National cancer control plan 2020 – 2030

The Republic of Croatia

March, 2019

NACIONALNI PLAN PROTIV RAKA

Content

1. Foreword by the NCCP lead

a. BURDEN OF CANCER

The number of cancer patients in the world and in Croatia is constantly rising. The World Health Organization predicts that the global number of new patients will increase from 18 million in 2018 to 29,5 million per year in 2040, whilst the number of deaths will rise from 9,5 million to 16,4 million per year. Unfortunately, cancer is the leading health problem in Croatia. In the last 15 years, on average, 11 510 cases of invasive cancer were diagnosed annually in men and 9 980 in women. The latest official data from The Cancer Registry of the Croatian Institute of Public Health confirmed 22 503 cases of malignant diseases (11 969 in men and 10 534 in women), furthermore the incidence was 535,3/100.000; 590,0/100.000 for men and 484,3/100.000 for women.

The number of cancer cases in Croatia is expected to rise along with the number of cases globally, mostly because of aging population. From 2001 to 2015 the average number of patients increased by 1% on year to year basis. With the help of age-standardized incidence in Croatia, we can see that the increase of incidence independent of aging population. The average age-standardized incidence in Croatia from 2001 to 2015 increased 0,63 % for women, but decreased 0,23% for men. The most common cancer in men is lung cancer, whilst in women it is breast cancer. It is also expected for prostate cancer to become most common cancer in men in the near future. Five most common cancer sites account for more than half of all cases in both genders.

Malignant diseases are the second most common cause of death (after cardio-vascular diseases), they were responsible for 26% of deaths in Croatia in 2017. With people under the age of 65 it is the leading cause of death, and cause 50% of deaths in women and 35% in men. The latest official data in Croatia says that in 2017 the number of people who died from invasive cancer (not including non-melanoma skin cancer) in total was 13.638 (330,7/100.000 rate), of which 7.789 male (391,3/100.000 rate) and 5.849 female (274,1/100.000 rate).

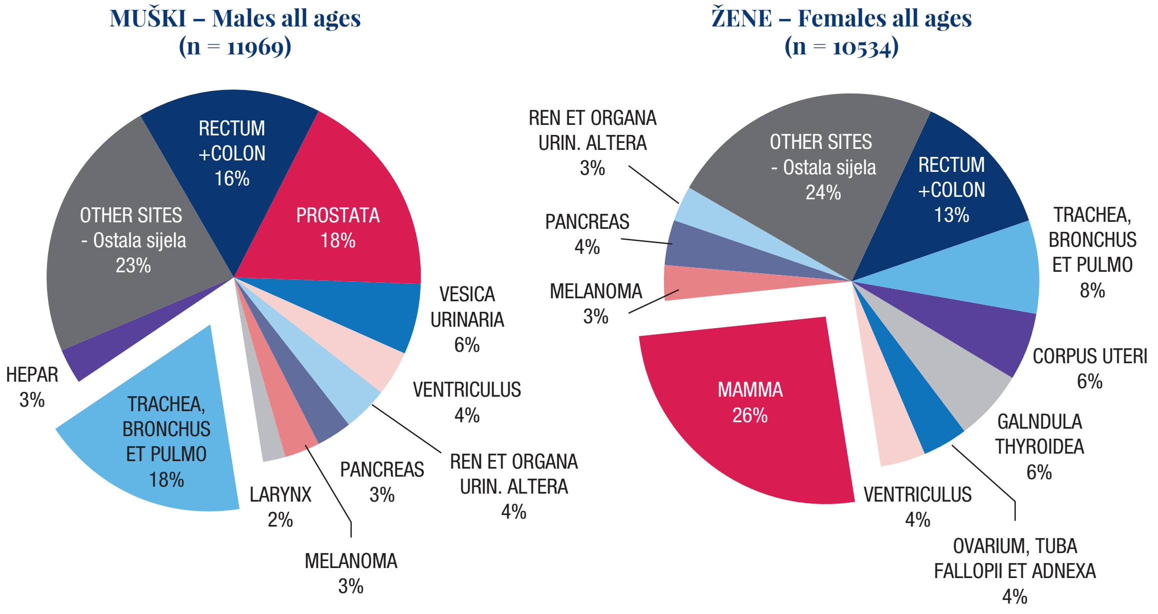
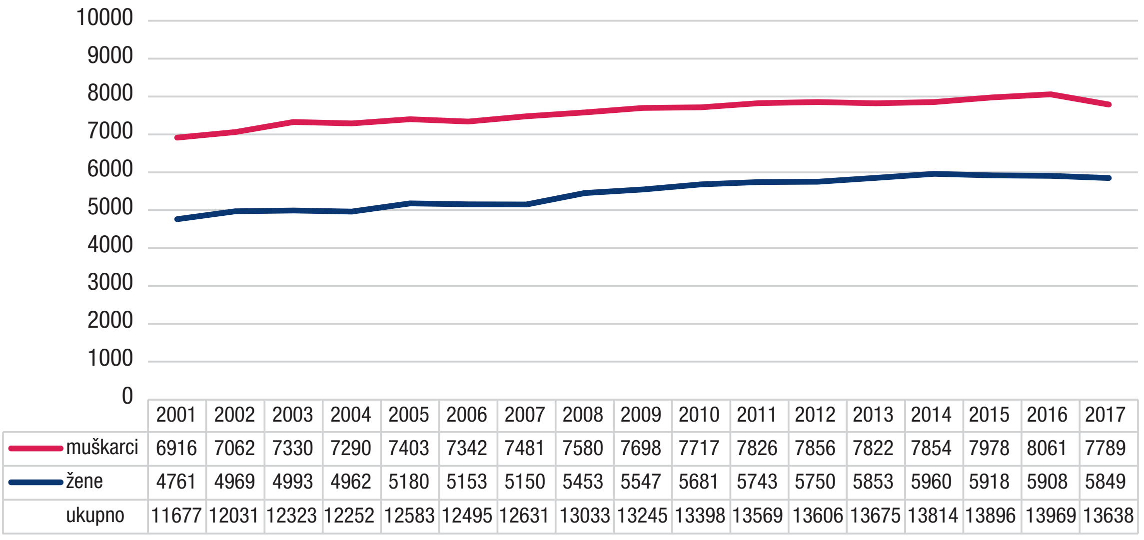


Figure 1 – Incidence of malignant diseases, rate of most common cancer types by gender, 2015

The most common cause of death in men was lung cancer (2.142), colorectal cancer (1.174) and prostate cancer (852), and in women it was colorectal cancer (863), breast cancer (853) and lung cancer (852). The proportion of population dying from cancer, among all causes of death, is constantly rising. Cancer was accountable for around 20% of all deaths in the mid 90-s, increasing to 25% in the last 10 years. Even though the proportion malignant diseases have in total mortality is increasing, the standardized mortality rate of cancer is decreasing. In most European countries that decrease is bigger than in Croatia. From 2001 to 2017 we can see a statistically significant fall in the age-standardized (E) mortality rate of 0,3% a year; in women there is no change in trend, while in men the annual decrease is 0,7%.



	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
muškarci	6916	7062	7330	7290	7403	7342	7481	7580	7698	7717	7826	7856	7822	7854	7978	8061	7789
žene	4761	4969	4993	4962	5180	5153	5150	5453	5547	5681	5743	5750	5853	5960	5918	5908	5849
ukupno	11677	12031	12323	12252	12583	12495	12631	13033	13245	13398	13569	13606	13675	13814	13896	13969	13638

Figure 2 – Number of cancer related deaths by gender, Croatia, 2001-2017

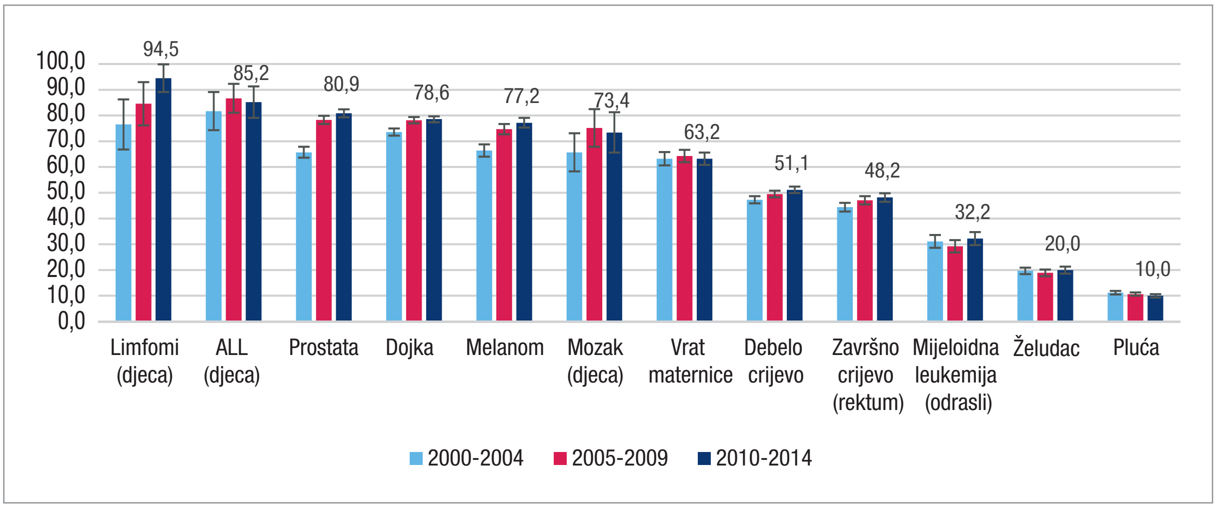


Figure 3 – Five-year survival from most common cancer sites in Croatia, for patients diagnosed from 2000 to 2014; the mark shows survival among patients diagnosed from 2010 to 2014

Survival rate in most cancer types is increasing, but there are significant differences between cancer sites. Five-year survival data for people who were diagnosed with some cancers between 2000 and 2014 and were recorder in the Croatian Cancer Registry were published in an international study on cancer survival, CONCORD-3.

This study included data for over 220.000 people who were diagnosed with a malignant disease in Croatia in the stated time period for 15 cancer sites in adults and 3 sites in children. Data on survival by site shows that Croatia is at the bottom of all the EU countries included in the research with better survival rates in children. Survival rate improvement is visible, but again, unfortunately, cancer survival in other European countries is improving on faster rate.

Out of the 30 EU countries included in the research, Croatia is among 5 with the worst survival for lung cancer (10%), prostate (81%), stomach (20%), colon and rectum (colon 51%, rectum 48%) and adult onset myeloid leukemia (32%). On the positive side, child survival (lymphomas (95%), brain tumors (73%) and acute lymphoblastic leukemia (85%)) is comparable to developed EU countries. We are also at the bottom for other common cancer sites in Croatia like breast cancer (79%), skin melanoma (77%) and cervical cancer (63%).

b. SOCIAL ASPECTS OF CANCER

Unfortunately, every third Croatian citizen will suffer from cancer. Every year more than 22.500 new cancer patients are diagnosed. The estimated number of people who are living with or without their cancer cured is 170.000. Obviously, these people don't live alone, but rather with their immediate or extended family. Taking into account that the average extended family has at minimum 4-5 members, we can easily hit a number of 850.000 Croatian citizens being impacted by cancer directly or indirectly in their daily lives, a number which makes up 20% of our society.

Because of modern oncology, we witness greater everyday oncological success with a greater ratio of cured patients. Therefore, two parallel processes have to be considered:

- cancer diagnosis, demanding therapy, sacrifice of a patient, family and society, pain, death, loss…
- cure, reintegration, rehabilitation, relations, right to work, right to a dignified life…

Respecting before mentioned numbers, specific historic and emotional truth about cancer and the fact it affects almost all Croatian families, cancer is and should be the primary societal concern. It should also be one of the most important aspects in national permanence. Even small improvements in this important public health issue will result in prosperity for many Croatian citizens. In the beginning the best starting point is to ensure that cancer is not publically treated as stigma and a myth which can only happen to somebody else. It can happen to each and every one of us. Lack of knowledge about cancer and historically determined fear of dying from cancer lead to escaping the truth, disrespect of the problem and leaving it unresolved. Accepting cancer as a possible diagnosis puts every citizen in the position to embrace education about preventive measures, early detection (screening) programs as well as determining, as a society, optimal treatment options, general oncology care, patient and family support initiatives, rehabilitation, re-integration and palliative care.

In conclusion, cancer is unfortunately part of our everyday lives, embedded in every pore of our society. With optimal and rigorous implementation of The National Cancer Control Plan, we can significantly minimize negative aspects of cancer to national health, improve overall population health status and build a happier society for many generations to come.

c. ECONOMIC IMPACTS OF CANCER

The cost of cancer and its development over time is impacted by a combination of different parameters and is mostly a reflection of the development in cancer incidence and mortality. For example, rising incidence increases the expenditures for diagnostics and treatment, whereas declining mortality in patients in working age reduces production loss. The share of cancer deaths out of total deaths is highest in the economically active age groups. In addition to epidemiological parameters and its direct impact, the cost of cancer over time is also a result of progress in cancer care. For instance, the introduction of new imaging techniques for diagnostics and new treatment modalities affects health expenditure in a complicated way, including both cost increasing and cost saving innovations.

Measured in current prices, per capita health expenditure on cancer in Europe, increased from €74 in 1995 to €164 in 2014, equaling an increase of 121%. Taking into account inflation, the health expenditure in 1995 was €105 per capita, equaling an increase of 56% between 1995 and 2014. During the same time, cancer incidence increased by approximately 30%. Thus, the mare increase in the number of cancer patients might be one explanatory factor of the observed development in total health expenditure. Other factors that could help to explain the increase over time are the roll out of mass screening programs for several cancer types and primary prevention measures (e.g. HPV vaccination), new cancer therapies (e.g. targeted cancer therapy and immunotherapy) that allow a greater share of patients to be treated and that come at a high price, and new but more expensive medical equipment for diagnostics and treatment (e.g. PET-CT scanners and linear accelerators).

In Croatia, the increase in per capita expenditures adjusted for PPP increased from €31 in 1995 to €80 in 2014 while the cancer-specific share of total health expenditure did not change (6.9% in both 1995 and 2014). Great disparities in health spending on cancer between countries persisted throughout 1995-2014. In 2014, per capita expenditures were highest in Luxembourg with €311 in 2014, followed by Central and Western European countries with more than €200. In Southern European countries (except Portugal and Croatia), per capita expenditures were between €155 and €100, whereas in countries along the eastern border of the EU (except Slovakia), the expenditures fell short of €100. In Romania, they were lowest with €53, which is six times lower than in Luxembourg.

Cancer drugs account for a growing share of total health expenditure on cancer in all countries. In the EU, this share increased from 12% in 2005 to 20% in 2010 and 23% in 2014. In Croatia, the increase was from 13% in 2005 to 22% in 2010 and 31% in 2014, however, the information for 2010 and 2014 could be overestimated as in 2009 mandatory confidential managed entry agreements were introduced to manage the overall expenditure of innovative cancer drugs. The relative burden of cancer has been increasing over time, while spending on cancer care has remained rather stable. Spending on cancer drugs has increased but at the same time balanced by reductions in spending on inpatient hospital care. In conclusion, the burden of cancer in terms of mortality and DALY is far higher than the health expenditure devoted to cancer care.

2. Executive summary

Cancer is the leading health problem in Croatia, and unfortunately every third Croatian citizen will suffer from cancer during his/her life. The latest official data from the Public Cancer Registry confirmed 22.503 new cases of malignant diseases in 2015 (11.969 men and 10.534 women), resulting with the incidence of 535,3/100.000 population (590,0/100.000 men and 484,3/100.000 women). The estimated number of people who are living with or without their cancer cured is 170.000. Obviously, these people don't live alone, but rather with their immediate or extended family. Taking into account that the average extended family has at minimum 4-5 members, we can easily hit a number of 850.000 Croatian citizens being impacted by cancer directly or indirectly in their daily lives, a number which makes up 20% of our society.

Cancer is the second most common cause of death in Croatia, after cardio-vascular diseases and is responsible for 26% of deaths in 2017. With people under the age of 65 it is the leading cause of death, and cause 50% of deaths in women and 35% in men. Data on survival by site shows that Croatia is at the bottom of all the EU countries, among 5 with the worst survival, except of children, who have comparable survival rates to EU. Survival rate improvement is visible, but again, unfortunately, cancer survival in other European countries is improving at a faster rate. The most probable causes for such unfavorable oncology outcomes in Croatia are multifactorial, and include great exposure to harming influences (primarily smoking and obesity), a lack of high-quality primary prevention programs, low health awareness and insufficient early detection programs, late diagnosis, higher share of more fatal forms of cancer, poor availability of high-quality oncology care, a lack of radiotherapy and other expensive and sophisticated equipment, a lack of true multidisciplinary approach in oncology, insufficient oncology databases and quality control, and, finally, insufficient investment in all aspects of oncology, from science and education to treatment and supportive symptomatic care for cancer patients

The most common cancer in men is lung cancer, whilst in women it is breast cancer. It is also expected for prostate cancer to become most common cancer in men in the near future. Five most common cancer sites account for more than half of all cases in both genders.

Because of modern oncology, we witness greater everyday oncological success with a greater ratio of cured patients. Therefore, two parallel processes have to be considered:

(1) cancer diagnosis, demanding therapy, sacrifice of a patient, family and society, pain, death, loss, and

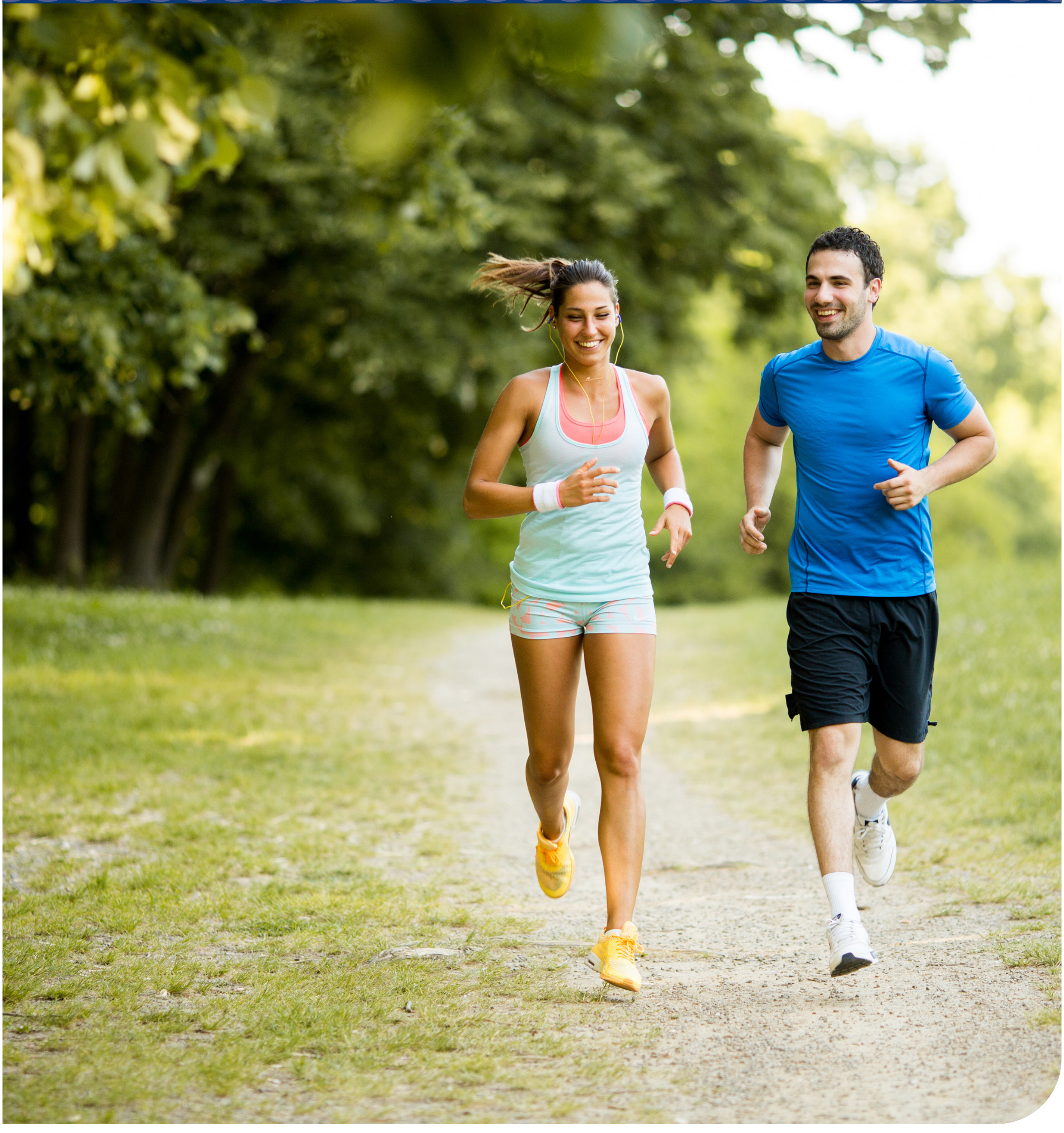
(2) cure, reintegration, rehabilitation, relations, right to work, right to a dignified life.

Interestingly, despite the clear increase in cancer burden, the share of total health expenditure devoted to cancer was constant in Europe and in Croatia (6.9%) over the last 20 years. While expenditures on cancer drugs increased during that period in both absolute and relative terms, other expenditures were decreasing what resulted in the flat share of investment, despite increases in cancer incidence driven by ageing population.

Considering everything said above, the decision was made to develop a comprehensive and cross functional National Cancer Control Plan for which 135 stakeholders were pulled together to collaborate through 21 Working Groups. After 3 years of consultations, research and brainstorming, they developed a robust plan with 12 Chapters, 112 objective and sub-objectives and most importantly with 228 measures which will enable the oncology community in Croatia to improve patients' outcomes to the level above the EU average.

The NCCP was developed in line with relevant WHO and EU guidelines and was offered for a public consultations and Experts' review in country and abroad. Economic evaluation was done in collaboration with foreign experts to ensure critical assessment and prioritization of activities based on the financial impacts. Implementation and the funding of this robust National Plan will be secured from budgeted state (public) healthcare resources, special unbudgeted local investments, as well as from the EU and WB funds or loans with the ultimate objective to prolong cancer survival in Croatia to the level of the Western European countries.

3. Primary prevention



3. Primary prevention

Introduction

Malignant diseases in their incidence and as a cause of death present one of the greatest public health challenges we are facing today. There are numerous risk factors for the occurrence and development of malignant diseases – family history, genetic predisposition, lifestyle (smoking, drinking alcohol, inadequate diet, excessive weight, insufficient physical activity), exposure to radiation, professional exposure, exposure to carcinogens in the environment, infections, some immunodeficiencies and medicines. According to the World Health Organisation 30 – 50 % of malignant tumours are preventable.

Primary prevention of malignant tumours includes educating the public on the related risk factors, eliminating risks or reducing exposure, and preserving and improving general health conditions by adopting healthy habits. Primary prevention measures should be introduced before the disease develops, with the aim of timely prevention.

Raising awareness of these factors in society as a whole is a continuous process, which has to be conducted among healthcare professionals and expert groups with a significant role in society, adjusting it at the same time to all age groups of the population. Strengthening public awareness of the role of risk factors in the development of malignant diseases is one of the key steps toward reducing cancer incidence rate.

For these activities to be successfully carried out, public health needs further strengthening in terms of know-how, skills and staff, and cooperation between health professionals, creators of public policies not only in health, but also in economy, education, social protection, labour, pension system and demography improved, including the general public as well, as a precondition for implementing prevention programmes on all levels.

In implementing the primary prevention measures, cross-sectorial and multidisciplinary approach is crucial, as it involves a greater number of stakeholders, including national and local government, educational and health institutions, NGOs and the media, but also relevant EU stakeholders who could provide additional guidance and support.

Planning preventive activities in the years to come should be based on improving the efficient monitoring of all measures in the area of promoting health and primary prevention by applying indicators comparable to those used in other countries.

