytostatics is continued. A decision concerning surgical removal of the primary tumour is made depending on presence or absence of characteristics of the risk of digestive tract obstruction and the possibility of simultaneous metastases resection with local treatment. Patients in which disease dissemination does not allow planning the above sequential treatment are subject to palliative systemic treatment, i.e. targeted therapy and chemotherapy.

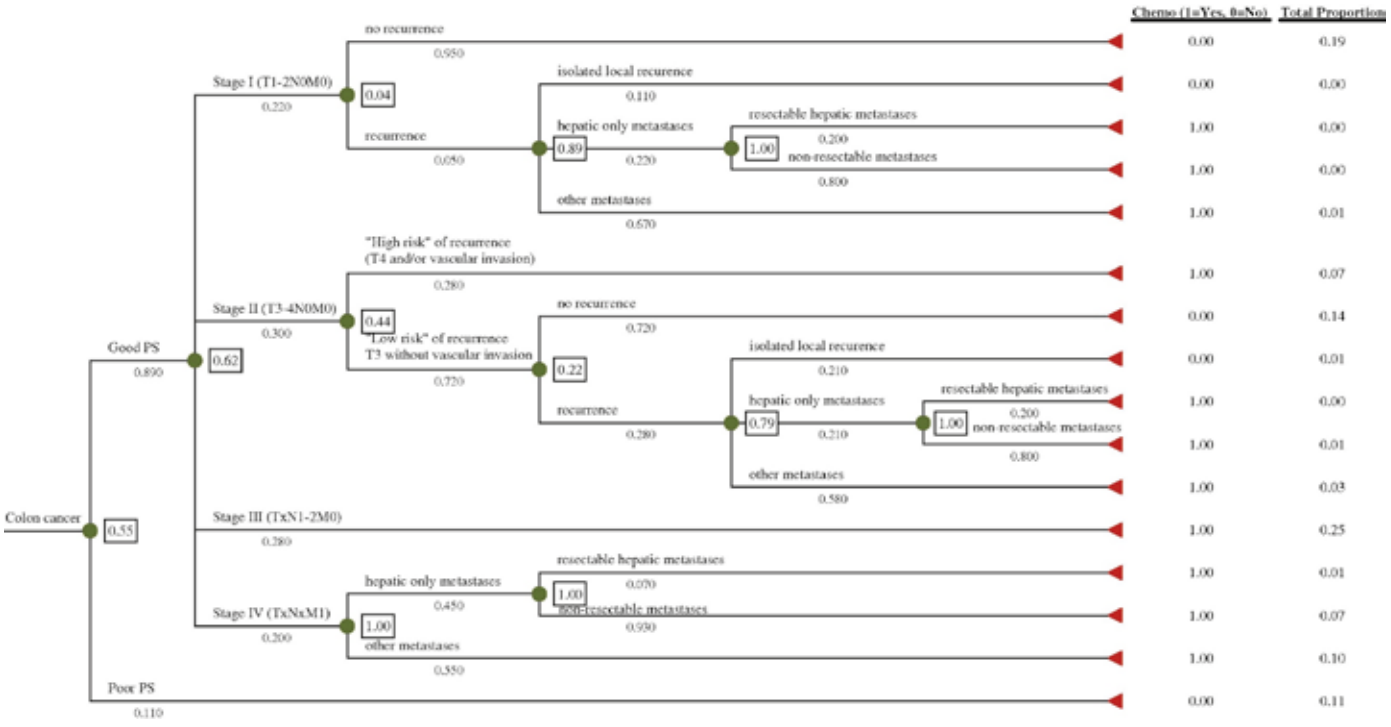
Chemotherapy of malignant neoplasm of intestine is based on pyridine derivatives and relatively new cytostatics, i.e. oxaliplatin and irinotecan, administered in various protocols and sequences. Targeted therapy is administered to patients who, after molecular tests, display likelihood of response to such treatment. At present in Poland targeted therapy is used in the third line of treatment (patients must undergo two types of chemotherapy first).

Treatment of anal carcinoma (C21) depends on its histopathology and location. The treatment of choice in rectal ampulla adenocarcinoma is a surgical procedure. In the case of planoepithelial carcinoma, a surgery can be performed only in the case of low stage (cT1N0M0), and the therapeutic standard in other cases in radiochemotherapy.

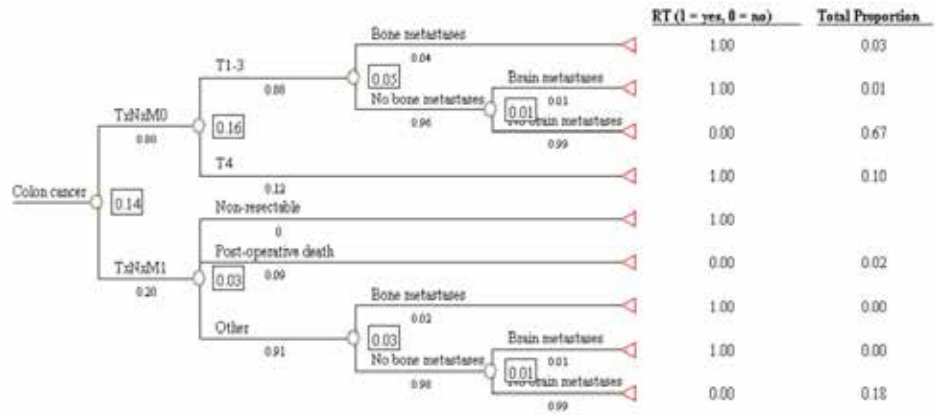
Decision-making models in treatment of malignant neoplasms of large intestine

In literature, decision-making models in treatment of malignant neoplasm of large intestine are presented in the form of decision trees. The models reproduce treatment regimens applied in a given country and allow defining demand for specific services depending on assumptions. Due to differences in treatment regimens, colon cancer and rectal carcinoma have separate trees. Due to a small number of cases and similarity of treatment methods, anal carcinomas (C21) have been added to rectal carcinomas (C20).

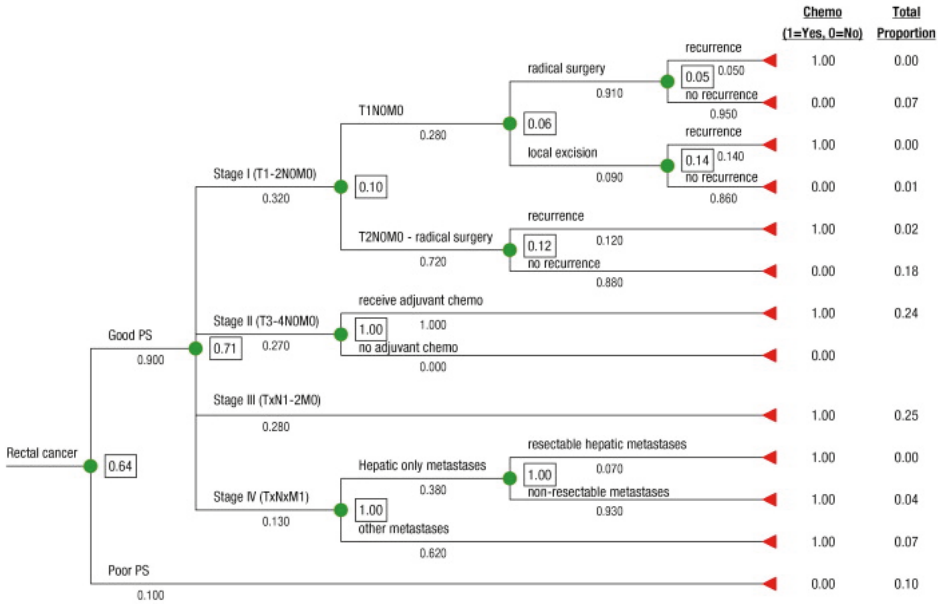
Australian decision trees in the area of chemotherapy were published by Ng et al. (2010), while the model of radiotherapeutic treatment was developed and publicised by Barton (2013) for Australia and by NHS Scotland (2005) for Scotland, which is similar to Poland in epidemiological terms. Decision trees for colon cancer are presented in Flowcharts 1-2, while Flowcharts 3-5 depict relevant decision trees for rectal carcinomas.



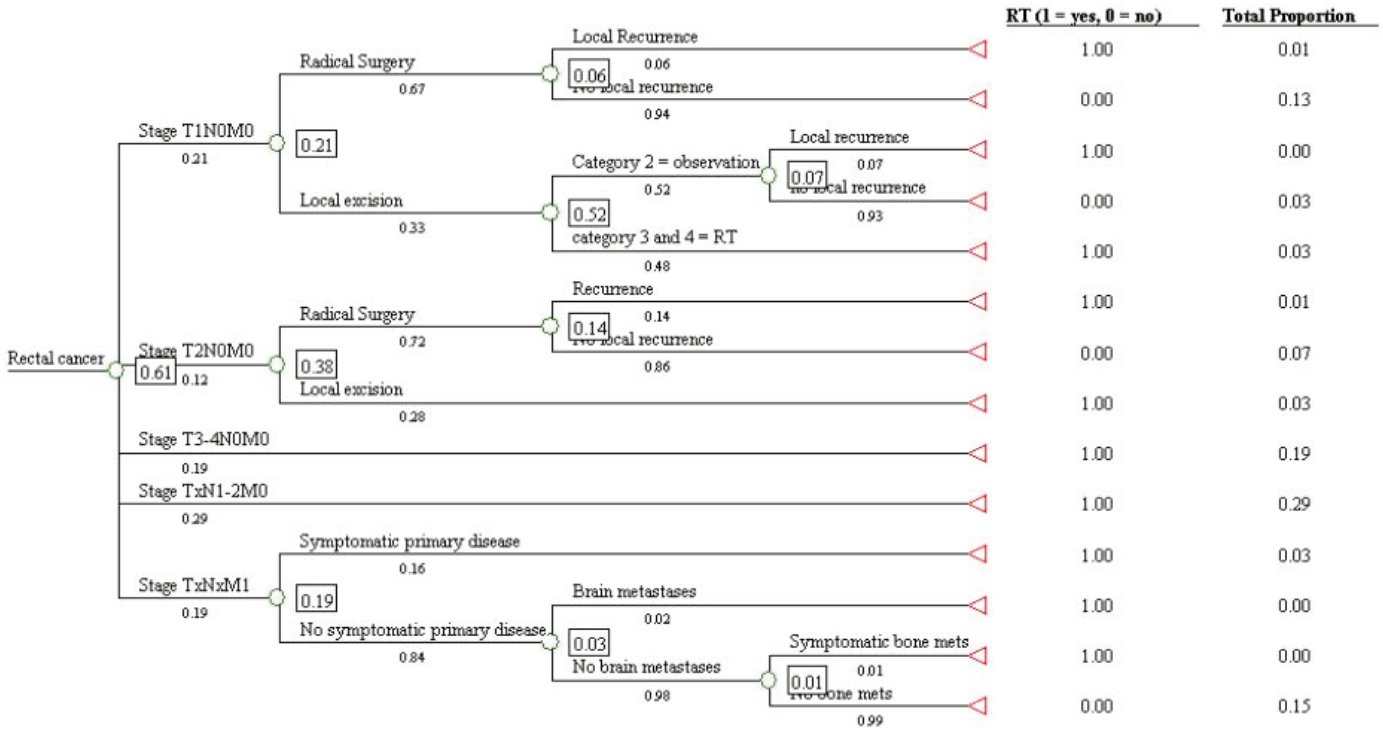
Flowchart 1. Decision tree for chemotherapy in colon cancer treatment in Australia (source: Ng et al. 2010)



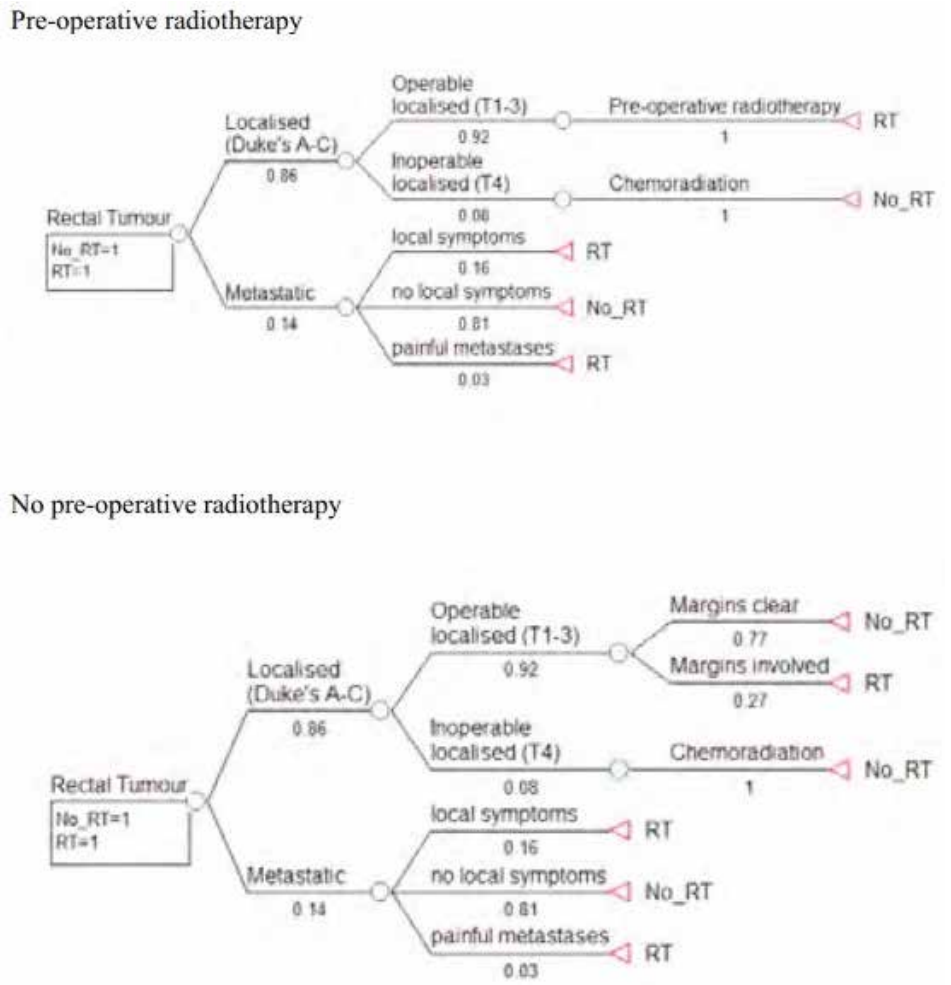
Flowchart 2. Decision tree for radiotherapy in colon cancer treatment in Australia (source: Barton 2013)



Flowchart 3. Decision tree for chemotherapy in rectal carcinoma treatment in Australia (source: Ng et al. 2010)

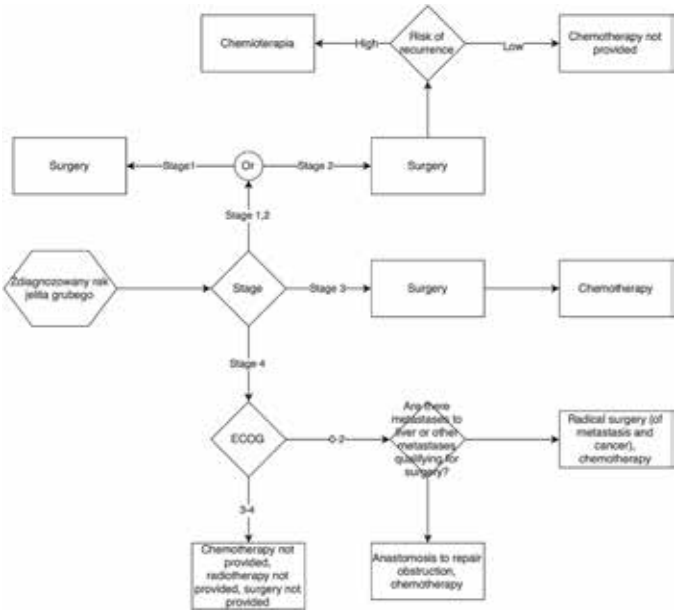


Flowchart 4. Decision tree for radiotherapy in rectal carcinoma treatment in Australia (source: Barton 2013)

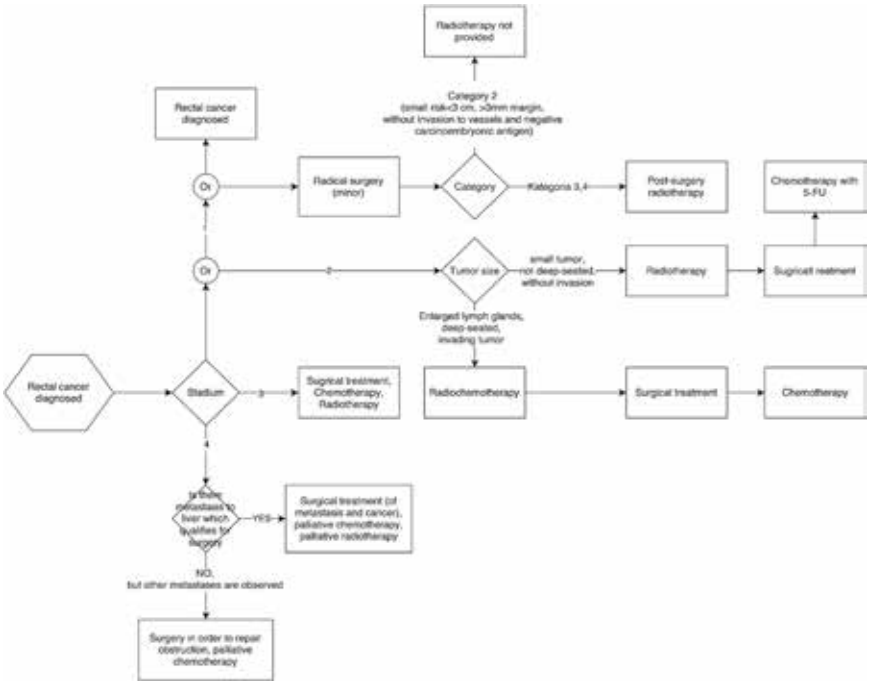


Flowchart 5. Decision tree for radiotherapy in rectal carcinoma treatment in Scotland (source: NHS Scotland 2005)

On the basis of analysis of the above models, a model of oncological treatment in Poland has been developed. The model, presented in Flowcharts 6-7, covers surgical treatment, chemotherapy, and radiotherapy. During work on the model, account was also taken of standards of oncological treatment, which are recommended by scientific societies in Poland and expertise concerning practical treatment of malignant neoplasms of large intestine.



Flowchart 6. Model of colon cancer treatment in Poland (source: own analysis)



Flowchart 7. Model of rectal carcinoma treatment in Poland (source: own analysis)

Empirical model of treatment of malignant neoplasms of large intestine

In order to supplement the theoretical model of counting malignant neoplasms of large intestine with empirical data, several analyses were carried out using available national sources. Supplementing the model would require access to data on stage, general health condition of the patient and histopathological structure of neoplasm. Data on stages are kept in the National Cancer Registry, the only such a registry on the national scale. As a result of analyses using reporting data of the National Health Fund, underreporting of data in the NCR were observed.

Absence of data was noticeable *inter alia* as concerns information on neoplastic disease stage. The results of data analyses provided by the NCR[107] are presented in Table 2 (colon neoplasms) and Table 4 (rectal carcinoma, anal carcinomas). The share of entries without information about the stage of progression of the disease oscillates between 22% and 27% depending on the year and neoplasm type. Tables 3 and 5 present the structure of patients reported to the National Cancer Registry (with supplemented information on stage). The very low share of patients in stage I is very disturbing. It may point to serious problems with timely diagnostics and quality of screening in Poland, as well as reporting problems. In the case of stage I, a diagnostic procedure is also a therapeutic procedure. It can be performed in a private centre and the patient does not require referral to highly specialised centres. It decreases the chances of fulfilling the statutory obligation of case registration (it is a bureaucratic burden to many).

[107] The figures presented by NCR have been initially verified based on NHF database. This means that they do not include patients who appeared for the first time in the NCR database in a given year with breast cancer diagnosis and who were recorded with the diagnosis in the NHF database before that year.

Table 2. Distribution of information on cancer stage in the NCR database for new patients – colorectal cancer (C18, C19) (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	1	0%	0%	0%
II	3,219	3,067	3,041	32%	30%	29%
III	2,546	2,544	2,423	25%	25%	23%
IV	2,171	2,276	2,268	21%	22%	22%
Stage not recorded in the NCR	2,203	2,487	2,805	22%	24%	27%
Total	10,139	10,375	10,538	100%	100%	100%

Table 3. Distribution of information on cancer stage in the NCR database for new patients with full information on stage – colorectal cancer (C18, C19) (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	1	0%	0%	0%
II	3,219	3,067	3,041	41%	39%	39%
III	2,546	2,544	2,423	32%	32%	31%
IV	2,171	2,276	2,268	27%	29%	29%
Total	7,936	7,888	7,733	100%	100%	100%

Table 4. Distribution of information on cancer stage in the NCR database for new patients – rectal and colorectal cancer (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	0	0%	0%	0%
II	1,988	1,941	1,854	35%	33%	32%
III	1,424	1,482	1,312	25%	25%	23%
IV	1,072	1,096	1,022	19%	18%	18%
Stage not recorded in the NCR	1,255	1,407	1,525	22%	24%	27%
Total	5,739	5,927	5,713	100%	100%	100%

Table 5. Distribution of information on cancer stage in the NCR database for new patients with full information on stage – rectal and anal cancer (C20, C21) (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	1	0	0%	0%	0%
II	1,988	1,941	1,854	44%	43%	44%
III	1,424	1,482	1,312	32%	33%	31%
IV	1,072	1,096	1,022	24%	24%	24%
Total	4,484	4,520	4,188	100%	100%	100%

Absence of data is also visible in a situation where a patient appears in the NHF system with a diagnosis of malignant neoplasm of large intestine (C18-C21), but does not appear in the National Cancer Registry. An analysis was carried out for patients who appeared in the NHF reporting systems with the first diagnosis of malignant neoplasm. On the basis of services provided, the stage of the patients who did not appear in the NCR or appeared without information on stage. Among them, patients in the follow-up process were identified: these were patients who underwent relevant therapy before the electronic reporting era. In addition, the patients whose services indicated treatment of other conditions despite reported diagnosis ICD-10 for malignant tumour of large intestine were identified as well.

Analysis of services provided in hospitals or within the SOC/OCIDA (Specialist Outpatient Care/Outpatient Cost-intensive Diagnostic Assistance) system, but who were not registered in the National Cancer Registry, allows a conclusion statement that about 4,000 patients with colon cancer and approximately 2,000 patients with rectal cancer a year are not registered in this database. In addition, there is still a (decreasing) group of patients at the follow-up stage who did not appear in the NCR (or appeared with a PESEL identification). Categorisation of patients based on services provided is presented in Tables 6 and 7.

Table 6. Cancer stage categorization of new patients who have not been recorded in the NCR database – colorectal cancer (c18, C19) (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	949	942	932	11%	12%	13%
II	804	777	779	10%	10%	11%
III	1,087	1,071	1,079	13%	14%	16%
IV	1,381	1,273	1,214	16%	17%	17%
Other cause	767	658	671	9%	9%	10%
Follow-up	3,450	2,817	2,286	41%	37%	33%
Total	8,438	7,538	6,961	100%	100%	100%

Table 7. Cancer stage categorization of new patients who have not been recorded in the NCR database – rectal and anal cancer (C20, C21) (source: own analysis)

	Absolute value			%		
Stage	2010	2011	2012	2010	2011	2012
I	336	317	292	7%	7%	7%
II	397	375	347	8%	8%	8%
III	383	377	443	8%	8%	11%
IV	1,482	1,307	1,186	30%	29%	28%
Coding errors	2	1	5	0%	0%	0%
Follow-up	2,404	2,120	1,933	48%	47%	46%
Total	5,004	4,497	4,206	100%	100%	100%

On the basis of data supplied by National Cancer Registry and expert analysis of treatment pathways of patients recorded in the National Health Fund system the colorectal cancer incidence in years 2010–2012 was determined. Tables 8 and 9 present results of the above mentioned analyses with the distribution in relation to cancer stage at the moment of making a diagnosis. Comparing these results with the structure of patients recorded in the NCR database (Table 8 with Table 2, Table 9 with Table 4) an increase of 33% (underassessment

of 25%) in the number of new diagnoses during a year and of 36% in case of rectal and anal cancers (underassessment of 26%) has been observed[108].

The structure of cancer stages at the moment of making a diagnosis has also changed. The percentage of patients in stage I of colon cancer increased to 9% and there were practically no such cases in the Table 2. In case of rectal cancer the percentage of patients in stage I is 6%. It should be noted that this number could still be underestimated due to the fact that colonoscopy with biopsy can be conducted in ambulatory conditions and therefore there is a possibility to conduct this diagnostic and therapeutic procedures without reporting to NCR and to payer system (NHF). It should be added that due to the fact that National Health Fund spends public money, the records of NHF are subject to appropriate controls and reporting is often connected with receiving funds. Thus this kind of reporting enables to obtain more comprehensive data than reporting without an appropriate enforcement mechanism.

Table 8. Distribution of incidence in relation to cancer stage for the period 2010–2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
1	1,249	1,276	1,341	9%	9%	10%
2	4,389	4,286	4,302	32%	31%	31%
3	3,916	3,953	3,864	28%	28%	28%
4	4,299	4,379	4,451	31%	31%	32%
impossible to define	23	22	26	0%	0%	0%
Total	13,876	13,916	13,984	100%	100%	100%

[108] The increase of 33% means that following the adjustments based on NHF database in Poland there was 33% more cases than reported in NCR. However, the underassessment of 25% means that among new cases 25% has not been recorded in the National Cancer Registry database (NCR includes in this situation 75% of cases).

Table 9. Distribution of incidence in relation to cancer stage for the period 2010–2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	472	462	470	6%	6%	6%
II	2,563	2,505	2,428	32%	31%	31%
III	2,177	2,302	2,231	27%	28%	29%
IV	2,905	2,805	2,620	36%	35%	34%
impossible to define	16	10	9	0%	0%	0%
Total	8,133	8,084	7,758	100%	100%	100%

The missing information in NCR was complemented based on the analysis of services provided to patients reported to the National Health Fund. This analysis involved therapies provided to patients within the first year in which they were diagnosed with malignant neoplasm. It was based on financial products reported to NHF (chemotherapy and radiotherapy services) and the reporting procedures according to International Classification of Medical Procedures ICD-9. On the basis of them for each patient the following parameters were defined:

- Whether the patient underwent major surgery – according to the developed procedure glossary, which can be considered as such in case of a treatment of a given type of cancer,
- Whether the patient received systemic treatment (chemotherapy, drug regimes, therapeutic regimens),
- Whether the patient was treated through radiation (teleradiotherapy or palliative teleradiotherapy, brachytherapy),
- Whether the patient was provided with services defined as palliative (treatment of metastases to bones, palliative radiotherapy),
- Whether the patient died within 365 days of being recorded in the system.

