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Efforts in Fighting against Cancer in Croatia Have to be Focused on the Primary Health Care

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A B S T R A C T

This manuscript is a comprehensive review of the long-lasting tradition and the state-of-the-art in the prevention and early detection of cancer in Croatia. Compared with other European countries, Croatia holds a high and unfavourable position in cancer morbidity and mortality. Global experience in implementation of national programmes for the early detection of cancer clearly shows that such approach is the most successful and in the long term the least expensive method for fighting against cancer. In Croatia, numerous separate actions in cancer care have been taken, but never systematically, nor included in a health care policy. The National Programme for the Prevention and Early Detection of Cancer of the common localizations for which effective screening tests are available (breast, uterine cervix, colon and prostate) has recently been launched. Local long-standing experience of the Osijek-Baranja County in implementation of programmes of cancer care contributed significantly to these initiatives. In this review, draft National Programme and the early results of its implementation were presented. In addition, preparations for the research project »Model of early cancer detection integrated in a practice of family physician«, recently set up by the Department of Family Medicine of the School of Medicine, University of Osijek, were described. In this project, the programme of the early detection of cancer in which family physicians take responsibility for the programme implementation is suggested. Possible advantages of this model, compared with the model proposed by the National Programme, centrally directed and mostly supplied by the public services, are pointed out.

Key words: *cancer, early detection, Croatia, the National Programme, primary health care, integrated model*

Introduction

Cancer is the second cause of death worldwide, accounting for 7.6 million (or 13%) of all deaths (2005). If the current trend were to continue, it is estimated that around 9 million people will die from cancer in 2015 and 11.4 million in 2030[1].

Cancer accounts for almost every fourth case of death in Croatia, ranking second in mortality causes. Only in the last year, about 22,000 of newly diagnosed patients and near 13,000 cancer-related deaths were recorded[2]. Compared with other European countries, in cancer statistics, Croatia holds a highly unfavourable position[3].

Both cancer incidence and mortality in Croatia are on a constant rise. Thus, between 1988 and 2005, the total cancer incidence rate (per 100,000) increased from 303.9 to 466.8 and the mortality rate increased from 217.7 in 1988 to 282.8 in 2006 (Table 1 and 2). A relatively sharp increase in incidence rates can be observed after 1997 (Figure 1).

Similar incidence and mortality data, but on a lower scale, has been recorded in the Osijek-Baranja (O-B) County (Table 1 and 2). Thus, between 1988 and 2005, the incidence rate increased from 314.5 to 429.0 and the mortality rate increased from 212.7 in 1988 to 269.6 in 2006. The matter of concern is that mortality rates, in the O-B County, increase to a higher extent than the average for Croatia (Figure 2). This clearly indicates that

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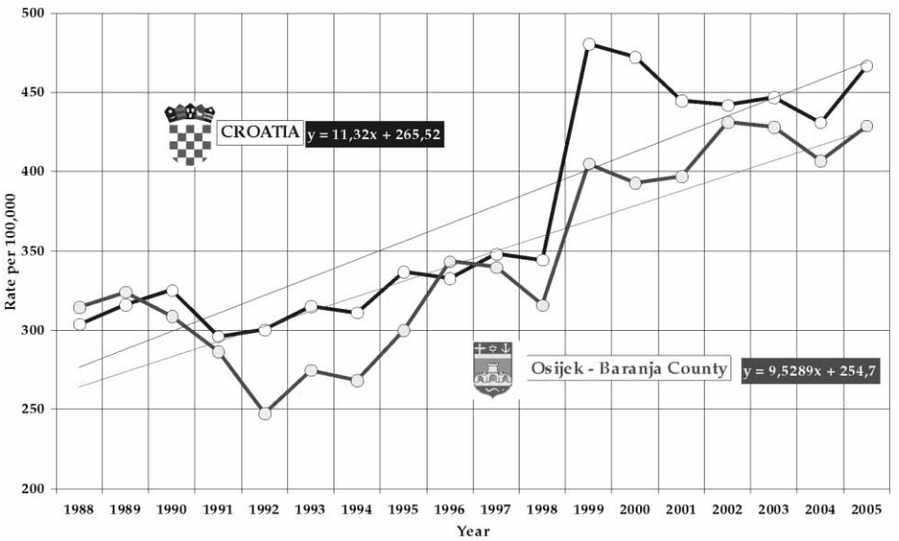

Fig. 1. Total cancer incidence rates (per100,000) in Croatia and the Osijek-Baranja County between 1988 and 2005 Source: Cancer register, Croatian Public Health Institute.

prevention and measures for the early detection of cancer, in the O-B County, should be intensified.