Overall Croatia has a high prevalence of many behavioural risk factors. Based on Institute for Health Metrics and Evaluation (IHME) estimations, more than one third (36%) of the overall burden of disease in Croatia in 2015 (measured in terms of DALYs) can be attributed to behavioural risk factors, most notably smoking, but also alcohol use, dietary risks and physical inactivity contributing to high body mass index (IHME, 2016).

Unhealthy diet and insufficient physical activity are some of the risk factors for development of cancer, as they contribute to excessive body mass. Obesity is an important risk factor for the development of a number of cancers, such as breast, ovarian, intestine, pancreas and other types of cancer. Changing lifestyle at an early age is highly beneficial not only for reducing the risk of developing cancer, but for health in general. Cancer prevention through balanced diet, physical activity and maintaining adequate body mass can also contribute to preventing other diseases, including type 2 diabetes and cardiovascular diseases. The diet which might have protective effect against some malignant diseases includes increasing the consumption of fruits, vegetables, food rich in fibre, and reducing the intake of fat. According to the *European Health Interview Survey* (EHIS) conducted in Croatia in 2014 and 2015, 18.0 % of adults are obese, with body mass index ITM > = 30 kg/m^2. In terms of gender distribution, excessive body mass is more prevalent among men than women. Since 2015 the Republic of Croatia has been involved in the WHO project *Childhood Obesity Surveillance Initiative* – COSI, thus becoming a part of international monitoring of obesity among children, with the aim of applying a unique system of standardised measuring in the European region by the WHO, including measuring trends of excessive body mass among elementary school children. Research has shown that 13.9 % of children in Croatia at the age of seven are obese.

The action plan for preventing and reducing excessive weight was passed for the period 2010-2012. National guidelines for elementary schools’ diet were passed in 2013, and they are more intensively implemented through the national *Living healthy* programme. The programme was initiated in 2014, and consists of health education, health tourism, health and nutrition, health at workplace, health and environment, and a network of health promotion centres, including those dedicated to healthy diet and physical activity. According to the EHIS data for Croatia for 2014 and 2015, only 23 % of examinees older than 15 reaches the necessary level of medium intensity aerobic activity of at least 2.5 hours per week. The same research has shown that 59.6 % of examinees walk less than 30 minutes, and 40.4 % more than 30 minutes a day, on a usual day. A detailed analysis indicates that the share of men walking more than 30 minutes a day (44.4 %) is greater than the share of women (35.8 %).

Health education should start in pre-schools, and it should be part of the curriculum during the entire educational process. Such a curriculum would provide continuous education for children and parents about the benefits of a balanced diet, the need for physical activity, avoiding addiction which also increases the risk of developing chronic, non-communicable and malignant diseases (smoking tobacco, drinking alcohol, imbalanced diet with excessive intake of sugar, salt and fat), the need for preventive activities through vaccination and regular check-ups, and responsible workplace behaviour. Such an educational program must be supported by the conditions for maintaining healthy habits among children – removing vending machines that contain sweets, snacks and sugary drinks from all (!) educational institutions, enabling sufficient time and space for moving, and balanced school meals based on nutritionists’ advice. This systematic approach, in cooperation with the Ministry of Science and Education, is the only path toward changing social awareness and the level of healthcare literacy among the public, the approach which cannot be replaced by promotional campaigns and public health actions alone.

Smoking is the single greatest preventable cause of premature mortality and morbidity in the world today. It is connected to the development of different cancer sites – lung, oral cavity, nasal cavity and sinus, pharynx, larynx, oesophagus, stomach, pancreas, livers, urinary bladder, kidney, cervix and myeloid leukaemia. In highly developed countries smoking accounts for 30 % of all cancers. The risk increases proportionally with the length of smoking and the number of cigarettes, it is similar in both genders, and gender differences in incidence and mortality are usually attributed to different smoking habits among genders. Around 10 – 15 % of lung cancer in non-smokers is attributed to passive smoking.

According to the EHIS survey conducted in the Republic of Croatia in 2014, 25.0 % of examinees, of which 29.5 % were men and 20.8 % women, smoked every day; 3.7 % smoked occasionally (3.2 % men and 4.2 % women); 71.3 % of them did not smoke (75.0 % women and 67.3 % men).Smoking represents a serious public health issue in Croatia among both adults and children, with little progress made over the last few years. One quarter of Croatian adults reported being daily smokers in 2014, well above the EU average (21%). Regular smoking among 15-year-olds, at 23% in 2013–14, is the second highest rate among EU countries (after Bulgaria) and nearly 1.5 times greater than the EU average, which can be linked to generally weak anti-smoking policies.

The plan for taking measures and activities in the area of strengthening control over tobacco has been defined by the Action Plan for Strengthening Tobacco Control adopted by the Croatian Government for the period between 2013 and 2016. The planned activities were based on the World Health Organization Framework Convention on Tobacco Control (WHO FCTC), The Act on Ratifying the World Health Organization Framework Convention on Tobacco Control (*Official Gazette*, No. 3/08), Council of Europe Recommendation on smoke-free environments 2009/C 296/02), and the Directive 2001/37/EC of the European Parliament concerning the manufacture, presentation and sale of tobacco products. The new Act on Restrictions on the Use of Tobacco and Related Products (*Official Gazette* No. 45/17) has been in effect since 18 May 2017. The restriction of use has been expanded from tobacco products to other related products, leading to introducing the ban on direct or indirect advertising of tobacco and related products, including smokeless tobacco products and herbal smoking products, electronic cigarettes, refill containers and single-use cartridges. It is prohibited to smoke and consume tobacco and related products, including smokeless tobacco products, electronic cigarettes and herbal products for smoking, during public performances or to show persons smoking or consuming the products referred to on television. It is prohibited to sell tobacco and related products, including smokeless tobacco products and herbal products for smoking, electronic cigarettes, refill containers and single use cartridges to persons under 18 years of age. It is prohibited to sell tobacco and related tobacco products online, and to sell tobacco and related tobacco through vending machines. The 2017 Act on Restrictions on the Use of Tobacco and Related Products enables local government to declare no-smoking zones in cities. The Act is excellent, but it requires consistent implementation (!). Continuing with and strengthening legislative and tax measures, further education on harmful effects and consequences of smoking tobacco, particularly among minors, are key to reducing cancer-related morbidity and mortality.

Excessive alcohol consumption is connected to the development of oral cavity cancer, pharynx, larynx, oesophagus, liver, colon, rectum and breast cancer. According to some estimates 1.8 million deaths a year are attributed to excessive alcohol consumption. The risk increases with greater consumption, it multiplies with smoking, and with the infection of hepatitis B or C virus for liver cancer.

According to the EHIS survey, 9.1 % of examinees drank alcohol daily in the previous 12 months; 14.9 % drank at least once a week, 19.9 % less than once a week, and more than half of the examinees (56.2 %) drank alcohol rarely or did not drink at all in the previous 12 months.

Men drank more than women – 16.3 % of men drank alcohol every day, 21.1 % at least once a week, and 22.1 % less than once a week. Almost three quarters of women (74.0 %) drank alcohol rarely or did not drink at all in the previous 12 months; 14.8 % of women drank less than once a week, and 11.1 % at least once a week or every day.

Recognising the health and social impact of alcohol abuse, National Strategy for Preventing Alcohol Abuse and Alcohol-Related Disorders was adopted in 2010, for 2011-2016. In the view of everything stated above, Croatia has legislative framework to fight against alcoholism and its consequences.

Ten infective factors have been classified into known (Group 1) of cancer factors in people according to the International Agency for Research on Cancer (IARC), as follows: Helicobacter pylori, Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human papilloma virus (HPV, types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, known as HPV high risk types), Epstein-Barr virus (EBV), human herpes virus type 8 (HHV-8, known as herpes virus connected to Kaposi sarcoma), Human T-lymphotropic virus (HTLV-1), Opisthorchis viverrini, Clonorchissinensis and Schistosoma haematobium.

Cancer types scientifically proven to have a causal relation with the aforementioned factors include oral cavity, oropharynx, including tonsils and tongue base, larynx, anus, cervix, vulva, vagina and penis cancer (HPV); leukaemia and T-cell lymphoma in adults (HTLV-1); Kaposi sarcoma (HHV-8); Hodgkin's lymphoma, Burkitt's lymphoma and nasopharynx carcinoma (EBV); stomach cancer, stomach non-Hodgkin lymphoma (H.pylori); liver cancer (HBV), liver cancer and non-Hodgkin lymphoma (HCV), bile ducts cancer (Opisthorchis viverrini and Clonorchissinensis) and urine bladder cancer (Schistosoma haematobium).

Vaccination has an important role in reducing the incidence of cancer caused by infections. Two vaccines are currently available – vaccine against HBV (hepatitis B virus) which can cause liver cancer, and vaccines against some types of HPV (human papilloma virus) which can cause cervix cancer, vagina, vulva, penis, anus, oral cavity and throat cancer.

Vaccination against hepatitis B for persons with increased risk of infection and healthcare professionals started in the Republic of Croatia in 1980s. Universal vaccination against hepatitis B was introduced into Mandatory Vaccination Programme in 1999 for 6th graders; in 2007 vaccination against hepatitis B was introduced for infants. When children vaccinated as infants reach 6th grade in elementary school, vaccination for school children will be cancelled. Immunization of persons with increased risk and infants within the Mandatory Vaccination Programme has been defined by the Ordinance on immunisation, seroprophylaxis, chemoprophylaxis against infectious diseases, and on persons who have to comply with this obligation (Official Gazette 103/2013). The results of the universal vaccination against hepatitis B, with high reach, are already visible. The incidence of acute hepatitis B has been reduced compared to pre-vaccination by 50 %, and the decline of incidence is most evident among the youth.

Vaccination against HPV became available in Croatia in 2008. In some cities and counties, it was carried out in an organised way for school-going children, depending on the capacity of local government to finance it. In early 2016 this vaccination became available and free of charge for certain age groups in the entire country. The recommendation regarding age groups has gradually changed in the last two years, and since 2018 vaccination has been free of charge for elementary school 8th grade boys and girls. This vaccination is recommended and free of charge, but it has not been included in the Mandatory Vaccination Programme. Free vaccination against HPV has been regulated by the Programme of immunisation, seroprophylaxis and chemoprophylaxis for special groups and individuals with increased risk of tuberculosis, hepatitis A and B, rabies, yellow fever, cholera, abdominal typhus, tetanus, malaria, streptococcus disease, haemophilus influenza invasive disease, meningococcal disease and HPV infection (the so-called Programme 2). Participation of elementary school 8th graders in vaccination was very low in Croatia in 2017, i.e. below 10 %.

Systematic education of educational institution staff and parents involved in the process is necessary in order to increase participation in vaccination against HPV infections even prior to children reaching the vaccination age. Only systematic cooperation between the Ministry of Health, Croatian Institute of Public Health and the Ministry of Science and Education can achieve significant steps toward greater participation.

Around 1/4 to 1/5 of the population disease burden is caused by environmental factors, so cancer can also be a consequence of the exposure to harmful factors from the environment. This includes exposure to different chemical, physical, biological and other factors (e.g. chemicals, tobacco smoke, or radiation) through environmental media – water, food, air or ground. Although exposure to some factors has been proven as harmful and can lead to cancer, it does not mean that the exposed individuals will in fact develop the disease, because other factors need to be taken into consideration as well, such as dose, manner and the length of exposure, as well as individual genetic basis and physiological features.

Individuals are exposed to carcinogens by breathing in polluted air or consuming food and water. Carcinogens can appear in food as a result of mould contamination (aflatoxin), the use of pesticides, or during thermic processing (acrylamid). Food and water for human consumption may be contaminated with arsenic, of natural origin or released to the environment as a result of human activity; arsenic contaminated water is considered more harmful for human health. Lengthy exposure to arsenic is related to the increased risk of developing bladder, lung, liver, kidney cancer, and hematopoietic system cancer.

Professionally exposed groups of people are particularly at risk, and a number of substances workers in different industries come in contact with have been recognised as carcinogens. The most frequent are lung cancer, connected to asbestos, beryllium, cadmium, silicon dioxide crystals, chrome and nickel exposure. Exposure to benzene and ethylene oxide connected to leukaemia among adults, whereas exposure to tar and mineral oils is connected to skin cancer. Due to professional exposure to harmful substances regulatory mechanisms aimed at reducing the exposure in some industries is necessary. Continuous monitoring of carcinogens at the workplace is important, through risk assessments and implementing measures for reducing their occurrence and workers' exposure, as well as continual monitoring of the exposed workers' health. Adequate levels of education about risks that the presence of carcinogens poses for employers and employees in the workplace is necessary. Workers, employees, physicians, experts and EHS inspectors need to have greater awareness on the consequences of exposure to carcinogens, and on the possibilities for preventing such exposure. Disease epidemic caused by asbestos exposure (mesothelioma) is at its peak due to long latency, so apart from preventing production and the use of asbestos it is important to eliminate and adequately manage disposal of any asbestos that is still in our surrounding.

Due to damage of the ozone layer, the change of lifestyle and new trends, there has been an increased incidence of melanoma as a result of grate exposure to ultraviolet (UV) light in the last years, irrespective of whether the exposure is to natural light or artificial light in tanning beds. Preventing skin exposure to UV radiation and early lesion discovery are key steps necessary for reducing the risk related to this disease and improving skin cancer treatment outcomes.

According to the latest available data from the Cancer Registry, in 2014 in the Republic of Croatia 587 people were diagnosed with melanoma, 305 of whom were men and 282 women. Although most patients belong to the older age group, melanoma patients on average belong to younger age groups compared to other types of cancer, so 20% of patients are under the age of 50. According to the latest mortality data, in 2016 138 men and 97 women died of melanoma. 5-year melanoma survival rate in Croatia, according to the CONCORD-3 international study, for persons diagnosed between 2010 and 2014 is 77 %, which marks a significant improvement compared to the data for persons diagnosed between 2000 and 2004, when the 5-year survival rate was 66 %. Although melanoma survival rate is somewhat higher than in other cancer types and a positive trend can be observed, Croatia still lags behind Europe and is ranked 21st out of 28 European countries, of which 20 have above 80 % survival rate. One of the measures for reducing the risk of skin cancer caused by UV exposure is educating the public on its harmful effects, and on the appropriate use of UV protection. Young people who use tanning beds are particularly important target groups.

It is necessary to establish cooperation between the Ministry of Health and the Ministry of Labour and Pension System and other stakeholders for systematic training of employers and their employees on workplace risk factors (exposure to hazardous agents, prolonged sun exposure, exposure to tobacco smoke, sedentary jobs which disable movement). During a certain period of time, awareness of healthy workplaces, which enable employees to maintain a healthy lifestyle (movement, availability of balanced diet) and reduce exposure to risk factors to the smallest possible extent, should be developed.

Alongside all specific measures listed below for each primary prevention objective, it is also very important to:

(a) strengthen capacities and infrastructure for implementing primary prevention measures,

(b) implement primary prevention measures through cross-sectorial and multidisciplinary approach, and (c) improve the system of indicators monitoring and assessing the efficiency of primary prevention measures.

Vision 2030

To have primary prevention programs fully implemented and controlled, consecutively public cancer awareness on the level of western EU countries average in order to reduce malignant disease incidence through primary prevention to the level of western EU countries average.

Objectives / Sub-objectives

1. **Promoting healthy eating habits and regular physical activity**
    - 1.1. Increase awareness of the importance of a healthy diet and the need for regular physical activity
    - 1.2. Improve eating habits and reduce the prevalence of obesity among children, youth and adults to the western EU average
    - 1.3. Increase the accessibility of healthy food and adequate diet for all groups in society
    - 1.4. Increase the accessibility of facilities for physical activity and improve the quality of targeted physical activity programmes for different age groups
    - 1.5. Ensure sufficient human and financial resources in public health institutes and in primary care with the aim of successful promotion of adequate nutrition and physical activity with health benefits
    - 1.6. Continuously introduce new effective measures, in line with EU strategies (https://ec.europa.eu/health/nutrition_physical_activity/platform_en)

2. **Preventing smoking-related cancer**
    - 2.1. Reduce tobacco smoking prevalence to western EU average prevalence
    - 2.2. Reduce the availability of tobacco and related products especially through tax policy
    - 2.3. Increase awareness and knowledge on the harmful effects of smoking
    - 2.4. Enable a smoke-free environment
    - 2.5. Continuously introduce new effective measures, in line with EU strategies https://ec.europa.eu/health/tobacco/overview_en

3. **Reducing the harmful effect of alcohol consumption**
    - 3.1. Strengthen awareness of alcohol as a harmful factor for the development of malignant diseases

3.2. Reduce drinking prevalence, particularly among adolescents to the level of western EU average
3.3. Reduce availability of alcoholic drinks through tax policy

4. **Preventing cancer caused by infections**
   4.1. Increase public awareness on the connection between infections and cancer, and on prevention possibilities
   4.2. Eliminate hepatitis B infections in infant and adult age by 2030
   4.3. Reduced HBsAg carriers' prevalence in general population, and reduce the risk of developing liver cancer connected to chronic hepatitis B
   4.4. Reduce the risk of premalignant and malignant lesions related to persistent HPV infection in persons undergoing vaccination
   4.5. Increase the participation in vaccination among elementary school 8th grade students to at least 50% by 2025
   4.6. Reduce the incidence of cervix premalignant lesion among girls and young women by at least 30% by 2030

5. **Preventing cancer caused by risk factors related to lifestyle and work environment**
   5.1. Ensure an adequate level of knowledge about the risks associated with the presence of carcinogenic substances in the environment and in the workplace and on the manners of effective prevention
   5.2. Reduce exposure to carcinogens in the workplace by implementing health and safety measures at the workplace and ensure early detection and treatment by conducting preventive examinations
   5.3. Ensure a safe and healthy environment by monitoring all environmental media, assessing the impact on health and adopting and implementing health protection measures against harmful environmental factors

Measures / Activities

1. **Promoting healthy eating habits and regular physical activity**
   a. Educate the general public and experts on adequate nutrition and physical activity with health benefits
   b. Apply national guidelines for elementary school nutrition
   c. Develop and implement guidelines for nutrition according to specific targeted groups
   d. Develop and implement national guidelines for physical activity with health benefits
   e. Implement physical activity consultancy services within the health system and refer to certified fitness programmes
   f. Implement tax policy measures with the view of improving nutrition – implementing comprehensive fiscal policy which includes accessibility, availability, and acceptability of healthier eating habits
   g. Increase the availability of healthy nutrition in public catering facilities

   Target groups: Healthcare professionals, particularly those working in public health institutes and primary healthcare, kindergarten, elementary and high school staff, children in kindergartens, elementary and high school students and their parents, socially vulnerable groups, sports and recreational clubs, fitness centres, other physical or legal persons providing physical activities with health benefits, the food industry, family farms, restaurant and other catering facilities owners.

2. **Preventing smoking-related cancer**
    a. Educate the general public on the harmful effects of smoking tobacco
    b. Develop a positive attitude about non-smoking among younger generations, and secure a positive environment
    c. Implement regulations with the aim of reducing smoking tobacco and ensuring smoke-free environment
    d. Implement tax policy measures with the view of reducing cigarette accessibility, particularly for younger age groups; increase cigarette tax as much as possible and direct it entirely or to a great extent into preventive activities, including fight against cancer (!)
    e. Support smokers in their efforts to quit smoking
    f. Enable physicians and nurses to treat tobacco addiction

    Target groups: general population, elementary, high school and university students and their parents, employees in these institutions, salesmen, healthcare professionals, marginalised groups and groups at the risk off social exclusion

3. **Reducing the harmful effect of alcohol consumption**
    a. Raise awareness of alcohol as a risk factor for a number of diseases, including malignant ones
    b. Develop positive attitude among younger generations about not drinking alcohol, and secure positive environment
    c. Develop and implement education programmes for marginalised groups and those at risk of social exclusion
    d. Control and supervise the implementation of regulations that reduce alcohol available to younger generations
    e. Support communities in adopting efficient approach and interventions for preventing and reducing alcohol abuse

    Target groups: general population and the media, elementary, high school and university students and their parents, high school and university students and their parents, persons who face problems as a result of alcohol abuse (including moderate consumers) and alcoholics, NGOs, and other providers of interventions for preventing and reducing alcohol abuse

4. **Preventing cancer caused by infections**
    a. HBsAg carriers testing for pregnant women, immunoprophylaxis of the newly born whose mothers tested positive for HBsAg, in accordance with the Act on Protecting the Public from Infectious Diseases;
    b. Continual maintenance of high vaccination coverage (> 95 %) against hepatitis B in infants and persons with increased risk of infection, in line with the Ordinance on

   immunisation, seroprophylaxis, chemoprophylaxis against infectious diseases, and on persons who have to comply with this obligation and the Vaccination Programme;
   c. Ensure financial means and organisation in the health system with the view of continually providing vaccination against hepatitis B for the purpose of implementing the Vaccination Programme and Programme 2;
   d. Ensure financial means and organisation in the health system with the view of continually providing vaccination against HPV, for the purpose of implementing Programme 2;
   e. Monitor the HPV vaccination response rate, vaccine safety and efficiency, and modify recommendations if necessary;
   f. Provide objective public information about benefits and risks of vaccination, in accordance with the vaccination safe application and efficiency monitoring results.

   Target groups: general population, infants, pregnant women, elementary school 6 and 8 graders, persons with increased risk

5. **Preventing cancer caused by risk factors related to lifestyle and work environment**
   a. Educate employers and employees about workplace exposure to carcinogens
   b. Ensure effective functioning of workplace control of the exposure to carcinogenic substances, as well as the application of occupational safety measures by strengthening the capacity of occupational health and safety at work and inspection services
   c. Education on the harmful effects of UV exposure and on the effective application of protective measures, including cosmetic agents with UV filter.
   d. Legal regulation of tanning bed use, including ban on use by minors, requiring licensing and UV lamps intensity control in these facilities
   e. Ensure effective safety monitoring of food and water for human consumption, as well as recreational waters, in particular with regard to the presence of carcinogenic substances.
   f. Carry out effective air pollution monitoring and ensure the implementation of pollution reduction and elimination measures, in particular with regard to carcinogens
   g. Establish a system of environmental pollution monitoring, in particular industrial contaminated areas and those with hot spots
   h. Adopt the asbestos and asbestos-based products elimination programs in all places where it exists

   Target groups: Croatian Employer Associations (HUP, UPUZ,), Institute for medical research and Occupational Health (IMI), Work Councils, Occupational Health Specialists, all employees

Stakeholders

- Ministries (Health, Science and Education, Economy, Labour and Pension, Environment and Energy, Tourism, Agriculture)
- Croatian Institute for Health Protection and Safety at Work
- Croatian Health Insurance Fund

- National and Regional (county) Institutes of Public Health
- Primary healthcare physicians and visiting nurses
- Specialists, gynaecologists, neonatologists
- Local Government
- Education and Teacher Training Agency
- Professional Associations
- NGOs
- Journalists
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- Government of Croatia
- EU or other international source of funding

Economic evaluation

Primary prevention activities are from economic evaluation perspective relatively cheap and feasible to implement, including tobacco control, dietary advice, and taxation policies that promote healthy lifestyles. As the costs of cancer diagnosis and therapy are already very high and keep growing, prevention will lead to net savings. Furthermore, risk factors are shared among many different non communicable diseases (NCDs). For example, smoking, obesity, and poor diet are risk factors for several major cancers but are also determinants of cardiovascular disease, diabetes, and some neurological diseases. Thus, prevention as in investment has a multiplying positive effect on the costs of care of multiple non-communicable diseases (NCDs).

There are many examples of the effectiveness and cost-effectiveness of primary prevention in terms of declining cancer rates. For example, 40% of the overall decrease in cancer mortality rate between 1991 and 2003 in men in the United States has been because of a reduction in cigarette smoking. A large scale smoking cessation program in Taipei (involving counselling and nicotine replacement) led to 215 million USD savings in 15 years. According to a simulation model, an intensive six-month mass media antismoking campaign in Australia would lead to an estimated $912 million savings over the lifetime of 190.000 quitters, which is equivalent to Australia’s government investment in early childhood education.