On the basis of the above mentioned analysis for each stage a decision tree presenting applied treatment methods was developed. At each level the size of a group obtained as a result of subsequent divisions, the share of these patients in the superior group and the share

in respect to the whole population of cancer patients from a given group (colon, rectum with anus, respectively) is presented. For groups smaller than 50 patients no further divisions were made. The decision trees for patients entering the system in 2012 have been presented in Flowcharts 8 and 9.

Treatment – colon

The empirical data confirm a crucial role of surgery in the treatment of colon cancers and an important role of chemotherapy. Using radical radiotherapy can be connected with:

- simultaneous occurrence of another malignant neoplasm, in case of which the radiotherapy is used,
- specifying the location of malignant neoplasm and changing the diagnosis (from C19 to C20),
- the reporting strategy of a centre (reporting the palliative radiotherapy as other products).

Table 10. Empirical model of colon cancer treatment in Poland, part 1 (source: own analysis)

Type of therapy	patients who underwent a given therapy
major surgeries	57.7%
chemotherapy	46.3%
radiotherapy	6.0%

Table 11. Empirical model of colon cancer treatment in Poland, part 2 - patients who underwent a given therapy depending on cancer stage (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
major surgeries	49%	77.0%	71.1%	30.0%
chemotherapy	0%	38.4%	68.8%	48.2%
radiotherapy	0%	7.1%	8.0%	4.9%

It is also worth mentioning that the patients in stage I were qualified on the basis of the services which were provided to them, thus making inferences will be fully justified after improving the quality of reporting data from NCR. Until that time one can only make inferences about the frequency of applying specific methods in the area of treating patients with cancer

in this stage. One of such conclusions is that 50% of radical surgeries (resection of intestine's part) in patients in (probably) first stage.

The analysis of Table 12 – shares of patients provided with various types of therapy without the division into stages – shows the similar level of monotherapy in the form of surgery (27.52%) and surgery with chemotherapy (25.12%). Other large groups are patients provided only with chemotherapy (17.15%) and patients, who did not receive radical treatment (both patients in stage I provided with diagnostic and therapeutic procedures and patients in stage IV with bowel obstruction, who receive palliative treatment due to their health condition).

Table 12. Empirical model of colon cancer treatment in Poland, part 3 (source: own analysis)

Was surgical treatment provided?			radiotherapy		Total
			NO	YES	
NO – 38.81%	chemotherapy	NO	22.94%	1.27%	24.21%
		YES	17.15%	2.11%	19.26%
	Total		40.09%	3.39%	43.47%
YES – 61.19%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	27.52%	1.28%	28.80%
		YES	25.12%	2.60%	27.73%
	Total		52.65%	3.88%	56.53%

The analysis of Flowchart 8 shows that the most common treatment method of cancer stage II is the surgery. In 1/3 cases it is combined with systemic treatment. This proportion changes in stage III, in which 2/3 of surgeries are combined with chemotherapy and it is even more important, if radical surgical treatment was not applied.

In stage IV in 30% of cases a major surgery is performed, however, chemotherapy plays a significantly more important role as does palliative treatment and (not included in the table) emergency surgery.

Stage					Including surgical treatment					Including surgical					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	1341	9.6%	166	12.4%	NO	680	50.7%	53	7.7%	NO	680	100.0%	53	7.7%	NO	680	100.0%	53	7.7%	NO	680	100.0%	53	7.7%
					YES	660	49.2%	114	17.2%	NO	660	100.0%	114	17.2%	NO	660	100.0%	114	17.2%	NO	660	100.0%	114	17.2%
2	4302	30.8%	559	13.0%	NO	990	23.0%	215	21.8%	NO	582	58.8%	132	22.7%	NO	522	89.7%	118	22.6%	NO	421	80.6%	86	20.4%
																				YES	101	19.4%	32	31.7%
															YES	60	10.3%	14	23.3%	NO	38	63.3%	8	21.0%
																				YES	22	36.7%	6	27.3%
										YES	408	41.2%	83	20.4%	NO	342	83.8%	77	22.6%	NO	263	76.9%	62	23.7%
																				YES	79	23.1%	15	19.0%
															YES	66	16.2%	6	9.1%	NO	40	60.6%	1	2.5%
																				YES	26	39.4%	5	19.2%
					YES	3312	77.0%	344	10.4%	NO	2067	62.4%	280	13.5%	NO	1985	96.0%	267	13.4%	NO	1983	99.9%	265	13.4%
																				YES	2	0.1%	2	100.0%
															YES	82	4.0%	13	15.8%	NO	82	100.0%	13	15.8%
										YES	1246	37.6%	64	5.1%	NO	1148	92.1%	63	5.5%	NO	1140	99.3%	61	5.3%
																				YES	8	0.7%	2	25.0%
															YES	98	7.9%	1	1.0%	NO	98	100.0%	1	1.0%
3	3864	27.7%	886	22.9%	NO	1116	28.9%	400	35.8%	NO	321	28.8%	183	57.0%	NO	287	89.4%	165	57.5%	NO	181	63.1%	88	48.6%
																				YES	106	36.9%	77	72.6%
															YES	34	10.6%	18	52.9%					
										YES	796	71.2%	216	27.2%	NO	692	87.0%	204	29.5%	NO	572	82.5%	158	27.7%
																				YES	121	17.5%	46	38.0%
															YES	103	13.0%	12	11.6%	NO	72	69.9%	7	9.7%
																				YES	31	30.1%	5	16.1%
					YES	2748	71.1%	486	17.7%	NO	883	32.1%	317	35.9%	NO	848	96.0%	301	35.5%	NO	844	99.5%	298	35.3%
																				YES	4	0.5%	3	75.0%
															YES	35	4.0%	16	45.7%					
										YES	1865	67.9%	169	9.1%	NO	1727	92.6%	157	9.1%	NO	1719	99.5%	154	9.0%
																				YES	8	0.5%	3	37.5%
															YES	138	7.4%	12	8.7%	NO	138	100.0%	12	8.7%
4	4451	31.9%	2581	58.0%	NO	3116	70.0%	1960	62.9%	NO	1772	56.9%	1412	79.7%	NO	1720	97.1%	1365	79.3%	NO	791	46.0%	695	87.8%
																				YES	929	54.0%	670	72.1%
															YES	52	2.9%	47	90.4%	NO	22	42.3%	19	86.4%
																				YES	30	57.7%	28	93.3%
										YES	1344	43.1%	548	40.8%	NO	1270	94.5%	519	40.9%	NO	615	48.4%	202	32.9%
																				YES	655	51.6%	317	48.4%
															YES	74	5.5%	29	39.2%	NO	26	35.1%	9	34.6%
																				YES	48	64.9%	20	41.7%
					YES	1335	30.0%	621	46.5%	NO	535	40.1%	439	82.1%	NO	505	94.4%	416	82.4%	NO	492	97.4%	407	82.7%
																				YES	13	2.6%	9	69.2%
															YES	30	5.6%	23	76.7%					
										YES	800	59.9%	182	22.7%	NO	737	92.1%	161	21.8%	NO	699	94.8%	144	20.6%
																				YES	38	5.2%	17	44.7%
															YES	63	7.9%	21	33.3%	NO	58	92.1%	18	31.0%
																				YES	5	7.9%	3	60.0%

Flowchart 8. Empirical model of colon cancer treatment in Poland, part (source: own analysis)

Treatment – rectum and anus

The empirical model confirms the comprehensive character of rectal and anal cancers treatment. Each of the main radical treatment methods concerns approx. half of patients. As in the example in case of colon cancer the mainstay is the surgical treatment.

Table 13. Empirical model of rectal and anal cancer treatment in Poland, part 1 (source: own analysis)

Type of therapy	patients who underwent a given therapy
radical surgical treatment	61.2%
chemotherapy	52.6%
radiotherapy	42.9%

Table 14. Empirical model of rectal and anal cancer treatment in Poland, part 2 - patients who underwent a given therapy depending on cancer stage (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
radical surgical treatment	95%	79.2%	74.6%	27%
chemotherapy	0%	32.8%	70.9%	65%
radiotherapy	16%	49.8%	69.4%	19%

It is also worth mentioning that the patients in stage I were qualified on the basis of the services which were provided to them, thus making inferences will be fully justified after improving the quality of reporting data from NCR. Until that time one can only make inferences about the frequency of applying specific methods in the area of treating patients with cancer in this stage. In stage IV both the important role of radiotherapy and chemotherapy (most probably palliative) can be observed.

The analysis of Table 15 – shares of patients provided with various types of therapy without the division into stages – shows that the most common rectal and anal cancers treatment is comprehensive therapy using all three methods (21.59% of patients), then the surgery alone (18.70% of patients), monotherapy in the form of chemotherapy (13.63%) and conservative treatment (13.83%).

Table 15. Empirical model of rectal and anal cancers treatment in Poland, part 3 (source: own analysis)

Was surgical treatment provided?			radiotherapy		Total
			NO	YES	
NO – 38.81%	chemotherapy	NO	13.83%	4.83%	18.66%
		YES	13.63%	6.52%	20.14%
	Total		27.46%	11.34%	38.81%
YES – 61.19%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	18.70%	10.00%	28.70%
		YES	10.90%	21.59%	32.49%
	Total		29.60%	31.59%	61.19%

The analysis of Flowchart 9 shows that the most common treatment method of stage II cancer is the surgery (approx. 80%). In almost half of cases it is combined with radiotherapy, in 1/3 cases with chemotherapy (the therapy using all three methods concerns approx. 23% of patients diagnosed in this stage).

In stage III approx. 3/4 of patients undergo surgery, of which 76.5% receive also chemotherapy and 71.7% radiotherapy. In stage IV major surgeries (rectum resections, etc.) are performed in 27% of cases, radiotherapy in 19%, chemotherapy in 65%.

Stage					Including surgical treatment					Including surgical					Including surgical					Including palliative				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	471	6.1%	105	22.4%	NO	22	4.7%	0	0.0%															
					YES	449	95.3%	105	23.5%	NO	449	100.0%	105	23.5%	NO	396	88.3%	102	25.8%	NO	396	100.0%	102	25.8%
															YES	53	11.7%	3	6.5%	NO	53	100.0%	3	6.5%
2	2428	31.3%	364	15.0%	NO	506	20.8%	126	24.9%	NO	367	72.5%	99	27.0%	NO	229	62.4%	61	26.6%	NO	178	77.7%	36	20.2%
																				YES	51	22.3%	25	49.0%
															YES	138	37.6%	38	27.5%	NO	121	87.7%	33	27.3%
																				YES	17	12.3%	5	29.4%
										YES	139	27.5%	27	19.4%	NO	34	24.5%	11	32.4%					
															YES	105	75.5%	16	15.2%	NO	67	63.8%	8	11.9%
																				YES	38	36.2%	8	21.0%
					YES	1922	79.2%	238	12.4%	NO	1265	65.8%	207	16.4%	NO	822	65.0%	155	18.9%	NO	817	99.4%	154	18.8%
																				YES	5	0.6%	1	20.0%
															YES	443	35.0%	52	11.8%	NO	440	99.3%	51	11.7%
																				YES	3	0.7%	1	33.3%
										YES	657	34.2%	31	4.7%	NO	134	20.4%	14	10.4%	NO	126	94.0%	14	11.1%
																				YES	8	6.0%	0	0.0%
															YES	523	79.6%	17	3.2%	NO	519	99.2%	17	3.3%
																				YES	4	0.8%	0	0.0%
3	2230	28.8%	327	14.7%	NO	567	25.4%	195	34.4%	NO	258	45.5%	118	45.7%	NO	152	58.9%	82	54.0%	NO	76	50.0%	36	47.4%
																				YES	76	50.0%	46	60.5%
															YES	106	41.1%	36	34.0%	NO	89	84.0%	30	33.7%
																				YES	17	16.0%	6	35.3%
										YES	309	54.5%	77	25.0%	NO	60	19.4%	27	45.0%	NO	16	26.7%	8	50.0%
																				YES	44	73.3%	19	43.2%
															YES	249	80.6%	50	20.1%	NO	138	55.6%	26	18.8%
																				YES	110	44.4%	24	21.7%
					YES	1664	74.6%	132	8.0%	NO	392	23.5%	69	17.7%	NO	143	36.5%	43	30.1%	NO	135	94.4%	41	30.4%
																				YES	8	5.6%	2	25.0%
															YES	249	63.5%	26	10.6%	NO	247	99.2%	26	10.7%
																				YES	2	0.8%	0	0.0%
										YES	1272	76.5%	63	5.0%	NO	328	25.8%	22	6.7%	NO	314	95.4%	17	5.4%
																				YES	15	4.6%	5	33.3%
															YES	944	74.2%	41	4.3%	NO	939	99.5%	39	4.2%
																				YES	5	0.5%	2	40.0%
4	2620	33.8%	1184	45.2%	NO	1912	73.0%	995	52.0%	NO	799	41.8%	540	67.6%	NO	691	86.5%	479	69.3%	NO	200	28.9%	144	72.0%
																				YES	491	71.1%	335	68.2%
															YES	108	13.5%	61	56.5%	NO	18	16.7%	13	72.2%
																				YES	90	83.3%	48	53.3%
										YES	1113	58.2%	455	40.9%	NO	962	86.4%	390	40.5%	NO	557	57.9%	207	37.2%
																				YES	405	42.1%	183	45.2%
															YES	151	13.6%	65	42.9%	NO	56	36.9%	29	52.0%
																				YES	96	63.1%	36	37.7%
					YES	708	27.0%	189	26.7%	NO	119	16.8%	77	64.7%	NO	88	74.0%	65	73.9%	NO	72	81.8%	57	79.2%
																				YES	16	18.2%	8	50.0%
															YES	31	26.0%	12	38.7%					
										YES	589	83.2%	112	19.0%	NO	382	65.0%	90	23.5%	NO	352	92.2%	78	22.1%
																				YES	30	7.8%	12	40.0%
															YES	206	35.0%	22	10.7%	NO	194	94.2%	21	10.8%
																				YES	12	5.8%	1	8.3%

Flowchart 9. Empirical model of rectal and anal cancer (C20-21) treatment in Poland, part 4 (source: own analysis)

Conclusion

The colorectal cancers are a group of cancers, which origin and development are quite well understood. They pose an epidemiological challenge due to their significant number. In Poland it is necessary to undertake diverse actions in order to reduce the number of cases, reduce the mortality and improve 5-year survival outcomes. Health education, improved reporting and ensuring high quality of screening programmes should result in improvement of outcomes (reduced number of cases) in about ten years. These actions are fully economically justified. Decreasing number of patients and early diagnosis are essential mechanisms for improving the current situation in the field of cancer control. The presented diagnostic and therapeutic procedures do not differ significantly from regimen applied in the highly developed countries, however the degree of their application may be considered insufficient. In case of diagnostics it should be noted that there is no possibility to perform imaging examinations such as MRI. As far as surgeries are concern the use of pre-surgical radiotherapy is standard only in large centres. The surgical techniques including CME are still too rarely used, as well as qualifications for radical metastasectomies.

However it should be noted that January 2015 in Poland saw the start of certain processes, which might bring about changes in this area. For example the requirement to provide cancer patients with multi-disciplinary treatment should improve the treatment results and have an impact on wider use of existing treatment standards using all kinds of available therapies. In subsequent years in most cases surgeries will be performed in centres specialised in oncology. As a result the quality of therapy will improve. The therapy models of rectal and anal cancers indicate that using radiotherapy is an integral part of treatment. The time factor and appropriate irradiation techniques are important factors having impact on long term survival. The therapy regimen of cytostatic drugs and their accessibility do not cause concern. In Poland patients still have a limited access to targeted and innovative therapies.

Bibliography

AJCC Cancer Staging Handbook. 7th Edition (2010). New York: Springer-Verlag, pp. 173–206.

ESMO Clinical Practice Guidelines: Gastrointestinal Cancers. Access: www.esmo.org/Guidelines/Gastrointestinal-Cancers, download date: 17.03.2015.

EUROCARE-5 Database, access: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx, download date: 2.04.2015.

EUROCARE-5 Working Group (2013) *Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5 – a population-based study*, www.thelancet.com/oncology Published online December 5, 2013.

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013) *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet], Lyon: International Agency for Research on Cancer. Access: http://globocan.iarc.fr, download date: 2.04.2015.

Fusch R. et al. (2012*) Nowotwory przewodu pokarmowego*. Warsaw.

Jassem J. et al. (2014)*Nowotwory układu pokarmowego*. Gdańsk.

National Cancer Registry. Access: www.onkologia.org.pl/nowotwory-zlosliwe-jelita-grubego-c18-21, download date: 8.03.2015.

Krzakowski et al. Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych, 2013. Access: www.onkologia.zalecenia.med.pl, download date: 10.03.2015.

NCCN GUIDELINES. Access: www.nccn.org/professionals/physician_gls/pdf/colon.pdf, download date: 13.03.2015.

Program Badań Przesiewowych. Access: www.pbp.org.pl, download date: 13.03.2015.

Treatment pathway model in bladder cancer

Iwona Skoneczna, Beata Koń

Introduction

Bladder cancer[109] is a malignant neoplasm, which is formed from the epithelium lining bladder. The most frequent type of bladder cancer is a transitional cell carcinoma, which constitutes over 90% of all bladder cancers. Other types of this kind of cancer occur less frequently, they may consist of combination of various types of abnormal tissue or other than cancer uniform structure consisting of transitional cells (for example adenocarcinoma or squamous cell carcinoma) (Krzakowski et al. 2011; NCCN 2015).

Smoking increases the risk of developing a bladder cancer – it is almost three times higher among smokers than in case of non-smokers. It is estimated that smoking is responsible for half of new bladder cancer cases, while approx. 1/3 of cases are connected with occupational exposure to carcinogens, including *inter alia* aromatic amines. Some professional groups are particularly exposed to contact with carcinogens. This concerns the workers of the leather industry, rubber industry, persons employed in textile industry, metalworking industry (production of aluminum and steel industry), in processing of crude oil and petroleum products and people having contact with dyes and tannins (Burger et al. 2013).

The aim of this article is to present the structural model of bladder cancer treatment in Poland. The first part of this paper presents an epidemiological analysis covering the the incidence of this type of malignant neoplasm in Poland in relation to other countries and the region. The next part contains an economic analysis of an oncological diagnosis, which includes prevention, screening tests and diagnostic procedures allowing for diagnosis of the cancer. Further, decisional methods describing the treatment regimen for bladder cancer are presented. These are Western empirical models and a theoretical model developed for Poland. Another element of this paper covers an empirical treatment model, which includes information on the structure of patients in Poland, and also information on the treatment

[109] C67 according to ICD-10 classification.

regimen applied in the last years. Based on the data presented, main conclusions from the paper and a summary of this article were formulated and discussed.

Epidemiology

In 2012 bladder cancer was the 9th most frequently diagnosed malignant neoplasm in the world. This type of cancer was diagnosed in 430 thousand patients, and occurred 3 times more often in men than in women. It was not included in the group characterised by the highest case-mortality rate – 165 thousand deaths due to this type of cancer were registered in 2012 (accounting for ca. 10% of deaths caused by lung cancer – which is the type of cancer causing the highest number of deaths) WHO, Cancer Research UK 2014).

According to international statistics prepared by GLOBOCAN[110], the 5-year prevalence of bladder cancer is lower than in the region, and the incidence rate is at the level of the EU average (cf. Figure 1). Additionally, bladder cancer accounted for almost 4% of deaths caused by malignant neoplasms. This value is lower than the average value for southern European or EU countries. When comparing Poland to other countries, one may notice that the percentage value of deaths caused by bladder cancer is higher than in other analysed countries. An equally high proportion is observed in the case of Denmark, and significantly lower in the case of Germany (cf. Figure 1).

[110] It is also worth mentioning the GLOBOCAN methodology – values for Poland were obtained based on three regional registers (Cracow, Kielce and Lower Silesia), which cover 13% of the population - it is disputable whether a sample made up in such a way is representative from the point of view of making inferences about the population of the whole Poland.

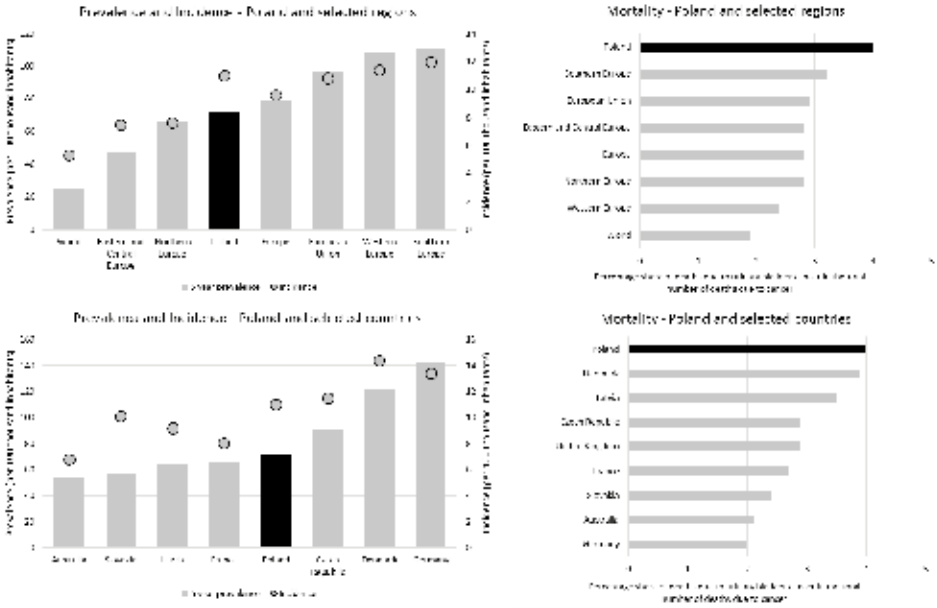


Figure 1. Basic statistics concerning the epidemiology of malignant neoplasm of bladder for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

The value of the unconditional 5-year survival rate for bladder cancer in Poland is 50.9%, which significantly departs from the value of average parameters observed in Western European countries (average value – 58.45%; the highest rates are observed in Southern Europe – 65%) and suggests a large proportion of patients who present with more advanced disease. When comparing the survival rates for Poland to other European countries, a significantly higher probability of surviving 5 years is observed in countries such as Germany or Great Britain. Also Denmark, which observes a similar proportion of deaths caused by bladder cancer as in the case of Poland, achieves higher 5-year survival rate values. In turn, the values for unconditional 5-year survival rate indicate that the most significant treatment phase is the first year from the basic diagnosis. Provided the treatment brings about effects and the patient survives the first year, the probability of him of her surviving the second year increases by almost 10 pp. (cf. Figure 2).

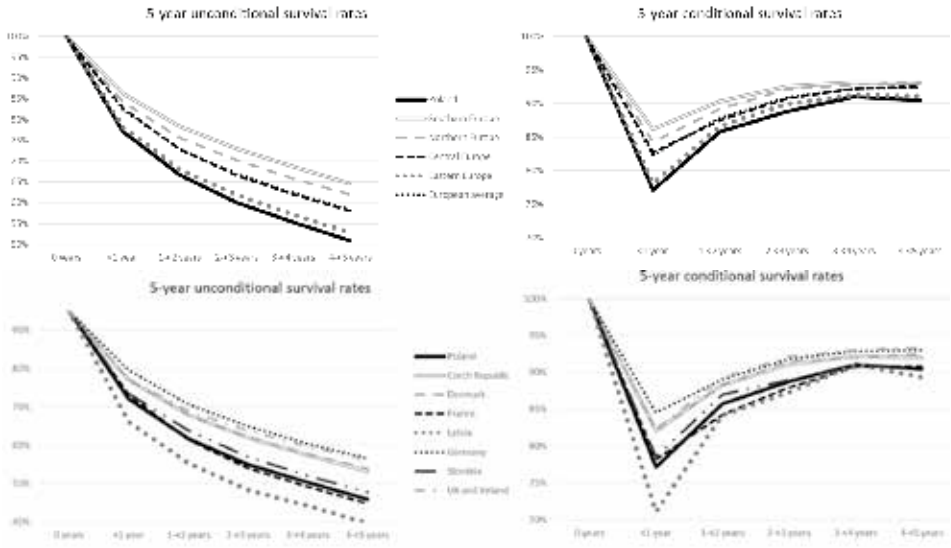


Figure 2. Five-year survival outcomes for patients suffering from malignant neoplasm of bladder in Poland and selected regions(source: own analysis based on EUROCARE – 5)

Economic analysis of cancer diagnostics

Prevention

The main factor increasing the risk of developing bladder cancer is smoking. Smoking is responsible for almost half of all the cases of this type of malignant neoplasm. Basic tasks of primary prevention include all efforts aiming at decreasing the percentage of smokers. Many countries undergo decrease in the rates of smoking, however, abandonment of this addiction is observed mainly among people with higher education and health-related interests. People who continue smoking more often have a lower economic status and represent professions related to chemical and processing industries, the result of which is an increased risk of developing bladder cancer. Popular educational programmes influencing the prevention of bladder cancer should be targeted mainly at supporting the fight against tobacco addiction. This concerns in particular people who are occupationally exposed to aromatic amines and polycyclic hydrocarbons or dyes. Increasing awareness in the context of occupational health and safety aimed at ensuring protection against carcinogen substances could also significantly

contribute to decreasing the incidence of these types of malignant neoplasms. Literature also points to reducing the risk of developing diseases by consuming large amounts of fluids as well as vegetables and fruit (Burger et al. 2013).

Screening tests

In the case of malignant neoplasms of bladder screenings do not have a documented suitability and are not normally recommended by leading scientific associations (cf. NCCN 2015; Babjuk et al. 2015; PTOK 2013; Witjes et al. 2014). It is however indicated that a simple general urinanalysis may in many cases help with early diagnosis of microscopic malignant neoplasm of bladder. Every person, where the urinanalysis reveals hematuria (both microscopic and macroscopic), should immediately be subjected to an ultrasound examination of the abdominal cavity with full bladder, and – in case of finding any irregularities – referred to a urological consultation with the view to undergoing a cystoscopic examination (endoscopy of the urinary bladder) (cf. McDougal et al. 2011; Burger et al. 2013; Krzakowski et al. 2011; NCCN 2015; Babjuk et al. 2015; PTOK 2013; Witjes et al. 2014).

Diagnostics

A characteristic first symptom of bladder cancer is the presence of red blood cells in the urine (hematuria), often with blood clots. Some patients also experience frequent painful urination or urinary retention (inability to empty the bladder despite the pressure on the bladder). Symptoms suggesting a significant advancement of the disease include losing weight, lack of appetite, lower back pain, perineum pain, oedemas of lower limbs. In the case of occurrence of even a single hematuria episode, it is necessary to perform tests aiming at confirming or eliminating the presence of a tumour in the urinary bladder.

The firsts tests should include a general urinanalysis and ultrasonography of the abdominal cavity with full bladder, and then cytoscopy. In case the ultrasonography confirms the presence of a tumour or an infiltration in the bladder wall, the patient is urgently referred to a urologist with a suspicion of neoplastic disease. In any case of the presence of hematuria or suspicion of a urinary bladder tumour, the patient should be immediately subjected to cytoscopy along

with the Transurethral Resection of Bladder Tumour (TURBT), during which it is possible to completely eliminate the disease[111].