Currently, the most prevalent cancer sites for men in Croatia are: the lung, the colon and the rectum, the prostate, the bladder and the stomach. In the O-B County, the order is as follows: the lung, the prostate, the colon and the rectum, the stomach and the bladder. The respective cancer sites in female population in Croatia are: the breast, the colon and the rectum, the lung, the ovary, corpus uteri, the stomach and cervix uteri. The leading cancer sites for women, in the O-B County, are: the breast, the colon and the rectum, the lung, cervix uteri, the ovary and corpus uteri[2].

For the purpose of this analysis, trends in the incidence and the mortality data of only those particular cancer sites proved to be preventable by means of the early detection methods were demonstrated, including: the breast, the colon and rectum, cervix uteri and the prostate. In the O-B County, a more rapid increase in incidence rates, compared to the whole of Croatia, can be observed for breast cancer (Figure 3). Other major differences concern trends in incidence rates of cervix uteri

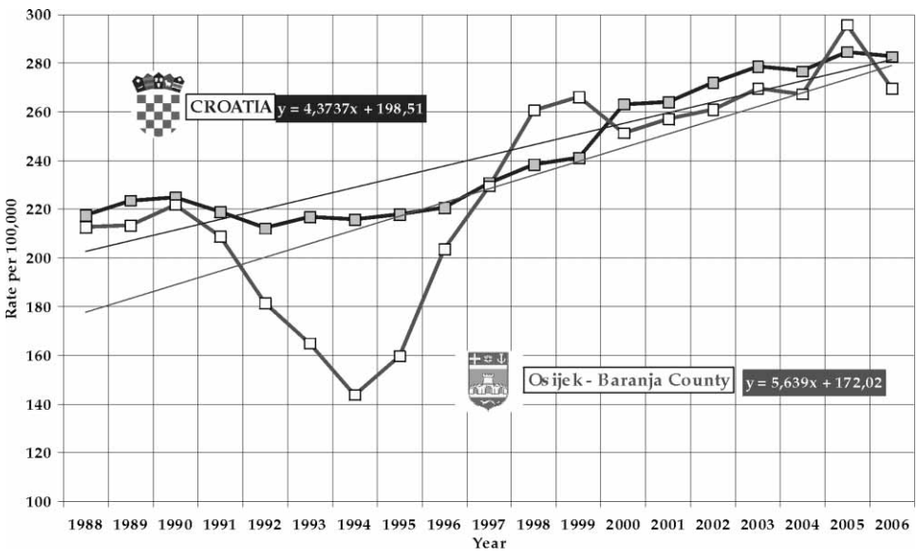

Fig. 2. Total cancer mortality rates (per100,000) in Croatia and the Osijek-Baranja County between 1988 and 2005 Source: Cancer register, Croatian Public Health Institute.

TABLE 1
TOTAL CANCER INCIDENCE RATES (PER 100,000) IN CROATIA AND THE OSIJEK-BARANJA COUNTY BETWEEN 1988 AND 2005

Year	All sites	
	Croatia	The Osijek-Baranja County
1988	303.9	314.5
1989	316.2	324.1
1990	325.3	308.8
1991	296.1	286.5
1992	300.3	247.6
1993	315.0	274.8
1994	311.1	268.3
1995	337.0	299.8
1996	332.8	343.4
1997	348.1	339.8
1998	344.3	315.9
1999	480.7	405.2
2000	472.3	393.0
2001	444.8	397.0
2002	442.1	431.2
2003	447.1	428.1
2004	431.1	407.0
2005	466.8	429.0