Tax and prices of tobacco are among the most effective policies on the side of demand. There is strong evidence from Thailand and Brazil that increases in taxes and prices had a large and durable impact on the decline in tobacco use. In Brazil, smoking prevalence declined by 46% between 1989 and 2008, with 48% and 14% of the relative decline attributed to taxes and advertisement bans, respectively. Similarly, increased taxes and advertisement bans, respectively, accounted for 61% and 22% of the relative decrease in smoking prevalence between 1991 and 2006 in Thailand.

Dietary advice to obese and overweight people in the Netherlands has been estimated to save up to $2.5 billion over five years. Very good evidence of the effectiveness of hepatitis B virus (HBV) vaccination is available from Taiwan, where vaccination started in 1984. Since then, liver cancer in children and young adults has decreased by as much as 80%. As with other preventive programs, the campaign had a number of positive outcomes: It has successfully lowered the prevalence of chronic HBV carriers, mortality from infant fulminant hepatitis, and chronic liver disease in vaccinated birth cohorts.

The predicted increase in the cancer burden can only be reduced if prevention strategies are prioritized. Only rapid acceleration in the implementation of cancer control programs at national levels is likely to have a major impact in reducing the projected burden. In the absence of the implementation of prevention, such a scenario can only amplify socio-economic differentials, making effective therapies a preserve of the richest in most societies.

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4. Secondary prevention (early detection)

4. Secondary prevention (early detection)

Introduction

The treatment of most types of cancer is more successful if cancer is diagnosed at an early stage. Survival rates for a number of common sites and types of cancer can be greatly improved by early diagnosis and treatment according to the most up-to-date knowledge. Secondary prevention therefore involves early identification of symptoms by an individual and timely diagnosis by a physician. On one hand, it is necessary to inform the public about early symptoms and signs of cancer through health education and on the other hand, enable physicians to properly diagnose these symptoms as soon as possible.

Through organized screening examinations programs, i.e. using simple tests, we can detect invasive or early invasive forms of cancer in people without clinical symptoms. Organized screening programs involve actively calling specific population groups to undergo testing, organizing screening programs, which include quality parameters monitoring according to relevant European guidelines. The primary goal of screenings is to reduce cancer mortality rate. Mortality is the most important long-term indicator of the screening program outcomes effectiveness. By monitoring early indicators, it is possible to evaluate the effects before reducing mortality. This effect can be analyzed using special methodology (cohort and periodic effect). Early detection of cancer is best achieved by organizing screening programs, which includes a series of activities that begin by regulating legal and financial basis, ensuring adequate equipment and specifically trained personnel, and defining target population and program algorithms. The targeted population group of a particular age is called in regular intervals to undergo cancer screenings for cancer sites that can be treated efficiently, followed by mandatory follow-up of procedures, treatment, and ultimate outcome. Special attention should be paid to healthcare users who are difficult to reach, as well as to persons without insurance. If cancer is detected in the screening program, the costs of treatment for those persons should be defined and covered. Organized screening also includes any measure and procedure aimed at securing and controlling the quality of the screening, which is also the basis for further improvement of the overall care, and ultimately is the most rational step.

According to scientifically based evidence and recommendations of the EU Council on cancer screening (2003/878/EC), three cancer sites are related to the implementation of organized screenings, i.e. breast and cervical cancer in women and colon cancer in both genders. Detailed guidelines for quality assurance of organized screening for breast, cervical and colon cancer have been published in the EU, and translated into Croatian. The Croatian Guidelines for Quality Assurance of Breast Cancer Screening and Diagnosis were published in 2017, and the guidelines for the other two sites are under development and will be available most probably before the implementation of the NCCP (expected date of publication 2019/2020). The implemented screening programs should achieve the highest possible response rate and quality level. They will be accompanied by appropriate promotional campaigns, as well as ongoing training of the staff running and managing the programs.

Based WHO and other relevant international criteria, all new screening programs should have:

(i) the evidence for the effectiveness of screening;

(ii) the evidence that the benefits of screening outweigh the harms;

(iii) the evidence that the screening is cost-effective.

Priority screening programs:

Breast cancer early detection screening

The national program for early detection of breast cancer, “Mamma” started with the implementation at the end of 2006. The main goal of the program is to reduce breast cancer related mortality by 25% within 5 years from Program implementation, to detect cancer at an early stage and to improve the quality of life of patients with breast cancer. The program includes all women50 to 69 years of age who are being invited for breast examination with mammography every two years, aiming to reach 70% response rate. In the first cycle of the program a total of 720,981 women were invited, and the response was 58.5% with 1,593 breast cancers discovered. In the second cycle 680,552 women were invited and the response was 57%, with 928 breast cancers discovered. The third cycle began in late 2011 and lasted until May 2014with a response rate of 45,1% and the fourth started in May 2014 and ended in autumn 2016. The Croatian Guidelines for Quality Assurance of Breast Cancer Screening and Diagnosis were published in 2017 which will contribute to additional quality of cancer screening program in Croatia.

Colon cancer early detection screening

Colon cancer is the second most common type of cancer, and the second leading cause of malignant cancer death in both genders. Around 3000 persons of both genders are diagnosed annually with this type of cancer in the Republic of Croatia, and around 2000 die, which has become a stable trend. In 2014 colon cancer was diagnosed in 3127 persons, and in 2016 there were 2169 persons who dies of this disease, making it the fourth cause of death in Croatia. Implementing the National Program for Early Detection of Colon Cancer began with the decision of the Government of Croatia made in late 2007. Every two years, persons of both genders between 50 and 74 years of age receive a letter inviting them to undergo fecal occult blood test. People with positive result are referred to colonoscopy via a centralized system. The age range and program implementation method is in line with the European Commission’s recommendations. A high share of patients with discovered and removed polyps, which is the best colon cancer prevention, makes this program particularly valuable. In order to achieve screening program efficiency, at least 45% of persons should have the fecal occult blood test performed, with the desirable response at 65%. Given the difficulties in the implementation so far, 30% of the total number of invited persons are expected to have the test performed. According to the EHIS survey conducted in Croatia on a self-assessment of health condition, about 27% of the target group had the fecal occult blood test within three years, and about 14% had colonoscopy within ten years. This suggests that only a small number of people of this age had the exam outside the organized program, mainly during regular check-up.

Unfortunately, current screening response in colon cancer program is rather low, only 17% of people invited to screening have returned their kits with a correctly placed stool specimen on FOBT cards.

Cervical cancer early detection screening – National Cervical Cancer Early Detection Program

The goal of the National Cervical Cancer Early Detection Program is aimed at maintaining women's health, reducing risk, early cervix cancer detection and improving the quality of life of the targeted population of women. According to the recommendation from the Twinning Project Improving the quality of the implementation of the National Cancer Screening Program, the call on public as a part of the Cervical Screening Programs was suspended until the basic implementation conditions are fulfilled.

Since the middle of the last century, opportunistic screening was implemented in the Republic of Croatia, and this led to a reduction in the incidence and mortality of cervical cancer. However, with the opportunistic program it is not possible to reduce the incidence of disease under 10/100.000, since most of the new cases arise from the part of the population that is not covered with screening. In December 2012 The Ministry of Health of the Croatian Government started the implementation of national organized cervical cancer screening program. The objectives of the program are to decrease the incidence of invasive cervical cancer by 60% in the age group 25-65 years after 8 years from the beginning of the program, reducing mortality by 80% in the age group 25 to 70 years after 13 years and gradual cessation of opportunistic screening. The program included women, "no opportunistic" (women who had a recent Pap-test are not invited), age range 25-64, every 3 years, index year 2013. Invitation coverage (on annual population) was 105.1% of all ages. Proportion of the target population screened in the index year after invitation was 10.8%. Participation rate of all ages was 10.3%.

Lung cancer

After recent publications of Nelson and NLST studies controversies about recommendation for the use of low dose lung CT for lung cancer screening have diminished. Now, it was proven that annual screening is associated with about 25% decrease in lung cancer mortality. The cost per QALY gained in annual screening with low-dose computed tomography in the tobacco-related risk groups has been estimated to vary between about US$ 13.000 and US$ 81.000 while interventions with the cost of up to 36.000 EUR could be considered cost effective in Croatia based on WHO threshold recommendation.

Due to fact that the national program for early detection of lung cancer has not started yet (will start on May 2019), we do not have previous screening response rates in Croatia.

Possible additional screening programs:

Prostate cancer

Cost-effectiveness with a single screen at age 55 was estimated at US$ 31.500. These cost-effectiveness ratios apply to health care costs as incurred in the United States and may be lower in European settings. For the Netherlands, cost-effectiveness has been estimated at €19.000 per QALY which could be, based on WHO recommendation, considered cost effective in Croatia too, at the level of 1.6x GDP. The European Randomized Study of Screening for Prostate Cancer has showed that screening using levels of prostate-specific antigen (PSA) results in a 21% prostate cancer mortality reduction in an intention-to-treat analysis, but questions remain on the optimal benefit-harm balance.

Gastric cancer

There are three types of screening programs: (i) screening for gastric cancer itself by endoscopy or fluoroscopy, (ii) screening for precancerous lesions by detecting the ratio between pepsinogen I and II or other biomarkers in the circulation, and (iii) screening for Helicobacter pylori, the major carcinogen for gastric cancer, with the aim to eradicate it in those testing positive (search-and-treat strategy).

As there are currently no conclusive cost effectiveness studies and there for no clear recommendation for the implementation of a specific screening program in Europe, more research is needed, especially whether and how to implement population-based H. pylori screening and treatment programs as well as the rationale for endoscopy and serology screening for gastric cancer and the associated risk-lesions.

Other cancer sites screening programs

Screening tests are available for many types of cancer, but so far their efficacy has not been proven in people with average risk. Therefore, for potential new sites the most recent findings with proven effectiveness are to be applied. In addition, guidelines for opportunistic early detection in people with elevated risk, in co-operation with a selected GP who is the only one with relevant data, has to be introduced.

Vision 2030

Improve ratio of early to late stage cancers at diagnosis by 20%, for all cancer sites with implemented screening programs (breast, cervical colon and lung) and implement new screening programs based on possible positive cost effectiveness analysis (prostate, gastric, melanoma)

Objectives

Breast cancer

1. Maximally improve the response to mammography screening within the framework of the existing national breast cancer early detection program to at least 76% in 2020 and 77% in 2021
2. Reduce mortality by 25%

Colon cancer

1. Maximally improve the response to screening within the framework of the existing national colon cancer early detection program to at least 45% in 2020 and 50% in 2021
2. Reduce mortality by 25%

Cervical cancer

1. Reduce cervical cancer incidence and mortality by 50% after three implementation cycles, through a well-organized National Program for early Detection of Cervical Cancer.
2. Maximally improve the response to the test up to at least 61% in 2020 and 62% in 2021.
3. Reduce mortality by 25%

Lung cancer

1. Implement National Lung Cancer screening program
2. Reach screening response rate of 60% in target population
3. Reduce cancer mortality by 25%
4. Increase 5-year survival from 6% to 15%

Other cancers:

1. Cost effectives analyses for the implementation of additional screening programs, e.g. prostate cancer, gastric cancer and melanoma.

Measures/Activities

General

1. Introduce specific screening targets and key performance indicators (KPIs) for GPs and related to that develop bonus/malus scheme to motivate high screening rates (e.g. if screening target reach is 75% than ensure bonus to all GPs who reached this target and if the reach is below 50% consider some financial penalties similar and within the scope of other measure implemented by HZZO)
2. For targeted patients who have not responded to screening programs consider making supplementary health insurance more expensive (alignment between HZZO and all other relevant insurance companies needed) and for those who are having free supplementary insurance consider revoking this benefit on a temporary basis.

Breast cancer

1. Encourage clinical self-examination and provide training
2. Mammography every two years; every year for women with positive family history who belong to a risk group; Target group: women between the age of 50 and 69
3. Introduce genetic counselling and gene testing for women, as well as special screening protocols for women with particularly high risk of breast cancer (the so-called high-risk screening), which includes annual breast MRI.
4. Regular renewal of mammography equipment and replacement with new one(please see Chapter 5 for further information); strict quality control of all segments of the program, by complying with all the elements of the adopted and published Croatian Guidelines for Quality Assurance of Screening and Diagnosis of Breast Cancer (2017, ISBN 978-953-7031-64-0) in the implementation of the National Breast Cancer Early Detection Program. These guidelines are comprehensive, they are divided into nine chapters, include epidemiological guidelines, quality control recommendations for mammography devices, radiography guidelines, radiological guidelines, multidisciplinary aspects of quality assurance, pathology and surgical guidelines, diagnostic and screening units' certification, and guidelines on communicating early detection of breast cancer. The existing IT program, which is inadequate, must be improved.

Colon cancer

1. Every two years, persons of both genders between 50 and 74 years of age receive a letter inviting them to undergo fecal occult blood test.
2. People with positive result are referred to colonoscopy via a centralized system. The age range and program implementation method is in line with the European Commission's recommendations. A high share of patients with discovered and removed polyps, which is the best colon cancer prevention, makes this program particularly valuable.
3. In order to achieve the screening program efficiency, at least 45%of persons should have the fecal occult blood test performed, with the desirable response at 65%. Given the difficulties in the implementation so far, 30% of the total number of invited persons are expected to have the test performed. According to the EHIS survey conducted in Croatia on a self-assessment of health condition, about 27% of the target group had the fecal occult blood test within three years, and about 14% had colonoscopy within ten years. This suggests that only a small number of people of this age had the exam outside the organized program, mainly during regular check-ups.
4. Introduce genetic counselling and gene testing for individuals, as well as special screening protocols for people with particularly high risk of colon cancer
5. Regular renewal of endoscopy equipment and strict quality control of all segments of the program
6. Measures to increase the effectiveness of screening and increase the percentage of responses to screening: PR campaigns, educating the public through electronic and non-electronic media, promoting patient participation in screenings by general practitioners, training persons to perform tests, understanding regional differences and their reduction and effective involvement of local government

Cervical cancer

1. Develop a legislative framework with clear definition of obligations and responsibilities of screening program participants
2. Continually work on raising awareness of women and the public about cervical cancer prevention
3. Continually train health professionals involved in the screening program and the public about the prevention of this cancer site. Targeted education and the better communication channels lead to both more useful and more rational referrals, and to better healthcare for patients. An educated physician will explain the importance of self-examination to a patient more easily, therefore will be able to detect early cancer symptoms better. Both the physician and the patient must be well informed about modern diagnostic methods and cancer treatment. The role of GPs in early detection of cancer is important because they are familiar (or should be familiar) with family history, social status, psychological condition (excessive stress), risk habits (alcohol, smoking), eating habits, exposure to carcinogenic substances at work and other risk factors. All the information provided must be documented, to make sure they are well connected after the occurrence of suspicious symptoms
4. Measures to increase the effectiveness of screening and increase the percentage of responses to screening: PR campaigns, educating the public through electronic and non-electronic media, promoting patient participation in screenings by general practitioners, training persons to perform tests, understanding regional differences and their reduction and effective involvement of local government. So far, screenings have been promoted through various marketing and educational programs. These initiatives include educational materials, press articles, and television or radio shows. At the local level, educational campaigns were organized in schools and workplaces. These measures should continue to be implemented and their effectiveness assessed.
5. For women under 30 years the primary screening would still a Pap smear.
6. Reduce opportunistic screening
7. Develop a functional IT system that will enable tracking, results storage, evaluation and quality control. Implement a pilot project of testing the IT system functionality in one county, various intervention strategies and a new HPV DNA screening for women over 30 years of age prior to national implementation, as recommended by the European guidelines on quality assurance of cervical cancer screening. National implementation can only be considered once the pilot project is proved successful and economically viable.
8. Ensure the necessary human, financial resources and facilities for smooth running of the program

Lung cancer

1. Publish recommendations for implementation with quality assurance measures
2. Develop materials for individuals who will be entering the screening programs, to transparently present all benefits and potential harms of screening
3. Establish public campaign (TV, radio, internet, social networks) to increase awareness and importance of Lung cancer screening program
4. Plan health service requirements and their delivery

5. Network of 15 centers with low-dose CTs will be established and radiologist will be educated and accredited to perform lung cancer screening programs
6. Patients who need further work – up will be sent to six accredited centers throughout Croatia
7. Plan to set up a registry of images and data
8. International and national quality assurance boards should be set up to oversee technical standards
9. Lung nodule management pathway will be done according to Lung – RADS guidelines
10. Population at risk of both genders, aged 50 – 75 years, will be sent to screening in collaboration with GPs.
    a. currently smoke or have quit within the past 15 years
    b. have at least a 30-pack-year smoking history
    c. have been involved in informed/shared decision making about the benefits, limitations, and harms of screening with LDCT scans
    d. receive smoking cessation counseling if they are current smokers
11. In persons at risk with initial normal LDCT, scans will be performed every three years. In persons at risk with emphysema features on LDCT scan, scans will be performed every two years.
12. Evaluate implementation after the first 12 months and review delivery strategy

Stakeholders

- Ministry of Health
- Croatian Institute of Public Health
- Croatian Institute of Telemedicine
- Croatian Health Insurance Fund
- Professional Associations
- Patient Associations
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources at HZJZ, HZZO
- Additional resources needed to improve the likelihood to reach target screening response rate and implement additional screening programs
- EU or other international source of funding

Economic evaluation

Developed countries around the world are investing heavily in secondary prevention with noticeable results. For instance, cervical cancer incidence rates in many western countries such as Finland and Sweden have decreased by more than 70%, largely because of organized screening. Earlier diagnosis, combined with more effective therapies have had a dramatic effect on the success of cancer treatment. In the case of breast cancer, mortality in Europe is decreasing in spite of an increasing incidence.

In terms of economic evaluation, much however depends on the organisation of the screening programs. International studies of the cost-effectiveness of breast cancer screening show substantial differences in cost per life-years gained. The cost-effectiveness ratio appears to be more favorable for well-organized screening programs, often European ones, than for spontaneous screening. The probable explanation is that having a special organization only for screening helps keep costs low, promotes more efficient use of resources, with high attendance of invited women and good quality screening leading to a health benefit. Moreover, as the direct cost for the screening examination is probably the most important single factor in total costs, organized large-scale screening may reduce the average cost per screen. A number of reviews of the cost-effectiveness of colorectal cancer screening reaffirms the results that any fecal occult blood test, sigmoidoscopy, colonoscopy, virtual colonoscopy, or stool DNA test is cost effective when compared with no screening.

Some of the first cost-effectiveness data from a lung cancer screening trial in Europe has come from the UK Lung Cancer Screening (UKLS), providing a more than acceptable figure of around UK £8.5K per QALY gained for screening. Also, there is now robust and consistent evidence for the cost-effectiveness of lung cancer computed tomography (CT) screening in Canada. Over 570 potential screening scenarios were evaluated, which included parameters such as the age to start or stop screening, screening interval, eligibility criteria (with respect to smoking history and quit time) as well as whether or not former smokers were excluded from further screening. Incorporating the provision of standard smoking cessation measures into the model modestly increases cost but results in a marked improvement in the QALY's saved.

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5. Diagnosis of cancer

5. Diagnosis of cancer

a. IMAGING TECHNIQUES

Introduction

One of the greatest problems in oncology care is a slow and fragmented diagnostic process, which includes imaging and functional diagnosis, cytological or pathohistological analysis, i.e. acquiring imaging methods using cells or tissue and molecular analysis. The scope of diagnostic options and optimal algorithms for the most common types of cancer in the Republic of Croatia need to be defined in detail.

After referral to a diagnostic treatment, patients are facing a problem of insufficient and unequal access to the optimal diagnostic procedures, from quality and time perspective. Radiology procedures, both diagnostic and interventional, need to be standardized at the national level for the most common types of cancer, and radiologists need to be included in all oncology multidisciplinary teams at individual institutional level. European standards for radiological equipment renewal and servicing need to be used, a register of radiological equipment to be established and kept at the Ministry of Health, and the number of examinations per device and per radiologist to be analyzed in details for each public institution in Croatia as well as the quality of radiological findings. Such data are necessary for the appropriate planning of equipment renewal as well as to ensure their optimal use. In the City of Zagreb, it is important to clearly define institutions in which patients are examined and by which team, to avoid having tests unnecessarily repeated in different hospitals. It is also important to introduce methods for quality control of assessing radiology tests in cancer patients, as about 25-30% of the patients are treated incorrectly due to inadequate radiological exams, and number of patients are being referred to certain exams unnecessarily (e.g. breast MRI). Clear criteria for the referral of patients to radiological examinations with long waiting lists need to be introduced, particularly for cancer patients. It is recommended to use the i-Guide, a clinical decision support system of the European Society of Radiology, which should be integrated into hospital information systems. Cancer patients must have separate, priority waiting lists, depending on clinical indication for the exam. In accordance to the European guidelines, in primary diagnosis of malignant diseases, adequate diagnostics should be provided within reasonable time, not longer than three weeks. Additional conditions need to be ensured, such as: availability of appropriate equipment and trained staff to carry out these procedures in all clinical hospitals and hospital centers, as well as in most county and general hospitals for specific, more frequent tumors. The second reading of oncological test results need to be mandated by law, as it is a burden for radiologists in clinical hospitals and rewarded only at a symbolic level. There is no alternative for radiology images revision in external institutions, if the imaging is of poor quality, which is frequently the case. Supplementing the findings with those from external institutions is proposed, instead of asking for new interpretation, and introducing financial regulation of such activity, with repeated testing only in the case of significant errors. Adequate PACS systems need to be introduced in all clinical hospitals in Croatia and a gradual transition to cloud technology to be planned. In some subspecialist areas in Croatia education for oncological imaging is inadequate, and a quality control system has yet to be introduced. GPs are not educated for performing some procedures such as breast ultrasound, and it is medically unjustified to diagnose breast cancer partially, without mammography, ultrasound, MRI and biopsy if necessary at the primary health care level, unless this diagnosis is performed by properly trained radiologists.

Unfortunately, we are witnessing a significant delay in the diagnostic of cancer patients. The reasons are a lack of diagnostic equipment, its uneven distribution and a lack of trained personnel. Irrational management of existing, limited diagnostic resources, due to the non-compliance with the guidelines and the fact that diagnostic specialists are often not consulted when the exam is indicated, pose additional challenges. The situation can be quickly improved by a strict implementation ofthe European guidelines and adequate use of existing equipment. In example, MRI should be more frequently used for cancer patients and less frequently for patients with chronic back pain, as results of this test would not have a significant impact on the treatment choice for the chronic back pain patients and could have for cancer patients.

Also, patients need to become more responsible to avoid multiple orders, not showing up for scheduled exams, and not taking over written findings, or in case they act irresponsibly, could be charged patients for the full cost of the exam.

In all institutions where a significant number of cancer patients undergo surgery and treatment, basic interventional radiological procedures for cancer patients have been introduced, as they have been found useful in validation processes at major centers abroad. Core procedures such as TACE, TAE, thermal ablation, and PEI should be used, followed by the evaluation of standard treatment methods that are available to Croatian patients.

Given that the diagnosis of cancer in most cases starts with a GP, primary health care plays an important role in this process. The areas where primary health care should play a key role are:

- Coordinating diagnostic procedures in line with the European guidelines for referring patient to radiology exams (ESR i-Guide)
- Long-term follow up of patients who are believed to be cured of cancer

The prerequisite for the optimal start of the diagnostic process is good medical education within the framework of primary health care, and understanding European guidelines that should be integrated into hospital information systems and as a second step to be introduced into primary healthcare system. After completing early cancer treatment, a primary care physician plays an important role in monitoring patients, in collaboration with the responsible oncologist. In order that the optimal conditions for the inclusion of GPs in the monitoring process of cancer patients are met, adequate education and knowledge about procedures are necessary. Therefore, timely diagnostic procedures and optimal monitoring of cancer patients during and after treatment are cornerstone of the successful treatment.