In order to diagnose and determine the disease stage and to select an optimal treatment regimen appropriate for the patient's condition, a medical examination, computed tomography or a MRI examination of the abdominal cavity and pelvis is performed. These examinations allow for assessing the disease stage and the condition of upper and lower urinary tracts as well as possible the difficulties in the outflow of urine from the bladder. To receive a complete diagnosis, it is necessary to perform an imaging examination of the chest (e.g. a chest radiograph in two projections or a chest CT scan), bone scintigraphy and CT scan of the brain in the case of a suspicion that the cancer metastasised to bones or the brain. A significant element of the diagnosis is the performance of peripheral blood analyses, paying particular attention to kidney function, which in this diagnosis is frequently compromised (NCCN 2015).

Cancer diagnosis is determined based on a histopathological examination of tissue removed during the Transurethral Resection of Bladder Tumour (TURBT). TURBT is a diagnostic procedure, but in many cases it also constitutes a treatment method. It is crucial that this procedure is performed correctly by an operating urologist – the process of collecting tissue samples should be performed deep enough to ensure that for the histopathological examination not only mucosa with carcinoma infiltration is removed, but also a deeper muscle layer of the urinary bladder. Then the histopathologist is able to actually assess the depth of carcinoma infiltration, which differentiates an invasive cancer from that of a non-invasive nature. In the case of no infiltration of the muscle layer by the cancer structure, the resection is also considered to constitute a complete treatment procedure. However, in some cases it requires the treatment to be complemented with intravesical infusions of cytostatics or BCG (vaccine against tuberculosis). In case of infiltration of the muscle layer of the bladder a more aggressive, usually combined therapy is necessary, and the transurethral resection is only of diagnostic value.

In assessing the malignancy of this neoplasm, instead of applying a traditional grading scale, different types of malignant neoplasm of bladder are divided into non-invasive neoplasms, such as bladder papilloma, of a low malignancy potential (neoplasm with no

[111] In the case of a non-invasive cancer, this type of treatment may be sufficient.

potential to metastasise or infiltrate the bladder, with the tendency to reappear locally), low-grade cancer types and high-grade cancer types related to an aggressive course of the disease. In assessing the disease stage, the TNM staging system is used, where 'T' describes the stage of the disease inside the urinary bladder, 'N' describes the condition of nearby lymph nodes, and 'M' describes distant metastasis (cf. Table 1).

Table 1. TNM classification of malignant neoplasms of bladder (source: own analysis based on AJCC Cancer Staging Manual Ed. 7 2010)

Clinical stage based on TNM			
Stage	**Primary tumour (T)**	**Regional lymph nodes (N)**	**Distant metastasis (M)**
0a	Ta	N0	M0
0is	Tis	N0	M0
I	T1	N0	M0
II	T2a	N0	M0
	T2b	N0	M0
III	T3a	N0	M0
	T3b	N0	M0
	T4a	N0	M0
IV	T4b	N0	M0
	Any T	N1-3	M0
	Any T	Any N	M1

Treatment

Bladder cancer treatment methods are above all dependant on the disease stage and the overall condition of the patient. For treating patients with urothelial cancer limited to the urinary bladder with no infiltration of the muscle layer, the transurethral resection (TURBT) procedure is used. In the case of multiple changes in the urinary bladder, the presence of intraepithelial cancer of high-grade (carcinoma in situ – CIS) or recurrent changes, intravesical infusions may be used as preventive or complementary treatment. These infusions involve injecting, through a bladder catheter, a solution containing the medicine – cytostatics or BCG tuberculosis vaccination. Patients diagnosed with bladder cancer that has infiltrated the muscle layer, but with no distant metastases, must have their urinary bladders removed – i.e.

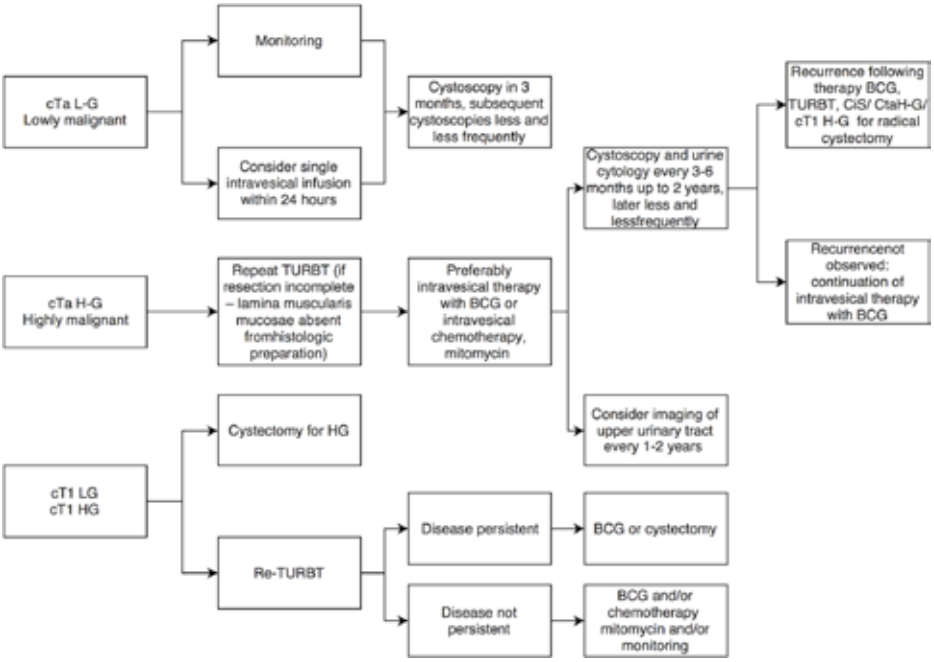
they must undergo the so-called radical cystectomy in case of women or cysto-prostatectomy in case of men, which requires creating a method for the drainage of urine, most frequently in the form of urostomy. The procedure performed in patients in a good overall condition and with proper kidney function parameters should be preceded by a systemic chemotherapy with cisplatin (most frequently applied chemotherapy programmes include: M-VAC, MVC and PG, or more intense ones: HD M-VAC, DD M-VAC, DD PG) (cf. McDougal et al. 2011; Krzakowski et al. 2011; NCCN 2015; PTOK 2013; Witjes et al. 2014). In the case the patient does not consent to bladder removal or there are contraindications to performing such surgery, teleradiotherapy is offered. Patients diagnosed with bladder cancer with distant metastases are referred to oncological consultations in order to determine whether the patient should be subjected to systemic chemotherapy or palliative radiotherapy with the view to extending the survival period and improving the quality of life. All patients undergo palliative procedures, i.e. treatment which aims at reducing disease severity (cf. McDougal et al. 2011; Krzakowski et al. 2011; NCCN 2015; PTOK 2013; Witjes et al. 2014).

Decision-making models in the treatment of malignant neoplasms of bladder

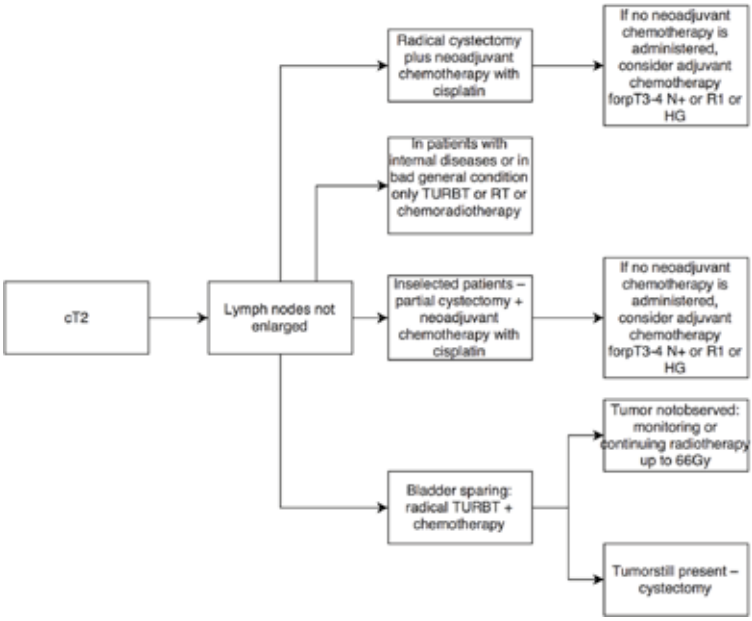
Foreign decision trees

The main treatment option of an advanced, locally invasive bladder cancer is surgery which involves a radical removal of the bladder or the bladder with prostate in the case of men. Alternatively, radiotherapy is considered in the case of patients who do not consent to complete bladder removal or those who cannot undergo such a procedure due to an advanced disease stage or due to the existence of concomitant diseases. Also, the procedure often cannot be performed because of an old age of the patient or his or her poor overall condition. For this reason, in countries where a conservative approach towards therapy dominates (such as Great Britain and Australia), a number of oncological treatment algorithms indicate that radiotherapy is applied to a larger extent than it results from European and American recommendations of urological associations. Treatment programmes involving the so-called ‘saving’ of the urinary bladder through the application of complex combined treatment programmes using transurethral resection procedures and the combination of chemotherapy and radiotherapy may only be offered to a selected group of patients and in specialised

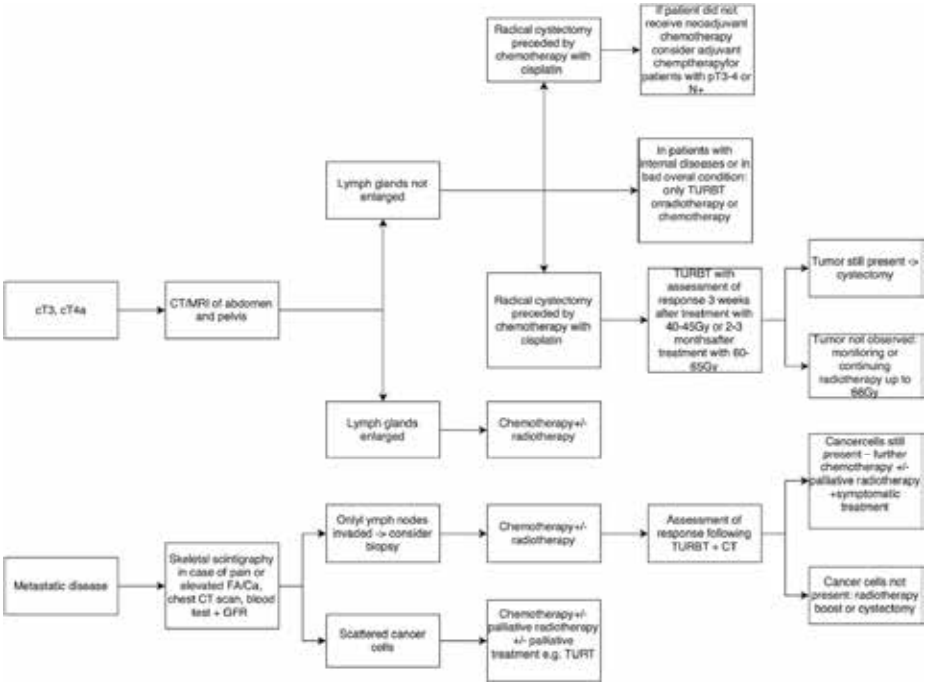
clinics. This results from the necessity for applying therapies in accordance with an approved protocol which aims at minimising the risk of deterioration in the oncological outcome of such an approach (cf. McDougal et al. 2011; Krzakowski et al. 2011; NCCN 2015; PTOK 2013; Witjes et al. 2014). Flowcharts 1, 2 and 3 show a comprehensive approach towards bladder cancer treatment, prepared by the National Comprehensive Cancer Network (NCCN), where the individual approach depends on the cancer grade.



Flowchart 1. Decision tree compliant with NCCN recommendations for bladder cancer from 2015 – grades: cTa LG – low-grade, cTa H-G – high-grade, cT1 LG, cT1HG
(source: own analysis based on NCCN 2015)

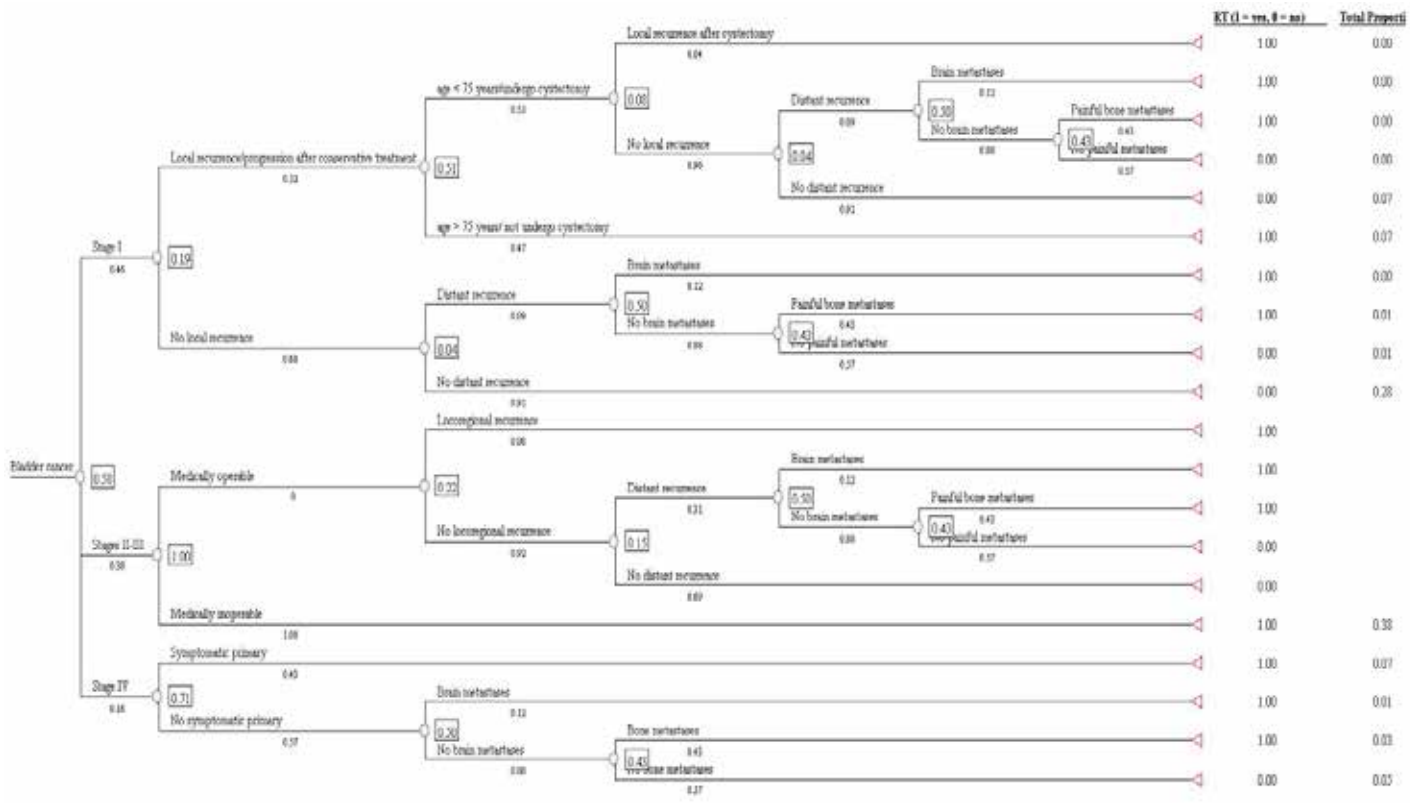


Flowchart 2. Decision tree compliant with NCCN recommendations for bladder cancer from 2015 – grade: cT2 (source: own analysis based on NCCN 2015)



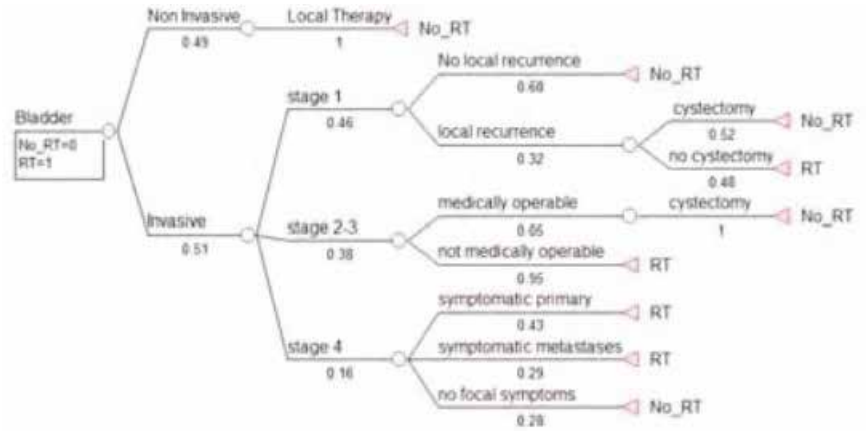
Flowchart 3. Decision tree compliant with NCCN recommendations for bladder cancer from 2015 – grades: cT3, cT4a and metastasised disease (source: own analysis based on NCCN 2015)

The literature also indicates separate recommendations concerning the application of radiotherapy in malignant neoplasm of bladder treatment (cf. Barton et al. 2013, NHS Scotland RT 2005). These recommendations are developed based on treatment outcomes, i.e. in line with the evidence-based medicine approach. Barton et al. (2013) present a decision tree on the application of radiotherapy in malignant neoplasm of bladder treatment developed based on Australian data. The decision on subjecting a patient to radiotherapy is based i.a. on the information on the disease stage, patient's age, metastases or tumour characteristics. It assumes that radiotherapy should be applied mainly where there are metastases or there is no possibility of removing the tumour. In some cases the decision on applying radiotherapy depends on the possibility to perform cystectomy.



Flowchart 4. Decision tree for the application of radiotherapy in Australia (source: Barton et al. 2013)

On the other hand, the recommendations on the alternative application of radiotherapy based on Scottish data are simplified to a larger extent than the Australian recommendations (NHS Scotland RT 2005). However, the conclusions are similar and recommend radiotherapy only in the case or recurrence of the disease or metastases, or if the tumour is inoperable. Pursuant to Western recommendations, radical radiotherapy in the treatment of malignant neoplasm of bladder is used only in rare cases, whereas palliative radiotherapy is often used in metastases causing various ailments or in a locally advanced disease.



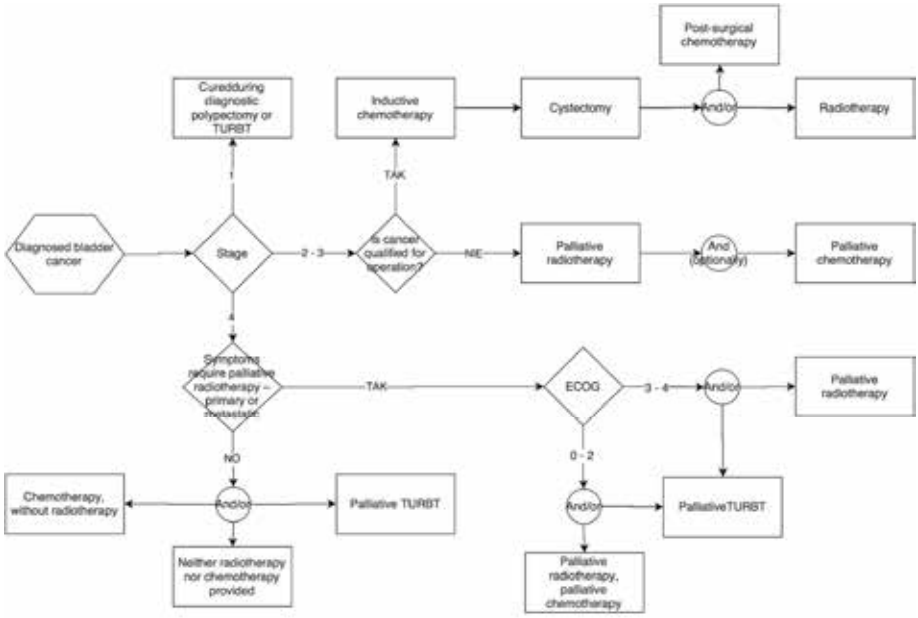
Flowchart 5. Decision tree for the application of radiotherapy in Scotland (source: NHS Scotland 2005)

Decision tree for treatment of malignant neoplasm of bladder in Poland

In Poland the recommendations concerning the treatment of malignant neoplasm of bladder are developed by Polish Society of Clinical Oncology (PTOK 2013) and the Polish Urological Association (PTU), based on recommendations of the European Association of Urology (EAU 2014). They include diagnostic and therapeutic standards in case of this type of neoplasm and other urogenital neoplasms. On the basis of them, as well as international recommendations, a theoretical decision-making model of diagnosed malignant neoplasm of bladder was developed (cf. Flowchart 6).

The developed model of bladder cancer treatment shows that initial stages are treated mainly based on diagnostic and therapeutic procedures, such as TURBT. BCG infusions

and active patient observation are also used. In stages II and III, when the tumour may be removed, radical surgical treatment, i.e. cystectomy or cystoprostatectomy in men, is also applied. Radical cystectomy or cystoprostatectomy is usually preceded by transurethral diagnostic and therapeutic procedure, i.e. transurethral resection of bladder tumour (TURBT). In line with international recommendations for patients who qualify for cisplatin treatment regimens, radical cystectomy or cystoprostatectomy should be preceded by chemotherapy, and in some cases additionally followed by chemotherapy or radiotherapy. In the bladder cancer is as an advanced stage with metastases, palliative chemotherapy or radiotherapy is used (NCCN 2015; PTOK 2013, EAU 2014).



Flowchart 6. Model of bladder cancer treatment in Poland (source: own analysis)

Empirical model of bladder cancer treatment

The first necessary element to develop an empirical treatment model is to estimate annual incidence, i.e. the number of patients with newly diagnosed malignant neoplasm of bladder. The National Cancer Registry database is the main source of such information.

According to the NCR database[112], in 2012, 5,833 new cases of bladder cancer were diagnosed, of which for over 30% the disease stage was not specified. In addition, the share of such patients was relatively stable in the years 2010-2012 and has not improved in recent years (cf. Table 2).

Table 2. Distribution of information on cancer stage in NCR database for new patients (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	1	7	3	0%	0%	0%
II	3,327	3,155	3,113	54%	53%	53%
III	607	551	468	10%	9%	8%
IV	483	455	417	8%	8%	7%
Stage not recorded in NCR	1,696	1,773	1,832	28%	30%	31%
Total	6,114	5,941	5,833	100%	100%	100%

Among persons with a known cancer stage, the largest group of patients in the NCR database comprises patients with stage II of the diseases (approx. 75%); the share of patients with advanced bladder cancer is relatively small. The notable fact is the insignificant number of patients with the initial stage of the disease (stage I) in the NCR database (cf. Table 3). Such data may be due to the moment of reporting the neoplastic disease to the NCR, which may take place after the diagnostic transurethral resection of bladder tumour (TURBT). At this stage of the diseases, only histopathological results are available, which in practice prevents the classification of patients into those with disease in stage I (non-invasive) and stage II or further (invasive cancer).

Due to a significant proportion of patients with an unidentified stage of cancer in the NCR database, the stage of malignant neoplasm was estimated on the basis of an analysis including information about services provided to patients with C67 diagnosis and reported to the National Health Fund. However, an assumption was made that some persons who did

[112]The figures presented by NCR have been initially verified based on NHF database. This means that they do not include patients who appeared for the first time in the NCR database in a given year with breast cancer diagnosis and who were recorded with the diagnosis in the NHF database before that year.

not have the NCR entry, but received services in relation to malignant neoplasm of bladder, are not new patients. They are persons who did not receive appropriate treatment for this time of cancer during 365 days from the diagnosis and the services provided included mostly diagnostic procedures. In line with the adopted methodology, a significant part of this group of patients was classified as persons under observation. Some of them were classified into the group of patients with a wrong C67 diagnosis in the NHF reports.

In order to estimate the stage of the diseases in patients who were not reported to the NCR database, but received services, settled by the NHF, in relation to bladder cancer diagnosis, and to identify the groups of patients with wrong diagnosis or under observation, the analysis of procedures performed within 365 from the first service provided with the C67 diagnosis was carried out. The categorisation used allowed to classify approx. 32% persons from that group as patients wrongly reported as diagnosed with bladder cancer. They are persons who were not entered into the NCR and did not receive services in relation to bladder cancer since 2009 in hospital treatment and outpatient specialist care, and the medical services provided to those persons within 365 days of their entry into the system concerned diagnostic procedures and procedures that were not appropriate for diagnosis and treatment of bladder cancer. They most likely included patients who, despite recommendations, were not reported to the NCR or were subject to diagnostic procedures with reported diagnosed malignant neoplasm, although the histopathological analysis did not confirm that diagnosis. The group of another 33% of patients are persons under observation, and a further 26% are patients with stage IV of the disease (cf. Table 3). A significant percentage of persons with stage IV of the disease points to a particularly low reporting of this stage to the NCR. In an analysis based on the NHF data, only a small percentage of patients were classified into stages I-III, which demonstrates the completeness of the NCR database for early stages of bladder cancer.

Table 3. Cancer stage categorization of new patients who were not recorded in NCR database, but who received oncological services according to NHF database (source: own analysis)

	Absolute value			%		
Stage	2010	2011	2012	2010	2011	2012
I	63	64	67	1%	1%	1%
II	167	181	169	2%	2%	2%
III	443	462	421	6%	6%	6%
IV	1,983	1,972	1,831	25%	26%	26%
other cause	2,611	2,429	2,312	33%	32%	32%
follow-up	2,620	2,440	2,321	33%	32%	33%
Total	7,887	7,548	7,121	100%	100%	100%

The above approach was also used with respect to patients entered into the NCR database, with an unspecified stage of the disease. However, the assumption of a wrong bladder cancer diagnosis in this group of patients was abandoned. Therefore, patients without the specified stage in the NCR were assigned to groups with stage I-IV of the disease or patients under observation. The cumulative distribution of newly diagnosed patients according to the adopted methodology is presented in Table 4. It also includes patients for whom it was impossible to defined the cancer stage. They are persons who were included in the National Cancer Registry database, but did not receive any medical services settled by the NHF. They are most likely the patients who started the bladder cancer treatment in private health care service.

Table 4. Cumulative distribution of incidence against cancer stage for years 2010-2012 (source: own analysis)

Stage	Absolute value			%		
	2010	2011	2012	2010	2011	2012
1	567	632	647	6%	7%	8%
2	3,623	3,477	3,435	42%	41%	41%
3	1,205	1,173	1,054	14%	14%	13%
4	3,316	3,285	3,143	38%	38%	38%
impossible to define	17	12	13	0%	0%	0%
Total	8,728	8,579	8,292	100%	100%	100%

The completeness of NCR database for newly diagnosed patients in 2010–2012 amounted to 70%, 69% and 70%, respectively. However, in terms of completeness of data with information about the stage of cancer, the values are significantly lower and amount to 51%, 49% and 48%, respectively, for 2010-2012.

Summing up, the largest group of patients with bladder cancer in Poland are patients with stage II and stage IV of the disease. The group with stage I cancer is small.