TABLE 2
TOTAL CANCER MORTALITY RATES (PER 100,000) IN CROATIA AND THE OSIJEK-BARANJA COUNTY BETWEEN 1988 AND 2006

Year	All sites	
	Croatia	The Osijek-Baranja County
1988	217.7	212.7
1989	223.7	213.5
1990	224.9	222.0
1991	219.0	208.9
1992	212.3	181.4
1993	216.9	165.0
1994	215.8	143.8
1995	217.9	159.9
1996	220.8	203.6
1997	230.9	229.6
1998	238.5	260.8
1999	241.2	266.3
2000	263.3	251.4
2001	264.2	257.2
2002	272.2	261.1
2003	278.8	269.6
2004	276.9	267.5
2005	284.8	295.9
2006	282.8	269.6

carcinoma (Figure 4). In contrast to its stagnation in the scale of Croatia as a whole, in the O-B County, the trend is still increasing. Mortality rates for colon, breast and prostate cancer have been growing up more rapidly in the O-B County, compared to the average for Croatia (Figure 5-7). Similar as for the incidence data, mortality rates for cervix uteri cancer have been declining steadily in Croatia as a whole, while in the O-B County they continue to increase, although with a variable course (Figure 8).

Considering such cancer statistics, it is understandable then, that in Croatia and the O-B County the implementation of the comprehensive programme of measures

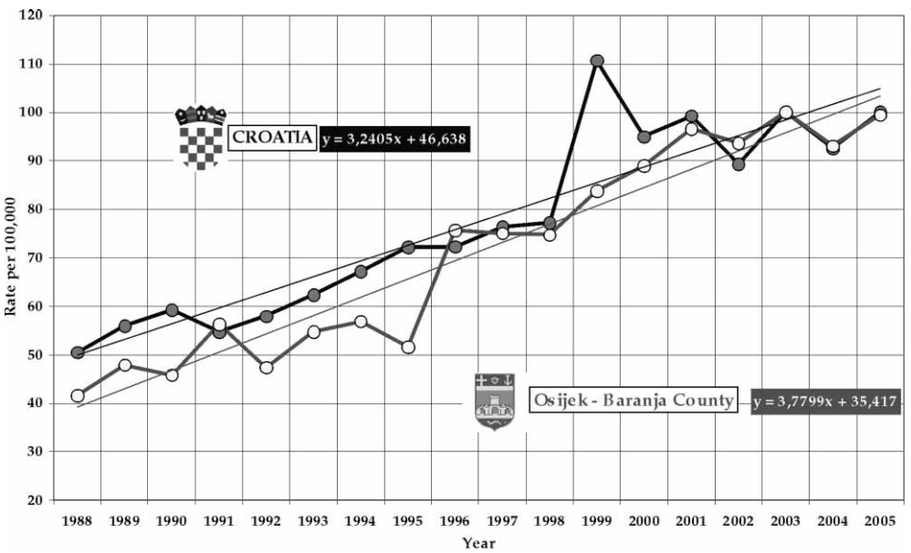

Fig. 3. The breast cancer incidence rates (per100,000) in Croatia and the Osijek-Baranja County between 1988 and 2005
Source: Cancer register, Croatian Public Health Institute.