Summary of key issues:

- Delayed diagnosis and consequently delayed onset of treatment play significant role in high mortality to incidence ratio for cancer in Croatia
- Insufficient availability of optimal diagnostic procedures
- Non-compliance with standardized protocols for diagnosing and monitoring treatment effects and outcomes
- Irrational use of limited resources

Vision 2030

Improve capacity and capabilities for diagnostic procedures, treatment monitoring and cancer after-care in Croatia to meet all of the western EU standards by 2025.

Objectives

1. Improve the organizational and quality aspects of oncological diagnostics and treatment monitoring
2. Improve the access to optimal cancer diagnostic procedures to patients
3. Improve collaboration and coordination among all relevant stakeholders in the healthcare system, especially GPs, oncologists and radiologists in order to ensure rational use of diagnostic resources.

Measures/Activities

1. Develop optimal diagnostic and treatment monitoring algorithms for the most common types of cancer (in line with European guidelines, not longer than three weeks for primary diagnosis)
2. Standardize diagnostic and interventional radiology procedures for the most common types of cancer at the national level
3. Implement PET-CT technology at all University centers in Croatia (currently Split, Rijeka and Osijek do not have that essential diagnostic tool for cancer patients)
4. Ensure that radiologists are included in all MDTs at individual institutional level
5. Ensure that all other specialists performing cancer diagnostic procedures are part of MDT (gastroenterologists, pulmonologists, gynecologists, etc.)
6. Develop a national network of optimal diagnostic procedures to ensure equal availability to all patients

7. Develop clear criteria for patients' referral to radiological examinations, prioritizing those with long waiting lists. It is recommended to use the ESR (European Society of Radiology) i-Guide clinical decision support system which should be integrated into hospital information systems.
8. GP's and other specialist's education and training on how to coordinate and monitor diagnostic processes by using ESR i-Guide.
9. Long-term follow up of patients who are believed to be cured of cancer and collaboration with patient's oncologist.
10. Ministry of Health to develop and maintain a register of radiological equipment as well as other diagnostic equipment used in cancer diagnosis (endoscopy or bronchoscopy equipment for example)
11. Promote / mandate the use of European standards for radiological equipment renewal and servicing
12. On a continuous basis, perform the utilization analysis (per device, radiologist, and institution at the national level).
13. Introduce quality control processes to improve accuracy of diagnostic tests readouts (currently, 25-30% of the patients are treated incorrectly due to inadequate radiological exam, and numerous patients are referred to certain exams unnecessarily)
14. Regulate the process and rewarding system for the second reading of diagnostic test results
15. Introduce adequate PACS systems in all clinical institutions and a gradual transition to a cloud technology

Stakeholders

- Ministry of Health
- Professional Associations
- Croatian Medical Association (HLZ)
- Croatian Health Insurance Fund
- Hospitals
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources (Ministry of health, HZZO, Hospitals)
- Additional resources needed to implement planned measures
- EU or other international source of funding

Economic evaluation

Effective early diagnosis can help detect cancer in patients at an earlier stage, enabling treatment that is generally more effective, less complex, and less expensive. For example, studies in high-income countries have shown that treatment for cancer patients who have been diagnosed early are 2 to 4 times less expensive compared to treating people diagnosed with cancer at more advanced stages. This is the reason why the WHO is strongly recommending investments in strengthening and equipping health services and training health workers so they can conduct accurate and timely diagnostics.

While lower cost options such as MRI and CT have been the cornerstone of imaging diagnostics in cancer treatment for decades, PET-CT technology, even though it has been around since 1998, due to higher costs still occasionally provokes discussions on its cost-effectiveness as a diagnostic tool.

PET/CT is a technique with high sensitivity and specificity as far as malignant lesions are concerned. It has dramatically improved PET interpretation; it has reduced equivocal interpretations; and it has increased diagnostic accuracy. More accurate staging, restaging, and prompt evaluation of therapy lead to appropriate changes in patient management. It is evident that apart from additional costs, potential savings are associated with PET/CT as a result of avoiding additional imaging examinations or invasive procedures and by helping clinicians make the optimum treatment decisions. These arguments point towards its cost-effectiveness in treatment. The evidence continues to accumulate on its usefulness in clinical practice as a profound imaging modality with expanding applications in a variety of oncological fields.

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b. PATHOLOGY AND MOLECULAR DIAGNOSTICS

Introduction

Pathohistological and molecular diagnostics represent the basis of modern cancer therapy. Various molecular tests are used in tumour diagnostics. These tests are often necessary to establish accurate tumour diagnosis and classification of tumours in specific prognostic categories, detect minimal residual disease, and for predicting response to treatment. Molecular diagnostic tests may also reveal familiar tendency to developing malignant tumours at different sites.

Until recently, molecular tumour studies have included only individual genes analyses. Over the past several years, the introduction of new technology enabled rapid sequencing of the entire genome by using new generation sequencing, epigenetic changes analyses (epigenomics), determination of RNA expression in cell population (transcriptsomic), and simultaneous measurement of a large number of proteins (proteomics) and metabolites (metalobolomics) in tumour cells.

Molecular diagnostic tests can also be performed by circulating tumour DNA analysis, and/or isolated tumour cells from the patient's blood stream (liquid biopsy), so the liquid biopsy technique could have a place in early diagnosis, assessing treatment response, detecting drug resistance, and discovering relapse.

Vision 2030

Implementation of new, validated and cost effective cancer molecular testing procedures with the aim of applying targeted oncological therapies. The main goals are to determine the type of treatment that is the most effective for an individual patient, targeting the subpopulation of patients who will benefit most from the particular medicine, and avoiding toxic therapies for patients who do not need them. In addition, this type of research has a very important role in public health because of more efficient cost control.

Objectives

1. Encourage cooperation with international, highly specialized centres through consultations with foreign experts.
2. Define highly specific reference centres in molecular and clinical genetics, immunological diagnosis and pathohistology, which would be involved in quality control through additional analyses
3. Enable the development of new and more effective screening programs by further refining the molecular diagnostics, developing new targeted drugs, and based on specific genomic changes in each patient, obtain information for monitoring of treatment efficacy and evaluating the response to therapy
4. Contribute to cancer patients' treatment individualization through multidisciplinary approach and further advancement of molecular diagnostics.

5. Encourage the development of translation research. Translational research creates continuity between a fundamental research and clinical practice and explores molecular biomarkers and new technologies for predicting tumour susceptibility to a particular therapy.
6. Support a collaboration of specialists from clinical hospital centres and scientists employed at medical schools or institutes, with the aim of incorporating basic research into clinical research and clinical practice and vice versa.

Measures/Activities

1. Continue to educate national experts, through collaboration with international, highly specialized centres (within 1-2 years of acceptance of NCCP)
2. Ensure appropriate financing of infrastructure and procure modern equipment (within 3 year of acceptance of NCCP)
3. Get donation of equipment and chemicals for molecular tests from pharmaceutical and biotechnology companies (within 2 year of acceptance of NCCP).
4. Set up tumour banks for collection and storing of tumour tissue samples and establish collaboration between clinical hospital centres and general hospitals with the aim of optimizing tumour sample analysis (additional analysis, detecting new biomarkers as a result of a drug unknown at the time of diagnosis, or due to potential testing of new drugs) to improve patient care (within 1-2 years of acceptance of NCCP).
5. Adopt rules and regulations on recording medical data and methods of handling samples in tissue banks, which are a guarantee for the biological quality of samples and the correct use of the stored materials (within 1-2 years of acceptance of NCCP)
6. Create a virtual tumour bank that combines databases from different tumour banks, to facilitate information exchange, access to a larger number of samples, thus achieving results faster within the framework of initiatives for cooperation between academic institutions and hospitals, as well as to promote translation research (within 3 year of acceptance of NCCP)
7. Create a quality control system for molecular diagnostic labs by introducing test performance standards, assessing the quality of results (internal and external laboratory control) and meeting accreditation requirements for personnel, equipment and testing quality (within 1-2 years of acceptance of NCCP)
8. Continuous adaptation, implementation of emerging pathologic diagnostic modalities

Stakeholders

- Ministry of Health
- Croatian Health Insurance Fund
- Pharmaceutical and biotechnology companies
- Molecular diagnostic laboratories in Departments of pathology in Clinical hospitals and Medical Schools in Split, Zagreb, Rijeka and Osijek University.
- Professional Associations
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources (Croatian Government, Ministry of Health, HZZO, Hospitals)
- Additional resources needed to implement planned measures (external financing (EU funds, WB))
- EU or other international source of funding

Economic evaluation

as the era of personalization in cancer medicine approaches, clinically relevant genetic alterations are increasingly used to stratify patients for specific targeted therapeutics. In the context of personalized oncology, screening for somatic tumour mutations is crucial for prediction of an individual patient's response to therapy. The continuous decrease of costs of these tests is contributing to their everyday use in clinical medicine in western countries.

A growing body of literature evaluates their cost-effectiveness in clinical practice. For instance, massive parallel sequencing (MPS) allows to rapidly uncover genomic alterations in tumours in unprecedented detail and with relatively low cost. With the drop in costs over recent years, this technology can be expected to become increasingly more affordable for daily routine testing and is already approaching diagnostically acceptable cost rates. Using novel molecular tests for differential diagnosis of cytologically indeterminate thyroid nodules can potentially avoid almost three fourths of currently performed surgeries in patients with benign nodules. Compared with current practice based on cytological findings alone, this may result in lower overall costs and modestly improved quality of life for patients with indeterminate thyroid nodules.

Using KRAS testing to restrict use of EGFR-inhibitor therapy to patients with KRAS wild-type tumours has been found as cost saving for some patients in a review that focused on both the United States and Germany.

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c. GENETIC TESTING AND COUNSELLING

Introduction

About 5 to 10% of malignant tumors are hereditary, i.e. they result from inherited mutations that usually affect tumor suppressor genes. Today, more than 30 different genes are known to be associated with increased risk of certain cancers. Among them, most common are breast and ovarian cancer/fallopian tube cancer/primary peritoneal cancer associated with mutations in BRCA1/2 genes, hereditary nonpolyposis colorectal cancer (HNPCC), familial adenomatous polyposis colon cancer (FAP), hereditary melanoma and medullary thyroid cancer in multiple endocrine neoplasia type 2 (MEN 2) syndrome. In families where the existing criteria point to the possibility of hereditary cancer, both the patient and healthy blood relatives should be referred to a genetic counselling center. At present, genetic counselling for hereditary types of cancer has not been adequately organized in the Republic of Croatia, especially for the adult population. Genetic counselling for hereditary cancer should be comprehensive and address all cancer types counselling, and should be in the domain of medical/clinical geneticist educated for hereditary cancer, who then consults other specialists. People at risk should be familiar with the possibilities of genetic testing. After genetic counselling and individual risk assessment, a decision is made on the need for genetic testing. Based on the genetic testing results and the data from personal and family history, persons are classified into different risk categories for specific tumors and are therefore referred to regular preventive examinations; alternatively, preventive pharmacological or surgical interventions are made. Genetic counselling should exist for all genetically-conditioned tumors, especially breast and ovarian/fallopian tubes/primary peritoneal tumors, colon cancer and melanoma.

Vision 2030

Improve early detection and outcomes of most prevalent hereditary cancers to reach western European average.

Objectives

1. Equal access to high quality genetic counselling, diagnostics and preventive treatment for all patients at risk and their blood relatives.
2. Comprehensive screening program aiming to early detection of cancer in patients with genetic predisposition.
3. Effective preventive treatment options

Measures/Activities

1. Ensure the availability of adequate genetic counselling and diagnostic centers. The number of genetic counselling facilities in the Republic of Croatia must be optimally defined, to make it easily accessible to patients and healthy relatives, taking into account geographical characteristics, population numbers and prevalence of hereditary cancer

types. It has been estimated that at least four to five genetic counselling centers, linked to clinical hospital centers or medical schools, should be established in the Republic of Croatia. The testing itself can be centralized, i.e. it is not necessary for each counselling center to have its own laboratory. Major genetic counselling centers linked to clinical hospital centers may, if necessary, establish branch offices in county centers, with a clear instruction on referring patients from a specific area. It is also advisable to set up a telephone counselling center, which would not be a substitute for the complex process of genetic counselling, but would act as assistance in providing patients and healthy persons at risk with basic information. Within the genetic counselling center, the procedures for the so-called therapeutic testing should be separated, when the information on mutation has to be obtained fast, as it directly affects decisions about therapy (a priority procedure with available rapid test results), as well as counselling and testing of healthy individuals to assess cancer risk; in the event of a limited number of tests per month, the advantage needs to be given the so-called therapeutic tests.

2. All patients suspected or diagnosed with a genetically-conditioned tumor, as well as their blood relatives who are potential hereditary mutation carriers, should be sent to genetic counselling at major centers in the Republic of Croatia which provide the possibility of genetic testing.
3. Develop and implement an early screening program for people with genetic predispositions to develop cancer and ensure tracking of hereditary mutations in a personalized care program. For example, 80% of the HNPCC gene carriers will develop colon cancer. Associated malignant tumors such as endometrial and ovarian tumors are frequent. Patients also have an increased risk of ureter, kidney, stomach, biliary system and small bowel cancer. Each hereditary cancer patient or a healthy person carrying mutation should receive clear follow-up recommendations for early cancer detection, depending on the type of mutation carried, in the genetic counselling center.
4. Ensure access to effective preventive interventions for all hereditary mutation carriers to reduce the risk of tumor formation (e.g. prophylactic mastectomy and adnexectomy in mutations in BRCA 1/2, prophylactic colectomy in FAP and HNPCC). Prior to any prophylactic measures planning, particularly surgical interventions (e.g. prophylactic ovarian and oviduct removal in mutant carriers), it is necessary to provide advice on the conservation of fertility (oncofertility counselling). Psychological counselling should be provided to a person who wants it or receives such recommendations from a genetic counsellor.
5. Initiate studies to investigate the link between genetic markers (mutations) and increased frequency of certain tumors. In addition, it is important to determine the percentage of cancer patients with a single marker who will actually develop cancer.
6. Establish a reference center for genetically-conditioned tumors and genetic counselling.
7. Improving the Molecular Genetics Laboratory (defining laboratories are appropriate for testing and their accreditation and certification system, internal and external control). Greater investment in academic and multidisciplinary research and public health research in oncology should be ensured. In particular, support should be provided to programs for the development of new genetic and epigenetic indicators of genetically-conditioned tumors (e.g. in the search for indicators among patients with hereditary breast cancer in which no BRCA1/2 genes mutation was found, who in fact represent two-thirds of all cases of hereditary breast and ovarian/fallopian tubes/primary peritoneal cancer). For other professionals (biologists, pharmacists, medical biochemist sand

others) planning training in laboratory genetics is important. The link between fundamental and clinical research institutions and research groups in cancer research needs to be strengthened, clinical and research part linked, and in obtaining an informed testing consent offer patients and healthy family members a separate informed consent which would include using samples for further research.

8. Expedite approval for a new 5-year residency program, and an adequate number of interested physicians to residency training sent as soon as possible. According to the EU directive, medical/clinical genetics has been recognized as an independent residency that should last at least four years. In the transitional period before such residency program is completed and for the purpose of better functioning of the genetic counselling center, it is recommended to train a certain number of genetic counsellors and to devise additional education for nurses who would work in a genetic counselling centers, clearly defining their scope of work.
9. Educate primary, secondary and tertiary level physicians in this area and improving public awareness on early cancer prevention programs and initiatives.
10. Establish a central register of biological samples banks, which, besides being a source of information, would have defined standards of the quality of samples, isolation methods, storage, as well as introduced rules on access to such data and materials.

Stakeholders

- Ministry of Health
- Molecular diagnostic labs in clinical hospital centers
- Institute Ruđer Bošković
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources (Ministry of Health, Croatian Health Insurance Fund, Hospitals)
- Additional resources needed to implement planned measures (external financing /EU funds, WB/)
- EU or other international source of funding

Economic evaluation

Genetic testing and counselling appears to be most cost-effective when focused on at risk populations. A number of analyses testify that a program of genetic testing and screening for breast cancer in high-risk populations may be cost-effective. For both breast and ovarian cancer, results indicate that despite the costs associated with testing and prophylactic procedures, testing women who are concerned about developing breast and ovarian cancers is economically advantageous because it allows women at high risk for these diseases to have a prophylactic surgery and avoid high costs, morbidity, and mortality associated with having these cancers. The costs and benefits for each testing and no-testing strategies are very similar when considered over the entire lifespan. This implies that the costs of testing and prophylactic surgery are approximately equivalent to the increased costs associated with the higher incidence of cancers in the no-test strategy. Some research even points to favorable economic outcomes of screening entire female populations for breast cancer.

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6. Treatment of cancer

6. Treatment of cancer

a. PROMOTING MULTIDISCIPLINARY ONCOLOGY TEAMS

Introduction

In order to improve and optimize oncological treatment with the existing resources, it is necessary to significantly improve the organization of oncological care in Croatia. Multidisciplinary approach and the development of multidisciplinary teams in oncology are the cheapest and potentially most effective way to quickly improve the success of cancer treatment, so they should become mandatory. Multidisciplinary team (MDT) makes a joint decision on the initial treatment plan. Since the initial treatment plan is the most important element in contemporary successful cancer treatment and affects the final result, this decision should be binding. The MDT also makes decisions on rational diagnostic treatment of patients, enabling faster initial and more efficient further treatment of patients with malignant disease. Teamwork involves several professionals working to achieve a common goal. The work must not be fragmented and unconnected, but well-coordinated by the team leader (coordinator). The conclusions of the MDT must be recorded and saved in the form of standardized documentation, be a part of the national oncology and the Cancer Registry database. Therefore, all team reports must be forwarded to a joint national database. Effective teamwork and good communication with patients and family members can prevent mistakes and the dissatisfaction with the service provided, as well as complaints against healthcare professionals. Numerous researches have shown the value and benefits of team work, but have also pointed to difficulties in organization.

Vision 2030

To have more than 90% cancer patients presented before properly staffed, organized and financed multidisciplinary teams to ensure joint decision about the best treatment option.

Objectives

1. The initial treatment plan for all cancer patients must comply with accepted guidelines and must be made by multidisciplinary teams.
2. A multidisciplinary team should consist of oncologist (specialist in oncology and radiotherapy and/or medical oncology), surgeon, pathologist, radiologist, nurse, psychiatrist

or psychologist, as well as other specialists depending on the cancer site, e.g. a pulmonologist, gastroenterologist, gynecologist, ORL specialist, dermatologist, nuclear medicine specialist. Teams are formed according to the tumor site, and specialists involved in its work must be relevant for their respective topics.

3. For oncological multidisciplinary teams to work well, team members must have the following competencies:
    a. High level of professional knowledge on a specific issue related to the core objective of a particular team
    b. Each member of the multidisciplinary team should have the skills and competences for cooperation, establish good communication, and readiness to hear others and respect their opinions.
    c. Apart from hospital specialists, it is very important to involve family medicine practitioners (GPs) in the process of caring for cancer patients and to determine their role and position within an oncological network. There is a need for continuous training of family doctors with the view of providing better care for cancer patients.
    d. The presence in the team is an obligation, not an option. The head of the institution in which the team is formed is responsible for specialists' participation in the team, and so are the heads of the units whose staff are team members.
    e. Ideally, a patient is also physically present during the case presentation before the team, enabling all team members' optimal insight into the patient's general condition, capacity to receive the defined diagnostic and therapeutic modalities.
    f. Multidisciplinarity must be legally defined; institutions that treat cancer patients without a decision by the MDT, should not be paid for it, but sanctioned, unless oncological urgency has been proved.
    g. The work of an MDT must be valued both financially and in terms of time invested.

Measures/Activities

1. The Ministry of Health should ensure legislation for obligatory implementation of proper multidisciplinary approach in oncology
2. Documentation on multidisciplinary treatment must be standardized and submitted to the national database.
3. All regional oncological institutions must define multidisciplinary teams for all cancer sites they will deal with, appoint team members, define the team meeting timing and organizational structure, and how to present a cancer patient case in front of the team.
4. All local oncological institutions that cannot form their own qualified MDT are obliged to refer their patients to regional institutions, and their oncologists should prepare the patient for case presentation in front of the team (universal form) and if possible participate in the team virtually (IT network should be established to ensure virtual MDT work).
5. Secure sufficient human resources to allow optimal MDT work (make sure physicians and administrative staff are given time devoted to prepare and present patients to MDT as well as to do the paper work – input the patient information's in national oncology data base).

6. Secure sufficient financial resources to allow optimal MDT work (physicians and administrative staff are properly financially compensated for time devoted to prepare and present patients to MDT as well as to do the paper work – input the patient information's in national oncology data base).
7. Implement, supervise and control these measures through the Cancer Agency at the Ministry of Health.

Stakeholders

- Ministry of Health
- Regional oncology institutions / all oncology institutions
- Oncological societies
- Croatian Health Insurance Fund
- Cancer Agency at the Ministry of Health
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources (Ministry of Health, HZZO, Hospitals)
- Additional resources needed to implement planned measures (external financing (EU funds, WB))
- EU or other international source of funding

Economic evaluation

The benefits of multidisciplinary working in oncology are now accepted as the norm and widely acknowledged as being pivotal to the delivery of optimal cancer care. It has been also shown that multidisciplinary-based care results in more robust decision making processes, can improve survival, shorten the time taken to accurately stage patients, and reduce waiting times for treatment. There is also evidence that the patient experience is improved with the use of MDMs.

Central to this are the multidisciplinary meetings (MDMs) for which decision outcomes and financial costs need to be evaluated at the institutional and national level. In UK as an example, the cost per month of MDMs ranged from £2192 to £10 050 (median £5136) with total cost of £80 850 per month and the cost per new patient discussed was £415 which is substantially less costly in Croatia. In the currently challenged health-care financial environment MDM efficiency needs to be continuously monitored and ensured without losing the considerable benefits for both patients and clinicians associated with regular MDMs.

The results from many identified publications showed that there is a high degree of heterogeneity among reported costs of MDT approach. Current evidence is insufficient to determine whether MDT working is cost-effective or not in oncology care and further studies aimed at understanding the key aspects of MDT working that lead to cost-effective cancer care are required. However, all other relevant aspects of the MDT approach have been proven positive, so the costs of MDT will be included in the economic evaluation.

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b. ONCOLOGICAL SURGERY

Introduction

By definition, oncological surgery is surgery aimed at treating malignant tumors and eliminating the resulting disturbances. It is well known that oncological surgery requires extensive knowledge, experience, continuous training and adequate equipment, as well as a high level of overall complementary diagnostics, supportive therapy, intensive medicine and oncology.

The role of a contemporary surgical oncologist is that of an equal member of a multidisciplinary team; together with experts from complementary areas, they cooperate in all aspects of cancer patient treatment – prevention, diagnosis, treatment, monitoring and palliative care. In addition to specialized knowledge of surgical procedures, surgical oncology must include the knowledge of various diagnostic, clinical, supportive, and reconstructive and rehabilitative medical procedures that ensure patients survival in the best possible conditions.

Surgical oncology is not properly organized in Croatia. There is no systematic network of such surgical centers, nor are minimum preconditions for performing certain oncological surgical procedures clearly and uniquely defined. Oncological surgical treatment is often performed by surgeons who are not closely specialized in treating tumors. At this moment there are no unambiguous guidelines for indicating and performing certain surgical procedures. There are no clear definitions of standard operating procedures.

Vision 2030

To have majority of oncological surgery patients (more than 80%) operated by accredited oncology surgeons in accredited surgery institutions after MDT decision and strategy within the radicality frame of western EU average

Objectives

Raise the quality of surgical oncology and consequently better treatment outcomes (at the level of average western EU) for oncologic patients, with more rational use of available resources.

Measures/Activities

1. The network of tertiary institutions where surgical procedures are performed (general surgery, urological surgery, gynecologic surgery as well as other disciplines where oncological surgery is performed) needs to be well defined; these facilities should be arranged in such a way to provide surgical treatment of the most common tumors as close to the patient’s residence as possible.
2. These institutions need to be equipped with infrastructure and a sufficient number of adequate experts, including the entire surgical team.