The definition of the group of new patients allows to project the treatment model for malignant neoplasm of bladder in Poland. Due to the specific characteristics of malignant neoplasm of bladder, the analysis covered surgical treatment, chemotherapy and radiotherapy, as well as transurethral diagnostic and treatment procedures[113], which are often used in early stage bladder cancer treatment (they are also necessary to diagnose a more advanced cancer). The infusions of BCG vaccine were also quantified. The data for 2012 reveal that transurethral diagnostic and therapeutic procedures were very often used in bladder cancer and were provided to over 75% of patients. Surgical procedures (radical procedures, i.e. cystectomies or cystoprostatectomies) were significantly less frequent and were performed only in 16.8% of newly diagnosed patients. Almost 16% of patients received chemotherapy, which shows that a significant part of patients who underwent radical surgeries had the disease in a more advanced stage, requiring combined treatment. Radiotherapy was relatively seldom used in this type of malignant neoplasm. BCG infusion was used in over 3% of patients (cf. Table 5).

Table 5. Empirical model of malignant neoplasm of bladder treatment in Poland, part 1 (source: own analysis)

Type of therapy	Patients who underwent a given therapy
transurethral diagnostic and therapeutic procedures	77.9%
surgical treatment	16.8%
chemotherapy	15.9%
radiotherapy	4.8%
BCG infusion	3.3%

[113] Pursuant to the treatment description, this group involves mainly transurethral electroresections of bladder tumour (TURBT).

The cancer treatment method depends largely on the stage of the disease. Based on this assumption, as attempt was made at estimating the stage of the disease in subsequent years, on the basis of the NHF data from reporting on individual services provided. Empirical data on provided services were assigned to the stage of the disease. The main treatment methods in stage I included transurethral diagnostic and therapeutic procedures or BCG infusions. The assumption was that that stage did not involve any chemotherapy, radiotherapy or major surgical procedures appropriate for that malignant neoplasm. Transurethral diagnostic and therapeutic procedures were often used for patients with stage II in the NCR and for patients for whom the stage was estimated, with 90% of patients receiving such procedures. Surgical procedures were reported for almost 40% of patients for whom stage III of the disease was estimated based on provided services and for patients with this stage included in the NCR. The percentage of patients who received chemotherapy or radiotherapy was higher. Patients with malignant neoplasm at the most advanced stage, after the tumour diagnosis (TURBT), are usually treated using chemotherapy (cf. Table 6). Special attention should also be paid to transurethral diagnostic and therapeutic procedures, and in particular to their nature. At early stages of the disease, they may be classified into treatment procedures, but as the disease progresses, their function becomes mainly diagnostic.

Table 6. Empirical model of malignant neoplasm of bladder treatment in Poland, part 2 - patients who underwent a given therapy depending on stage (source: own analysis)

Type of therapy	stage I	stage II	stage III	stage IV
transurethral diagnostic and therapeutic procedures	91%	90.0%	70.4%	64.5%
surgical treatment	0%	17.7%	39.6%	11.7%
chemotherapy	0%	10.6%	14.3%	25.4%
radiotherapy	0%	5.8%	8.3%	3.6%
BCG infusion	10%	2.4%	3.7%	2.9%

The subsequent stage of the analysis is to identify the simultaneous use of transurethral diagnostic and therapeutic procedures, surgical procedures, chemotherapy and radiotherapy. The largest group comprises patients who underwent only diagnostic and therapeutic treatment procedures (cf. Table 7). They are mainly patients with stage I of the disease, where treatment consists in transurethral procedures, such as TURBT, and patients with terminal

stage of the disease who did not manage to receive palliative care services. Subsequent groups in terms of number are patients who did not undergo any of the four above-mentioned treatments. They most likely include also patients with stage IV of the disease with their only treatment being palliative care. Another group consists of patients who underwent both surgical treatment and transurethral diagnostic and therapeutic procedures.

In addition, Flowcharts 7, 8 and 9 present precise treatment pathways for patients with a diagnosed malignant neoplasm of bladder. They include additional information about patient deaths within 365 days from the diagnosis, as well as about the use of palliative treatment (including palliative radiotherapy) or BCG infusion.

Table 7. Empirical model of malignant neoplasm of bladder treatment in Poland, part 3 (source: own analysis)

Transurethral diagnostic and therapeutic procedures	Radical surgery					
YES – 77.87%	YES – 13.33%			radiotherapy		Total
				NO	YES	
		chemotherapy	NO	9.53%	0.30%	9.83%
			YES	3.29%	0.21%	3.50%
		Total		12.82%	0.51%	13.33%
	NO – 64.54%			radiotherapy		Total
				NO	YES	
		chemotherapy	NO	54.30%	2.17%	56.47%
			YES	7.40%	0.67%	8.06%
		Total		61.70%	2.83%	64.54%
NO – 22.13%	YES – 3.51%			radiotherapy		Total
				NO	YES	
		chemotherapy	NO	2.70%	0.06%	2.76%
			YES	0.62%	0.13%	0.75%
		Total		3.32%	0.19%	3.51%
	NO – 18.62%			radiotherapy		Total
				NO	YES	
		chemotherapy	NO	14.21%	0.86%	15.07%
			YES	3.11%	0.44%	3.55%
		Total		17.33%	1.30%	18.62%

Stage					Including intravesical diagnostic and therapeutic tratment					Including BCG infusion					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
1	647	7.8%	0	0.0%	NO	60	9.2%	0	0.0%	NO	40	66.4%	0	0.0%																				
										YES	20	33.6%	0	0.0%																				
					YES	587	90.8%	0	0.0%	NO	544	92.7%	0	0.0%	NO	544	100.0%	0	0.0%	NO	544	100.0%	0	0.0%	NO	544	100.0%	0	0.0%	NO	544	100.0%	0	0%
										YES	43	7.3%	0	0.0%																				
2	3422	41.4%	412	12.0%	NO	343	10.0%	62	18.1%	NO	335	97.8%	61	18.2%	NO	224	66.8%	40	17.9%	NO	215	96.0%	38	17.7%	NO	188	87.2%	38	20.3%	NO	146	77.6%	21	14%
																														YES	42	22.4%	17	40%
																									YES	27	12.8%	0	0.0%					
																				YES	9	4.0%	2	22.2%										
															YES	112	33.2%	21	18.8%	NO	94	83.9%	16	17.1%	NO	93	99.5%	16	17.2%	NO	92	98.9%	15	16%
																														YES	1	1.1%	1	100%
																									YES	0	0.5%	0	0.0%					
																				YES	18	16.1%	5	27.8%										
										YES	8	2.2%	1	13.3%																				
					YES	3079	90.0%	350	11.4%	NO	3006	97.6%	339	11.3%	NO	2529	84.1%	266	10.5%	NO	2308	91.3%	243	10.5%	NO	2198	95.3%	225	10.2%	NO	1710	77.8%	86	5%
																														YES	488	22.2%	139	28%
																									YES	109	4.7%	18	16.4%	NO	61	55.7%	6	10%
																														YES	48	44.3%	12	25%
																				YES	221	8.7%	23	10.4%	NO	191	86.4%	22	11.5%	NO	119	62.3%	8	7%
																														YES	72	37.7%	14	19%
																									YES	30	13.6%	1	3.3%					
															YES	477	15.9%	73	15.3%	NO	387	81.1%	58	15.0%	NO	371	95.9%	55	14.8%	NO	359	96.8%	50	14%
																														YES	12	3.2%	5	42%
																									YES	16	4.1%	3	18.8%					
																				YES	90	18.9%	15	16.7%	NO	85	94.4%	14	16.5%	NO	78	91.8%	10	13%
																														YES	7	8.2%	4	57%
																									YES	5	5.6%	1	20.0%					
										YES	74	2.4%	11	15.0%	NO	58	78.9%	7	12.1%	NO	43	74.1%	7	16.3%										
																				YES	15	25.9%	0	0.0%										
															YES	16	21.1%	4	25.8%																

Flowchart 7. Empirical model of bladder cancer treatment in Poland, part 4a (source: own analysis)

Stage					Including intravesical diagnostic and therapeutic tratment					Including BCG infusion					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
3	1054	12.8%	382	36.3%	NO	312	29.6%	133	42.7%	NO	302	96.8%	129	42.8%	NO	207	68.4%	116	56.0%	NO	196	94.7%	114	58.2%	NO	170	86.8%	111	65.3%	NO	109	64.0%	61	56%
																														YES	61	36.0%	50	82%
																									YES	26	13.2%	3	10.8%					
																				YES	11	5.3%	2	18.2%										
															YES	96	31.6%	13	14.0%	NO	78	81.6%	13	17.2%	NO	76	98.1%	13	17.5%	NO	75	98.7%	13	18%
																														YES	1	1.3%	0	0%
																									YES	2	1.9%	0	0.0%					
																				YES	18	18.4%	0	0.0%										
										YES	10	3.2%	4	40.6%																				
					YES	741	70.4%	249	33.6%	NO	713	96.1%	235	33.0%	NO	407	57.2%	177	43.5%	NO	364	89.3%	160	44.0%	NO	331	91.0%	156	46.9%	NO	156	47.1%	56	36%
																														YES	175	52.9%	100	57%
																									YES	33	9.0%	5	14.1%					
																				YES	43	10.6%	17	39.2%										
															YES	305	42.8%	58	18.9%	NO	235	77.1%	39	16.4%	NO	232	98.7%	38	16.2%	NO	223	96.1%	33	15%
																														YES	9	3.9%	5	56%
																									YES	3	1.3%	1	33.3%					
																				YES	70	22.9%	19	27.1%	NO	67	95.1%	18	27.0%	NO	59	88.0%	13	22%
																														YES	8	12.0%	5	62%
																									YES	3	4.9%	1	29.4%					
										YES	29	3.9%	14	49.3%																				

Flowchart 8. Empirical model of bladder cancer treatment in Poland, part 4b (source: own analysis)

Stage					Including intravesical diagnostic and therapeutic tratment					Including BCG infusion					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths	NO/YES	Number of cases	Share	Number of deaths	% of deaths
4	3137	38.0%	1321	42.1%	NO	1113	35.5%	534	48.0%	NO	1087	97.6%	522	48.0%	NO	1014	93.3%	477	47.1%	NO	751	74.1%	375	50.0%	NO	738	98.3%	368	49.9%	NO	241	32.7%	190	79%
																														YES	497	67.3%	178	36%
																									YES	13	1.7%	7	56.2%					
																				YES	263	25.9%	102	38.8%	NO	240	91.2%	95	39.6%	NO	139	57.9%	37	27%
																														YES	101	42.1%	58	57%
																									YES	23	8.7%	7	30.4%					
															YES	73	6.7%	45	61.2%	NO	47	63.9%	31	65.7%										
																				YES	26	36.1%	14	53.2%										
										YES	26	2.4%	12	45.1%																				
					YES	2024	64.5%	787	38.9%	NO	1959	96.8%	761	38.8%	NO	1679	85.7%	638	38.0%	NO	1313	78.2%	562	42.8%	NO	1280	97.5%	546	42.7%	NO	281	21.9%	216	77%
																														YES	1000	78.1%	330	33%
																									YES	33	2.5%	15	46.7%					
																				YES	366	21.8%	76	20.8%	NO	349	95.5%	72	20.6%	NO	206	59.0%	23	11%
																														YES	143	41.0%	49	34%
																									YES	17	4.5%	4	24.1%					
															YES	280	14.3%	123	44.0%	NO	170	60.6%	90	53.2%	NO	165	97.1%	86	52.4%	NO	153	92.7%	80	53%
																														YES	12	7.3%	6	50%
																									YES	5	2.9%	4	80.0%					
																				YES	110	39.4%	33	29.9%	NO	102	92.2%	30	29.5%	NO	88	86.2%	21	24%
																														YES	14	13.8%	9	64%
																									YES	9	7.8%	3	34.9%					
										YES	65	3.2%	26	40.1%	NO	53	81.6%	22	42.1%	NO	35	65.8%	14	40.9%										
																				YES	18	34.2%	8	44.4%										
															YES	12	18.4%	4	31.1%																

Flowchart 9. Empirical model of bladder cancer treatment in Poland, part 4c (source: own analysis)

Conclusion

Malignant neoplasm of bladder is the 9th most common neoplasm in the world, which occurs predominantly in the male population. International comparisons indicate that Poland faces an unfavourable epidemiological situation. This requires the introduction of some changes in the oncological care system, which would allow for improvement in disease outcomes. Health education of Poles and promoting preventive measures seems to be of particular importance.

Results of the analysis indicate underestimation in the National Cancer Registry database, which may lead to an incorrect analysis of the entire oncological care system in Poland. The low level of completeness (ca. 50%) of data for patients in specified stages of disease progression is particularly problematic. The methodology used allowed to determine the dimension of this problem and estimate the missing values, however it is necessary to improve the reporting of data to the NCR in the future.

The empirical data derived based on the methodology addressing the missing values in the NCR indicate a relatively large proportion of patients who were treated only by means of transurethral resection procedures. According to the recommendations, such procedures should only be used in the case of patients in stage I cancer, as the relevant recommendation for stage II patients should be radical treatment. However, of very particular concern is the negligible percentage of patients who receive intravesical treatment, which should be characteristic of stage I disease, and illustrates the virtual absence of a proper procedure, i.e. the combination of a urological procedure with chemotherapy applied within the first 24 hours from performing the transurethral resection. What is more, the developed empirical model of treatment indicates that patients who were treated using transurethral diagnostic and therapeutic procedures constitute the largest group of patients. Such procedures constituted a treatment method offered to patients in early disease stages. However, of very particular concern is the small number of patients who received treatment complemented with BCG infusions, as well as the complete absence of intravesical chemotherapy applied within the first 24 hours from performing transurethral resection, which is recommended by all scientific associations (lack of technical capacity to prepare the cytostatic in the majority of urological wards and absence of a procedure for simultaneous refund of chemotherapy and surgery).

Another issue is the low percentage of radical surgical procedures – cystectomy and cysto-prostatectomy, which may be due to various reasons. Radical cystectomy or cysto-prostatectomy is a burdensome procedure for the patient. Global and national epidemiological data indicate a large percentage of elderly patients, who, as a general rule, are in more advanced stages of disease progression. These patients often have co-existing conditions that preclude the possibility of performing such procedures. Some patients refuse consent to have their urinary bladders removed – usually these patients are referred to undergo radiotherapeutic treatment. Another problem are constraints from urologists and the refund system. Radical cystectomy and cystoprostatectomy are one of the most extensive and most difficult surgeries in urologic oncology. The surgery requires the removal of the bladder and the reproductive organs in women and the removal of the bladder and the prostrate in men. The next stage is to create a new way to pass urine from the body and it may consist of creating an urostomy or reconstructing the bladder from the intestine (the so-called intestinal bladder). The third stage of the procedure is an extensive removal of the lymph nodes (it is recommended to remove more than 15 nodes). All these elements require the urological surgeon to have a vast surgical experience. The average time needed to perform such a surgery in specialist medical centres is 3-4 hours and the hospitalisation time is approximately 14 days. There are still few urology centres in Poland that have experience in performing such surgeries. Increasing the surgical capacity of centres which are prepared for it, so those which currently perform for instance a minimum of 50 cystectomy or cystoprostatectomy surgeries a year, should be considered.

Bibliography

AJCC Cancer Staging Manual. 8th Edition 2014. Accessed on: https://cancerstaging.org, date downloaded: 4.05.2015.

Babjuk M., Böhle A., Burger M., Compérat E., Kaasinen E., Palou J., Rouprêt M., van Rhijn B.W.G., Shariat S., Sylvester R., Zigeuner R., *Guidelines on Non-muscle-invasive Bladder Cancer (Ta, T1 and CIS)*. Accessed on: http://uroweb.org/guideline/non-muscle-invasive-bladder-cancer.

Barton M., Jacob S., Shafiq J., Hsin Wen Wong K., Thompson S., Delaney G., Hanna T. (2013) *Review of optimal radiotherapy utilization rates*.

Burger M., Catto J.W.F., Dalbagni G., Grossman H.B., Herr H., Karakiewicz P., Kassouf W., Kiemeney L.A., La Vecchia C., Shariat S., Lotan Y. (2013) Epidemiology and Risk factors of Urothelial Bladder Cancer. *European Urology*, Volume 63 Issue 2, pp. 234–241.

EUROCARE-5 Database, Accessed on: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx, date downloaded: 2.04.2015.

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013), *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet], Lyon: International Agency for Research on Cancer. Accessed on: http://globocan.iarc.fr, date downloaded: 2.04.2015.

National Cancer Registry, accessed on: http://epid.coi.waw.pl/krn, date downloaded: 8.04.2015.

Krzakowski M., Dziadziuszko R., Fijuth J. et al. (eds.) (2011) *Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych*. Gdańsk: Wydawnictwo Via Medica.

McDougal W.S., Shipley W.U., Kaufman D.S., Dahl D.M., Michaelson M.D., Zietman A.L. (2011) *Cancer of the Bladder, Ureter, and Renal Pelvis*, [in]: De Vita V.T., Lawrence T.S., Rosenberg S.A., eds. Cancer, Principles and Practice of Oncology. Vol. I, No. 159, pp. 1358–1384.

NCCN Guidelines ver. 1.2015. Bladder Cancer. Accessed on: http://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf, date downloaded: 8.04.2015.

Polskie Towarzystwo Onkologii Klinicznej, Stelmach A., Potemski P. (eds.) (2013) *Nowotwory układu moczowo-płciowego*. Accessed on: http://www.onkologia.zalecenia.med.pl/pdf/PTOK_2013_07_Nowotwory%20ukladu%20moczowo-plciowego.pdf, date downloaded: 13.04.2015.

Witjes J.A., Compérat E., Cowan N.C., De Santis M., Gakis G., Lebret T., Ribal M.J., Van der Heijden A.G., Sherif A. (2014) *EAU guidelines on muscle-invasive and metastatic bladder cancer*, European Association of Urology, Vol. 65, No. 4, pp. 778–792.

World Health Organization, Cancer Research UK (2014) World Cancer Factsheet, 2014. Accessed on: http://publications.cancerresearchuk.org/downloads/Product/CS_REPORT_WORLD.pdf, date downloaded: 8.04.2015.

Treatment pathway model in prostate cancer

Iwona Skoneczna, Janusz Dagiel

Introduction

Cancer of the prostatic gland, also referred to as prostate cancer, is a malignant neoplasm developing within this gland. The prostatic gland produces seminal fluid which serves as a natural environment for sperm cells. The majority of malignant neoplasms of the prostatic gland are cancers of the glandular tissue of the prostate – the so-called adenocarcinomas of the prostate or prostatic gland. One can usually establish whether a given person can be suspected of suffering from prostatic gland cancer after measuring the concentration of PSA (Prostatic Specific Antigen) in the serum and by means of a *per rectum* examination. The alarming symptoms include the detection of hard nodule within the prostatic gland or increased compactness of the prostate. If a diagnostician suspects that the patient may be suffering from prostate cancer, he usually orders histopathological samples to be taken – nowadays mostly by means of core needle biopsy monitored via trans-rectal ultrasound.

The aim of this article is to present how prostate cancers are treated in Poland. The first part of the article presents medical aspects, i.e. epidemiology, diagnostic methods and treatment of cancer in Poland. The second part is a presentation of the results of an analysis of estimated prostate cancer incidence in Poland, taking account of an empirical model of patient treatment.

Epidemiological analysis

Prostatic gland cancer is a common malignant neoplasm among men both in terms of new cases, as well as in terms of prevalence and case-fatality rate. In 2012 there were 10 798 new cases (14.34% of all cases, second most common malignant neoplasm among men, standardised incidence factor = 36.1) and 4 199 deaths (7.97% of all deaths, second greatest death frequency, standardised deaths factor) caused by this malignant neoplasm in Poland (NCR). Prostate cancer is a disease diagnosed most frequently among men over 65 years of age (70% of new cases, 90% of deaths), while the risk of death increases with age. The 5-year

survival rate for prostate cancer in Poland is 53.26% and is significantly divergent from the values observed in Western European countries (average: 69.7%, highest values in France – 75.79%), which may suggest a significant percentage of patients suffering from initially advanced disease (EUROCARE 5). Five and ten year prevalence amounts to, respectively, 37 396 and 55 698 persons (NCR). Prostate cancer is the most common cancer in the world (aside from skin neoplasms) and the second most common cause of death due to neoplastic diseases. In Europe there were 400 thousand new cases and 92 thousand deaths in 2012, while the 5-year prevalence amounted to nearly 1.5 million people (GLOBOCAN).

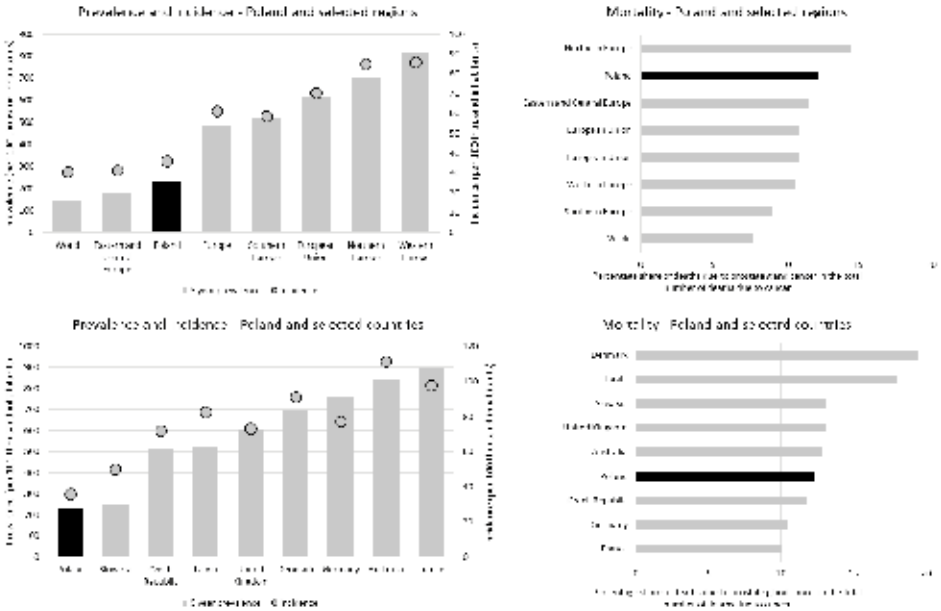


Figure 1. Basic statistics concerning the epidemiology of malignant neoplasm of prostate for Poland and selected regions (source: own analysis based on GLOBOCAN 2012)

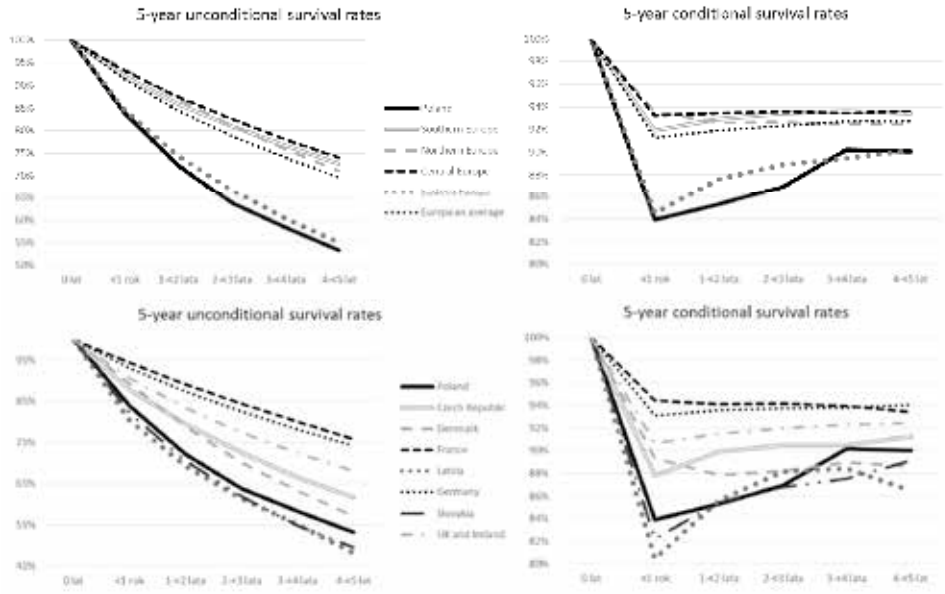


Figure 2. Five-year survival outcomes for patients suffering from malignant neoplasm of prostate for Poland and selected regions(source: own analysis based on EUROCARE – 5)

Cancer diagnostics

The diagnosis of prostate cancer is based on microscopic examination of patient's tissue samples (usually it is a prostate biopsy). Additionally, blood tests and imaging studies are necessary in order to determine the stage of the disease and plan therapy.

To evaluate the stage, the four-stage system of the American Joint Committee on Cancer (AJCC) is used where subsequent stages are marked with I, II, III, and IV, the TNM staging system is used, where 'T' describes the stage of the disease inside the prostate, 'N' describes the condition of the lymph nodes, and 'M' describes distant metastasis.

Table 1. Anatomic stage of malignant neoplasm of prostate based on TNM staging (source: own analysis based on Edge et al. 2010)

Clinical stage based on TNM					
Stage	**Primary tumour (T)**	**Regional lymph nodes (N)**	**Distant metastasis (M)**	**PSA**	**Gleason**
I	T1a-c	N0	M0	<10	<=6
	Twa	N0	M0	<10	<=6
	T1-2a	N0	M0	X	X
IIA	T1a-c	N0	M0	<20	7
	T1a-c	N0	M0	<10;20)	<=6
	T2a	N0	M0	<20	<=7
	T2b	N0	M0	<20	<=7
	T2b	N0	M0	X	X
IIB	T2c	N0	M0	Any	Any
	T1-2	N0	M0	>=20	Any
	T1-2	N0	M0	Any	Any
III	T3a-b	N0	M0	Any	>=8
	T4	N0	M0	Any	Any
IV	Any	N1	M0	Any	Any
	Any	Any	M1	Any	Any

To determine the stage and optimal treatment, a medical examination is performed (including necessarily the *per rectum* examination), a TRUS examination (a transrectal ultrasound examination), PSA is determined, a histopathological/microscopic examination of biopsy samples from the prostate, imaging study of the chest and abdomen, such as pelvis MRI (Magnetic Resonance Imaging), chest X-ray, abdomen ultrasound examination, possibly also a CT scan od the chest, abdomen, and pelvis, bone scintigraphy, and bone X-ray or MRI if metastasis to bones is suspected. The grade is determined by a histopathologist on the basis of a microscopic image of biopsy specimens (tumour samples collected during a biopsy) or neoplastic tissue samples. The so-called Gleason Score or Gleason Sum is the most commonly used scale. A cancer can be attributed between 2 and 10 points. The higher the score, the greater the cancer grade (and a more aggressive course of the disease is predicted).

Treatment

The modalities of prostate cancer treatment depend primarily on the stage, but also on age of the diagnosis, general condition of the patient, and co-occurring diseases, such as heart disease, hypertension, diabetes, and excessive weight. In many cases, it is advisable that the patient consults various specialists taking part in his therapy before making the decision on treatment. These are the so-called multidisciplinary consultation with a team of physicians, including an urologist (surgeon), oncologist, radiotherapist and often also a clinical oncologist. The team may also include a psycho-oncologist and physiotherapist. Preferences of patients, who may decide about their treatment based on information obtained from the specialist physician, are increasingly important in oncological treatment. Regrettably, despite the progress in medicine and oncology, some therapies still entail the risk of complications, such as change in the patient's appearance or limitations in everyday functioning, and therefore it is important that a patient is made aware of it.