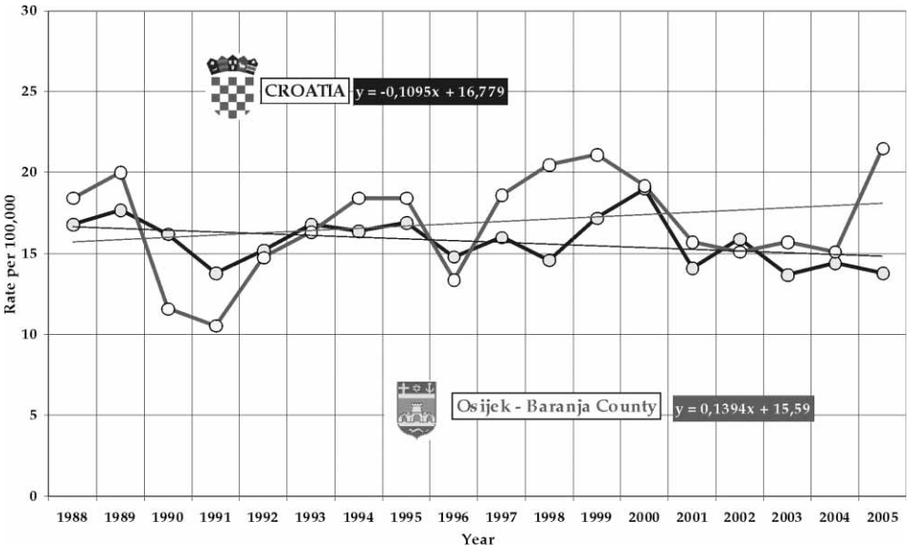

Fig. 4. The cervix uteri cancer incidence rates (per100,000) in Croatia and the Osijek-Baranja county between 1988 and 2005
Source: Cancer register, Croatian Public Health Institute.

aimed at achieving better cancer control should be a task of the highest public health care and social relevance[4].

Global initiatives for the implementation of national programmes for prevention and the early detection of cancer

Based on the experience of developed Western countries, it is proposed that up to one third of cases of cancer can be prevented merely by implementing principles of a healthy life-style, mainly by means of a healthy diet, a regular physical activity, no smoking and only a moderate alcohol consumption[1,5]. Other primary preventive measures known to deal with the reduction of the total cancer incidence are: changes in sexual behaviour, immunization against Human Papilloma Virus (HPV) infection and Hepatitis B Virus infection, taking the control on occupational hazards, avoidance of cancer-causing substances in the global environment and attentive exposure to sunlight[1].

The curability of a malignant disease is considerably higher when it is detected in the early, localised stage[6,7]. Programmes for the early detection of cancer, if implemented, allow heavy forms of treatment to be avoided

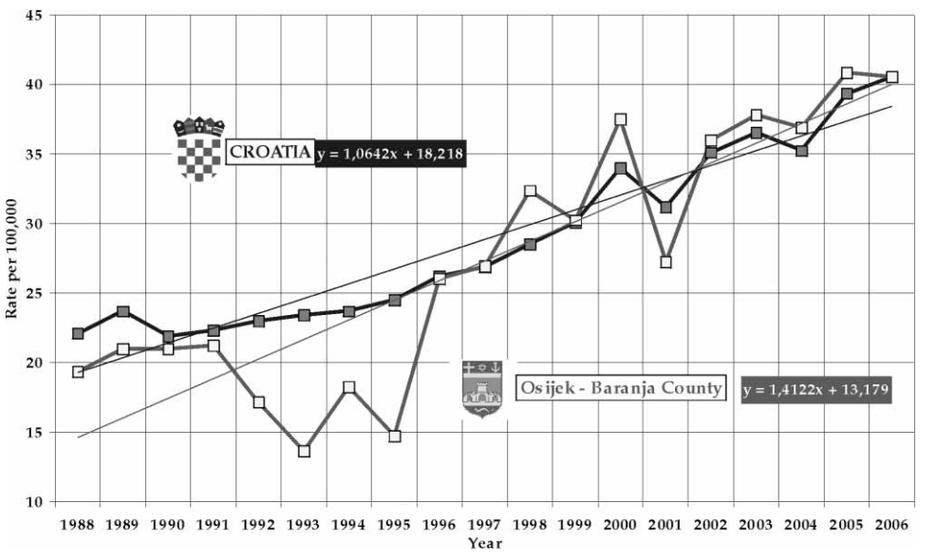

Fig. 5. The colon cancer mortality rates (per100,000) in Croatia and the Osijek-Baranja county between 1988 and 2005
Source: Cancer register, Croatian Public Health Institute.