3. Provide professional staff first with initial, followed by continuing training.
4. Create a unique database that will monitor and supervise the quality of treatment through clinically relevant parameters such as complications, infections, and mortality, and define the accreditations of individual centers through continuous re-evaluation.
5. Integrate all patients and treatment outcomes data into a single database. Hire administrative staff to create the database, fill in and analyze the data.
6. Define standard operational procedures for surgical treatment, from preoperative preparation, postoperative care, treatment of perioperative nutritional status, complications etc.
7. Develop guidelines for surgical oncological treatment of the most common tumors.
8. Specifically define institutions for the treatment of rare tumors and sarcomas; the treatment of such diseases should be centralized.
9. Define financing methods, and how prosthetics (e.g. breast implants, cannulas, growing prosthetics, artificial joints, etc.) are to be obtained.
10. Define exactly the conditions for going abroad for surgical oncological treatment and the sources of funding.
11. Introduce a statutory obligation for presenting patient cases before a multidisciplinary team prior to the operation.

Stakeholders

- Oncological and Surgical Professional societies
- Ministry of Health
- Croatian Institute of Telemedicine
- Croatian Health Insurance Fund.
- Relevant EU stakeholders who could provide guidance and support

Resources

- Existing, already budgeted resources (Ministry of Health, HZZO, Hospitals)
- Additional resources needed to implement planned measures (external financing (EU funds, WB))
- EU or other international source of funding

Economic evaluation

There are still scarce studies evaluating cost effectiveness of surgical interventions. Several recent studies have shed light on the value of various surgical approaches. Relevant disparities were detected among studies, mainly based on effectiveness. These apparently contradictory results may be reflecting the difficulty of interpreting small differences between treatments regarding QALY gains. For example, one study in the World Journal of Urology found no increase in cost with laparoscopic vs open radical nephrectomy. Another example, it is still unclear whether the benefits of radical nephrectomy outweigh the risks in elderly patients. Even when studies do reveal differences that are statistically significant, physicians need to determine whether those differences are clinically significant. For some interventions considered as dominant strategies in example of prostate cancer, QALY gain was 0.013 for active surveillance over radical prostatectomy; and 0.007 for robotic-assisted over non-robotic techniques. The highest QALY gains were 0.57-0.86 for radical prostatectomy vs watchful waiting, and 0.72 for brachytherapy vs conventional radiotherapy.

More studies are needed to address the question of value in the surgical care of patients. The optimal care is defined as a procedure associated with no readmissions, no patient safety indicators, no infections, and no hospital-acquired conditions. From economic evaluation perspective, the “optimal” surgical care is relatively common only in few cancer types such as prostate and kidney. Considering the lack of validated cost effectiveness data for existing surgeries, it will be very difficult to understand the economic impact of the emerging techniques such as robotic nephrectomy, for which the purchase of a piece of equipment that costs nearly $2 million is required. In addition, the hospital must spend money on drapes, fluorescence imaging, ligatures, sutures, clips, hemostatic agents, sponges, ports, ultrasound, and instruments—all of which can cost an additional $3000 for each procedure.

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c. RADIOTHERAPY

Introduction

As a treatment method, radiotherapy is used in 60 % or more of cancer patients. The role of radiotherapy in the treatment of malignant diseases is multiple. We use it as the primary, fundamental treatment modality (either alone or in combination with chemotherapy, hormone or immunotherapy), in the treatment of locally restricted and locally advanced tumors, to prevent the recurrence of the disease after radical surgical treatment, to potentially reduce major tumors, i.e. the conversion of initially inoperable into operative, and palliative (for the relief of pain, pressure and bleeding) when the tumor is incurable.

Radiotherapy requires great initial investment, planning of space and equipment. In countries with low or medium income, such as Croatia, there is a different rate of distribution of cancer types and stages (multiple smoking-provoked tumors and a later stage at diagnosis on average), which creates an even greater need for radiotherapy compared to countries with high average incomes. According to the estimates for Croatia, out of 1,000 patients with cancer, 520 of them will be treated with radiotherapy, and additional 120 will receive radiotherapy again, repeatedly during further treatment of their disease. To conclude, out of 1000 newly diagnosed patients, 640 radiotherapy planning and treatment are planned.

Most radiotherapy treatments in Croatia are done with three-dimensional conformal radiotherapy. However, in developed countries, modern radiotherapy techniques have an unavoidable and very important role in treatment, aiming at better local control of the disease and better protection of the surrounding healthy tissue.

Modern techniques are Image-Guided Radiation Therapy (IGRT), Intensity-Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy / Rapid Arc (VMAT), Stereotactic Body Radiation Therapy / Cyber Knife (SBRT).

These modern techniques rely on increasingly demanding technologies and techniques, which need to provide more money, time and people for their implementation. However, performing radiotherapy with modern techniques results in more successful treatment of cancer patients.

In Croatia, there are five radiotherapy facilities in four regional centers. Radiotherapy centers are organized in scientific-educational institutions due to the complexity of planning and conducting radiotherapy by a radiotherapy team.

The main obstacles to better and more effective radiotherapy at the national level are:

- The absence of a networked organizational structure to connect radiotherapy centers to make a wide spectrum of radiotherapy available to patients, and its work financially and clinically the most effective;
- Organization of work focused on everyday tasks, a lack of mid-term or long-term strategic planning;
- A lack of self-evaluation system based on carefully observed clinical outcomes;

- Inadequate capital investment with the consequent lack of equipment. There are 15 linear accelerators in the Republic of Croatia, which puts us in the group of under-equipped European countries (3.5 units per million inhabitants), while the European average is 5.3 units per million inhabitants. The average age of linear accelerators in the Republic of Croatia (2016) was 7.7 years (range 3 - 18 years). The use of modern radiotherapy techniques at most linear accelerators in the Republic of Croatia is not possible. Within public health system stereotactic radiotherapy is only possible for head tumors, on one device only;
- A lack of professional staff.
- Having analyzed the condition and needs of radiotherapy equipment in the Republic of Croatia, as well as the radiotherapy standards in Europe and the world, we can conclude the following:
- The number of radiotherapy institutions and their regional distribution is optimal and there is no need to set up new radiotherapy centers.
- The number of radiotherapy devices in Croatia is critically lower than the European average.
- Regional equipment load is not uniform, and some centers have significantly higher number of patients per device annually than others

Radiotherapy is one of the most promising medical disciplines. It is therefore important to purchase the latest, state-of-the-art devices when purchasing new radiotherapy equipment. Creating a system that would provide continuous high-quality care to radiotherapy patients across the country is a very complex and financially demanding project. It is therefore important to ensure continuous funding from all the available resources, such as the Government of the Republic of Croatia, the Ministry of Health, EU funds, international organizations, local self-government, and non-governmental organizations.

Vision 2030

To have all required radiotherapy treatments given without delay, according to the internationally defined standards using modern radiotherapy techniques with continuous quality control of equipment and treatment plans within the average of western EU countries

Objectives

1. Provide optimum radiotherapy to all oncological patients in Croatia without waiting for treatment
2. Use of modern radiotherapy techniques for cancer
3. Networking of all radiotherapy institutions in Croatia in order to optimize equipment utilization and quality control in radiotherapy

Measures/Activities

1. Immediately ensure one linear accelerator for the radiotherapy facilities with the biggest load (Clinical Hospital Centers in Split (ST), Rijeka (RI) and Osijek (OS)) as soon as possible, and redistribute patients in Zagreb region, to make the burden on the equipment more even.
2. Plan the acquisition of six new linear accelerators (Clinical Hospital Centre Zagreb (ZG), Tumor Clinic (KZT),2x Department of Oncology and Nuclear Medicine at Sestre Milosrdnice University Hospital Centre (SM), Clinical Hospital Centre Rijeka and Clinical Hospital Centre Osijek) in the next two years to achieve the European average, and improve the quality of radiotherapy treatment. By acquiring a total of nine new radiation devices we would get closer to the European average of the number of linear accelerators.
3. SBRT (Stereotactic Body Radiation Therapy – Radiosurgery) should be immediately developed in two centers which have the highest number of patients and geographically cover these needs best – Zagreb and Split. It is therefore, necessary to purchase a SBRT device at Clinical Hospital Centre Split and Clinical Hospital Centre Zagreb as soon as possible, thus introducing a modern radiotherapy treatment in the healthcare system of the Republic of Croatia.
4. New treatment modalities, options in radiotherapy are emerging very fast, so is important to continuously adapt, implement them to give to radiotherapy patients the best treatment opportunities.
5. Plan the purchase of new devices for brachytherapy for the Tumor Clinic at the Clinical Hospital Centers Sestre Milosrdnice, Zagreb and Rijeka, and provide software for other's (Clinical Hospital Centers Split) as soon as possible.
6. Carefully plan and carry out maintenance and renewal of the existing equipment, as well as introduce new technologies in radiotherapy; gradual replacement of the old linear accelerators should be planned and considered separately from the aforementioned procurement of new devices.
7. Provide sufficient staff as a prerequisite for improving radiotherapy techniques and the operation of newly-equipped radiation devices. This includes employing as well as initial and ongoing training of the entire radiotherapy team, i.e. oncology and radiotherapy specialists, medical physics engineers and radiology technicians.
8. Organize network of radiotherapy institutions in the Republic of Croatia with the role of optimizing (maximizing) the use of the overall radiotherapy equipment and to monitor the quality control of the radiotherapy system and the results of the treatment.
9. Plan to increase the capacity of all radiotherapy institutions in the Republic of Croatia in the next ten years, due to the increase of malignant diseases incidence both in the European Union and in the Republic of Croatia. Investments should follow modern trends in radiotherapy, as well as the needs of individual institutions. This implies the purchase of 4 more radiotherapy devices (15 in total).
10. Establish a good, financially viable system that will be able to meet the needs of radiotherapy facilities in the Republic of Croatia as soon as possible, thus providing all patients with advanced and innovative radiotherapy, which will result in improved treatment outcomes by increasing the share of cured patients, with fewer undesirable consequences of treatment.

Stakeholders

- Ministry of Health
- Oncology centers
- Professional societies
- Relevant EU stakeholders who could provide guidance and support

Resources

1. Ministry of Health's own sources within the budget
2. EU funds and other available international funding opportunities, particularly grant programs. The Republic of Croatia is eligible to absorb funds for the modernization of healthcare; however, there are no projects to apply for the funds in oncology and RT (or there are projects to a lesser extent). The most important document for absorbing the EU funds is the National Oncology (and Radiotherapy) Strategy.
3. Lease funding

Sources of funding for capital projects can be secured in cooperation with leading manufacturers with much more favorable conditions than those currently offered by the commercial banks in Croatia. Planning and purchasing equipment through packages would greatly reduce these financial costs. If around EUR 45.9 million is spent on annual maintenance of 30 linear accelerators in a 10-year period, which is approximately 33% of the total amount, and aware that this value is significantly reduced when manufacturers have a larger installed base (service risk per device is reduced), it is realistic to expect that manufacturers will also rationalize the total cost. With the aggregated procurement at intervals after three years in a 10-year period (3 x 10 accelerators) the estimated reduction in the total procurement costs is at up to 20%.

Economic evaluation

The field of radiation therapy has made dramatic technical advances over the past 20 years. 3D conformal radiotherapy, intensity-modulated radiation therapy and proton beam therapy have all been developed in an attempt to improve the therapeutic ratio: higher cure rates with lower toxicity. There are limited number of publications analyzing the cost effectiveness of one type of radiotherapy over the other.

According to a report published in the Lancet, in low- and middle-income countries, with a $97 billion upfront investment, the economic benefits and cost savings are sizable: between $278 billion to $365 billion over the next 20 years. More importantly, these policies and investments would positively impact people living with cancer. It is estimated that if all patients had access by 2035, radiation therapy would prevent cancer from progressing in 2.5 million people and it would lead to an overall survival benefit for 950,000 people.

Clinical and patient-reported outcomes data are also needed to understand short-term and long-term factors that affect the cost-effectiveness of various RT modalities. If patients place great importance on avoiding short-term toxicity or upon shorter RT schedules (such as with brachytherapy), they may feel that more expensive treatment is justified, despite a lack of a longer-term benefit. For example, if brachytherapy is associated with less severe acute skin reactions compared with EBRT, this may lead to a transiently increased utility for brachytherapy but a minimal effect on the long-term QALY forecast. In contrast, if brachytherapy substantially improves long-term breast outcomes such as cosmesis or late effects on the lung and heart, the effect on QALYs could be more substantial. Other factors that may affect long-term utility and costs of newer modalities include subsequent related procedures, screening, and late toxicity. Thus, there is a need to assess patient-reported outcomes to improve our understanding of the utility of newer modalities.

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d. SYSTEMIC CANCER TREATMENT

Introduction

As cancer is frequently a systemic disease, systemic oncological treatment is the basis for successful cancer therapy. Systemic cancer treatment consists of antitumor and supportive treatment. Antitumor treatment includes chemotherapy, endocrine therapy, targeted therapy, immunotherapy, biological therapy, and sometimes isotope treatment. Systemic oncological treatment is complex and demanding, frequently accompanied by significant unwanted effects, potentially environmentally damaging (chemotherapy, isotopes) and often expensive. Taking into account the number of cancer patients in Croatia, the cost and potential toxicity of systemic oncological treatment, the need for continuous monitoring of treatment outcomes and its adverse effects, the use of systemic oncological therapy should be limited to defined oncological care institutions (National Oncology Network) and specialists trained in its application (oncology and radiotherapy specialists, medical oncology specialists, hematology specialists and pediatric specialists with sub-specialization in hematology and oncology).

Systemic cancer treatment in Croatia should be carried out in institutions where conditions for the application of systemic oncological therapy exist, in accordance with the national oncology network. Systemic cancer treatment is one of the most promising medical areas where changes occur almost daily. The National Cancer Plan must ensure conditions for cancer patients in Croatia to receive systematic therapies that significantly contribute to prolonging life without progression of the disease and improving the quality of life.

Possible financial limitations for the application of some therapies must be clearly and explicitly defined by relevant state bodies (Croatian Parliament, Government of the Republic of Croatia, Ministry of Health) and apply to all such patients in the Republic of Croatia. The system of putting new medicines on the list of the Croatian Health Insurance Fund (or another mechanism which makes drugs available to patients) must be transparent, clear and fast. When approving therapies and defining indications, the opinion of appropriate professional medical societies should also be considered, not just the registration of the drug. The decision on the method of systemic treatment should be made after deliberation in a multidisciplinary team, in accordance with national or EU guidelines. The results of treatment, efficacy and toxicity should be monitored, stored in national registers and regularly checked. The Ministry of Health must ensure all human, material and legal conditions for the functioning of such registers as soon as possible. Sufficient resources should be secured for all approved systemic oncological therapies. Taking into account the high price of therapies and the burden on hospital budgets, consideration should be given to the formation of a special fund at the state level for the treatment of patients with malignant diseases. Also, a special department should be organized at the Croatian Health Insurance Fund which would deal exclusively with oncological issues.

The administrative burden on medical staff needs to be reduced; therefore, the approval of the Committee for Medicines or similar bodies is to be requested only as an exception. Healthcare in institutions where systemic oncology therapy is applied should be organized in a way to provide ongoing care and treatment of patients and the availability of appropriate qualified medical staff 24/7, seven days a week. For this purpose, participation of oncological medical personnel in activities which are not a part of their sub-specialization should be reduced to a minimum (e.g. outpatient clinic for ultrasound, being on-call in the ER, etc.)

Vision 2030

Patient access to all systemic cancer treatments according to the nationally and internationally defined treatment guidelines with continuous monitoring of treatment specific outcomes and with drug expenditures within the average of western EU countries measured as GDP percentage adjusted for PPP.

Objectives

1. Within the options available in the Croatian public health care system, all citizens diagnosed with cancer should be allowed access to treatment of equal quality at all levels of health care.
2. All cancer patients in Croatia must be given a better chance of survival as well as the possibility of better quality of life through the availability of systematic therapies that undoubtedly prolong life without progression of the disease.
3. It is necessary to create financial and organizational conditions for data collection and professional monitoring of treatment results, which will also enable a good comparison of different levels of health care.
4. Professional and scientific data on treatment outcomes, appropriately processed, should be made available to the public.
5. Provide multidisciplinary treatment of patients.
6. Ensure administrative and financial conditions and encourage clinical studies to increase the availability of innovative therapy to as many people as possible.
7. Ensure administrative support at the Ministry of Health for the application of new systemic forms of treatment before they are placed on the market, the so-called compassionate drug use.
8. Faster application of scientific discoveries in clinical practice.
9. Analyze the care system through the model of patients' report on the success of the therapy performed, based on occasional, coordinated and standardized patient satisfaction surveys.
10. Major part of therapy, anti-tumor and supportive, should be administered in day hospitals.
11. Provide incentives to ensure access to new therapies, concurrently creating the framework for ensuring compulsory access to products of particular interest from the public interest point of view.
12. Provide a transparent, public, fast, flexible system for approving new oncological drugs as well as a system for controlling the success of their application

Measures/Activities

1. Institutions accredited for the implementation of systemic oncological therapies should organize health services so as to provide continuous care and treatment of cancer patients and the continued availability of qualified medical staff.
2. Establish a special oncology department at the Croatian Health Insurance Fund.
3. Professional societies should regularly develop and review clinical guidelines for the treatment of certain diseases.
4. Clinical guidelines for systemic oncological treatment must be available electronically (online).
5. Ensure optimum availability of new anticancer medicines to all cancer patients by Croatian Health Insurance Fund based on rigorous scientific evidence, significant overall survival advantage, progression free survival or improvement of quality of life.
6. Supervise and implement these measures through the Cancer Agency at the Ministry of Health.
7. Require from the Ministry of Health and the Agency for Medicinal Products and Medical Devices, its bodies and clinic-hospital institutions, to enable the biggest possible number of different clinical research to be carried out in the Republic of Croatia in the shortest time possible (through legal acts, human and IT resources, and facilities, etc.).
8. Ensure maximum availability of new medicines through European and global compassionate programs (Expanded Access), through the Cancer Agency, as relevant body at the Ministry of Health.
9. All regional oncological institutions must define multidisciplinary teams for all cancer sites they will deal with, appoint team members, define the team meeting timing and organizational structure, and how to present a cancer patient case in front of the team.
10. Establish a transparent, public, fast, flexible system for approving new oncological drugs as well as a system for controlling the success of their application.
11. Establish a network of daily hospitals where systemic oncology therapy is given

Stakeholders

- Oncology institutions with National Oncology Network
- Ministry of Health
- Croatian Health Insurance Fund
- Oncological Societies
- Cancer Agency at the Ministry of Health
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding
- Supplementary ‘Oncospecific’ Insurance Card or similar innovative approaches

Economic evaluation

Although the perceived high price of cancer drugs and their perceived marginal benefits (often only weeks to months) have been increasingly criticized, cost-effectiveness analyses (CEAs) commonly show favorable conclusions based on which these drugs become available to patients through public health system.

Interestingly, the share of total health expenditure devoted to cancer was mostly constant (around 6-7% average in Europe and 6.9% in Croatia) over the last 20 years. While expenditures on cancer drugs increased in both absolute and relative terms, other expenditures were stable or decreased, despite increases in cancer incidence driven by a growing and ageing population. Reductions in cancer mortality during working age resulted in decreasing production loss due to premature mortality. Problems to reallocate funding in health care systems under economic pressure may be one explanation for maintaining the same share of costs, and shifting costs from inpatient to ambulatory care another.

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e. PSYCHOLOGICAL SUPPORT, REHABILITATION AND REINTEGRATION OF CANCER PATIENTS

Introduction

According to research, about 60% of patients need at least initial psychological support, and about 30% need continuous support and follow-up for more severe psychological problems in the form of anxiety-depressive reactions, difficulty adjusting, posttraumatic stress disorder symptoms, cognitive disabilities, psycho-sexual and other difficulties. The psychological distress is also expressed by family members, especially care-givers during treatment, and they need to be provided psychological help during patient treatment, and immediately following the passing away of the patient. Psycho-therapeutic treatment includes interventions aimed at reducing the effects of cancer on emotional experiences and improving the ability of the patient to meet the requirements of the disease, its treatment, and the changed lifestyle as a result of the disease. It is necessary to identify ways of recognizing psychologically most vulnerable patients and to provide early intervention, i.e. psychological treatment and assistance. An important professional component of psychosocial support, which all healthcare professionals and others involved in the treatment and support of cancer patients must respect, is to develop appropriate communication skills. Within the category of cancer patients, it is necessary to take into account the particularities of the groups, which include children and their families, and palliative patients and their families.

The prognosis for most types of cancer is improving, so it is all the more important to provide cancer patients with the best possible chance to function well in their future life roles. An increasing number of patients survive cancer, but the consequences of their illness and/or treatment become obstacles in their daily life. Rehabilitation measures (psychological, social, health) must be introduced from the beginning of treatment, for the rest of patient’s life. Patient self-esteem and general physical and mental well-being must be preserved as long as possible with the help of rehabilitation. Rehabilitation is (primarily) aimed at improving the quality of life of a patient, not just prolonging life expectancy. According to framework estimates, 50% of cancer patients need rehabilitation. Its aim is to reduce the adverse consequences of the disease and the side effects of cancer treatment, encouraging the patient to take a more active approach to their treatment (strengthening their own ability, self-confidence) and helping the families of patients to understand their needs and thereby change the attitude of the society to cancer. It is necessary to become aware of psychological problems patients face within the medical, but also wider community, and to develop a system for early detection of mental disorders and their care.

Oncology patients have the right to work and adapt both the workplace and working conditions to their capabilities. It is necessary to plan specific measures with the Croatian Institute for Occupational Health to raise awareness among employers and the working environment, and encourage cancer patients to work, when their health permits them to.

Vision 2030

Health care services in Croatia will be optimized to better support cancer patients and help them re-connect with their family members and re-establish daily life routines. All stakeholders will collaborate in creating positive attitude and conditions in the society to aid rehabilitation and reintegration of cancer patients.

Objectives

Psycho-oncological treatment and psychological interventions

1. Make the psycho-oncological treatment and care a standard and accessible component of the treatment of cancer patient and their families, at all levels of health care and in all stages of diagnosis, treatment and rehabilitation.
2. Develop specific psycho-oncological interventions (psychotherapy, psychopharmaco therapy) as a standard element of the treatment of cancer patients and their families.
3. Provide the appropriate number of professionals (e.g. psychologists, social workers, psychiatrists, psychotherapists, etc.) for psychological counselling and treatment of cancer patients and their families' at all three levels of health care, taking into account the special needs of children and palliative patients.
4. Incorporate psycho-oncological content into the process of vocational and continual training of all health care professionals and others providing direct treatment and care to cancer patients.

Rehabilitation and reintegration of cancer patients

1. Improve conditions in a wider social environment, raise awareness among the public for the difficulties of cancer patients, ensure community and civil society programs, and facilitate social reintegration of patients.
2. Reduce the harmful bodily and mental consequences of illness and treatment by empowering patients to develop new patterns of behavior and new life skills to reduce the consequences of illness and treatment.
3. Establish a system that will speed up the processing of requests for assessment of disability, bodily harm and decision-making on compensation for cancer patients.

Measures/Activities

Psycho-oncological treatment and psychological interventions

1. Integration of psycho-oncological therapy and care into the overall process of cancer patients' diagnosis, treatment and monitoring.
2. Organizing psycho-oncological counselling centers in health care facilities for patients and their families.
3. Raising awareness, empowering and motivating associations providing mutual self-help and/or professional psychological and psycho-oncological counselling to patients and their families, particularly in the field of palliative care and support for children patients and their parents.

4. Incorporating the elements of psycho-oncology into education and continual training of oncologists in order to detect the psychological difficulties that occur in patients and families on time. Providing additional education of experts working in psycho-counselling centers in the field of psycho-oncology and basic oncological treatment. Creating guidelines and rulebooks on forms and methods of providing support in psychological treatment and counselling, and on the choice of instrumentation and research of patients' needs.
5. Mutual networking, sharing experiences and knowledge and organizing training for professionals working in the field of psycho-oncological counselling of patients and family members.