As a result of greater accessibility of such tests as PSA, the number of cancers diagnosed at early stages is increasing around the world, some of them are more benign and progress so slowly that they pose no threat to the patient; in such case aggressive treatment is not required. However, at the same time urological and oncological observation is conducted to ensure that the appropriate treatment will be initiated if necessary. Such procedure is called active surveillance.

Apart from division into TNM stages and stages I-IV, according to the AJCC, prostate cancer is also divided, depending on predicted risk of progression and course of the disease, into low (good prognosis), intermediate and high risk cancers.

Radical treatment is the treatment aimed at full recovery. It is possible only at early stages of the disease when cancer cells are located only in the prostatic gland. Until recently, metastatic lesions were the factor excluding radical treatment, but for several years radical therapies have been allowed in young patients with single metastases. There are two basic types of radical treatment: surgical treatment and irradiation.

Surgical treatment consists in resection of the entire prostatic gland along with seminal vesicles (radical prostatectomy). It is usually done by open surgery (incision in the lower abdomen) or by laparoscopic surgery in specialist centres. The surgery is offered to patients

in good condition, with the predicted survival over 10 years. The possible complications, as in the case of other surgeries, include bleeding and infections. Specific complications after such procedures, in particular in the case of large tumours, include erectile dysfunction, urinary incontinence (uncontrolled leakage of urine from the bladder) and sometimes also postoperative urethral stricture which results in difficulties in urinating. After each procedure, microscopic analysis of the removed tissues is performed and the type and size of cancer is finally determined. This provides the basis for the urologist or oncologist to plan further procedures or observation.

Radiotherapy consists of irradiation of the entire prostatic gland where the cancer was found. The radiotherapist carries out computed tomography in the patient to determine the location of the prostate – the so-called radiotherapy field. Then the treatment is planned and the specific parameters (place, duration of irradiation) are calculated for each patient. Radiotherapy of the prostate is normally combined with hormonal therapy, usually for several months before, during and – for a proportion of patients – up to 3 years after the end of radiotherapy. Radiotherapy complications are associated with simultaneous and hardly avoidable irradiation of organs adjoining the prostatic gland: the urinary bladder and the rectum. Among the complications those most often encountered include irritation of the urinary bladder that presents with passing urine more frequently, sometimes by haematuria and irritation of the rectum, leading to predisposition to diarrhoea, the presence of blood in the stool or some discomfort within that area. The side effect of irradiation may become manifest only after a long period, sometimes even as late as several years after treatment. Irradiation may be effected in two ways. One of them, teleradiotherapy, consists in irradiating the prostatic gland from an external device located outside the patient's body; the second way, brachytherapy, consists in locating the radioactive source directly in the prostatic gland. At present both these methods of radiotherapy are frequently combined.

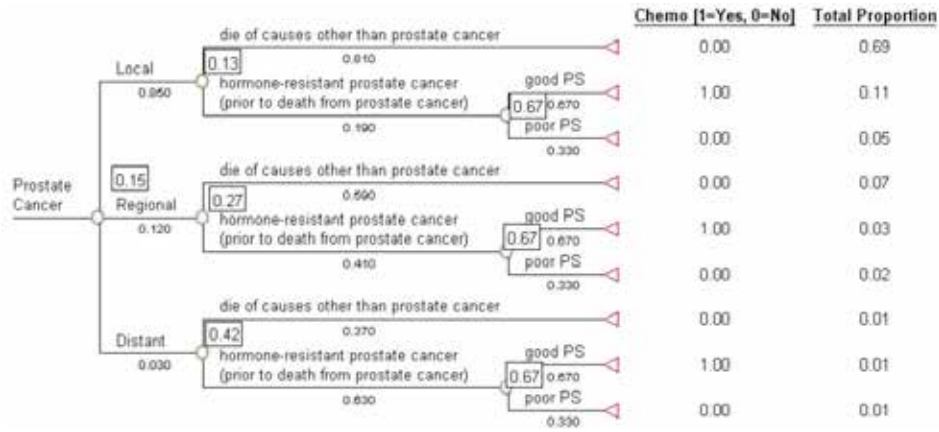
In the case of a more advanced disease – normally at the third or fourth stage of disease – hormonal therapy is indicated to eliminate the impact of male hormones (mainly testosterone) on cancer cells. Hormonal therapy may be used as an stand alone therapy in patients with advanced disease, but also as an element in therapy integrated with irradiation. Long-term hormonal treatment poses a risk of intensification of metabolic disorders, particularly with respect to predispositions to obesity, diabetes, osteoporosis, fat metabolism disorders, cardiac

diseases. In patients with advanced prostate cancer treatment with palliative chemotherapy and radiotherapy could also be considered.

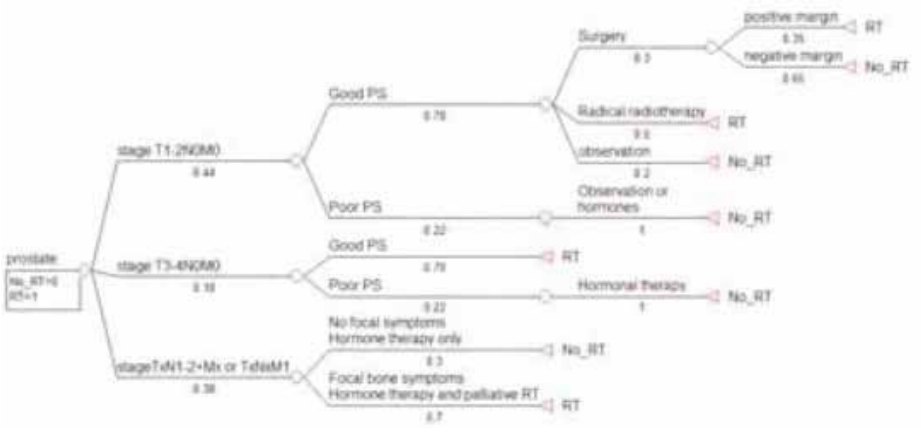
Decision models in treatment of prostate cancer

In literature the decision models in prostatic gland treatment are normally presented in form of decision trees. Ng et al. (2010) described the chemotherapeutical treatment model for Australia. The radiotherapeutical treatment model for Scotland was developed by NHS Scotland (2005), whereas for Australia it was published by Barton (2013). The trees representing these models are presented in Figures 1-3.

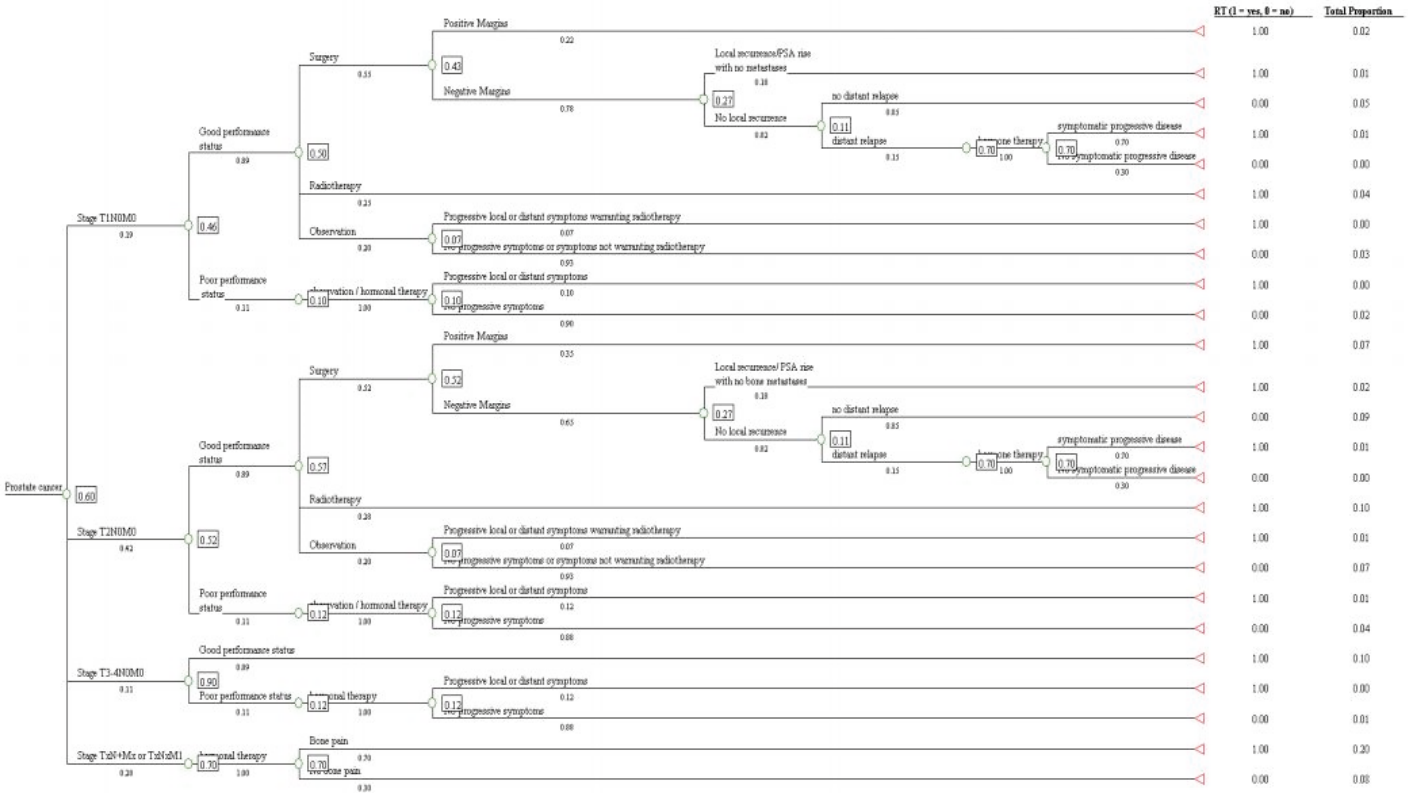
Decision trees represent treatment schemes applied in a given country. They allow determination of the demand for specific treatment methods depending on assumed or empirical values: the cancer stage structure at the time of diagnosis or decisions at individual levels.



Flowchart 1. Decision tree for chemotherapy in Australia (source: Ng et al. 2010)

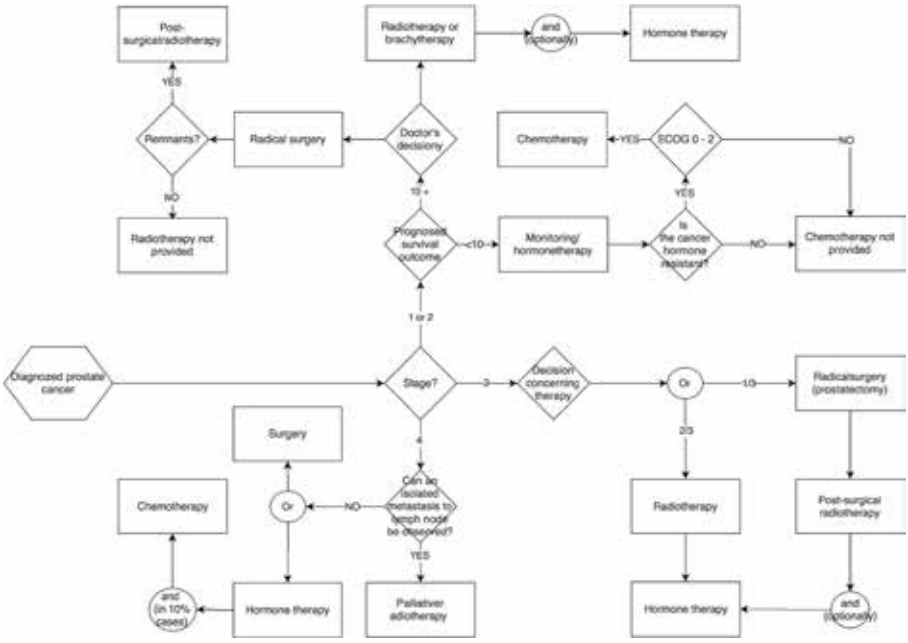


Flowchart 2. Decision tree for radiotherapy in Scotland (source: NHS Scotland 2005)



Flowchart 3. Decision tree for radiotherapy in Australia (Source: own study based on Barton 2013)

The theoretical model of oncological treatment in Poland, including surgical treatment, chemotherapy and radiotherapy, is presented in Figure 4. This model was generated based on analyses of the models presented above, corrected by oncological treatment standards recommended by scientific associations in Poland and by expertise in the field of prostate cancer treatment practice in Poland.



Flowchart 4. Model of oncological treatment in Poland (Source: own study)

Empirical model of prostatic gland cancer treatment

Based on data contained in the National Cancer Register (NCR) a number of analyses were carried out with respect to malignant neoplasms of the prostatic gland. In accordance with the transferred data, 9 796 malignant neoplasms of prostate were registered in 2012[114]. It is the

[114] The value presented here is a value developed based on the set of data transferred by the NCR. The patients were verified in terms of their occurrence in the National Health Fund systems with cancer diagnosed in the preceding years. Thus the resulting number is smaller than the number of new neoplasm cases reported in a given year, shown in the NCR website.

second (right after the lung cancer), most frequently occurring malignant neoplasm in men (14.5% of all cases of malignant neoplasms). This number is increasing and in accordance with the NCR data during the three past decades the incidence of this type of cancer grew about fivefold.

In terms of deaths caused by neoplastic diseases in men prostate cancer is the second (after the lung cancer). In 2012 about 4.2 thousand men died for this reason, representing 8% of cancer related deaths. Incidence is increasing, but mortality has been stabilised at the level of about 13 deaths per 100 thousand.

Supplementation of the theoretical model of prostate cancer treatment with empirical data would require access to data on the disease progression status or the general condition of the patient. The National Cancer Register base is the sole nationwide Polish source of information about the cancer progression. An analysis of the NCR base, together with the use of the National Health Fund base, delivered evidence of significant underreporting in the former one. Firstly, as presented in Table 2, the staging has not been reported for a considerable number of patients. The share of entries without information about the degree of progression of the disease oscillates between 28% and 30% depending on the year. At the same time a very low percentage of persons with stage I of disease is of concern – this may indicate late diagnosis in Poland, but also poor regularity of reporting: the longer the treatment, concentrated in oncological centres the patient requires, the longer the odds on reporting the case to the Register during the treatment. The structure of patients with supplemented stage of progression is presented in Table 2.

Table 2. Breakdown of information about the cancer progression in the NCR base for new patients (Source: own study)

Stage of progression	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	6	0	0%	0%	0%
II	4 462	4 841	5 254	50%	50%	53%
III	723	710	649	8%	7%	7%
IV	1 161	1 182	1 146	13%	12%	12%
Stage not recorded in the NCR	2 649	2 862	2 786	29%	30%	28%
Total	8 995	9 601	9 835	100%	100%	100%

Table 3. Breakdown of information about the cancer progression in the NCR base for new patients with full information about the degree of cancer progression (Source: own analysis)

Stage of progression	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	0	6	0	0%	0%	0%
II	4 462	4 841	5 254	70%	72%	75%
III	723	710	649	11%	11%	9%
IV	1 161	1 182	1 146	18%	18%	16%
Total	6 346	6 739	7 049	100%	100%	100%

Another manifestation of data deficiency in the NCR consists in the lack of registration, despite the inclusion of the patient into the NHF system, with C61 diagnosis. An analysis was carried out for patients who appeared in the NHF reporting systems with the first diagnosis of cancer. Services provided to them were analysed and on those grounds the stage was estimated for those patients who did not appear in the NCR. A proportion of them were defined as patients monitored following earlier treatment, whose first appearance in the NHF system (and respective treatment) took place before the reporting period. Another group consists of patients who were at the given time treated for reasons other than cancer, despite the reported ICD-10 corresponding to prostate cancer.

Analysis of services for patients treated in hospitals or within the AOS/ASDK (Specialist Out-patient Care/Out-patient Cost-intensive Diagnostic Assistance) system, but who were not registered in the NCR, allows to conclude that about 6 thousand patients a year are not registered in this base. Categorisation of patients based on services received is presented in Table 4. The 1st stage includes also those patients who did not undergo any other treatment since it was assumed that in their case a decision on active monitoring was made.

Table 4. Categorisation in terms of the degree of cancer progression in new patients, who were not registered in the NCR base (Source: own analysys)

Stage of progression	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	2 774	2 934	2 778	28%	31%	31%
II	646	730	748	6%	8%	8%
III	611	704	751	6%	7%	8%
IV	1 554	1 490	1 451	16%	16%	16%
Patients in *follow-up*	4 413	3 696	3 356	44%	39%	37%
Total	9 998	9 554	9 084	100%	100%	100%

The prostate cancer incidence for 2010-2012 was determined based on data transferred by the NCR and on analysis of patient paths appearing in the National Health Fund system. The results, complete with breakdown in terms of the estimated degree of progression, are presented in Table 5. Comparison of the results with the structure of patients whose NCR data were supplemented with the stage of progression shows that the number of newly diagnosed prostate cancer increases as much as by 60% over that period. The structure in terms of the stage of progression has also changed, e.g. the share of patients at the 1st stage of progression of the prostate cancer grew to 20% (as compared with actually nil number of such cases in Table 2), and the share of patients with the highest degree of progression remained at the 16% level, i.e. such as may be observed among patients with a specified stage of progression. It should be noted that because of spending public money, the National Health Fund reporting undergoes periodic audits. Although errors may happen, reporting related to financial flows often provides data of better quality than the voluntary (or mandatory, however without any enforcement and verification mechanism) data registration with the NCR.

Table 5. Incidence breakdown in terms of the degree of cancer progression for 2010-2012 (Source: own study)

Stage of progression	Absolute value			%		
	2010	2011	2012	2010	2011	2012
I	2 939	3 125	2 940	21%	21%	20%
II	5 658	6 186	6 541	41%	42%	45%
III	1 871	2 017	1 936	14%	14%	13%
IV	3 324	3 296	3 263	24%	23%	22%
indefinable	27	24	12	0%	0%	0%
Total	13 819	14 648	14 692	100%	100%	100%

Analysis of the services provided used as a basis for i.a. supplementing the deficiencies in information occurring in the NCR was based on examination of procedures and treatments within one year of the appearance of the patient with cancer diagnosis in the system. The analysis of products in the National Health Fund (complete with Homogeneous Patient Groups) and procedures reported according to the International Classification of Medical Procedures ICD-9 was used as a basis for estimation of information about the patient path in the system:

- has the patient undergone surgery – a dictionary of procedures indicating such treatment was defined for this purpose,
- has the patient undergone chemotherapy,
- has the patient undergone radiotherapy (both in form of teleradiotherapy and brachytherapy),
- has the patient received assistance defined as palliative (e.g. bone metastasis treatment),
- has the patient died within 365 days of the moment of appearance in the system with malignant neoplasm of the gland diagnosis.

This allowed development of a tree presenting the results of the analysis for each stage. They present the size of the groups obtained from consecutive breakdowns, the share of these patients in a group before the breakdown and vs. the whole population of prostate cancer patients. Groups of less than 50 patients were not broken down any further. The presented data relate to patients who entered the system in 2012 (cf. . Figure 5)

The empirical model confirms that the radical methods of prostate cancer treatment include radiotherapy or radical surgery, whereas chemotherapy[115] is provided to patients in the advanced stage of disease. The one year survival rate in prostate cancer crucially depends on the stage – 100% for the stage I, 97% for stages II and III and 60.5% for stage IV.

Table 6. Empirical model of prostate cancer treatment in Poland part 1 (Source: own study)

Type of therapy	per cent of patients undergoing the given therapy
radical surgery	18.5%
chemotherapy	11.4%
radiotherapy	38.2%

Table 7. Empirical model of prostate cancer treatment in Poland part 2 – per cent of patients undergoing the given therapy depending on the stage (Source: own study) 2 - patients who underwent a given therapy depending on cancer stage (source: own analysis)

Type of therapy	1st stage	2nd stage	3rd stage	4th stage
radical surgery	2%	27.4%	39.7%	3%
chemotherapy	0%	6.9%	3.3%	35.5%
radiotherapy	8%	54.3%	58.4%	21.1%

Again it should be noted that the patient group in Stage I included persons to whom no radical therapy was assigned. Such decision was most often made in treatment of patients with the lowest stage of progression. In the case of the 2nd and 3rd stages radiotherapy is the treatment method most often used in Poland, whereas the patients at the last stage of the disease most often undergo chemotherapy.

Analysis of Table 8 – the shares of patients undergoing various types of therapy, without differentiation of the stage of progression – shows that the most common decision in prostate cancer treatment is that of no radical treatment, i.e. conservative therapy, in a part of the patients with the assumption of active monitoring or with possible hormonal therapy. The second place is taken by radical radiotherapy (29.1%), followed by radical prostatectomy (18.02%), integrated in 4.56% with post-surgery radiotherapy.

[115] Substances indicated in the chemotherapy catalogue (bicalutamide included).

Table 8. Empirical model of prostate cancer treatment in Poland part 3 (Source: own study)

Surgery of the prostate?					
NO – 81.5%			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	41.39%	29.17%	70.56%
		YES	6.67%	4.27%	10.95%
	Total		48.06%	33.44%	81.50%
YES – **18.5%**			radiotherapy		Total
			NO	YES	
	chemotherapy	NO	13.46%	4.56%	18.02%
		YES	0.26%	0.22%	0.48%
	Total		13.72%	4.77%	18.50%

The analysis of treatment schemes stage I is subject to an error related to determination of the patient's stage. These stage I patients have actually been determined based on the treatment they received, therefore we are dealing with theoretical, not empirical treatment schemes. However, conclusions on the most prevalent treatment is not groundless – it allows determination which of the theoretically developed schemes is implemented most often. In the case of stage I patients it is active monitoring with possible hormonal therapy. Solely surgical treatment was undergone by 2% of patients and irradiation monotherapy was offered to 8.2% of patients.

Stage					Including surgical treatment					Including surgical chemotherapy					Including surgical radiotherapy					Including palliative treatment				
Stage	Number of cases	Share	Number of deaths	% of deaths	NIE/YES	Number of cases	Share	Number of deaths	% of deaths	NIE/YES	Number of cases	Share	Number of deaths	% of deaths	NIE/YES	Number of cases	Share	Number of deaths	% of deaths	NIE/YES	Number of cases	Share	Number of deaths	% of deaths
1	2939	20,0%	0	0,00%	NIE	2881	98,0%	0	0,00%	NIE	2881	100,0%	0	0,0%	NIE	2644	91,8%	0	0,0%	NIE	2644	100,0%	0	0,0%
															YES	237	8,2%	0	0,0%	NIE	237	100,0%	0	0,0%
					YES	58	2,0%	0	0,00%	NIE	58	100,0%	0	0,0%	NIE	58	100,0%	0	0,0%	NIE	58	100,0%	0	0,0%
2	6540	44,6%	200	3,10%	NIE	4752	72,6%	192	4,00%	NIE	4336	91,2%	171	3,9%	NIE	1431	33,0%	139	9,7%	NIE	1296	90,6%	118	9,1%
																				YES	135	9,4%	21	15,6%
															YES	2905	67,0%	32	1,1%	NIE	2825	97,2%	23	0,8%
																				YES	80	2,8%	9	11,2%
										YES	416	8,7%	21	5,0%	NIE	133	32,0%	17	12,8%	NIE	100	75,2%	10	10,0%
																				YES	33	24,8%	7	21,2%
															YES	283	68,0%	4	1,4%	NIE	264	93,3%	3	1,1%
																				YES	19	6,7%	1	5,3%
					YES	1788	27,4%	8	0,40%	NIE	1750	97,9%	8	0,5%	NIE	1402	80,1%	4	0,3%	NIE	1398	99,7%	4	0,3%
																				YES	4	0,3%	0	0,0%
															YES	349	19,9%	4	1,2%	NIE	344	98,6%	3	0,9%
																				YES	5	1,4%	1	20,0%
										YES	38	2,1%	0	0,0%										
3	1936	13,2%	66	3,40%	NIE	1167	60,3%	66	5,70%	NIE	1110	95,1%	60	5,4%	NIE	274	24,7%	52	18,9%	NIE	206	74,9%	43	20,9%
																				YES	69	25,1%	9	13,0%
															YES	835	75,3%	8	1,0%	NIE	792	94,8%	8	1,0%
																				YES	43	5,1%	0	0,0%
										YES	57	4,9%	6	10,5%	NIE	33	57,9%	5	15,2%					
															YES	24	42,1%	1	4,2%					
					YES	769	39,7%	0	0,00%	NIE	762	99,1%	0	0,0%	NIE	497	65,2%	0	0,0%	NIE	497	100,0%	0	0,0%
															YES	265	34,8%	0	0,0%	NIE	265	100,0%	0	0,0%
										YES	7	0,9%	0	0,0%										
4	3262	22,2%	1287	39,40%	NIE	3163	97,0%	1276	40,30%	NIE	2029	64,2%	1056	52,0%	NIE	1725	85,0%	914	53,0%	NIE	1129	65,4%	734	65,0%
																				YES	596	34,5%	181	30,4%
															YES	304	15,0%	142	46,6%	NIE	161	52,8%	97	60,5%
																				YES	144	47,2%	45	31,1%
										YES	1134	35,8%	220	19,4%	NIE	814	71,8%	175	21,5%	NIE	629	77,3%	109	17,3%
																				YES	185	22,7%	66	35,5%
															YES	320	28,2%	45	14,1%	NIE	254	79,3%	25	9,8%
																				YES	66	20,7%	20	30,7%
					YES	99	3,0%	11	10,90%	NIE	75	75,0%	7	9,4%	NIE	20	26,8%	7	35,0%					
															YES	55	73,2%	0	0,0%	NIE	54	98,2%	0	0,0%
																				YES	1	1,8%	0	0,0%
										YES	25	25,0%	4	15,3%										

Flowchart 5. Empirical model of prostate cancer (C61) treatment in Poland part 4 (Source: own study)

In the case of stage II patients 44.4% of patients underwent solely treatment by irradiation, 21.4% underwent solely radical surgery, 5.3% surgery combined with irradiation and for 21.9% of patients the decision was conservative therapy. Chemotherapy was used in 6.9% of patients (in 4.3% in combination with radiotherapy).

In patients with Stage III irradiation was the most frequently chosen therapy (43.1% patients), with surgery in the second position – 39.7%, where in 25.7% of patients it was surgery alone and in 13.7% of patients – surgery combined with irradiation and in 0.3% - surgery combined with chemotherapy (7 cases).

For stage IV patients radical surgery was used in 3% of cases only. Most often (52,9%) the decision was to apply conservative therapy. Chemotherapy was applied to 35.5% patients (9.8% combined with radiotherapy, 25% solely chemotherapy, 0.7% combined with surgery). A total of 30.4% of the 4th stage patients received various types of palliative treatment.