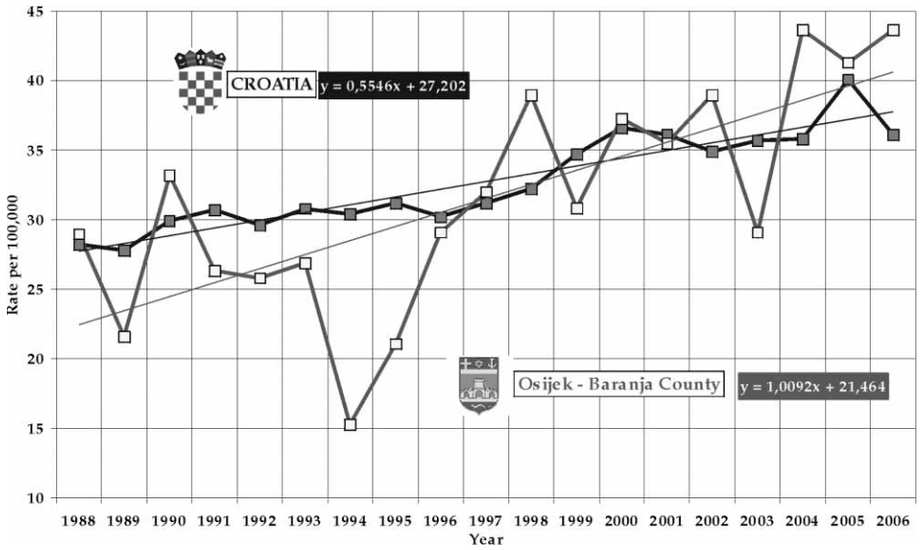

Fig. 6. The breast cancer mortality rates (per100,000) in Croatia and the Osijek-Baranja county between 1988 and 2005
Source: Cancer register, Croatian Public Health Institute.

and more favourable prognosis for a relatively large numbers of people affected with cancer. These programmes may be two-way oriented. One way is promotion of the early diagnosis by recognizing the early signs and symptoms of cancer, based on health education programmes, performed for both primary health care physicians and the population[1,8]. The other way is screening of an apparently healthy target population, before clinical signs of cancer are detectable, in order to find individuals with the early cancer or pre-cancer stages[9-11]. Fundamental for the latter approach is to have available and effective tests. Unfortunately, this is not possible for all cancer sites. Screening tests, which were accepted for wide implementation and proved to be cost-effective, include: high-quality mammography (for breast cancer), Pap cytology test (for cervical cancer) and testing for occult faecal bleeding (for colorectal cancer)[9]. The screening on prostate cancer has not yet been carried out routinely on population base, although a rather simple early detection test is available[9]. The increasing amount of evidence confirms that the early detection of this main form of cancer in men considerably increases survival, reduces mortality and is economically justified[11]. Efforts have constantly being made to improve the screening methods

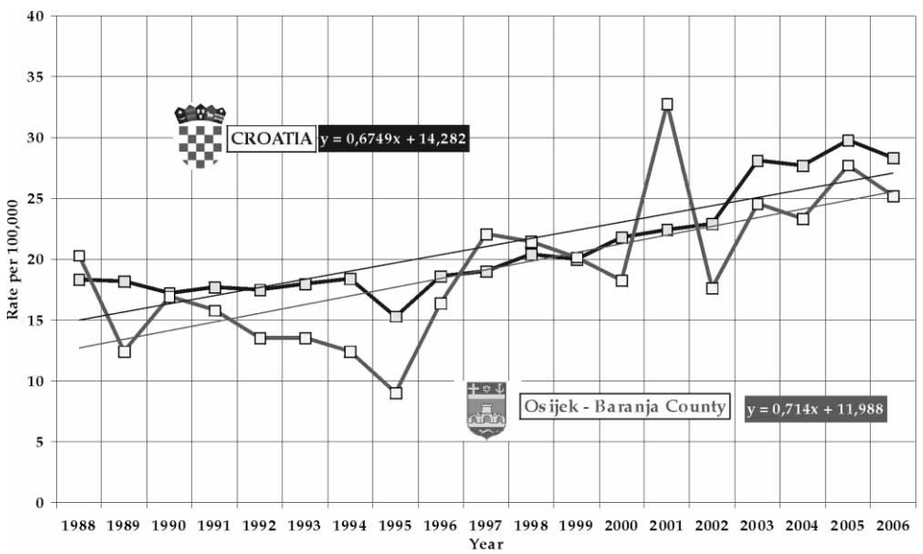

Fig. 7. The prostate cancer mortality rates (per100,000) in Croatia and the Osijek-Baranja county between 1988 and 2005
Source: Cancer register, Croatian Public Health Institute.