Rehabilitation and reintegration of cancer patients

1. Institutions, professional societies and patient associations will address the public, and the awareness of the nature of problems experienced by patients and their families will be raised through various charitable and public health actions and lectures; malignant disease and patients in the general population to be destigmatized.
2. Analyze the needs, define the rehabilitation team, and develop guidelines for the rehabilitation of cancer patients during and after treatment, in the part related to physical and mental health to improve the quality of life, assume all life roles in the family and society, and return to work.
3. Develop modalities and ways of financing the modified working hours for patients suffering from malignant diseases so that they can actively participate in their work and life community despite their condition. Together with employers' organizations and professional occupational medicine associations work on the program of raising awareness among employers about the need to adapt the working conditions of cancer patients.
4. Develop an accelerated procedure to address the requirements of cancer patients, the criteria and conditions for determining temporary and permanent disability of cancer patients whose treatment is extremely long term, whose condition is not expected to improve or who are in their terminal phase.

Stakeholders

- Ministry of Health
- Ministry of Demography, Family, Youth and Social Policy
- Ministry of Labour and Pension System
- Croatian Health Insurance Fund
- Croatian Pension Insurance Institute
- The Croatian Institute for Medical Research and Occupational Health
- Croatian Medical Association
- NGOs
- Media
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- Ministry of Demography, Family, Youth and Social Policy
- Ministry of Labour and Pension System
- EU or other international source of funding

Economic evaluation

Cancer survivors experience late and long-term effects of treatment, emotional distress and potentially tumour recurrence. These effects represent challenges for public health care systems, which have to ensure their appropriate follow-up care and quality of life: moving from "how long" people live after diagnosis to "how well" people can expect to live from diagnosis onward.

Although the effectiveness of many psychosocial interventions for people with cancer has been established, one barrier to implementation in routine clinical care is a lack of data on cost-effectiveness. Several psychosocial interventions, particularly those based on cognitive-behavioral therapy, have been demonstrated to represent good value for money in cancer care. Future research should include a clear definition of the economic question, inclusion of all relevant costs, and consideration of utility-based quality of life measures for QALY estimation.

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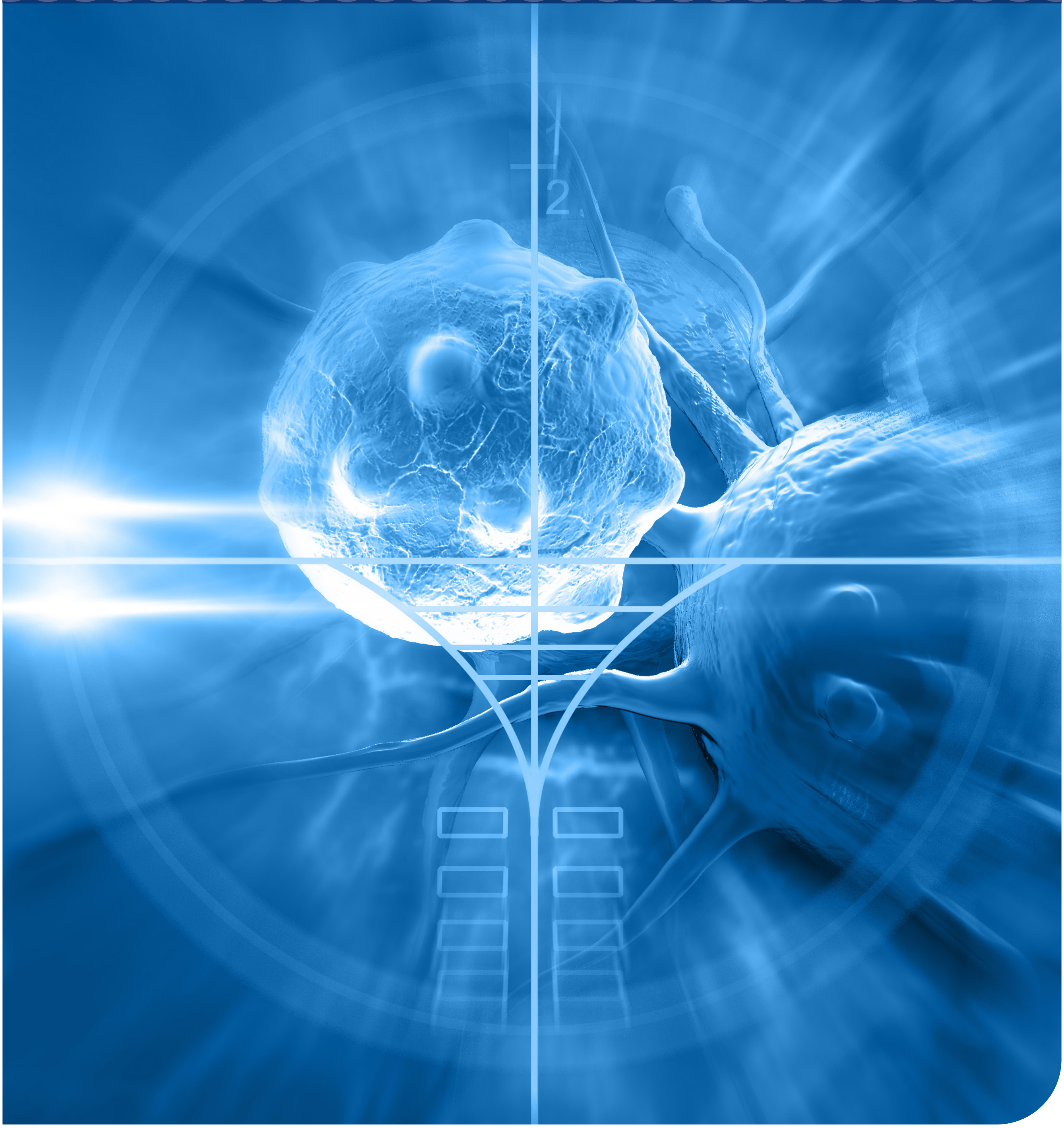
7. Specific oncology areas



7. Specific oncology areas

a. PAEDIATRIC ONCOLOGY

Introduction

Malignant diseases in children are not only medical, but also a psychosocial problem of the child, the family and the wider community. Given the high levels of tumor curability in children and a relatively low incidence and the need for excellence in their treatment, tumors in children present a demanding clinical, organizational and educational problem.

The basis of action in the field of pediatric oncology is the strategic plan of the European Society for Pediatric Oncology (SIOPE). This document formally regulates international professional cooperation among staff dealing with the issues of children with malignant tumors, for the purpose of applying a single working method (link: www.siope.eu/SIOPE_StrategicPlan2015). The previously adopted European standard of care for children with malignant diseases provides basic guidelines for adequate care of ill children and young people (link: www.siope.eu/wp-content/uploads/2013/06/Croatian.pdf).

Vision 2030

To have all pediatric cancer care given according to the internationally defined guidelines with continuous quality control and with drug access/methods within the average of western EU countries

Objectives

Optimization of health care for children suffering from malignant diseases, by raising the level of overall healthcare, with psychosocial care provided to the family

Measures/Activities

1. Categorize healthcare institutions and accurately define diagnostic and treatment methods
2. Create a network of pediatric institutions dealing with children with malignant tumors to make the data on each child continuously available. The development of adequate

administrative support is required. This also addresses the treatment of children with high-risk tumors, and treatment at reference centers.

3. Ensure a sufficient number of highly specialized professionals of all profiles, and provide continuous education and training.
4. Develop a comprehensive care program in pediatric oncology, along with defined guidelines for diagnosis and treatment, respecting priorities and achieving an adequate quality of life of the child and his / her family.
5. Develop a preventive program: increased diagnostic control of children in risk groups (e.g. neurofibromatosis, genitourinary malformations, and families with Wilms tumor, retinoblastoma and other tumors associated with a hereditary component or other risk factors).
6. Implement palliative care procedures that respect the personality and dignity of a child, in accordance with the IMPACT criteria that ensure mobility that will contribute to child spending more time at home. Good communication between the hospital palliative team, the county (local) hospital and/or the primary healthcare medical team is needed. It is important to make sure parents are well informed, and to avoid therapeutic violence. Psychosocial support must be provided to the whole family.
7. Track late treatment complications through outpatient work. Today, 80% of children and adolescents with malignant diseases are successfully treated. It is estimated that 60% of survivors have at least one chronic health problem, and 30% serious health damage.
8. Implementation of the Survivorship Passport for childhood neoplasia survivors, which enables every person in Europe treated for malignant childhood illness better access to health care and adequate long-term care.
9. Encourage national and international pre-clinical and clinical trials and take part in them.
10. Develop doctors’ activities in tumor working groups: BFM group, SIOP brain tumor group, SIOPEN group for neuroblastoma, EMSOS group for musculoskeletal tumors, a group for kidney tumors, rare tumors and late complications of treatment (PanCare).
11. Permanent postgraduate education of medical staff and the country and abroad, focused on primary health care for the earliest possible tumor detection.
12. Secure a permanent source of funding for employee training and planned participation of medical staff in meetings of individual groups in Europe. After meeting, a report is made and information shared with all centers in Croatia.
13. Improving common clinical epidemiological registries, making a national data base for pediatric oncology as a separate part of oncology data base.
14. Establish a special fund for innovative therapies and treating children abroad by methods proven to be effective in prolonging survival, but unavailable in Croatia.
15. Participation of hematooncologists in the work of the commission for the approval of expensive drug treatment and evaluation of the justification of using innovative medicines, i.e. participation in clinical studies based on professional medical and team decision.
16. Implementing preschool, elementary and high school programs, physical and work therapy, nutritional support and work of psychologists and social workers, with the implementation of rehabilitation projects and projects of psychosocial support (psycho-rehabilitation team).

17. Provide children and parents with accommodation during outpatient treatment, and parents with rights to sick leave, care-giver status or shorter working hours.
18. Synchronize activities of associations with the needs of departments where diagnostics, treatment, complications monitoring and rehabilitation of children with malignant tumor are carried out, prioritizing donations; harmonizing needs and ensuring a clear and transparent donation system. The possibility of engaging educated volunteers in the departments for pediatric oncology, who could significantly improve the quality of life of children and their families, as well as the working conditions of the employees in these departments, was considered. It is necessary to give precise descriptions of volunteering, make volunteer contracts, and let associations select and educate potential volunteers, who can be recruited from a group of survivors. All of these apply to other oncological institutions and departments through co-operation with civil society organizations.
19. Create a network of associations dealing with the problem of families with a malignant tumor in childhood; the network should have a united front in performance, to achieve optimal result, i.e. make sure families have social rights, and solve the problem of out-of-hospital accommodation.
20. Organize young malignant tumor survivors, setting up rehabilitation camps, with the help of associations.
21. Education and planned participation of competent volunteers.
22. Apply a protocol for communication in difficult situations.
23. Systematic supervision and psychological support for employees in pediatric oncological care.
24. Introducing radiosurgery treatment of children with solid tumors, with all the necessary technical and personnel support.

Stakeholders

- Professional societies
- Ministry of Health
- Croatian Institute of Telemedicine
- Pediatric Oncology Institutions.
- Accredited pediatric oncology institutions
- Associated International Pediatric Oncology institutions
- Croatian Institute of Public Health
- Croatian Health Insurance Fund
- Ministry of Science and Education
- Ministry of Demography, Family, Youth and Social Policy
- NGOs
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

Although scarcely analyzed and published, it can be assumed that the cost-effectiveness of pediatric oncology programs is well below the WHO-CHOICE threshold of 'very cost-effective'. This is based on the estimated number of annual new patients diagnosed and their 5-year survival which in Croatia is already comparable to EU average.

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b. MALIGNANT TUMOURS OF THE HAEMATOPOIETIC SYSTEM

Introduction

Hematopoietic malignancies are small in numbers or percentages in comparison to solid tumors, but they present scientifically as well as clinically extremely important group of tumors. Hematooncology lead the way too many breakthroughs in oncology, transplantation medicine including. Now, the best results in therapy in oncology in general are seen in treatment of different types of leukemia's and lymphomas.

Vision 2030

To improve the care of patients suffering from malignant tumors of the haematopoietic systems in the Republic of Croatia, to meet western EU standards.

Objectives

1. Create a standard of care for patients with hematopoietic systems malignant tumors and the manner of its implementation on the basis of good medical practice in hospitals and other institutions
2. Propose measures and procedures for medicines availability, as well as the criteria for their implementation
3. Define the system of quality control of the treatment and care of haematological patients

Measures/Activities

1. Develop national guidelines for the treatment of malignant tumors of the hematopoietic system, in order to harmonize procedures for the diagnosis, treatment and monitoring of patients in Croatia
2. Define and elaborate the level of hematological clinical care (diagnosis and treatment in hospitals of the Republic of Croatia, which determines the possibility of application i.e. the availability of services at a hospital institution.
3. Develop a procedure for transferring patients from one hospital to another based on the criteria of urgency and severity of the disease; defining the criteria for treating patient abroad.
4. Define criteria for reference centers, which perform the most complex procedures of diagnosis and treatment; propose what their obligations and rights, as well as financial needs, are.
5. Create criteria based on professional and financial indicators on new drugs for the positive list of the Croatian Health Insurance Fund.
6. Develop a procedure for conducting clinical trials, as well as compassionate treatment.
7. Create a database of patients suffering from haematopoietic system malignant tumor.

8. Educate citizens on all important indicators of care for haematological malignant tumors patients
9. Establish cooperation with patient associations and strengthen their capacities.
10. Institutional and structural support for haematopoietic stem cells banks – establish a center to coordinate all stem cell banks in the Republic of Croatia and contribute to even better cooperation with international stem cell banks
11. Encourage and promote clinical research in haemato-oncology

Stakeholders

- Professional societies
- Croatian Cooperative Group for Haematology – KROHEM,
- Ministry of Health's working bodies
- Croatian Health Insurance Fund
- Public Sector, Volunteering groups
- Patient associations
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

In study published in 'Blood' in 2015, the cost-effectiveness of innovative treatment for hematologic malignancies was studied using the data from 29 studies published in the years 1996-2012 (including 44 cost-effectiveness ratios). Most ratios fell below $50 000 per quality-adjusted life-years (QALY) (73%) and $100 000/QALY (86%). Published data suggest that innovative treatments for hematologic malignancies may provide reasonable value for money.

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c. RARE TUMOURS

Introduction

Rare tumors are those whose incidence is less than 6/100,000 inhabitants. The biggest problems faced by patients with rare tumors are late diagnosis, inadequate treatment in non-specialized centers, poor availability of clinical knowledge and adequate therapy in the treatment of rare tumors, given that the research in this area is also limited by a small number of patients, and therefore of potentially less interest to pharmaceutical companies. On the other hand, not less important, the absence of a national register of patients makes it impossible to perceive the actual dimension of this problem and to plan a national strategy.

Vision 2030

To have all rare tumors diagnosed, treated and follow up according to the internationally defined guidelines and with individualized diagnosis and drug access/expenditure within the average of western EU countries.

Objectives

Optimize early diagnostics, treatment and monitoring patients suffering from rare malignant diseases.

Measures/Activities

1. Reorganize the Cancer Registry and set up a national oncological database to enter patients' data accurately and reliably, in order to know the actual incidence, prevalence, treatment outcomes and survival of patients with rare tumors.
2. Form a unique database of patients with rare tumors (within the Cancer Registry and the national oncology base); provide infrastructure for its development and maintenance, with regular reporting on the state of rare tumors in the Republic of Croatia.
3. Define reference centers, centers of excellence for certain groups of rare tumors to ensure better health care quality, early diagnosis, diagnostic accuracy and advanced diagnostics, scientific and clinical research and staff training programs. As a rule, these are clinical hospital centers. Reference centers (centers of excellence) where all patients with rare tumors (according to the previously defined list of rare tumors) should be treated, should establish a national bank of rare tumors with a reference laboratory for rare tumors, which would serve as the basis for further research in this area. Taking into account incidence, it is sufficient to establish a unique national bank and laboratory that would be competent for genetic diagnostics, without which it will not be possible to determine future therapy, within the personalized therapy paradigm in modern oncology. In that sense, it would be desirable to cooperate with institutions that are not in the health care system and can greatly assist and develop their activities, such as medical schools or Ruđer Bošković Institute. It also strengthens the national network of institu-

tions, increasing competitiveness, competence and the use of existing resources. It is important to try to withdraw EU funds, or, alternatively, engage in cooperation with other European centers, primarily regional ones (Italy, Austria, and Germany).

4. Develop diagnostic guidelines (harmonizing pathohistological and radiological criteria), surgical and oncological treatment and overall healthcare for patients with rare tumors and supervision of their implementation. The guidelines should be created by centers of excellence.
5. Medical staff training in diagnosing and treating rare tumors (in centers of excellence).
6. Secure financial resources and logistics needed for patients to be referred to the center of excellence at the earliest possible stage of the disease in order to ensure optimal treatment. For this purpose, it is necessary to create a website with links that would enable direct communication and guidance of the patient towards centers of excellence (include all healthcare institutions in Croatia, but also make it accessible to the patients themselves).
7. Ensure cooperation with international institutions and organizations dealing with this issue and carrying out international clinical research on rare tumors.
8. Involvement in a comprehensive Rare Cancers Europe initiative that brings together all stakeholders involved in rare cancer issues.
9. Set up a special fund for rare diseases, including rare tumors.
10. Promotion of non-commercial clinical studies, given that the research of these tumors cannot be financed as commercial activity, due to a small number of cases and high costs.

Stakeholders

- Croatian Institute of Public Health
- Ministry of Health
- Oncology institutions
- Professional societies
- Croatian Health Insurance Fund
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

A number of weaknesses in the current orphan drugs policy and legislative framework need to be addressed not only in Croatia but across Europe. Due to high burden of illness and price of medicine, improvements in data collection with the creation of registries are needed and have been accounted for in previous chapter. Overall, a better and more holistic value assessment framework that explicitly accounts for the peculiarities of rare diseases in the context of value based assessment needs to be developed and consistently implemented.

It is commonly perceived that ICERs for drugs that treat rare diseases are much higher than those of common drugs, but results from the study published in Pharmacoeconomics suggest differently. The proportion of ICERs that were cost effective at both thresholds does not appear to be significantly different between the two groups, so rarity is not associated with cost effectiveness, even when adjusted for important covariates.

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8. Palliative care and pain relief

8. Palliative care and pain relief

Introduction

According to the definition of the European Association for Palliative Care and the World Health Organization, palliative care can be defined as follows:

- Palliative care is an approach aimed at improving the quality of life of patients and their families faced with the problems of incurable, advanced diseases, by preventing and alleviating suffering through early and impeccable judgment, by treating pain and addressing other physical, psychosocial and spiritual issues. Palliative care is an interdisciplinary approach and involves patients, the families and the community. Palliative care includes taking care of the patients' needs wherever care is provided, at home or at an institution.
- Palliative care affirms life, and perceived death as an integral part of life that comes at its end, and it neither accelerates not delays death. It strives to preserve the best possible quality of life until death.

Current state of play and future plans

The number and the position of palliative care facilities are laid out in the Public Health Service Network. Along with the implementation of a general level of palliative care in the area of general/family medicine, visiting nurse service, home care and pre-school health care protection, at the primary health care level the Network also envisages 52 palliative care coordinators and mobile palliative teams, and 83 palliative beds in health centers' inpatient clinic, providing specialist palliative care. In the stationary health care 352 palliative beds are envisaged, including 215 beds in general hospitals, 108 in special and psychiatric hospitals, 15 in Vrapče Psychiatric Clinic and 14 in Marija Krucifiksa Kozulić Hospice. There are also 83 palliative beds in inpatients clinics at health centers.

As of 31 December 2017, there are nine contracted coordinators for palliative care and seven mobile palliative teams in the Health Centers of Varaždin County, Požeško-Slavonska County, Čakovec, Istrian health centers, Osijek Health Centre and Karlovac Health Centre. In 13 counties formal written decisions were made on the beginning of performing palliative care at the primary health care level (coordination of palliative care / mobile palliative team): Varaždinska, Požeško-slavonska, Osječko-baranjska, Međimurska, Istarska, Karlovačka, Vukovarsko-srijemska, Dubrovačko-neretvanska, Zadarska, Primorsko-goranska and Šibensko-kninska counties, for 12 health centres (health centres DZ Varaždinska County, DZ Požeško-Slavonska County, DZ Osijek, DZ Čakovec, Istrian health centres, DZ Karlovac, DZ Vinkovci, DZ Vukovar, DZ Zadar County, DZ Primorsko-goranska County and DZ Knin). The Public Health Service Network provides palliative care beds in the following hospitals: Bjelovar General Hospital, Dr. Josip Benčević Slavonski Brod General Hospital, Sveti Rafael Strmac Special Hospital for Psychiatry and Palliative Care, Dubrovnik General Hospital, Vrapče Psychiatric Clinic, Sveti Ivan Zagreb Psychiatric Clinic, Special Pulmonary Diseases Hospital, Pula General Hospital, Karlovac General Hospital, Ogulin General and Veterans' Hospital, Duga Resa Special Hospital for Extended Treatment, Dr. Tomislav Bardek Koprivnica General Hospital, Zabok General and Veterans' Hospital, Gospić General Hospital, Čakovec County Hospital, Našice General County Hospital, Požega General County Hospital, Rab Psychiatric Hospital, Dr. Ivo Pediši" Sisak General Hospital, Dr. Ivan Barbo" Popovača Neuro-Psychiatric Hospital, Šibensko-kninska General County Hospital, Hrvatski ponos Knin General and Veterans' Hospital, Varaždin General Hospital, Virovitica General Hospital, Vinkovci General County Hospital, Vukovar General County and Veterans' Hospital, Zadar General Hospital and Ugljan Psychiatric Hospital.

In addition, due to the status changes and the separation of Pakrac General and Veterans' Hospital from Požega General County Hospital, and the separation of Nova Gradiška General Hospital from Dr. Josip Benčević Slavonski Brod General Hospital, in 2018 the palliative care beds were planned for newly established hospitals as well. At the same time, the Public Health Network envisaged palliative care beds and the Marija Krucifiksa Kozulić Hospice in Rijeka, as well as in the health centers' inpatient clinics. Pilot projects are carried out at Primorsko-goranska County Health Centre, Vinkovci Health Centre, Vukovar Health Centre, Dubrovnik Health Centre, Krapinsko-zagorska County Health Centre and Zagreb-Centre Health Centre (of the ten initial pilot projects for mobile palliative teams), funded by a special program of the Croatian Health Insurance Fund, and cease the contraction of teams in regular palliative care. There are also 31 pain clinics in hospitals, 47 free equipment rental centers and 16 volunteer organizations in palliative care.

The Ordinance on minimum conditions in terms of space, staff and medical and technical equipment for healthcare prescribes minimum conditions to be met by a palliative care institution. Mobile palliative teams carry out a specialist palliative care level and are envisaged by the Public Health Service Network with palliative care coordinators at the primary health care level.

The funds have been secured by the Croatian Health Insurance Fund for contracted teams in palliative care activities. In line with the palliative care coordinators network at the primary level of health care in the Republic of Croatia, and in view of the planned dynamics of establishing palliative care coordinators and mobile teams, for 2017 the Croatian Health Insurance Fund planned funds in the amount of HRK 8,000,000, for 2018 the amount of HRK 14,000,000 and for 2019 the amount of HRK 28,400,000. For palliative healthcare, which is conducted at the primary level by visiting nurses and home care nurses, funds planned for 2017 amounted to HRK 29,412,000, for 2018 HRK 29,559,000 and for 2019 HRK 29,707,000, and they include, among other things, funds for the implementation of 15 primary health care activities and stationary health care, which includes the care of palliative patients in 29 hospital institutions for the total of 352 beds, as well as the activity of the Reference Centre of the Ministry of Health for the protection of the elderly, which carries out activities for three gerontological and public health interdisciplinary teams, for the development of a monitoring program and the study of health needs for palliative care of the elderly.