Summary

Analysis of the data obtained makes one wonder why as many as 60% of patients included in the NHF reports have not been reported to the NCR. In the majority of cancer registries data the assumed level of data deficiency is considerably lower. Linkage of data between both these registers should be taken into consideration, as this could improve their completeness and eliminate double reporting of the same data. The payment for procedures in patients with neoplastic disease by NHF could contain a requirement for the degree of cancer progression; the data could be then routinely transferred for epidemiological analysis and this could maybe reduce the need for double reporting in the future.

Another aspect related to the analysis of trends in the prostatic cancer treatment in Poland is the fact that a relatively small group of patients undergo radical therapy. Due to the nature of the analysis based on reporting procedures and not the applied pharmacotherapy, the above analysis does not differentiate patients who did not receive pharmacotherapy from those who were treated e.g. with hormones. Based on the data on the application of hormonal therapies in Poland it may be assessed that annually hormonal therapy is applied in about 42% of newly diagnosed patients. Such factors as the low percentage of patients who undergo radical therapies, who are treated with hormonal monotherapy may be i.a. responsible for the lower survival indicators in prostatic gland cancer in Poland.

Bibliography

Edge SB., Byrd DR., Compton CC. et al. (eds.) (2010) AJCC Cancer Staging Manual, 7th ed. New York: Springer.

EUROCARE-5 Database, Access: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx, date of download: 2.04.2015.

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F. (2013), *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11* [Internet], Lyon: International Agency for Research on Cancer. Access: http://globocan.iarc.fr, date of download: 2.04.2015.

Heidenreich A., Bastian P.J., Bellmunt J., Bolla M., Joniau S., van der Kwast T., Mason M., Matveev V., Wiegel T., Zattoni F., Mottet N. (2014) EAU Guidelines on Prostate Cancer. Part I: Screening, Diagnosis, and Local Treatment with Curative Intent – Update 2013. *European Urology*, Volume 65, Issue 1, p. 124–137.

Heidenreich A., Bastian P.J., Bellmunt J., Bolla M., Joniau S., van der Kwast T., Mason M., Matveev V., Wiegel T., Zattoni F., Mottet N. (2014) EAU Guidelines on Prostate Cancer. Part II: Treatment of Advanced, Relapsing, and Castration-Resistant Prostate Cancer. *European Urology, Volume 65, Issue 1, p. 467–479.*

National Cancer Registry. http://epid.coi.waw.pl/krn.

Krzakowski M., Dziadziuszko R., Fijuth J. et al. (eds.) (2011) *Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych*. Gdańsk: Wydawnictwo Via Medica.

NCCN Guidelines ver. 1.2015. *Prostate Cancer*. Access: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.

Zelefsky M.J., Eastham J.A., Sartor O.A., Kantoff P. (2011) Cancer of the Prostate. In: De Vita V.T., Lawrence T.S., Rosenberg S.A. (eds.) *Cancer, Principles and Practice of Oncology*. Vol. I. 159: 1392–1452.

Cancer care in Poland – the results of the predictive model for 2015-2025

Barbara Więckowska, Beata Koń, Janusz Dagiel, Filip Urbański

Introduction

Modelling the disease pathways is an essential element of the health care system analysis. It allows generation of an accurate description of the present epidemiological situation and identification of existing relations and presentations. Definition of the disease processes is essential in the context of health needs of the population, as it allows identification of factors crucial to the modelling of the health situation of the population. These are defined with the use of quantitative methods. In modelling of the disease processes elements taken into consideration include the incidence rate, the mortality rate and prevalence. These values are most often obtained based on empirical data drawn from available registers, which are then used for development of predictive elements. Their generation is particularly essential in terms of the currently developed health strategies for regions, as they allow determination of the future health situation of the population and hence improved adjustment to changes occurring in the surroundings and attenuation of difficulties and differences occurring between regions.

This publication is designed to present the results of the predictive model with respect to prevalence of solid tumours. The first part of the paper describes the epidemiological indicators (such as incidence rates) and determines the survival curves, which are a prerequisite element for estimation of 5-year prevalence. This information provides essential input data for forecast development. Particular attention was paid to the sources of the data used to ensure that the results obtained are reliable and verifiable. The second section of the paper consists of the forecast results relating to the incidence and 5-year prevalence of solid tumours in Poland for years 2015-2025. The final part of the paper includes the summary of results and lists the key conclusions.

Historical data as input information for predictive purposes

Development of forecasts requires accurate definition of input information, i.e. the historical data that will be used for their development. In Poland data on oncological patients are registered in the National Cancer Registry (NCR) and information about services provided to them is reported to the National Health Fund (NHF). The use of empirical data in forecasts is an example of an approach based on the assumptions of the so-called evidence-based medicine, where decisions on health care are made on the grounds of real data and not based on discretionary decisions and expertise (Evidence-Based Medicine Working Group 1992).

Incidence of cancer in Poland in 2012-2012

Incidence, defined as the number of newly diagnosed patients in the given year is the key element used in epidemiological analyses (Rothman, Greenland 2005). Its definition allows determination of the risk of falling ill with a given cancer. It is also a determinant of the costs borne by the oncological care system, as the costs generated during the first year of oncological treatment are among the highest in the oncological care (National Cancer Institute 2010).

Based on the adopted methodology, described in detail in section *Sources and quality of data relating to cancer epidemiology in Poland – methodology of data analysis,* the total incidence of malignant neoplasms in 2010-2012 was determined (taking into account D05 exclusive of C44, C81-C96 acc. to ICD10). It was determined linking data from the NCR base with the NHF reporting data. Determination of the incidence consisted of 4 stages: i) determination for each patient of the first date of appearance in the system (defined as the first date of entry into the NCR with a given diagnosis or the first date of service provision with respect to the given cancer), ii) determination of the number of patients who appeared for the first time in the system in the given year (i.e. in NCR or NHF reporting), iii) analysis of the patient treatment path (covering 365 days from the moment of the first appearance in the system and comprising information about completed procedures acc. to ICD-9, application of chemotherapy, radiotherapy and possible death of the patient), iv) based on the treatment path estimation of the stage of progression (probability) for patients, who were not entered into the NCR or their stage of progression was not determined in the register[116]. It is worth

[116] See: *Sources and Quality of Cancer Epidemiological Data in Poland - Data Analysis Methodology*, Figure 1.

noticing that element ii) defines the potential number of new oncological patients and is insufficient to determine the annual incidence. In order to determine the stage of progression it is necessary to define the patient treatment path separately for every cancer stream. It is also necessary to indicate patients for whom the treatment pathway is inappropriate for a new oncological patient, i.e. to indicate patients whose treatment pathway shows they are in the *follow up* process and patients for whom the registration as a malignant neoplasm was incorrect (in the case of patients, who were not reported to the NCR). Only after rejection of these patient groups on the grounds of the treatment path analysis it will be possible to determine the incidence based on the linked NCR and NHF data. It should also be noted that because of the use of both data sources, the incidence calculated on the NCR data does not include those patients who received treatment with respect to the given cancer at least 365 days before the entry in the NCR; therefore the values presented further on in this paper will differ slightly from the NCR statistics (Wojciechowska et al. 2012; 2013; 2014).

Empirical data obtained based on the NCR base show that the incidence of malignant neoplasms in Poland was relatively constant and stabilised at the level of about 120 thousand new cases a year (cf. Figure 1).

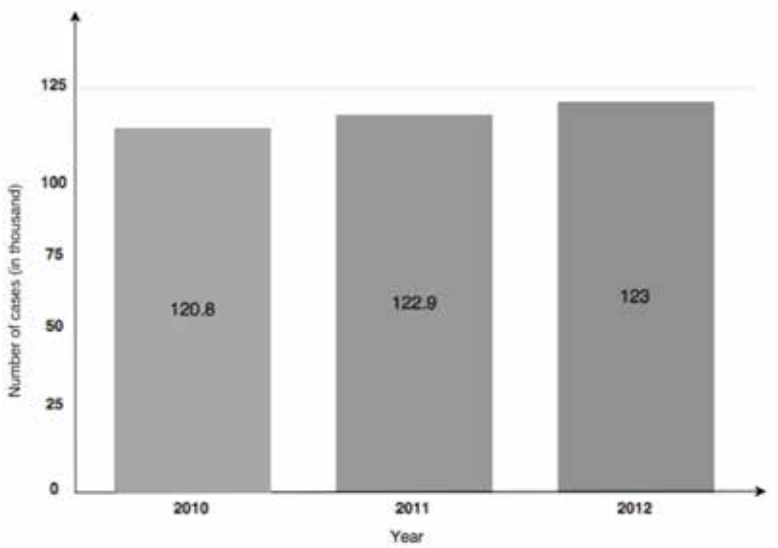


Figure 1. The incidence of malignant neoplasms in 2010-2012 acc. to the NCR base, taking into account D05 exclusive of C44, C81-C96 acc. to ICD10 (Source: own study based on NCR and NCR data).

Supplementation of NCR data with NHF reporting, and taking into account the appropriateness of occurrence of the given treatment path in the given type of cancer has allowed for the determination of the total incidence of solid tumours in Poland. In 2010-2012 it was 163 thousand, 164.5 thousand and 164.7 thousand respectively. Completeness of the NCR base did not improve over this period and during this period amounted to 73%, 74% and 74% respectively (cf. Figure 2).

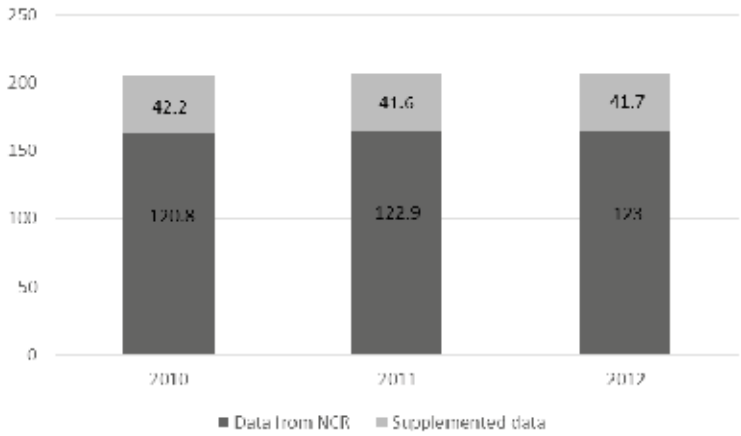


Figure 2. The total incidence of malignant neoplasms in 2010-2012, taking into account D05 and exclusive of C44, C81-C96 acc. to ICD10 (Source: own study based on NCR and NHF data).

New cases of cancer were defined according to 25 cancer streams. Data presenting the epidemiological situation in Poland in 2012 show that the largest numbers of newly diagnosed cases related to the lung, breast, prostate, colon and the urinary bladder cancer (cf. Figure 3). What's more, the largest 5 groups of cancers summed up to about 50% of all new cases of malignant neoplasms.

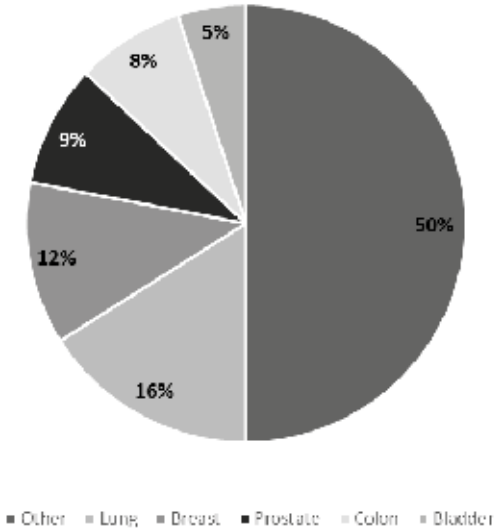


Figure 3. The structure of new cases of malignant neoplasms in 2012
(Source: own study based on NCR and NHF data).

The most frequently occurring cancers, i.e. the lung and breast cancer, were diagnosed in 2012 in more than 25.5 thousand persons and 20 thousand persons respectively. Among the identified cancer streams the lowest incidence occurred in the case of the lip cancer (almost 600 cases) and salivary gland cancer (about 670 cases). In the case of the first two most frequently occurring cancers, i.e. the lung and breast cancer, completeness of NCR data amounted to about 80%. Accurate values are presented in Figure 4, which, however, does not include “other” cancers, which in total add up to 6% of new cases nationwide.

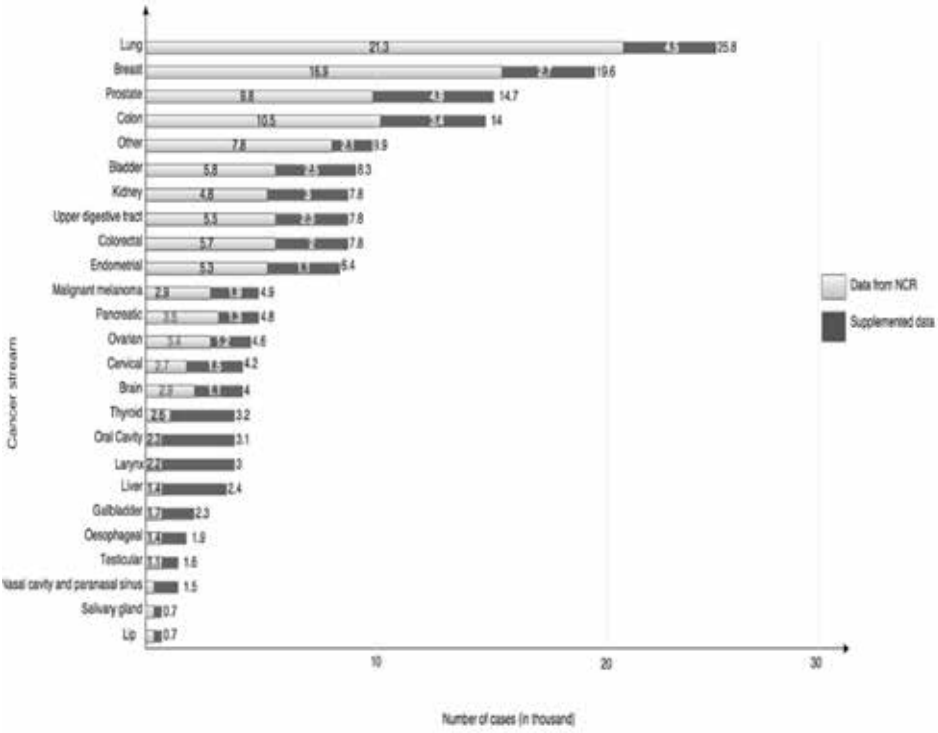


Figure 4. The total incidence of malignant neoplasms in Poland in 2012, by the type of neoplasm (Source: own study based on NCR and NHF data).

The aforesaid supplementation of NCR data with services reported to the NHF was carried out separately for each cancer stream. The highest proportion of supplementation was required for the salivary gland and the nasopharynx and piriform sinus cancer – completeness of the NCR register was only of about 50% (cf. Figure 5). However, this mainly results from the small size of this group of cancers. The lowest supplementation was required for data on patients with breast cancer (14%), which means that the indicator for reporting this cancer to the NCR is high. Accurate information about data on the incidence is presented in Table 1, comprising information about cases registered in NCR[117] for the first time in the given year and information supplemented based on services provided with respect to diagnosis of the given cancer.

[117] Corrected in accordance with the adopted methodology.

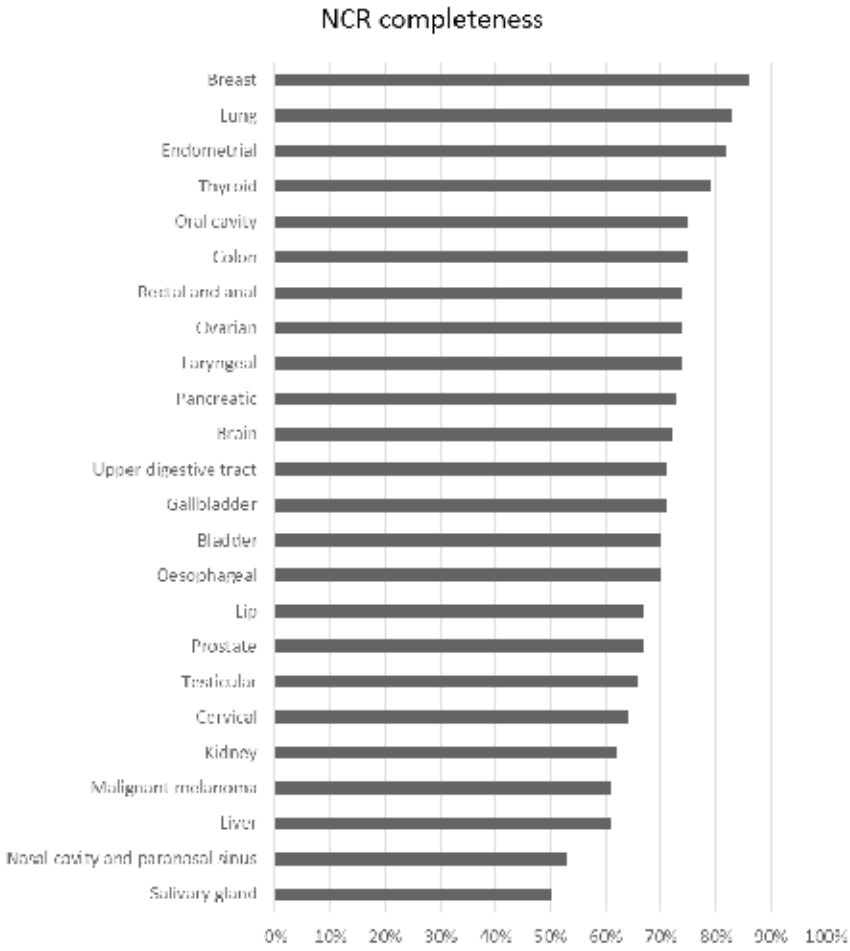
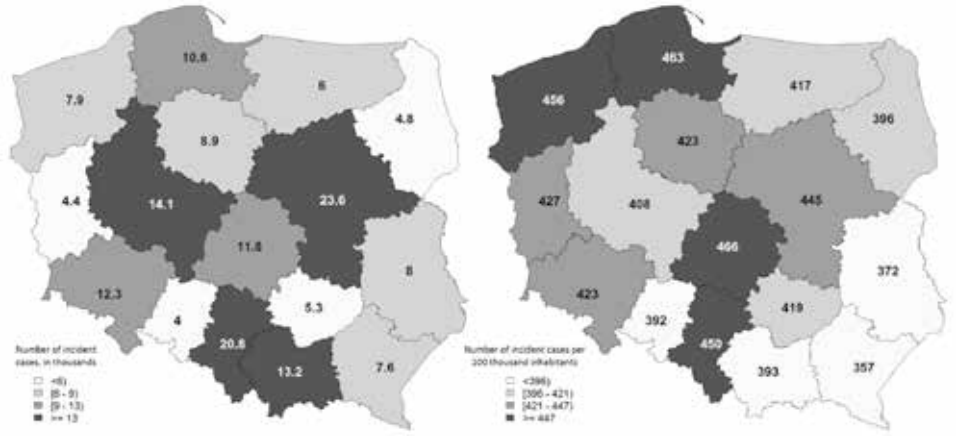


Figure 5. The NCR completeness by per cent (Source: own study based on NCR and NHF data)

Table 1. Incidence of malignant neoplasms in 2010-2012, by neoplasm groups (Source: own study based on NCR and NHF data).

Neoplasm Group	ICD-10	NCR			After supplementation		
		2010	2011	2012	2010	2011	2012
lip	**C00**	407	440	389	547	609	583
oral cavity	**C01, C02, C03, C04, C05, C06, C09, C10, C14**	2 372	2 352	2 347	3 165	3 103	3 115
salivary glands	**C07, C08**	346	299	334	607	589	668
nasopharynx and piriform sinus	**C11, C12, C13, C30, C31**	756	782	791	1 439	1 438	1 485
esophagus	**C15**	1 179	1 283	1 369	1 772	1 802	1 944
stomach,	**C16, C26**	5 613	5 637	5 502	8 525	8 045	7 781
colon, rectosigmoid junction	**C18, C19**	10 139	10 375	10 538	13 876	13 916	13 984
rectum and anus	**C20, C21**	5 739	5 927	5 713	8 133	8 084	7 758
liver	**C22**	1 436	1 405	1 449	2 354	2 282	2 367
gallbladder	**C23, C24**	1 588	1 667	1 654	2 258	2 340	2 321
pancreas	**C25**	3 268	3 357	3 519	4 454	4 584	4 831
larynx	**C32**	2 209	2 181	2 227	3 034	2 989	2 990
lung	**C33, C34**	20 879	20 851	21 272	25 550	25 313	25 759
melanoma of skin	**C43**	2 515	2 696	2 946	3 974	4 480	4 858
breast	**C50, D05**	16 378	17 306	16 866	19 080	19 879	19 614
cervix uteri	**C53**	3 091	2 993	2 684	4 113	4 065	3 932
corpus uteri	**C54**	5 158	5 327	5 252	6 016	6 342	6 392
ovary	**C56**	3 593	3 603	3 390	5 165	4 729	4 571
prostate	**C61**	8 995	9 601	9 835	13 819	14 648	14 692
testis	**C62**	1 085	1 013	1 051	1 558	1 493	1 595
kidney	**C64, C65, C66**	4 923	4 766	4 842	7 693	7 796	7 805
bladder	**C67**	6 114	5 941	5 833	8 728	8 579	8 292
central nervous system	**C70, C71, C72**	2 979	2 954	2 901	4 202	4 280	4 014
thyroid gland	**C73**	2 250	2 384	2 556	2 927	3 067	3 242
other	**other**	7 791	7 808	7 789	9 873	9 967	9 980
TOTAL		**120 803**	**122 948**	**123 049**	**162 862**	**164 419**	**164 573**

In Poland the largest number of new oncological patients lived in the following regions (voivodeships): Mazovia, Silesia, Greater Poland and Lesser Poland (cf. . Map 1)118 The lowest numbers, in turn, lived in the following regions: Opolskie, Lubuskie, Podlaskie and Świętokrzyskie. However, this mainly results from the population size of those voivodeships – in voivodeships with the largest population numbers the largest numbers of new cancer cases should be expected and similarly, in voivodeships with the smallest number of population – a smaller number respectively. That is why, beside the incidence, the incidence rate is also mentioned, which determines the number of newly diagnosed patients per 100 thousand inhabitants. It attenuates the impact of the number of inhabitants in the region and allows determination of differences in malignant neoplasm incidence models. In Poland the incidence rate differs considerably between the voivodeships. The highest values of the coefficient were observed in the Łódzkie and Pomerania, the lowest – mainly in south-eastern Poland and in the Opolskie voivodeship. Differences between the extreme voivodeships, i.e. Łódzkie and Sub-Carpathian reach 30%. However, certain precautions should be taken in interpreting these values, as they do not eliminate the effects of the sex structure nor the age groups.



Map 1. Incidence (the left hand side map) and the incidence rate (the right hand side map) in individual voivodeships in 2012. (Source: own study based on NCR and NHF data)

[118] Analysis of incidence and the incidence rate by regions does not take into account about 900 persons, with no determined place of residence. These are the persons who were reported in the given year to the NCR but no assistance was reported for them to the NHF (most probably these persons used solely the private health care).

In Poland empirical data on oncological patients are registered by the NCR. However, information about malignant neoplasm incidence in Poland is also provided by foreign sources, such as e.g. GLOBOCAN[119]. The cancer incidence provided by GLOBOCAN is considerably higher than those reported by NCR and fairly similar to the values obtained after supplementation of data with NHF reporting (cf. Figure 6). Higher values for breast cancer vs. the GLOBOCAN base result from the additional inclusion in the adopted methodology of the breast cancer *in situ* (D05 acc. to ICD10).

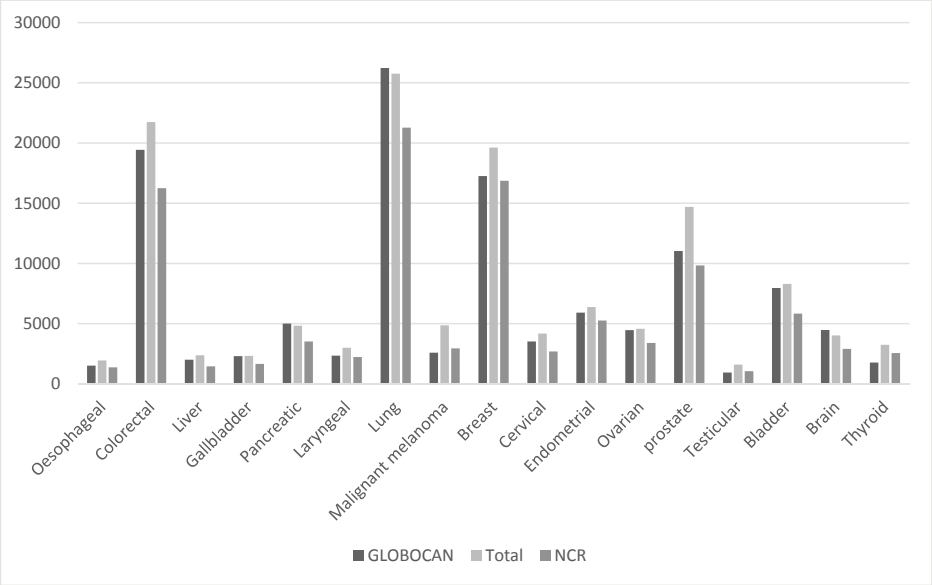


Figure 6. The NCR data structure, supplements vs. GLOBOCAN
(Source: own analysis based on GLOBOCAN, NCR and NHF data)

Incidence is often identified with the probability of falling ill with a given disease. However, its analysis requires differentiation of the stage of disease at diagnosis which provides information about the structure of patients. Figure 7 presents the structure of patients registered in the NCR base for all the studied cancer streams. Patients presenting

[119] It is also worthwhile to mention the methodology used by GLOBOCAN – the values for Poland have been acquired based on three regional registers (Kraków, Kielce and Lower Silesia), covering 13% of the population – the disputable issue is, whether a sample thus constructed is representative for the purposes of drawing conclusions as to the population of the whole country.

in stage II were largest group in the oncological patient structure. According to the NCR they represented 35% of all patients. Patients at stage I were the fewest (about 1%). This scanty number of patients at the initial stage of the disease is highly disturbing. It may be caused by at least two factors. The first of them is the late detectability of malignant neoplasms and their diagnosis at the stage when the disease already provides clear symptoms. However, it may also result from significant deficiencies in the 1st stage reporting to the NCR. Additionally, particular attention should be paid to a significant percentage of cases without a defined stage in the entries to the NCR – such situation relates to almost 26% of cases registered with the NCR in 2012.