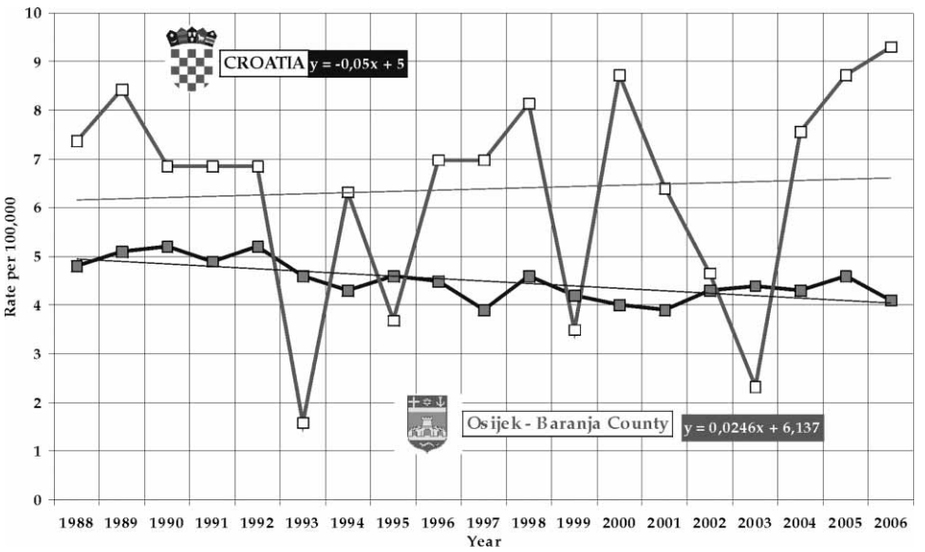

Fig. 8. The cervix uteri cancer mortality rates (per100,000) in Croatia and the Osijek-Baranja county between 1988 and 2005 Source: Cancer register, Croatian Public Health Institute

by means of looking for more sophisticated methods, or entirely new tests which would be suitable for other cancer sites[12].

Results of randomised trials as well as experience of the countries where the national programmes of prevention and the early detection of cancer have already been implemented clearly show that the implementation of such programmes, especially when they are well prepared and monitored, encompassing entire population, is the most effective and, in the long term, the least expensive method for fighting against cancer[13–15]. Based on the analysis of these results, respective agencies such as: the American Cancer Society (ACS), United States Preventive Services Task Force, the World Health Organization (WHO) and the European Union Advisory Committee on Cancer Prevention, set up recommendations for the early detection of cancer[9,16].

Awareness worldwide is growing that global initiatives are needed to make a dramatic stride in fighting against cancer. The framework for this call for a global movement is given in a form of basic documents, such as World Cancer Declaration 2006[17]. According to this document, the plan is to increase the number of countries that have the national cancer control programme, covering cancer prevention, early detection, treatment, palliative care and support for cancer patients. Cancer surveillance systems, including cancer registries, should be developed if they do not exist. The importance of these systems will be in collecting data on the cancer burden, its likely future evolution, trends in risk factors and effects of measures done with the aim to achieve better cancer control. As more than 70% of all cancer deaths occur in lower income countries, these countries will be especially encouraged and supported by the international bodies to be able to deal with their growing cancer burden.