For the purpose of standardizing palliative care education in the Republic of Croatia, the professional chambers (the Croatian Chamber of Physicians, the Croatian Chamber of Nurses, the Croatian Chamber of Physiotherapists, the Croatian Psychological Chamber, the Croatian Chamber of Social Workers, the Croatian Chamber of Health Workers and the Croatian Pharmacy Chamber) started the initiative to create the education program and the catalogue of competences in palliative care; their drafts are currently being adopted. Given the need for professional guidance for the development and provision of palliative care, in 2014 the Ministry of Health launched an initiative for their development of all the activities involved in providing palliative care and invited experts and chambers to submit their proposals; some guidelines have been made. Before the definition and adoption of the Croatian National Guidelines, the Ministry of Health submitted recommendations for using the existing recognized global and European guidelines for the recognition of palliative patient GSF-PIG (Gold Standards Framework - Prognostic Indicator Guidance) as a fundamental tool for early recognition of patients nearing the end of their lives, and SPICT, CriSTAL and QUICK GUIDE as auxiliary tools. Other tools and guidelines for reporting bad news, understanding symptoms, providing some forms of care, etc. are also being used. The Croatian Institute for Emergency Medicine has published the National Guidelines for Outpatient and Hospital Emergency Medical Services with patients requiring palliative care, for healthcare professionals in emergency medical services. In addition, the new National Program foresees the development of strategic guidelines for the development of palliative care of children in the Republic of Croatia, based on the IM104 PaCCT standards for the development of pediatric palliative care in Europe. Palliative care education is being developed on several levels. At the higher education level, there is education on palliative care in the form of compulsory or elective subjects, including studies in medicine, nursing, social work, etc. In addition, medical schools in Zagreb (via the Centre for Palliative Medicine, Medical Ethics and Communication Skills - CEPAMET), Split and Osijek, the Faculty of Health Sciences of the University of Rijeka and the Croatian Catholic University of Zagreb have additional courses on palliative care or courses of continuing education for all professionals and volunteers involved in palliative care. The Faculty of Pharmacy and Biochemistry in Zagreb has included palliative care within a compulsory subject on pharmacy care. Furthermore, palliative care education often takes place in the form of workshops, lectures or courses in hospitals, health centers, homes for the elderly and other institutions organized by the institutions themselves for their employees. Palliative care associations also participate in the organization and implementation of education for volunteers as well as professionals and citizens. Local communities throughout Croatia have organized numerous lectures and forums, appearances in the media and other public information activities, raising public awareness about the importance and availability of palliative care.

To date, around 560 persons from different professions from all over Croatia (doctors, nurses, psychologists, social workers, psychologists, pharmacists, etc.) have completed the Palliative Medicine Basics course, 250 colleges completed the Communicating Skills in Oncology and Palliative Medicine course, and 100 persons the Psychological Aspects in Palliative Medicine course at the Centre for Palliative Medicine, Medical Ethics and Communication Skills (CEPAMET) of the Medical School in Zagreb. For the past ten years, category 1 physicians' continuing education postgraduate course in Child Pain and Palliative Care has been held at the Medical School in Zagreb; around a hundred doctors, psychologists and social workers have been educated about the specifics of pediatric palliative care

It has been proposed that professional chambers should adopt rulebooks on further training, as a horizontal form of education for palliative team members. It is also important to raise awareness among the general, non-governmental and religious associations to actively participate in the palliative care system, volunteering system or counselling center for patients and families.

Vision 2030

Equal access to high-quality palliative care, integrated into all levels of healthcare systems to assure that any oncology patient's or family caregiver's suffering is relieved to the greatest extent possible.

Objectives

1. Define the sufficiency of the existing capacities for palliative care through:
    1.1. Number and place of palliative care facilities
    1.2. Profiles and number of experts from the mentioned area
    1.3. Number and arrangement of mobile palliative teams.
2. Define the way of financing and realizing patients' rights to palliative care services.
3. Define the manner of informing all healthcare professionals involved in the treatment of cancer patients about the existing palliative care system and any new changes.
4. Define the way of informing oncologic patients about the existing palliative care system.
5. Define the education of professionals required for palliative medicine as well as education of all health professionals during regular education and compulsory continuing professional training.
6. Secure funding for facilities, equipment and personnel needed to carry out palliative care.
7. Raise awareness among the public, non-governmental and religious associations to actively engage in palliative care, either through volunteering systems or counselling centers for patients and families.
8. Monitor the implementation of the measures.

Measures/Activities

1. Explore the situation in the field and determine the real needs for palliative care capacities through field visits, data analysis of the Croatian Institute of Public Health, etc.
2. Establish new palliative institutions, mobile palliative teams and counselling centers based on the number of residents in individual counties.
3. Educate a sufficient number of professional staff of all profiles to be available for work in palliative care.
4. Create a platform for informing all healthcare professionals involved in the treatment of cancer patients about the existing palliative care system and about any change.
5. Create a platform for informing cancer patients about all the existing possibilities of the palliative care system and merge it with other information patients might need during treatment.

6. Set aside adequate resources from the state budget for the implementation of measures.
7. Reach out to the public through the media, by educating the population and organizing a volunteer system through non-governmental organizations.
8. Create a national palliative care cancer network with national palliative cancer care database
9. Establish a commission for the quality control of measures taken on the ground and review the existing system depending on current needs.

Stakeholders

- Ministry of Health
- Health Insurance Fund
- Professional Associations
- Patient Associations
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

Randomized trials among advanced cancer patients demonstrate that early palliative care integration into usual oncology care reduces symptom burden, improves quality of life and caregiver outcomes, and may improve survival. The impact of palliative care on health economics remains poorly defined and reported cost savings are an unintentional consequence of providing care aligned with patient goals. This study determined the impact of palliative care on healthcare costs among elderly patients with advanced cancer.

There are limited but indicative studies which demonstrate that palliative care has the capacity to substantially reduce healthcare expenditures among advanced cancer patients. The impact is linked to the timing of calculations. Palliative care consultation within 7 days of death decreased healthcare costs by $975, whereas palliative care consultation more than 4 weeks from death decreased costs by $5,362.

Another study suggests that changes in palliative care cost can only come from dramatic changes in how the care is being provided. One model is coordinated, expert, high-volume care that can prevent end-of-life hospitalization, with early use of advance directives. Preliminary data supports the hypothesis that costs may be reduced by 40% to 70%.

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9. Cancer education

9. Cancer education

a. NATIONAL

Introduction

Cancer has become a growing public health, medical and economic problem both in the world and in the Republic of Croatia. Taking into account the biological, scientific and multidisciplinary complexity of oncology and cancer, the explosive development of the profession, significant advances in treatment and their application, education represents the basis of progress in oncology.

Education in oncology is of national importance, especially when it comes to the general population. Generally speaking, oncology education can be divided into the one directed towards the general population, and the one for medical professionals.

Vision 2030

To have optimal and continuous education of all medical professionals according to international standards as well as to significantly increase general public knowledge about cancer related issues

Objectives

Education of medical professionals

1. Adequate education in the field of clinical oncology provided to healthcare professionals of all profiles and qualifications level.
2. Education is very important for creating opportunities for integrated, multidisciplinary and ongoing care of oncologists. The emphasis must be on a holistic approach to the patient, not only in the use of diagnostic and therapeutic modalities or in the treatment of individual symptoms. The intent of treating a patient is curing or controlling the disease, achieving the highest possible quality of life, depending on the extent of the malignant disease and other comorbid diseases and conditions. Education must include knowledge of palliative-supportive treatment, as some patients will experience progression of the disease despite active oncological treatment. It also needs to include communicative skills, necessary for patients' psychological wellbeing through a friendly communication with the staff.

Education of general population

1. Educate the general public on cancer-related issues, with focus on incidence and curability of malignant diseases, as well as on the role of primary and secondary prevention of malignant diseases in this context

Measures/Activities

Education of medical professionals

1. Increase the number of hours in the Clinical Oncology and in the Cancer Patients Care courses in secondary school education (primarily nurses), with the syllabus containing specific clinical exercises and practice on the ground, in palliative care institutions and mobile palliative teams.
2. Increase the number of hours in the Clinical Oncology course in undergraduate higher education health studies. In educating radiology technicians, increase the number of hours in radiotherapy courses. For nurses in high or higher education increase the number of hours in Healthcare Processes for Cancer Patients course, as well as in palliative medicine course, with an adequate clinical exercises course.
3. Integrate an additional course in Clinical Oncology into university biomedicine and healthcare courses; additionally, emphasize diagnostics and non-oncological treatment of patients with malignant diseases in other clinical courses. Cancer patients unfortunately develop other (chronic) diseases (cardiovascular diseases, diabetes, hepatitis, rheumatic diseases, etc.). This primarily refers to courses in internal medicine, radiology, gynecology and surgery.
4. Permanent education of health professionals of all profiles, especially in the field of cancer patient's treatment and care. Check education level through the relicensing system in relevant professional chambers.
5. Include training abroad as an objective of education, and a possible obligation among residents in clinical hospital centers. Similarly, residents in clinical hospital centers should be able to attend professional training courses organized by European oncology societies (ESTRO, ESMO).
6. Develop a human resources management system, plan the residencies of required specialists, develop new staff profiles that will become necessary in oncology, e.g. specialized oncological nurses, highly educated non-medical experts needed for the implementation and management of new technologies, IT specialists with adequate education, all in order to establish a functional national oncology network.

Education of general population

1. Introduction of cancer related health education programs in all educational institutions, including universities.
2. Education of the general population through public health forums, lectures and workshops on healthy lifestyles, early detection of diseases, etc.
3. Encourage people to go for preventive check-ups, e.g. by giving them a day off.

4. Involvement of volunteers, non-governmental organizations and patient associations to raise awareness of the need to combat cancer.

Stakeholders

- Ministry of Science and Education
- Professional societies
- Ministry of Health
- Croatian Institute of Telemedicine
- Relevant healthcare professionals – nurses and educators in pre-schools and schools
- Physicians in public health institutions
- Young doctors and medical students
- Legislator, i.e. the Ministry of Health to regulate legal and financial framework
- NGOs and patients' association
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

There are no publications analyzing the cost-effectiveness of different educational programs in cancer care, neither those intended for healthcare professionals nor those for patients. If performed, it could support investment decisions for the educational programs and enable them to reach measurable outcomes. Therefore, the cost effectiveness analysis is a useful tool for policymakers and practitioners to decide which programs will provide the greatest return for their investment and is highly recommended to be used when new educational programs are being implemented or current programs amended.

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b. INTERNATIONAL

Introduction

International cooperation with scientific, clinical and public health institutions aims to improve the quality of services for oncologists, improve oncological care by collaborating on scientific and research projects, educating healthcare staff, consultations or treatment abroad or providing advice on oncological healthcare policy in general. Croatia, unfortunately do not have extensive, appropriate international cooperation with other countries, especially those with developed oncology infrastructure.

Vision 2030

To increase international cooperation, scientific and clinical, in oncology to the level of western EU average.

Objectives

1. Education of our experts abroad to profile them into experts in narrow field of oncology, raising the awareness of the need for true multidisciplinarity, quality control, and comparability in the treatment of cancer patients
2. Facilitating the involvement of patients in clinical trials that can help the patient, and that are not conducted in the Republic of Croatia, by defining and removing barriers that lead to a small number of clinical trials.
3. Integrating our data into a single European register, especially those on rare diseases, in order to contribute to global knowledge.
4. Continuous improvement, comparison, correction of our diagnostic and therapeutic procedures through comparison with the practice in the EU and Western countries in general.
5. Providing the possibility of consultations for patients abroad, especially for rare tumors and very complex cases.
6. Providing the possibility of sending patients abroad for treatment which have been proven effective, but are not carried out in the Republic of Croatia.
7. Equal participation in the creation and implementation of oncological research by the exchange of scientists.
8. Maximum use of international sources of oncological funding, especially the compassionate oncological drugs use.

Measures/Activities

1. Define the obligation to carry out a part of the internship in oncology disciplines (oncology and radiotherapy specialization and internal oncology and surgical sub-specialization in oncology) in a reputable international institution (two months).
2. Provide three scholarships per year in the amount of HRK 180,000 annually for study visits designed to adopt new knowledge and skills in oncology.

3. Supervise and implement these measures through the Cancer Agency at the Ministry of Health.
4. Require from the Ministry of Health and the Agency for Medicinal Products and Medical Devices, its bodies and clinic-hospital institutions, to enable the biggest possible number of different clinical research to be carried out in the Republic of Croatia in the shortest time possible (through legal acts, human and IT resources, and facilities, etc.).
5. Ensure maximum availability of new medicines through European and global compassionate programs (Expanded Access), through the Cancer Agency, as relevant body at the Ministry of Health.
6. The Ministry of Health should ensure legislation for their implementation.

Stakeholders

- Ministry of Health
- Ministry of Science and Education
- Croatian Health Insurance Fund
- Oncological Professional Societies
- Agency for Medicinal Products and Medical Devices
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

There are no publications analyzing the cost-effectiveness of different educational programs in cancer care, neither those intended for healthcare professionals nor those for patients. If performed, it could support investment decisions for the educational programs and enable them to reach measurable outcomes. Therefore, the cost effectiveness analysis is a useful tool for policymakers and practitioners to decide which programs will provide the greatest return for their investment and is highly recommended to be used when new educational programs are being implemented or current programs amended.

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10. Cancer research

10. Cancer research

Introduction

It is well known that research in oncology, including clinical trials, results in improved patient care and may in the future also lead to findings that can help cure majority of cancers.

Over the last decade, there has been a shift in the tumor treatment paradigm, especially in the field of personalized medicine and immune-oncology, which has led to significantly improved treatment outcomes, even in patients with metastatic diseases. Understanding etiology, biology, pathophysiology and cancer treatment is the result of biomedical research, both in basic science and in clinical studies, but also in regular clinical practice, after placing a drug or a medical product on the market (Real World Evidence). Cancer research on all levels is a necessary step to further improve treatment outcomes, requiring extensive medical knowledge, expertise in planning and conducting clinical trials, equipment and significant human and financial resources. Clinical research is a prerequisite of modern oncology and is often the first choice in treating advanced stages according to the international guidelines for cancer treatment, enabling better treatment outcomes for patients, with significant savings in drug use. Unfortunately, such research is underrepresented in Croatia, and only a small number of cancer patients get the opportunity to be included. Nearly all clinical studies in the world and in Croatia are sponsored by pharmaceutical companies. These studies bring new scientific evidence on the one hand, and financial savings for society on the other; patients included in control groups receive the gold standard of treatment with optimal monitoring and treatment of side effects borne by the sponsor, and patients in the study group receive a new drug from the sponsor, which represents a significant savings in the already limited health care budget. Likewise, various retrospective and non-interventional studies may provide insight in the quality of treatment and efficacy of drugs in daily clinical practice, compared with the results obtained from controlled clinical trials. Prospective academic studies can also lead to new insights. Basic trials, which are a prerequisite for further progress, have been relying on translational testing recently, which check the insights from pre-clinics directly under clinical conditions. Positive changes in this field are key to moving the Republic of Croatia from the devastating position, one before the last, in the EU28 in the malignant diseases survival category.

Vision 2030

To increase scientific coverage, output, in oncology to the level of western EU average.

Objectives

1. Increase the number of pre-clinical, clinical, non-interventional, academic and translational research in oncology to the average level of western EU countries and thus contribute more to global knowledge, enable the advancement of our scientists and clinicians, and provide patients with access to new medicines and ways of treatment in order to achieve better treatment outcomes.
2. The specific objective is to include more patients in clinical studies, doubling number of enrolled patients in first five years and quadrupling in period of 10 years in comparison to number of patients enrolled in studies in 2019.
3. Also, the specific objective is to have more published scientific articles in internationally recognized journals, doubling number of enrolled patients in first five years and quadrupling in period of 10 years in comparison to number of articles published by Croatian oncology scientist in 2019.

Measures/Activities

1. Ensure clear and simpler legal and financial frameworks for planning and conducting clinical trials based on positive practice of EU countries.
2. Create new rules for clinical, non-interventional and academic studies that will motivate physicians, especially clinicians, as well as other health professionals and experts from basic biomedical professions to conduct academic studies, and will also be motivating for sponsors (Note: Creating a new rulebook is also important for the purpose of aligning national procedure with the new, EU procedure in accordance with EU Regulation No 536/2014. The centralized procedure for clinical trials approval defined by this Regulation must be fully implemented, and the EU Member States can determine which part is implemented at national level, but in the way that everything is carried out within the timeframes defined by the Regulation. The deadline for its full implementation in the EU is 2019, and the activities related to establishing a centralized e-platform for application and approval of clinical trials has already begun).
3. Encourage the development of academic research through legislative measures and incentives.
4. Documentation required to obtain a study authorization as well as the approval process itself should be made simpler, making sure the submitted documentation is reviewed by trained experts in competent bodies such as the Ministry of Health, the Agency for Medicinal Products and Medical Devices, and the Central Ethics Committee for clinical trials. Approval system should be set up to enable the entire process to be carried out through a web application, which would ensure a shortening of the approval procedure and greater competitiveness of the Republic of Croatia in the area of sponsored clinical trials, but not to the detriment of the time required for the reviewers to review documents; only time that has so far been put in unnecessary administration would be saved.
5. Establish collaboration between universities, medical institutes and clinics to conduct interdisciplinary and translation studies.
6. Set aside special funds in the budget to carry out research, to the minimum extent those of the public health interest for Croatia, in order to improve cancer treatment and achieve better treatment outcomes.

7. Secure sufficient human resources to conduct research (make sure physicians and other staff are given time devoted to research alone) and a continuous education system in the field of good clinical practice, but also in areas that are important for independent planning, preparation and implementation of clinical, academic and non-interventional research.
8. Ensure appropriate education of the entire population and/or individual interest groups in order to better understand the importance of conducting clinical and other research, both for the individual patient and for the entire community. This can be done in cooperation with various non-governmental organizations, patient associations, etc. as it has already been established in EU countries that have achieved the best results in this field, such as Denmark or the UK.
9. Active involvement of patient associations in promotion of clinical research.
10. Fund the development and maintenance of the tumor tissue biobanks.
11. Achieve international cooperation with the aim of enabling our patients take part in clinical trials conducted abroad.
12. Establish a scientific unit in each clinical hospital center that will have the task of achieving a relevant translation project.
13. Establish a comprehensive clinical trial register with the aim of monitoring the results achieved and establishing a system of continuous progression. The results monitored can be roughly divided into: (1) clinical (e.g. treatment outcome of the patients involved in the tests), (2) administrative (e.g. testing approval speed) and (3) financial (e.g. monitoring investments related to clinical trials that have come to Croatia in this way, as it is well known that conducting clinical and other trials can significantly contribute to economy and affect the increase of gross national income).

Stakeholders

- Professional societies
- Ministry of Health
- Ministry of Science and Education.
- Central Ethics Committee for clinical trials
- Agency for Medicinal Products and Medical Devices
- Representatives of Clinical Trial Sponsors
- Universities
- Clinics in the tertiary healthcare system
- Patient associations
- Croatian Institute of Public Health
- Research labs
- Government of the Republic of Croatia
- NGOs
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Science
- Ministry of Health
- EU or other international source of funding

Economic evaluation

In addition to the main objective of bringing new medicines to patients that will improve their health and quality of life, clinical trial activity also provides significant benefits to national and local economies in terms of economic impact generated through activities as development of clinical trial protocols; selection of clinical trial sites; implementation trials including the recruitment of staff, contractors, vendors, and patient volunteer; manufacture of small batches for testing; care to patients, including lab tests and ongoing health monitoring; analysis of the enormous amount of data generated; and providing diagnostic and treatment options free of charge – just to name some of the activities occurring at particular trial sites which require significant expenditures by biopharmaceutical companies and their vendors and contractors.

Economic impact broadly consists of three types of effects:

1. **direct effects** (the specific impact of the actual "first round" spending on clinical trials activities by the biopharmaceutical companies and/or contract research organizations spent with clinical trial service providers)
2. **indirect effects** (the impact of expenditures by suppliers to these clinical trial service providers), and
3. **induced effects** (the additional economic impact of the spending of clinical trial service provider employees and suppliers' employees in the overall economy that can be attributed to the actual "first round" expenditures).

One report on impact of clinical trials on State Economies from the U.S., using conservative data sources and assumptions, identified 6,199 industry-sponsored clinical trials, involving 1.1 million volunteer trial participants in 2013 and the investment of $10 billion in these trials, with an overall economic impact of nearly $25 billion across the communities where the trials were located.

For Croatia it is important to understand the current economic impact, but also the missed opportunity related to low number of clinical trials conducted in Croatia when compared with EU average.

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11. Creating a national oncology network, quality control, monitoring & reporting

11. Creating a national oncology network, quality control, monitoring & reporting

a. NATIONAL ONCOLOGY NETWORK (NON)

Introduction

In terms of its surface area, Croatia is a small country with relatively clearly defined structure of basic oncological institutions. They are distributed well geographically (Zagreb, Split, Rijeka and Osijek), linked to the academic and scientific base: medical schools integrated into a multidisciplinary base (parts of clinical hospital centers or clinical hospitals).

Over the last 20 years, we have witnessed the development of small, local oncology centers (out-patient clinics, departments) that do not have the capacity for good multidisciplinary work and providing all aspects of modern oncological treatment. Unfortunately, the establishment of these oncological centers in Croatia was not coordinated, nor did the epidemiological demand analysis preceded. One of the reasons is the lack of a central institution that would have a clear mission of coordinating and implementing key requirements for an effective cancer control program. The goal of the National Cancer Plan is to provide equal and high-quality oncology care to all citizens of Croatia, despite relatively limited resources, and regardless of where they come from or where they are treated.

Considering Croatia's size and geographic shape, the distribution of oncological institutions, the public health importance of oncology, the enormous need to improve the cancer patients' treatment results, the need for optimal oncology from the point of view of pharmaco-economy, there is no doubt that a national oncological network needs to be established to include all oncological institutions, and prevent any treatment of cancer patients outside the network (it would not be funded).

The starting point for the National Cancer Plan implementation should be the update on infrastructure, equipment and human resources available in Croatia's cancer control institutions. The demand should be based on the current level of cancer incidence and predicting incidence by 2030. Such a resource and needs plan should be a basic tool in planning organizational and structural changes (investment, training) and should be prepared in the earliest possible stage of Plan implementation.

Access to data on the types of cancer and their characteristics, tracking processes and outcomes based on these data are necessary for risk recognition and decision-making in health policy. This information should also be one of the key tools for assessing the implementation of the Plan. This data is the basis for further research and dissemination of cancer information and knowledge. Despite a significant improvement in epidemiological data on cancer collected in Croatia, primarily due to the introduction of the Cancer Registry, there are numerous obstacles preventing further progress in this area.

Unfortunately, there are no specific instructions and regulations on the type of data that the medical record of an oncological patient must contain (case history, pathologist findings, report on surgery, etc.). Medical records are usually descriptive or narrative and are difficult to use them later. For all these reasons data collection, data types, sources of data and their use and interpretation should be standardized. As there is no standardized information, it is impossible to compare the quality of treatment in various hospitals. These barriers include: a lack of data link between institutions that have access to data on cancer, fragmentation of information collected, insufficient infrastructure of information on participants in the health care system and insufficient level of knowledge on the quality of oncology care in Croatia. This data would be extremely important for institutions that fund oncology care (above-average number of complications basically means significantly higher treatment costs), as well as for the patients themselves (the patient can consult data to choose the institution that achieves the best results). Therefore, it is necessary to establish a national oncology network (National Oncological Database) which would make it possible to import all documents from hospital information systems (IBIS) automatically, and which would be compatible and parallel to BISs, and should not additionally burden the medical staff and would result in meeting the set goals.

The precondition for creating a national oncological network is to create a common and unified medical documentation in electronic format with electronic data delivery to the national oncology base and the Cancer Registry. All oncological care institutions, basic (at medical schools) or local ones, would have to be included in the network; otherwise it should not be possible to finance the treatment of patients. Within this kind of IT network, appropriate algorithms of the basic diagnostic procedures necessary for initiating the treatment of the most common diagnoses could be built, to standardize treatment at all levels in Croatia, from small oncology outpatient clinics to clinical hospital centers.