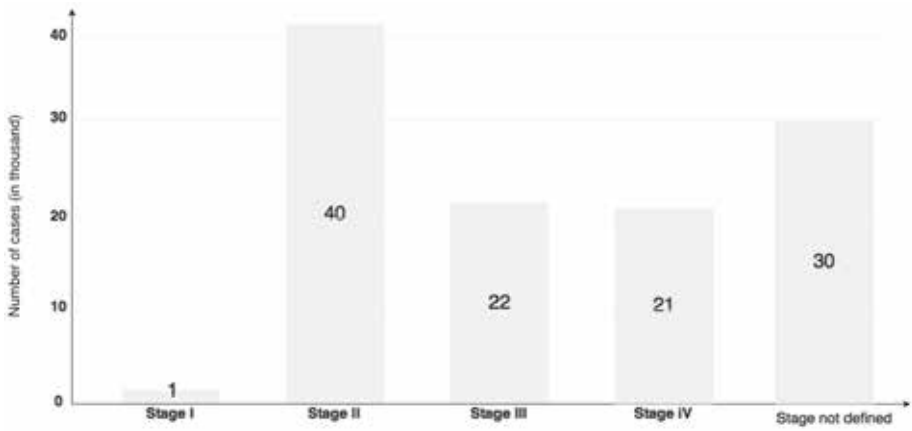


Figure 7. The structure of the stages of cancer progression according to the NCR base without taking into consideration the "Other" category, taking into consideration D05 and with exclusion of C44, C81-C96 acc. to ICD10 in 2012 (Source: own study based on NCR and NHF data)

Information about the patient treatment path allowed assessment of the cancer progression stage for the remaining patients, i.e. such patients whose stage of progression was not defined in the NCR base and patients who were not reported for registration. The rules defining the probability of occurrence of the given stage of progression for patients with the given treatment path (including the information about procedures acc. to ICD-9. the chemotherapy and radiotherapy used and the patient's death within the period of 365 days) were developed separately for each of the 24 cancer streams (excluding the "Other" group). Supplementation of information based on treatments provided to the patients shows that

significant supplementation of information is required for the 1st stage (cf. Figure 8). Based on the patient pathway it was assessed that in 2012 there were 17 thousand persons at this stage of the disease and not – as shown by entries to the NCR base – 1 thousand persons. Serious problems with reporting were also observed for the 4th stage of disease – only 41% of information about this stage of disease is reported to the NCR. Furthermore, the methodology used did not allow determination of the stage of progression for 185 patients (1‰ of patients). These are patients who were registered with the NCR, whose stage of disease progression was not determined, nor was any medical treatment reported for them to the NHF (also such which was inappropriate for oncological treatment or diagnostics). Also, those patients were alive one year after entry into the NCR base. This means that probably these persons used solely the private health care system.

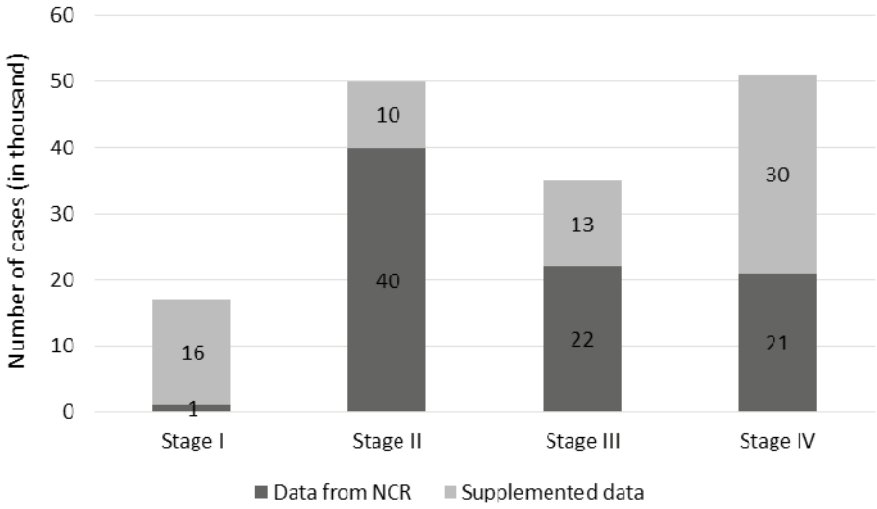


Figure 8. The total structure of the stages of cancer progression in 2012
(Source: own analysis based on NCR and NHF data)

Therefore, supplementation of information about the stage of progression based on information about treatments reported to the NHF has significantly changed the structure of the stages of malignant neoplasm at presentation in Poland (cf. Figure 9).

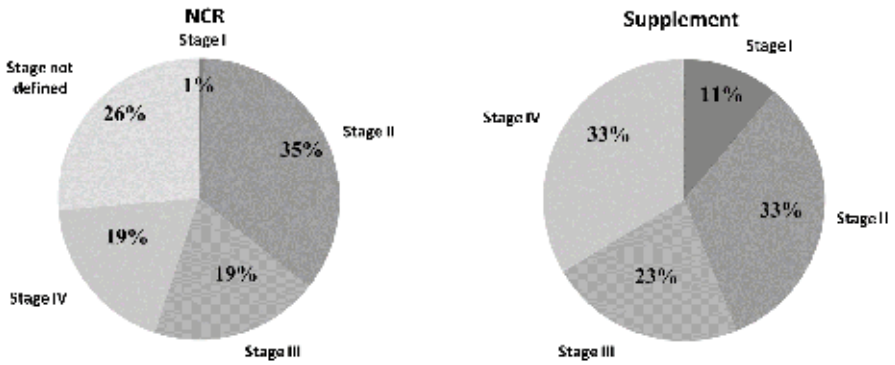


Figure 9. The structure of the stages of cancer progression in the NCR base and after supplementation of information in 2012 (Source: own analysis based on NCR and NHF data)

It is worth highlighting, however, that the stage of at presentation differs depending on the cancer stream (cf. Figure 10). In certain cancers, such as the prostate or cervical cancer, the 1st stage represented about 20% of patients in 2012, whereas in other cases, such as e.g. oral cavity cancers, it was only 4% of all cases. There is also a group of cancers in which the share of patients at an advanced stage of disease is predominant. These are mainly pancreas, liver, stomach and digestive organs and lung cancers, where the share of patients at the 4th stage of disease was over 50%. In the case of pancreatic cancer it was almost 70% of patients. For these cancer streams low survival rates should be expected, with high risk of death within one year of the diagnosis. Accurate values with respect to the stage of disease at diagnosis are presented in Table 2.

Table 2. Cancer structure in 2012 by the stages of progression (Source: own analysis based on NCR and NHF data)

Cancer Stream	ICD-10	NCR					After supplementation				
		stage									
		I	II	III	IV	NA	I	II	III	IV	NA
lip	**C00**	0	271	30	7	81	107	335	64	78	0
oral cavity	**C01, C02, C03, C04, C05, C06, C09, C10, C14**	1	606	1 035	172	533	126	759	1 415	814	1
salivary glands	**C07, C08**	0	115	93	23	103	131	223	181	133	0
nasopharynx and piriform sinus	**C11, C12, C13, C30, C31**	0	205	324	65	197	90	300	561	535	0
oesophagus	**C15**	0	247	326	357	439	79	299	419	1 146	1
stomach,	**C16, C26**	0	951	1 280	1 672	1 599	65	1 261	2 202	4 242	11
colon	**C18, C19**	1	3 041	2 423	2 268	2 805	1 341	4 302	3 864	4 451	26
rectum and anus	**C20, C21**	0	1 854	1 312	1 022	1 525	470	2 428	2 231	2 620	9
liver	**C22**	0	219	222	473	535	430	219	222	1 491	5
gallbladder	**C23, C24**	0	296	339	522	497	356	329	416	1 217	3
pancreas	**C25**	0	319	635	1 635	930	346	356	809	3 312	8
larynx	**C32**	0	1 025	569	106	527	290	1 295	866	539	0
lung	**C33, C34**	0	2 714	4 981	7 751	5 826	1 422	3 165	7 410	13 720	42
melanoma of skin	**C43**	3	1 524	313	257	849	609	2 724	781	742	2
breast	**C50, D05**	758	7 165	4 299	955	3 689	2 394	8 721	5 697	2 783	19
cervix uteri	**C53**	4	1 121	688	263	608	807	1 358	1 058	939	6
corpus uteri	**C54**	1	3 174	658	254	1 165	1 252	3 440	921	755	6
ovary	**C56**	0	801	872	862	855	711	1 133	1 497	1 225	5
prostate	**C61**	0	5 254	649	1 146	2 786	2 940	6 541	1 936	3 263	12
testis	**C62**	1	558	121	94	277	309	737	274	275	0
kidney	**C64, C65, C66**	0	2 229	282	920	1 411	1 379	3 608	337	2 470	11
bladder	**C67**	3	3 113	468	417	1 832	647	3 435	1 054	3 143	13
thyroid gland	**C73**	3	1 771	259	80	443	477	2 052	454	259	0

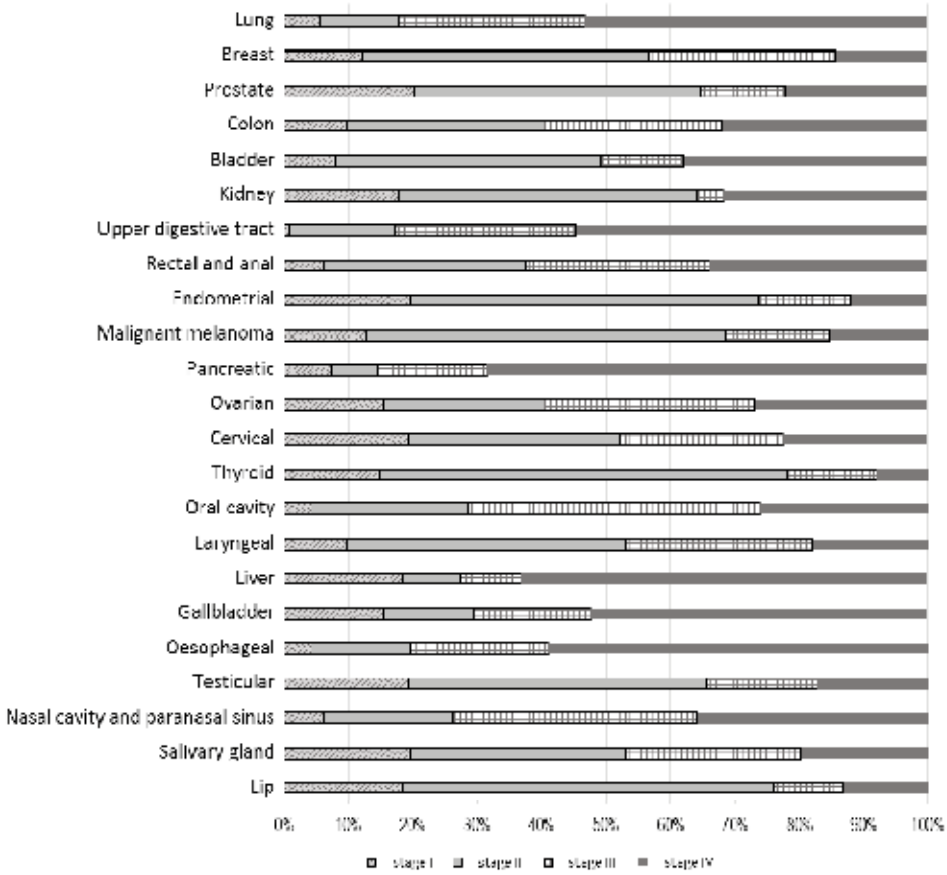


Figure 10. The total structure of the stages of cancer progression in 2012 after supplementation[120] (Source: own analysis based on NCR and NHF data)

Supplementation of information about patients registered with the NCR and the statement of incompleteness of this base could seem highly controversial. However, it should be noted that in their own publications the NCR point out that data deficiencies are possible and indicate to the on-going problems with their completeness (Wojciechowska et al. 2012). Figure 11 presents the structure of patients by the stage of progression for the most important cancer streams in Poland, the Czech Republic and in England. Data for Poland take

[120] The diagram does not include the 1‰ of patients for whom it was impossible to determine the stage of neoplasm progression.

into account the breakdown of stages according to the adopted methodology and the NCR base. Comparison of values for the chosen cancer streams shows that the supplementation of patient data that was carried out did not distort the relations between individual stages of progression occurring in the NCR, but the new breakdown of stages at presentation in Poland became closer to stage breakdown in other countries. The analysis introduced patients presenting with stage I disease into the structure. It also allowed determination of the stage at presentation for almost all oncological patients[121]. Furthermore it indicates that the problem with reporting the 1st stage to the NCR does not occur at such large a scale in other countries.

[121] The stage has not been determined for about 1‰ of patients.

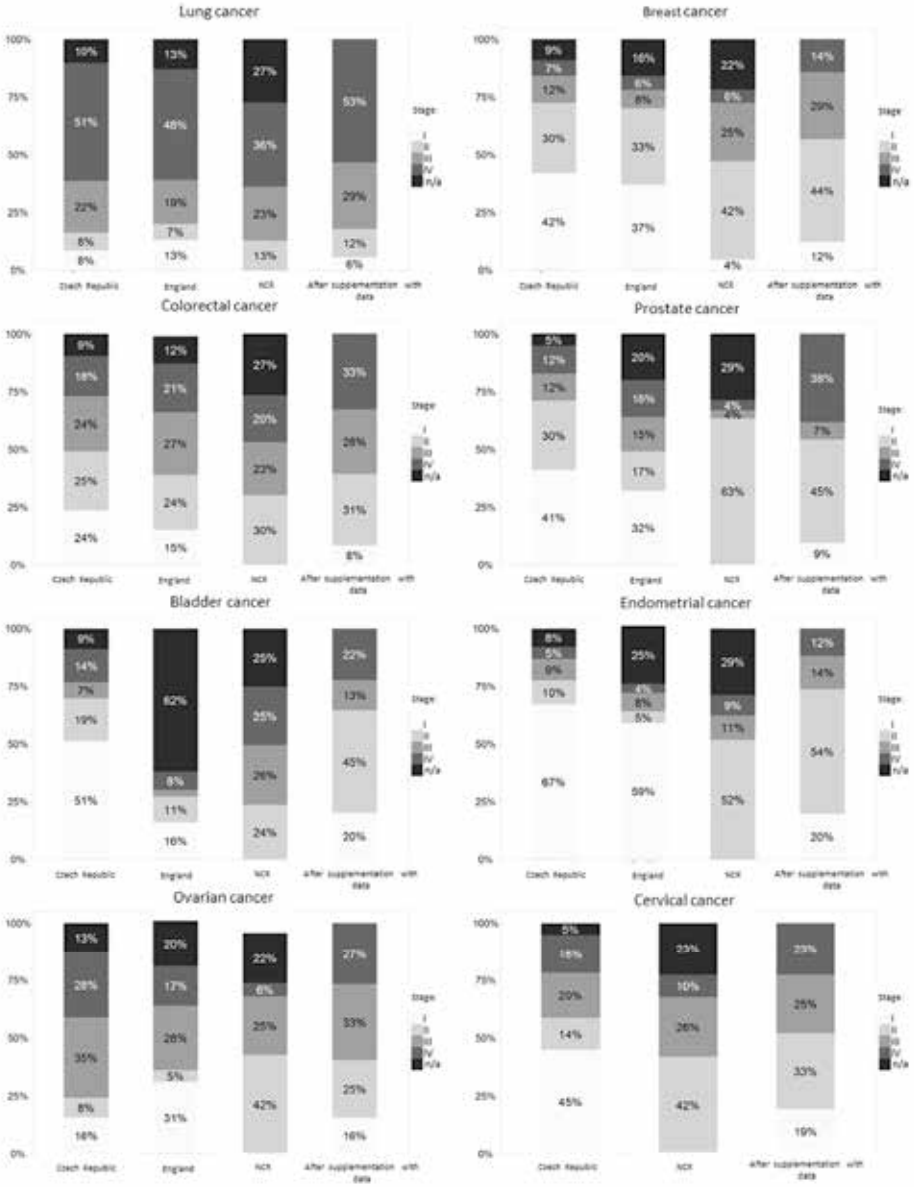


Figure 11. Breakdown of the stage of progression of the major cancer streams in Poland and in other countries (Source: own analysis based on NCR and NHF, Cancer Research UK[122], UZIS ČR data)[123])

[122] http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type
[123] http://www.svod.cz

Survival of cancer patients

Incidence determines the number of newly diagnosed oncological patients in the given year and defines the chances for falling ill with a given disease. The patient's life expectancy and the probability of living for a specified time after the date of diagnosis is another issue, also relating to epidemiology and the stage structure. Survival does not affect the incidence rate but in combination they allow determination of prevalence. It is an essential piece of information in terms of oncological patients, because it allows the definition of the scale of the phenomenon and burden for the health protection system.

Based on the estimated incidence it was possible to trace the length of the patient's life after the time of cancer diagnosis. It was used to estimate the so-called survival curves (cf. Figure 12) based on the Kaplan-Meier estimator (Kaplan, Meier; 1958). They determine the chances of the patient surviving for a specified number of years. The available empirical data made possible the use of a 5 year time horizon in the analysis.

The analysis shows that persons with diagnosed thyroid gland cancer, breast cancer, testis cancer and endometrial cancer have the best chances of survival one year after the diagnosis – this indicator amounts to over 90% (cf. Figure 12 and Table 3). The highest mortality rate involves pancreas, oesophagus and gallbladder cancers. In the case of the first of them, the chance of surviving a year after the diagnosis is only 23%. Note should also be taken of the very low survival rate in patients with the lung cancer, the cancer with the highest incidence rate in 2012. In the case of the most frequently diagnosed cancers the probability of surviving 5 years after the diagnosis are nearly 0.17 for the lung cancer, 0.79 for breast cancer, 0.51 in the case of the colon cancer and 0.74 for persons with diagnosed prostate cancer.

It should be noted also that in the case of neoplastic diseases the first year after the diagnosis is crucial. This is confirmed in Figure 13, which presents the death risk, i.e. probability of death in year *t* for a patient who lived till the year *t-1*. The risk of death during the first year after the diagnosis is strongly differentiated depending on the type of the cancer. During this period the highest death risk occurs in the cases of pancreas, oesophagus and gallbladder cancers. High risk of death during the first year also occurs in the case of the lung cancer, the cancer with the largest number of new cases – the risk of death during the first year is 0.62. After a period of about 3 years after the diagnosis the type of cancer no longer seems to be

a factor which differentiates the death risk. In consecutive years after diagnosis the risk of death becomes increasingly common for individual cancer streams.

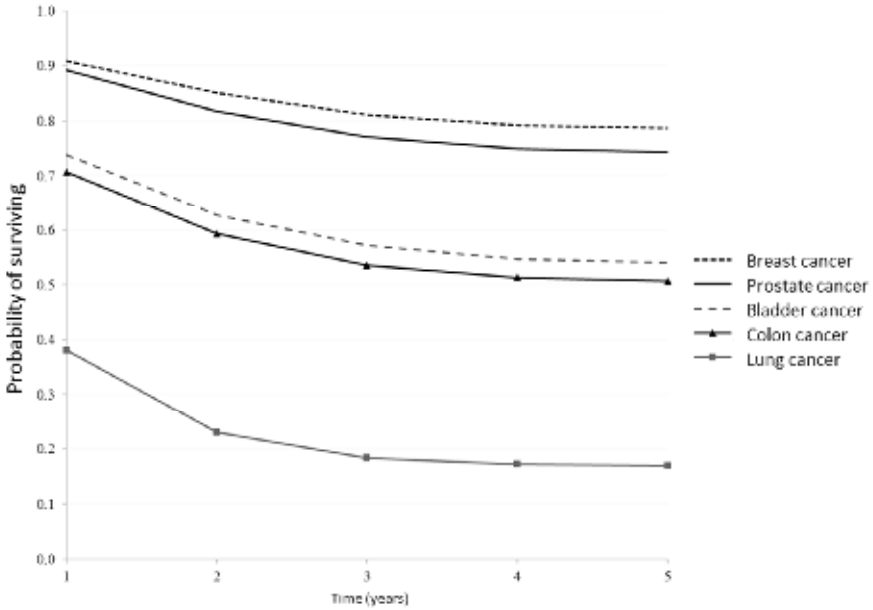


Figure 12. Unconditional survival curves for oncological patients
(Source: own analysis based on NCR and NHF data).

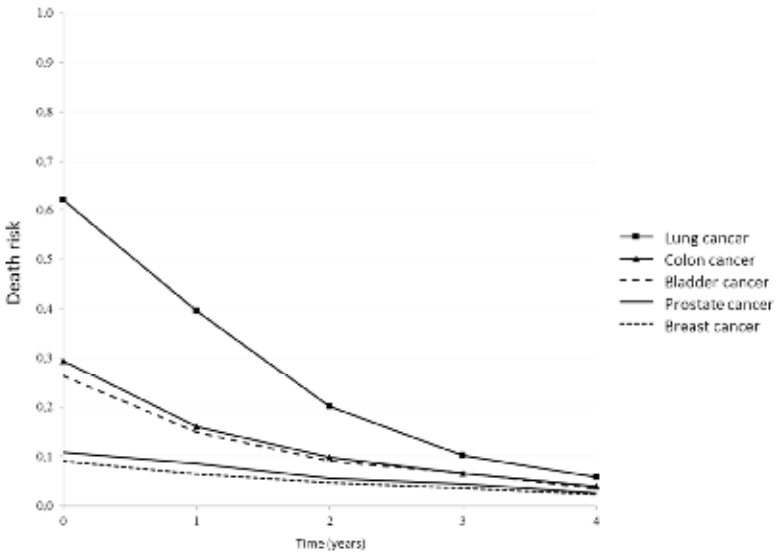


Figure 13. Death risk for new oncological patients
(Source: own analysis based on NCR and NHF data).

Table 3. Probability of survival and the death risk
(Source: own analysis based on NCR and NHF data).

Cancer stream	ICD Group	Probability of survival					Death risk				
		time (in years)					time (in years)				
		<0.1)	<1.2)	<2.3)	<3.4)	<4.5)	1	2	3	4	5
lip	**C00**	0.84	0.75	0.69	0.67	0.66	0.16	0.11	0.07	0.05	0.04
oral cavity	**C01, C02, C03, C04, C05, C06 C09, C10, C14**	0.59	0.45	0.39	0.38	0.37	0.41	0.24	0.12	0.07	0.05
salivary glands	**C07, C08**	0.74	0.63	0.59	0.58	0.57	0.26	0.15	0.07	0.03	0.03
nasopharynx and piriform sinus	**C11, C12, C13 C30, C31**	0.56	0.42	0.36	0.34	0.34	0.44	0.25	0.12	0.09	0.04
oesophagus	**C15**	0.29	0.15	0.12	0.11	0.11	0.71	0.47	0.19	0.16	0.06
stomach, digestive organs	**C16, C26**	0.42	0.29	0.25	0.23	0.23	0.58	0.30	0.15	0.09	0.04
colon	**C18, C19**	0.71	0.59	0.54	0.51	0.51	0.29	0.16	0.10	0.07	0.04
rectum and anus	**C20, C21**	0.74	0.60	0.52	0.49	0.49	0.26	0.19	0.13	0.09	0.05
liver	**C22**	0.32	0.22	0.17	0.16	0.16	0.68	0.32	0.20	0.11	0.08
gallbladder	**C23, C24**	0.29	0.19	0.15	0.14	0.14	0.71	0.36	0.18	0.11	0.07

In summary, development of two basic epidemiological statistics is crucial for defining the features of the studied population. These were determined with the use of available empirical data, use of the so-called evidence-based medicine approach and determination of the structure of patients suffering from cancer. This information provides the basic input data that will be used for development of forecasts for 2015-2025 and for determination of 5-year prevalence.

Results of forecasts for 2015-2025

In development of the forecast it is necessary to use historical input data to allow referring the current situation to the expected values. Their development is crucial in the process of building the health policy and possibilities for adjustment to the future health needs of the population.

Incidence

The previous part of this paper presents the number of new oncological patients in Poland in 2010-2012. It was used to determine the incidence rate which relates to the percentage of persons in an age group who were diagnosed with a given type of cancer. The incidence rate was determined separately for each of the 24 cancer streams in breakdown into 6 age groups (0–44, 45–54, 55–64, 65–74, 75–84, 85+)[124]. The 3-year incidence rate was used to generate a malignant neoplasm incidence forecast, also by stage progression. The generated forecast assumes a constant malignant neoplasm incidence rate and it is based to a major extent on a demographic forecast[125].

Therefore in the coming years we expect an increase in the number of newly diagnosed cancer (solid tumour) cases. In 2025 it will amount to nearly 199 thousand cases. This means growth by nearly 14% in the number of newly diagnosed persons with malignant neoplasm (cf. Figure 14).

[124] Incidence in the smaller neoplasm groups, specified in the "Other" group was taken into account as 6% of all cases nationwide.
[125] The paper used the demographic forecast developed by the Central Statistical Office, http://demografia.stat.gov.pl/bazademografia/Prognoza.aspx.

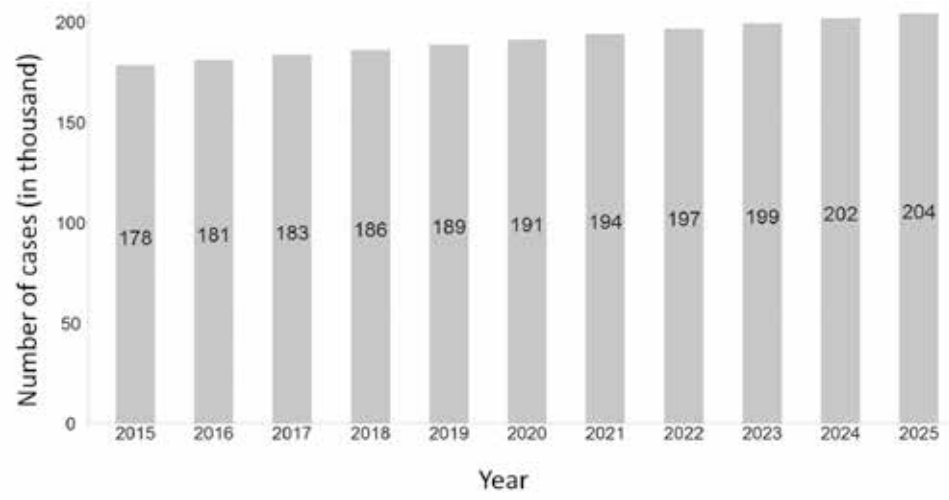
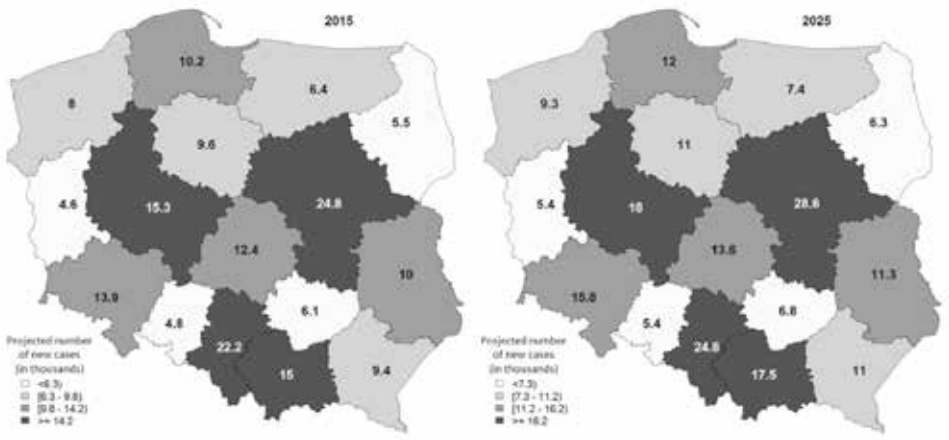


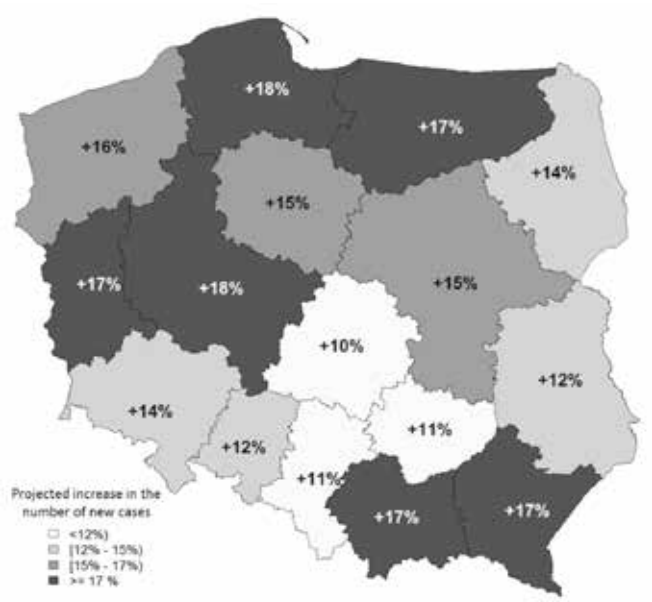
Figure 14. Forecast of total incidence rate of malignant neoplasms in 2015-2025 (Source: own analysis based on NCR and NHF data).

In terms of the place of residence of the patient, the largest number of new malignant neoplasm cases should be expected in the following voivodeships: Mazovia, Greater Poland, Silesia and Lesser Poland (cf. Map 2). Map 2. This relation is valid both for 2015 and 2025.



Map 2. The incidence of malignant neoplasm forecast for 2015 and 2025 (Source: own analysis based on NCR and NHF data).

Therefore within the coming 10 years the increase in malignant neoplasm incidence should be expected in Poland. It will be different in individual regions of Poland (cf. Map 3). Map 3. The largest 17% growth in incidence will occur in Warmia and Mazuria, Pomerania, Greater Poland and Sub-Carpathian regions, with the lowest growth to be seen in the Łódzkie region. The above relationships result mainly from changes in the demographic structure of regions and the share of older age groups in that structure, which are characteristic for oncological patients.



Map 3. Growth by per cent in the incidence of malignant neoplasms in Poland in 2015-2025 (Source: own analysis based on NCR and NHF data).

An assumption was also made during forecast developing that within such time horizon medical advancement shall not affect the baseline cancer incidence rate. It was also assumed that there would be no changes in the population behaviour that would affect exposure to factors posing neoplastic disease risks.

Figure 15 presents incidence forecast for 2015-2025 for each cancer stream. As expected, the highest growth in the incidence rate occurs with the most frequent cancers. The incidence rate forecasted for 2025 vs. the incidence rate in 2015 is presented in Figure 16. The highest

growth by per cent of the number of new cases should be expected in the lip cancer – however it results from the smallest size of this cancer stream. Additionally a decline in the testis cancer incident rate should be expected in the coming decade. The occurring changes will primarily result from on-going changes in the population age structure, i.e. mainly the increasing share of the 65+ age group.

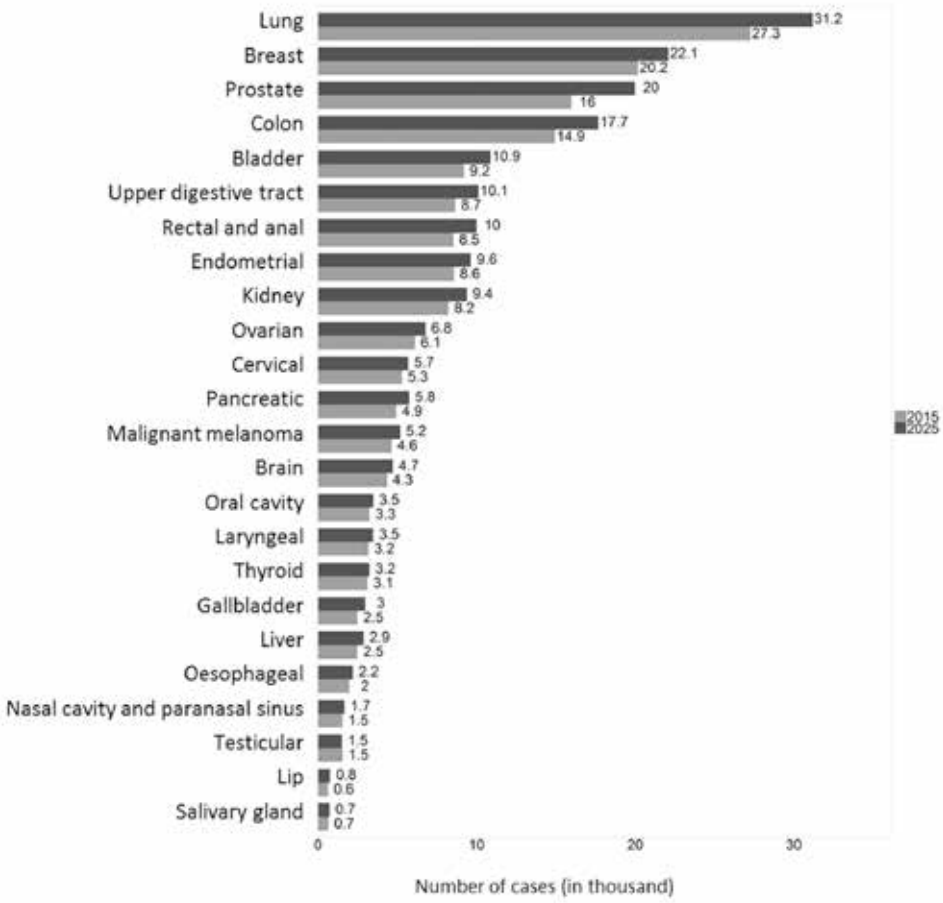


Figure 15. The incidence rate of malignant neoplasm forecast depending on the neoplasm group (Source: own analysis based on NCR and NHF data).

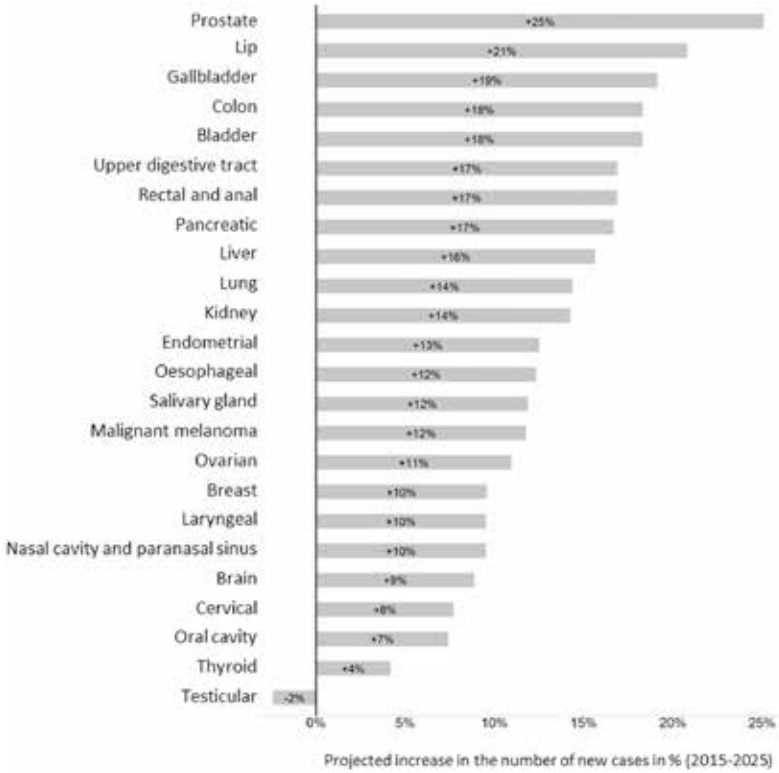


Figure 16. Changes in the incidence rate between 2015 and 2025 (Source: own analysis based on NCR and NHF data).

When comparing the patient age group structure in 2015 and 2025 one should mainly expect growth in the share of 45-54 and 65+ age group patients. The share of patients in 0–44 and 55–64 age groups will be smaller in 2025 than in 2015 (cf. Figure 17).

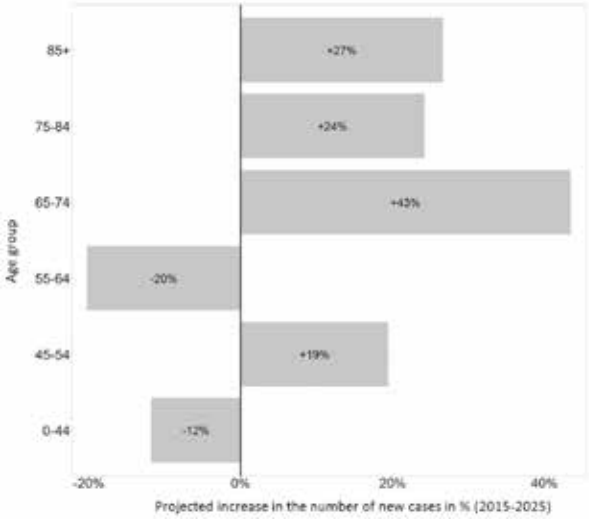


Figure 17. Changes in the patient age structure between 2015 and 2025
(Source: own analysis based on NCR, NHF and the Ministry of Internal Affairs data)

Therefore, in accordance with the presented incidence forecast, we expect an increase of about 14% in the number of new solid tumour cases over 2015-2025. This growth results from changes in the demographic structure of the population with the on-going ageing and the fact that oncological diseases are more common in older persons. What is more, growth in incidence will differ between voivodeships, thus indicating different future health needs of the population.

Prevalence

Assessment of incidence and survival curves allows observation of the epidemiological situation and definition of the features of the studied population. They may be then used as a basis for determination of prevalence, which defines the scale of the problem relating to oncological diseases and informs about the number of patients living with cancer in a given year. Prevalence is also used to measure the effects of the health care system functioning (Rothman, Greenland 2005). Registers dedicated to cancer often publish an indicator which uses the 5-year prevalence (relating it to the size of the population), and which takes into

consideration the number of patients living with cancer diagnosed during the past 5 years (i.a. Globocan[126], EUCAN[127], NCR[128]).

The 5-year prevalence determined for the given year uses information about 5-year survival and about the number of new cases during the past 5 years. Available data allowed the determination of 5-year survival, though they are insufficient to determine incidence within the 5 year period. Therefore, for the years when it was impossible to determine the level of incidence (also within the forecast years) estimation of incidence was made with the use of an assumption on constant incidence rate coefficients in age groups (determined based on 3-year data). This means, for instance, that 5-year prevalence for 2015 includes empirical information about patients diagnosed in 2010-2012 and their 5-year survivals as well as incidence forecasting for 2013-1014.

The 5-year prevalence forecast for 2015–2025 is presented in Figure 18. In 2015 the 5-year prevalence will amount to about 458 thousand and in 2025 nearly 533 thousand on the assumption that neither the survival rate of oncological patients nor the cancer incidence rate will change. Therefore, during 10 years the 5-year prevalence will grow by about 16%. This means that by 2015 1.19 out of 100 persons will be living with cancer diagnosed during the past 5 years. In 2025 this will already increase to 1.41 per 100 persons. Increase in oncological prevalence during the coming years results mainly from the process of ageing of the population. Figure 19 and Figure 20 present these values for individual cancer streams.

[126] http://globocan.iarc.fr/Default.aspx.
[127] http://eco.iarc.fr/eucan/.
[128] http://onkologia.org.pl/wp-content/uploads/Biul2012net.pdf.

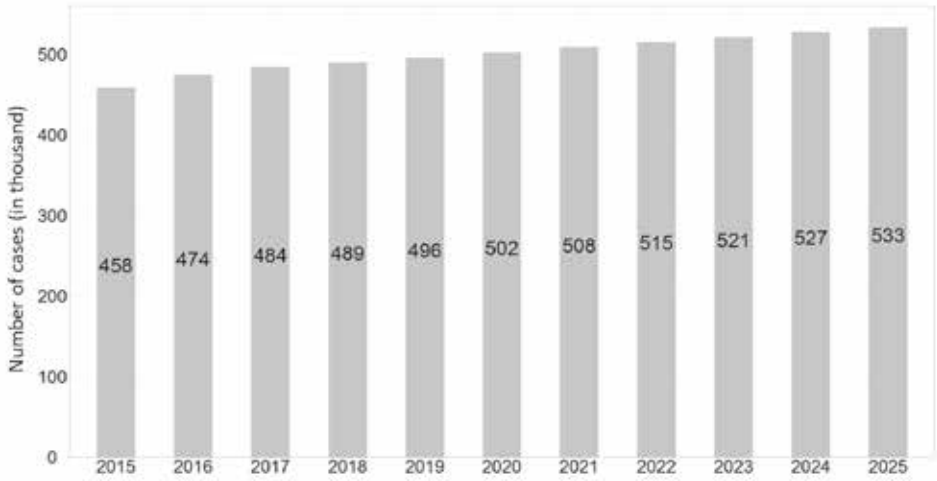


Figure 18. The 5-year prevalence forecast
(Source: own analysis based on CSO, NCR and NHF data).

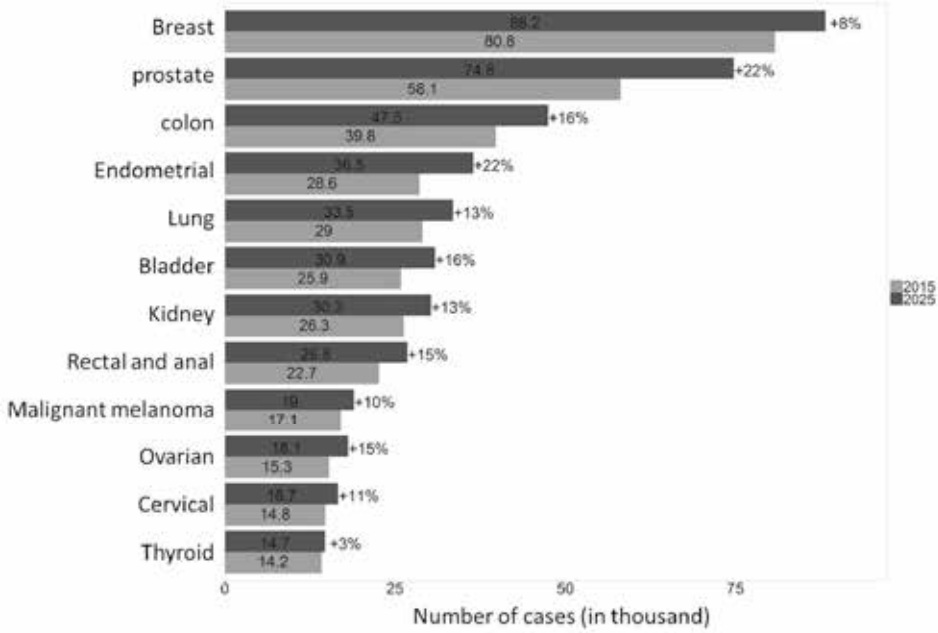


Figure 19. 5-year prevalence forecast for each cancer stream (1)
(Source: own analysis based on CSOS, NCR and NHF data).

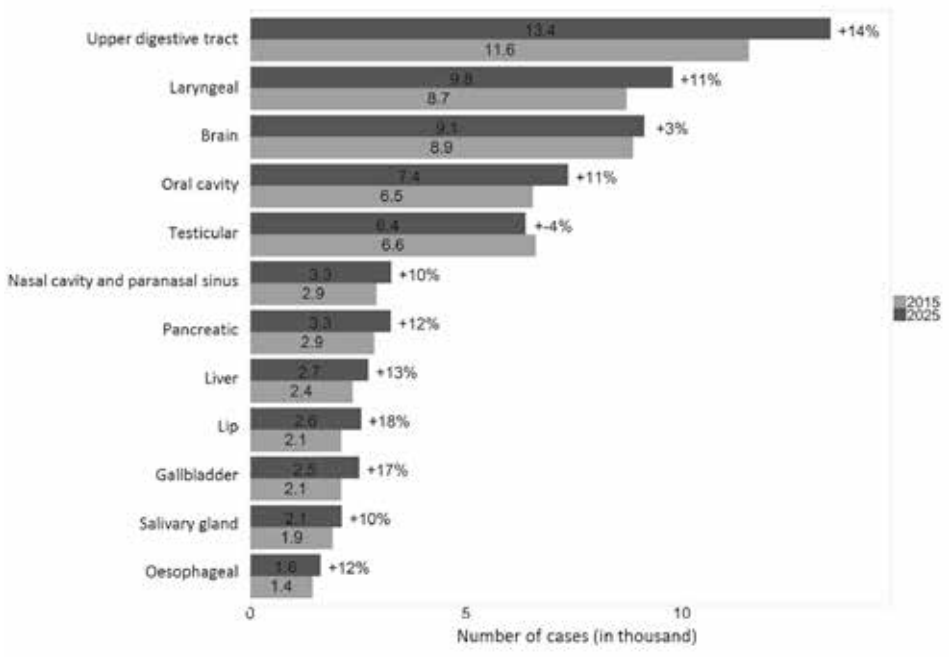
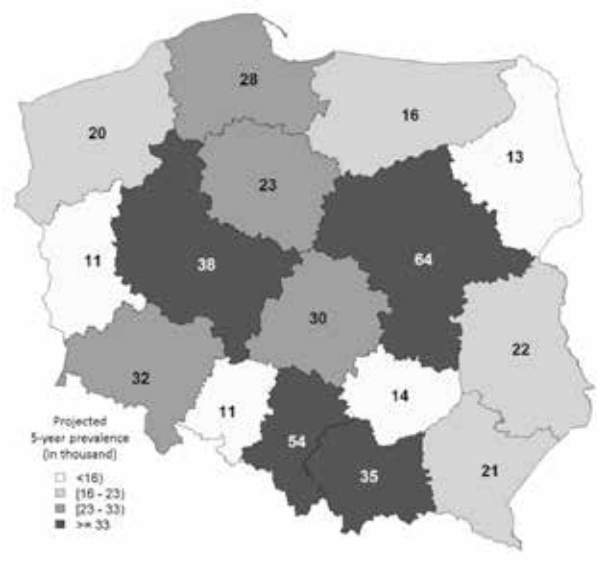
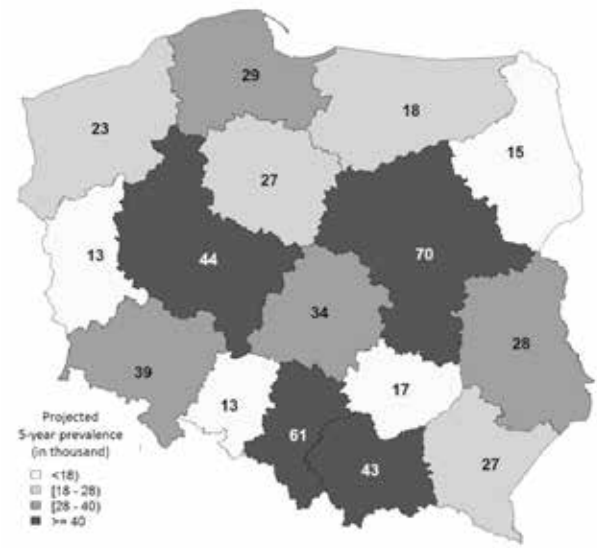


Figure 20. 5-year prevalence forecast for each cancer stream (2)
(Source: own analysis based on CSO, NCR and NHF data).

The 5-year prevalence in individual voivodeships is similar to incidence, i.e. the highest values should be expected in 2015 in the following voivodeships: Mazovia, Silesia, Greater Poland and Lesser Poland (cf. Map 4). It will amount to 64 thousand, 56 thousand, 38 thousand and 35 thousand respectively. This relationship will still hold in 2025 – the highest prevalence will still occur in Mazovia and will amount to 73 thousand (cf. Map 5). In Mazovia, Silesia, Greater Poland and Lesser Poland this will be: 61 thousand, 44 thousand and 43 thousand, respectively.

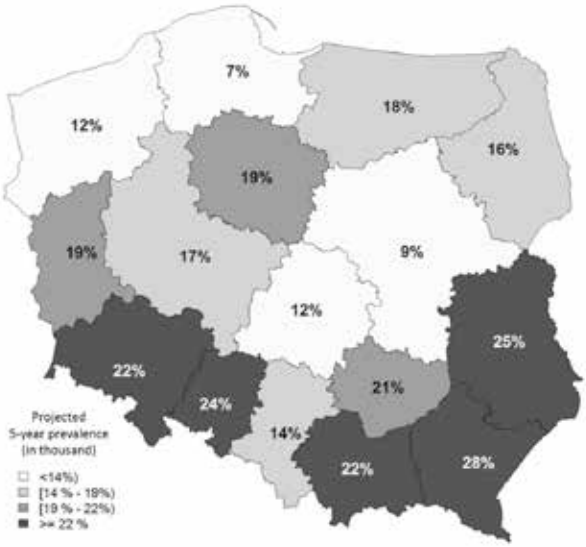


Map 4. The 5-year prevalence in 2015 (Source: own analysis based on CSO, NCR and NHF data)



Map 5. The 5-year prevalence in 2025 (Source: own analysis based on CSO, NCR and NHF data)

However, prevalence growth will differ between voivodeships. In the 2015-2025 perspective the highest growth in prevalence should be expected mainly in southern Poland voivodeships (cf. Map 6).. The largest increase will affect the following voivodeships: Sub-Carpathian (28%), Lubelskie (25%) and Opolskie (24%), but also Lower Silesia (22%) and Lesser Poland (21%). The lowest growth in prevalence over 2015-2025 will take place in Pomerania (7%), Mazovia (9%), Łódzkie (12%) and Western Pomerania (12%). The median of the prevalence increase is 19%, which means that in half of the voivodeships in Poland prevalence will grow by more than 19% in the 10 year perspective.



Map 6. Growth by per cent in the 5-year prevalence in 2015-2025
(Source: own analysis based on CSO, NCR and NHF data)

There were 458 thousand people living with cancer in Poland in 2015 and diagnosed in the past 5 years. As in the case of incidence, an increase in this value should be expected during the coming decade. Growth in prevalence will differ between the regions of Poland, which means differentiated burden on the oncological care system in individual regions of Poland.

Summary

Malignant neoplasms are the second most frequent cause of deaths in Poland (Wojtyniak et al. 2012). Due to their frequent occurrence, the process of treatment of this group of diseases has a major impact on the health care system, because expenditures on cancer care t are a significant burden on the system. Malignant neoplasms are most frequent among older people, therefore in view of the ageing society, growth in the number of new cases should be expected and hence – a growing number of persons suffering from malignant neoplasms. In the case of new diagnoses, they most common are cancers of the lung, breast, prostate, colon and the urinary bladder. On the other hand, analysis of the population of living patients diagnosed during the past five years shows, that the breast, prostate, colon and lung cancers will dominate. This forecast results from the number of diagnoses made annually, but also from survival in each cancer stream. In Poland the increase in new cases will differ between voivodeships. This is most probably the result of the age group structure, but also of the life style and access to medical care.

This paper was intended to present two elements: the present and the future situation with respect to oncological diseases. Assessment of historical data was crucial for identification of problematic areas. The forecast was designed to show the future incidence and prevalence rate with respect to neoplastic diseases. Their determination is crucial from the public health policy point of view, because it is important that the developments in health policy reflect as accurately as possible the changes in the health needs of the population. These estimates also provide essential information for projection of the future expenditures on cancer care, to ensure allocation of funds in line with the actual and projected health needs of the population. It should also be noted that in order to build accurate forecast, it is necessary to ensure reliable historical data that are the basis for its development.

Bibliography

Evidence-Based Medicine Working Group (1992) Evidence-based medicine. A new approach to teaching the practice of medicine, The Journal of the American Medical Association 268 (17), p. 2420-2425

Kaplan E.L., Meier P (1958) Nonparametric Estimation from Incomplete Observations, The Journal of the American Medical Association 53 (282), p. 457–481

National Cancer Institute (2010) Cancer Prevalence and Cost of Care Projections, http://costprojections.cancer.gov/annual.costs.html, date of access: 15.05.2015 15.05.2015.

Rothman K. J., Greenland S. (2005) Measures of Disease Frequency, in: Ahrens W., Pigeot I., Handbook of Epidemiology, Springer, p. 58–68.

Verdecchia A., De Angelis G. i Capocaccia R. (2002) Estimation and projections of cancer prevalence from cancer registry data, Statistics in Medicine, 21 (22), p. 3511–3526.

Wojciechowska U., Didkowska J., Zatoński W. (2012) Nowotwory Złośliwe w Polsce w 2010 roku, Krajowy Rejestr Nowotworów, Centrum Onkologii – Instytut im. Marii Skłodowskiej-Curie.

Wojciechowska U., Didkowska J., Zatoński W. (2012) Nowotwory Złośliwe w Polsce w 2010 roku, Krajowy Rejestr Nowotworów, Centrum Onkologii – Instytut im. Marii Skłodowskiej-Curie.

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Wojtyniak B., Rabczenko D., Pokarowski P., Poznańska A., Stokwiszewski J. (2012) Atlas umieralności ludności Polski w latach 1999–2001 i 2008–2010 – Internet edition: www.atlas.pzh.gov.pl.

The publication focuses on effective use of quantitative methods in the area of oncological diseases in Poland. It is a pioneering work on malignant neoplasms, combing the use of registry data (National Cancer Registry) and the data of the public payer (National Health Fund). The publication is particularly valuable because it includes extensive, objective analyses, which may help make decisions on priorities for contracting oncological services for the coming years. The book was written in line with the highest professional standards, using high qualifications, knowledge and experience of its authors. It is indispensable reading for decision-makers, advisors and analysts in the field of health care.

The publication is one of three volumes compiled by the team of experts working under the project "Improving the quality of management in health care by supporting the process of creating regional maps of health care needs as a tool streamlining the management processes in the health care system – training in estimating health care needs", implemented by the Department of Analyses and Strategy of the Ministry of Health, co-financed from the European Union funds under the European Social Fund.

In order to present the subject holistically, the publication is divided into two main parts: theoretical and empirical. It presents the basic terminology related to oncological diseases, demographic and sociological factors affecting the incidence of malignant neoplasms, and international experience in methodology of modelling of oncological diseases. It also presents descriptive empirical models for individual cancer groups which constitute the practical application of decision trees described in the theoretical part. The analyses allowed to present the projected incidence and 5-year prevalence of malignant neoplasms in Poland for the years 2015-2025.

Free copy

ISBN: 978-83-941589-3-4

Publication co-financed by the European Union under the European Social Fund

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