Oncological canters need to be integrated in a network in accordance with the latest IT standards, complying with all positive legal regulations, both national and European ones. This primarily refers to IT safety and personal data protection.

The main segments of the National Oncology Network system

1. Software solution
    1.1. Creating software
        1.1.1. Design and database creation
        1.1.2. Creating business solution for data management
        1.1.3. Creating user interface

        - 1.1.3.1. Web interface
        - 1.1.3.2. Desktop interface
        - 1.1.3.3. Mobile interface
    - 1.1.4. Creating communication links with hospital and other information systems
        - 1.1.4.1. Radiology systems
        - 1.1.4.2. Lab systems
        - 1.1.4.3. Hospital information system
        - 1.1.4.4. Croatian Health Insurance Fund
    - 1.1.5. Creating a reporting system

2. Software maintenance and update
    - 2.1. Regular system maintenance
    - 2.2. IT system update according to the needs of the National Oncology Network
3. Hardware demands
    - 3.1. Server support
        - 3.1.1. Software servers
        - 3.1.2. Database services
        - 3.1.3. Communication equipment
            - 3.1.3.1. Firewall
            - 3.1.3.2. VPN (Virtual Private Network) systems
    - 3.2. Hardware demands of oncology centres
    - 3.3. Hardware demand of ensuring permanent system availability (fail-over)
    - 3.4. Maintaining hardware resources
4. Software licences
    - 4.1. System software
    - 4.2. Licenses for database server
    - 4.3. Clients licenses
5. Analytical system
    - 5.1. Implementing modern analytical system
    - 5.2. Advanced predictive analytics
6. Communication demands
    - 6.1. Internet as a fundamental communication tool
    - 6.2. Ensuring secure communication for all participants
    - 6.3. Ensuring communication channel permanent availability
7. Human potential
    - 7.1. Educating users
    - 7.2. User support
    - 7.3. System maintenance
    - 7.4. Analytical support

Vision 2030

Existence of comprehensive, national oncological network where all patients will receive guidelines driven oncology care and with single and complete database which will generate continuous source of information about quality of oncology care.

Objectives

1. The idea is to partially separate oncology care as a medical discipline from the organizational structures of the existing hospital organization, and make it a national, unique, uniform platform for the optimal treatment of cancer patients, for the first time in the Republic of Croatia (partly, as it would continue to exists in the hospitals system). Such organizational structure would eliminate the barriers for cooperation of some oncological care institutions, provide the flow of cancer patients and the optimal use of existing, costly infrastructure, quality control, and would ultimately lead to the improvement of oncological treatment results in Croatia.
2. Telemedicine needs to be used for analysis and decision making and for arranging treatment in more complicated cases (e.g. treating severe side effects in patients who received differential therapies in clinical hospital centers, and are treated for the severity of adverse events in regional centers without the possibility of transport to clinical hospital centers; sending reports to another institution where more complex procedures or interventions can be performed). This platform would also be used to set up and conduct virtual multidisciplinary teams (telemedicine presentation of cases for team members located in different institutions). Institutions providing oncology care must urgently be linked to the Cancer Registry, which already collects and processes a large part of the data, at least at an expert level.
3. Therefore, an oncological care quality assurance system should be developed on the basis of comprehensive data collection on treatment outcomes, side effects and complications. In addition, regular review, processing and publication of the new data needs to be organized, all for the purpose of continuous improvement of oncological care. Since expertise and cost-effectiveness are directly related in oncology, they should not be separated in planning a unique information system. Such a system will provide insight into competence, professional qualifications and deadlines, as well as financial supervision, namely:
    - Tracking equipment use and staff burden
    - Real cost-based analysis, based on cancer type and stage
    - Evaluating treatment cost-effect ratio
    - This would allow daily monitoring of the quality of work of oncological institutions, which in turn requires well defined standards in treating cancer patients.
4. The quality of work, oncological care assessment, and the accuracy of the reported data of each institution would be determined and supervised by a special, newly established coordinating unit (agency) at the Ministry of Health. Such unit, with appropriate powers, should play a key role in achieving goals in a timely and successful manner. It would be in charge of monitoring the functioning of the oncological care system, taking initiatives to restructure the system, improving coordination and increasing its effective-

ness. The department should be assisted in its work by a cancer advisory committee, which would consist of representatives of all areas of oncological care (all three levels of health care), patient organizations and potentially NGOs. For this new coordinating body to be effective, cancer control should ensure the following:

- Legal authority to access data
- Collective transparent decision-making process, with the support of groups of experts with widely represented various bodies, as well as institutions involved in the cancer control program and patient organization
- Adequate budget

5. At the same time, it is necessary to proceed with the development of national guidelines for the diagnosis, treatment and follow up of specific cancer sites, regularly updating the changes in therapeutic approaches and/or diagnostics.
6. From a scientific point of view, the development of an oncology network in Croatia would make our country more interesting and more competitive, if clinical research included patients at the network level, not at the institution one. This would result in a significantly larger pool of potential subjects and greater weight in clinical trials, and it would probably make it possible for our patients to be included in some trials that are currently unavailable, because they are not performed by any institution for a number of more or less objective reasons.
7. It is particularly important to emphasize the need to ensure better cooperation between all levels of health care (primary, secondary, tertiary) as well as better communication between primary health care physicians and hospital doctors in the future joint oncology network, to improve collection and evaluation of data along with health status, quality of life and the economic and social situation of patients during and after treatment.
8. Finally, to improve oncological care, it is necessary to establish and define an oncology network (regional and local oncological institutions), the level of oncology care they need to provide, create an oncological electronic database, ensure the uniformity of oncological treatment, define quality parameters and its control, protection of the database and its use, and define a long-term national strategy for its development

Measures/Activities

1. The Ministry of Health should ensure legislation, organization and administrative framework for implementation of comprehensive national oncology network.
2. IT network should be established that will address the need of such complex system such as oncology care is. At the same time the system should be user friendly, not taking too much time from its users as well to be connected to all stakeholders, Cancer registry for example.
3. An oncological care quality assurance system should be developed on the basis of comprehensive data collection on treatment outcomes, side effects, relation of expenditures and results of therapy.
4. Supervise and implement above stated measures through establishment of Cancer Agency at the Ministry of Health.
5. Continuous development of national guidelines for the diagnosis, treatment and follow up of specific cancer sites by professional societies in oncology

6. Establishment a comprehensive clinical trial register within the NON with the aim of monitoring the results achieved and establishing a system of continuous progression.
7. Establishment of national oncology database within the IT structure of NON is essential.
8. The NON IT network should be connected with all levels of health care creating better communications, easier transfer of needs and consecutively better oncology outcomes and more satisfied patients

Stakeholders

- Ministry of Health
- External vendor
- Professional societies
- Croatian Institute of Telemedicine
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

National Oncology Network is a prerequisite and a backbone of all other NCCP initiatives, and related benefits are embedded across all outcomes.

Key references

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b. NATIONAL DATABASE AND PATIENT REGISTRY

Introduction

The basis for measuring oncological care quality and obtaining data important for its improvement lies in the creation of a comprehensive clinical oncology national database with an emphasis on treatment and care processes, and on improving the existing epidemiological Cancer Registry.

For oncological care to make progress a continuous insight into the data on cancer patients is necessary, and the only way to obtain them is to create a national database to collect and process data from all oncological centers in the Republic of Croatia. The existing oncology centers and institutional registers to be developed within them would be the basis for an improved registry and a national database of cancer patients. The process of upgrading the existing Registry and creating a national base is estimated to last approximately three years.

Ultimately, the national oncology base would include all the newly diagnosed patients since its establishment (statutory obligation), all major prognostic and predictive information on their illness and treatment, as well as information on the results of treatment and patients follow up. This way, in the future, we will be able to define basic problems, the quality of treatment, compare ourselves to each other and to the world, and allocate funds in the way that will bring maximum benefit. It is necessary to reach a consensus within the profession about priority diagnoses, which will be followed within the database, and about the parameters important for recording and monitoring.

The National Oncology Base and the Cancer Registry must have fully integrated data. It is necessary to use the ONKO + message defined within the European Twinning Project as the starting point for future reporting based on the database and the Cancer Registry, to adapt it to specific needs, and implement it in all hospital information systems in the country. This message will completely replace the current reporting by ONKO leaflets and significantly reduce the burden on clinicians and unnecessary administration. The message would be completed at a defined moment during patient’s hospital stay, and in the case of the same disease, it would not be completed again in the same department; rather, the data would be extracted from the existing systems.

A record of vaccination, cervical smear findings and biopsy findings would exist within the comprehensive registry of patients, and they would be linked to new cancer cases, including data analysis by region to interpret local phenomena.

Access to comprehensive, reliable and up-to-date information on cancer types and their characteristics, as well as monitoring treatment outcomes are prerequisites for risk recognition and the adoption of rational decisions in health policy. This data should also serve as a basis for further research, publications and disseminating information about cancer in the community. Publications and sharing data should be encouraged, complying with the rules on personal data protection and scientific productivity of the entire oncologic community.

Better understanding of the cancer-related phenomena in the Republic of Croatia requires not only the development and integration of databases, but also the development of new sources of information. There is currently no homogenous pathohistological database, which causes a lack of information needed before the onset of treatment. The following should contribute to further development of the knowledge of cancer: standardization of pathohistological reports, adoption of revised international classifications of morphological entities and stages of disease, and encryption of findings, computerization of all pathohistological laboratories, data collection and analysis from all segments of the system, development of authorized online oncology websites for patients and healthcare professionals, information on participation in clinical studies, databases on biobanks and an information system for assisting in making clinical decisions.

The success of the registry is ensured by long-term planning and exerting influence on political decisions and prevention programs.

Vision 2030

To have cancer registry and national oncology database coverage to the level of Nordic EU average.

Objectives

1. Improve the existing Cancer Registry according to four basic criteria agreed in the Cancer Registry professional community (comparability, reliability, timeliness, completeness)
2. Introduce a comprehensive national oncological database with defined inclusion criteria, monitored parameters and outcome measures
3. Enable the interoperability of the two databases
4. Introduce an ONKO + message as a reporting system according to the Cancer Registry and national early cancer detection programs, as a replacement for the present ONKO leaflet

Measures/Activities

1. Hold a discussion within the professional community about the fields within the ONKO+ message and the necessary reporting variables
2. Redefine the ONKO+ message according to the requirements and needs of the profession
3. Enable acceptance of ONKO+ messages on target systems (Cancer Registry, NPP Systems, national oncological data database / clinical registers)
4. Enable integration of ONKO+ messages in the starting systems (all hospital information systems) and CEZIH (central health information system)
5. Create national oncology database following best international examples (Nordic countries). Define the facilities where a pilot project for the collection of an extended set of data on the treatment of a particular malignant disease is being developed, which will then be extended to all institutions that treat cancer patients in any way

6. Introduce a two-week education on Cancer Registry and oncology database for medical oncology and oncology and radiotherapy specializations, and a one-week education for pathology specializations
7. Ensure regular financing of IT systems maintenance, necessary for storing high-quality epidemiological and clinical data
8. Provide training resources related to technical and scientific details necessary for successful implementation of these measures
9. Introduce the implementation of MKB-O-3 codebook, based on WHO's blue books in all pathohistological, cytological and immunohistochemical findings concerning malignant diseases
10. Provide funds for adequate data analysis in registers, to make sure expert and political decisions are based on the best possible data, displayed in the best possible way

Stakeholders

- Oncological Professional Societies
- Ministry of Health
- Croatian Institute of Telemedicine
- Relevant EU stakeholders who could provide guidance and support

Resources

- Croatian Government
- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

Cancer registration, generalized and consolidated is recommended in cancer control by the Union for International Cancer Control (UICC) World Cancer Declaration in its first article, and as recognized by many national cancer plans. Despite this favorable evolution, little is known about the economics of cancer registration, and no metrics have been developed so far for assessing costs and benefits. In term of costs, cancer registration has always been considered a low-technology and low-capital activity, and this has fed the prejudice that its costs were negligible. In term of benefits, the contribution of registry data has been indirect with respect to prevention, care, and research. This has made it difficult to define and quantify the added value attributable to registries.

Analysis of cost by productive factors indicated that almost all the registries were labor-intensive. On average, 79% of resources were spent on personnel, 10% on infrastructure and connected utilities, 6% on IT, and only 5% on materials (for example, printing books or bulletins and organization of events). Most of staff resources were devoted to data collection (24% of total budget), data management/analysis (21%), and research (21%), while management and administration, communication, and other activities received only 13% of total resources. Percentage of FTE units and salaries: 57% of staff was represented by registrars and IT technicians, 27% by scientific tasks, and 16% by administration and services.

With respect to the main routine product (incidence cases registered), it resulted that, on average, it took 1 FTE personnel unit to register 1,120 cases per year.

Key references

- Croatian Institute of Public Health, Croatian National Cancer Registry. Cancer incidence in Croatia 2015. Zagreb, 2018. Bulletin No. 40
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c. QUALITY CONTROL

Introduction

Quality control in oncology and assessing cost-effectiveness requires close cooperation between health care policy makers, healthcare service payers, experts and civil society. Taking into account the increasing incidence of cancer and the burden on the health system, assessing efficiency and cost effectiveness of each measure taken, as well as controlling quality is paramount, in order to increase the effectiveness of treatment and more rational funds management.

Vision 2030

Ensuring that the NCCP is implemented according to the highest possible quality standards.

Objectives

1. Define the existing situation in the scope of work of public health, primary, secondary and tertiary health care
2. Reduce malignant diseases mortality and detect them as soon as possible
3. Provide diagnosis, treatment and rehabilitation according to defined professional guidelines
4. Define precisely institutions for the implementation of specific procedures
5. Introduce the presentation of cancer patients' cases before multidisciplinary teams as a legal obligation
6. Introduce new medicines and medical procedures into a positive list rationally
7. Reorganize the Cancer Registry to provide comparable, timely, reliable and complete epidemiological data
8. Organize a national oncological database to track the results of treatment, data on the efficacy of certain drugs and procedures, total cost of diagnosis and treatment of cancer patients, results for individual institutions and doctors, and provide insight into the overall treatment of for cancer patients.
9. Create positive conditions for conducting clinical trials, as the availability of new therapies through clinical trials is one of the oncological care quality parameters.
10. Permanent education of all members of the working groups and monitoring the effectiveness of the measures introduced.

Measures/Activities

1. Define the working groups in charge of evaluating the situation in the field, determining the necessary measures and monitoring the implementation and effectiveness of the measures introduced. These groups would include representatives of the Ministry of Health, the Croatian Health Insurance Fund, the Croatian Institute of Public Health and

professional societies. This includes assessing the quality of preventive programs, as well as the diagnosis, treatment, monitoring and rehabilitation of cancer patients.

2. Identify the parameters to be used to analyze the current situation, and further monitor the quality of oncological care and the effectiveness of the measures introduced.
3. Ensure the reorganization of the Cancer Registry and a unique networking of hospitals across the country through a unique oncology network and a national oncology database as a prerequisite for achieving these goals by forming a working group composed of physicians, physicists, engineers, nurses, IT professionals, economists and politicians. Precisely define the concept of the Registry, the national oncology network, and the national oncology databases to ensure the possibility of analyzing economic costs, the burden placed on individual institutions, physicians and waiting lists, but also quality parameters such as survival, the ratio of the means spent and treatment results, any new measures that are introduced (e.g. the effect of a new drug, the effect of response rate to preventive check-ups and treatment, etc.).
4. Accreditation of centers (hospitals) for specific oncology care to determine exactly which part of the diagnostic, treatment and follow-up algorithm of an oncological patient can be performed at which hospital or hospital center. The accreditation process should include the Agency for Quality and Accreditation in Health Care.
5. Organize a working body at the Croatian Health Insurance Fund for the introduction of new medicines and oncology procedures, taking into account the medical aspect of an individual measure as well as its cost and the cost/outcome ratio, to fit into the anticipated allocation for healthcare. Members of this working body should be experts from accredited oncological institutions and representatives of the Ministry and patient associations.
6. Introduce the obligation to present a case and plan treatment in front of multidisciplinary teams to improve the quality of oncological care for patients.
7. Introduce measures that will encourage clinical research of oncological drugs by speeding up the necessary administrative procedures at all levels to ensure the availability of new oncology therapies through clinical trials. Additionally, enable communication on available clinical research in oncology to increase the availability of new therapies for cancer patients through the proposed national oncological network.
8. Supervise and implement above stated measures through establishment of Cancer Agency at the Ministry of Health.

Stakeholders

- Ministry of Health
- Croatian Health Insurance Fund
- Clinical hospital centers
- Relevant EU stakeholders who could provide guidance and support

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

Quality control depends on the ability to measure and report results through predefined indicators and in a consistent way. These have at least three dimensions, structure, process and outcome related, all of which can help health system managers to identify the strengths and weaknesses of the implementation. Data gathering systems for these indicators include registries of target population and screening activity, service user satisfaction surveys, quality audits for samples and diagnoses, mechanisms to monitor wait times, cancer registries with representative population coverage, and (to measure QALYs and cost-effectiveness) ad hoc methods and simulations models. It is very important to ensure linkages between screening services/registries with population-based cancer registries.

Most of these indicators will require no additional costs as they could be withdrawn from patient registry and similar already accounted measures.

Key references

- Tit Albreht et al. European Guide for Quality National Cancer Control Programmes. https://cancercontrol.eu/archived/uploads/images/European_Guide_for_Quality_National_Cancer_Control_Programmes_web.pdf

d. MONITORING & REPORTING

Introduction

Adequate monitoring of the NCCP is essential for its successful implementation. Focus should be on monitoring of goals and objectives, implementation of the measures proposed, regular evaluation of the plan with adjustment of strategies if necessary, with continuous and active participation of stakeholders in the process of monitoring and reporting.

Vision 2030

To ensure continuous and precise monitoring and reporting of all significant activities within the NCCP.

Objectives

1. To establish continuous and complete monitoring of all important activities within the frame of NCCP
2. To timely report all important findings of monitoring process
3. To oversee the implementation of the NCCP

Measures/Activities

1. The establishment of a Cancer Agency within the frame of Ministry of Health that will function as an independent supervisor for implementation of cancer policies defined within the frame of NCCP.
2. The Cancer Agency will have a steering committee comprised of all important stakeholders (patient representatives, payer's representatives, representatives of different medicine disciplines important for cancer care, other health professionals involved in cancer care, education and research)
3. The role of the Cancer Agency is to; continuously monitor and timely report all important and predefined activities of NCCP, assume responsibility for implementation of the plan, coordinate the work of all stakeholders that can contribute to cancer plan implementation, to ensure the best use of available resources for the NCCP implementation (oversee financial aspects of the program), implement legislative changes defined in the NCCP, oversee public education and participation on anticancer subjects, oversee professional education and development of planned activities in the NCCP, oversee development of national diagnosis and treatment guidelines, monitor cancer research activities defined in the NCCP, oversee the development and function of the National Comprehensive Cancer Network, monitor quality of cancer registry and of national cancer database, oversee complete cancer information systems, oversee primary and secondary cancer prevention programs, monitor development of diagnostic processes defined in the NCCP to allow the appropriate cancer treatment to all patients, monitor cancer treatment activities defined in the plan (radiotherapy network creation, purchase of new

linear accelerators, surgery centralization and accreditation, systemic therapy optimization and individualization), oversee the supportive and palliative care development, and finally, oversee the monitoring and evaluation process by itself in order to improve it.

4. Reporting of the results of the monitoring process is equally important. Cancer Agency should publish, make publically available, results of all monitoring activities continuously.
5. To facilitate the establishment of a Cancer Agency, a Technical Working Group will be appointed by the MOH with representatives of governmental and non-governmental organizations and chaired by a national cancer coordinator.

Stakeholders

- Ministry of Health
- Clinical hospital centers
- Patient organizations
- Professional cancer societies

Resources

- Ministry of Health
- Croatian Health Insurance Fund
- EU or other international source of funding

Economic evaluation

The quality of the NCCP implementation is directly linked to monitoring and reporting as well as to ensuring a robust coordination all key stakeholders in the health system – patients, health professionals, payers and policymakers. Securing leadership is essential in this sense and appointing the

right institution or organisation for the process is necessary. Special attention in the implementation should be dedicated to those objectives that are common for proactive and population-oriented health systems – improving access to services and reducing socio-economic inequalities in cancer.

Costs related to this chapter are mostly of administrative nature, required for the establishment of the Cancer Agency and similar activities, some of which have been accounted for in previous chapters.

Key references

- WHO National Cancer Control Programmes (NCCP) https://www.who.int/cancer/nccp/en/
- Romero Y et al. National cancer control plans: a global analysis. Lancet Oncol 2018; 19: e546–55

12. Integrated NCCP cost effectiveness analysis

NACIONALNI PLAN PROTIV RAKA

12. Integrated NCCP cost effectiveness analysis

An integrated economic evaluation of the incremental costs and effects of the NCCP has been undertaken based on the comparison of two scenarios:

a) implementation of all NCCP activities

b) no implementation of NCCP activities.

Results are reported as costs per life years gained due to the implementation of the NCCP and presented as an addendum to this document.

The following 10 cancer sites which are the most frequent in Croatia were in focus for the economic evaluation:

1. Prostate C61.9
2. Ovary (Ovary, fallopian tube and uterine ligaments, other and unspecified female genital organs, peritoneum, and retroperitoneum) C48.0–C48.2, C56.9, C57.0–C57.4, C57.7–C57.9
3. Cervix C53.0–C53.1, C53.8–C53.9
4. Breast C50.0–C50.6, C50.8–C50.9
5. Melanoma of the skin 8720–8790 provided topography was C44.0–C44.9, C51.0, C51.9, C60.9, or 63.2
6. Lung (Lung and bronchus) C34.0–C34.3, C34.8–C34.9
7. Stomach C16.0–C16.6, C16.8–C16.9
8. Colon and Rectum (Colon, rectosigmoid junction, rectum, anus and anal canal) C18.0–C18.9, C19.9
9. Pancreas C25.0–C25.4, C25.7–C25.9
10. Liver (And intrahepatic bile ducts) C22.0–C22.1

All costs and effects have been calculated by individual patient and for all patients diagnosed by year and in total; in years 2020-2030. Costs and effects arising from cancer diagnosed within these years have been taken into account regardless of how long it takes for them to occur. For instance, productivity losses due to early death have been calculated up to retirement age and life years gained have been calculated up to expected survival. All costs and lost earnings have been discounted at an 3.5% annual rate, but were also separately reported in absolute figures for budgeting purposes.

The economic analysis focuses on the following issues:

Cancer incidence: Number of patients developing 10 most frequent cancer sites from 2020-2030. Estimates have been undertaken based on incidence data and trends recorded by the Croatian Institute of Public Health, World Health Organization estimates, referenced data from other countries and expert opinion where necessary.

Survival: treatment success has been reported as life years gained, total number of cured patients (patients alive five years post diagnosis), and prolongation of life in years for patients not surviving the five-year threshold. Estimates are based on survival data and trends recorded by the Croatian Institute of Public Health, referenced data from other countries and expert opinion where necessary. For cancers subject to screening programs under the NCCP (breast, cervix, colon & rectum and lung), results are further reported by stage of disease (local, regional and disseminated).

Costs of medical care have been accounted for through Diagnosis Related Groups tariffs, expenditure on medicines financed from the expensive drugs fund as well as payments for outpatient care, emergency care and primary care, approximated through number of consultations. Estimates will be modelled based on actual Croatian Health Insurance Fund cost data and trends, adjusted by expert opinion where necessary.

Incremental programmatic costs due to the implementation of the NCCP, such as additional investments in primary and secondary prevention programs, diagnostic and radiotherapy equipment, molecular diagnostics, genetic testing, implementation of multidisciplinary teams, etc. have been attributed to incident patients.

Indirect costs, due to nonexistence of national data sources, such as costs of informal care, lost working days and productivity losses due to early death have been estimated based on international references, adjusted by expert opinion where necessary.

Sensitivity analyses have been undertaken to identify the impact of independent variables on the overall cost effectiveness of the NCCP.

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