In order to transfer proclaimed aims into practice, international committees establish global strategies in cancer control. Following the adoption of the Cancer Prevention and Control Resolution at the 58th World Health Assembly (WHA) in May 2005, WHO is developing the Global WHO Cancer Control Strategy[18]. The strategy is based on the following principles:

- people-centred (the goal is to improve the well-being of individuals, families and communities)
- equity (focused on the needs of low-income countries and marginalized populations)
- partnership (collaboration of all sectors)
- sustainability (to ensure the continuation of established programmes after financial and technical assistance has been completed)
- integration (integrated in the overall chronic disease prevention and control framework)
- evidence-based (based on research results and best practice evaluation)

In order to complement large-scale screening programs for breast and cervical cancer started in some European countries several decades ago, the EU Commission set up in 2003 recommendations for the early detection of colorectal cancer[19].

Colorectal cancer has become the most common newly diagnosed cancer in EU, proposed to be modified with the diet and modern lifestyle. On the other hand, it has excellent possibilities to be cut if recognized and cured at an early stage[19].

Until now, no more than half of the EU member states have followed EU Commission recommendations either by introducing a national screening programme or by performing preliminary studies for its eventual launch. Being aware of the importance of the issue for im-

proving the general health of the European citizens, policy makers, scientists, cancer specialists and other competent authorities, signed last year, on May 10th, »the Brussels Declaration for the prevention of Colon Cancer Across Europe«[20]. Declaration calls upon the Commission to implement an action plan »Europe against Colon Cancer«, aimed at the establishing the European guidelines and the implementation of quality-assured national screening programs[20]. Experience from the Finnish screening programme, with the highest participation rate (71% on average), may serve as a best practice example for wider implementation of the programme across Europe[19].

Prevention and the early detection of cancer in Croatia and the Osijek-Baranja County

In Croatia, measures of primary prevention and the early detection of cancer have never been systematically performed although declared as a task in the primary health care programmes of measures[4]. Clinical assessment on cancer and the occult faecal blood test have become an integral part of preventive examination for persons aged 50 years and more, recently included as an obligatory procedure in the contract between family physicians and the Croatian Institute for Health Insurance. In addition, many separate actions have been taken, carried out by non-governmental organizations and professional societies. The Croatian League against Cancer has a special role, by joining the resources and creating the strategies for fighting against cancer[21].

In the Osijek-Baranja County, intensive activities of the local League against Cancer on implementation of programmes of cancer care have been performed for years, contributing awareness of the local community on the social relevance of the issue to rise[22–24]. The attitudes of the League are that cancer prevention should be comprehensive and include: 1. change of unhealthy behaviour, 2. increase in screening coverage, 3. increase in the quality of palliative care, 4. education of general practitioners on cancer care, 5. investment in equipment, 6. establisment of guidelines for cancer prevention and early detection. The emphasis is, however, put on primary prevention measures, such as: 1. general preventive measures, 2. informing the population about the cancer risk factors, 3. intensive care for persons at increased risk, 4. education of personnel, especially in the primary health care, on early detection methods, 5. establishment of units for health promotion and prevention of chronic diseases in the county departments that will coordinate the activities, 6. implementation and monitoring of the prevention programmes.

The League has taken a large set of preventive measures. Health education activities are especially intensive, by informing the community about: 1. risk factors for the most frequent cancer sites, 2. methods of protection from sexually transmitted diseases, 3. the necessity of recognizing the first symptoms of a disease, 4. self-examination methods, and 5. early detection methods. For that purpose, the League has issued a number of publications in the form of lectures, brochures and posters, entitled: »Fighting cancer by knowledge«, »Breast self-inspection«, »Life after breast cancer«, »With food against cancer« and »Colorectal cancer«, 20.000 copies each. Some publications were issued in collaboration with the Ministry of Health and the Croatian League against Cancer, including: »Men and cancer«, »Women and cancer« and »Prostate cancer«, 100.000 copies each and »Colon cancer«, 492.000 copies, and the book »Smoking related diseases«, 20.000 copies[23,24]. Recently, a brochure entitled: «Cancer of skin, breast, large intestine, cervix uteri and prostate – symptoms and early detection methods«, have been issued to support the implementation of the National Programme of early cancer detection.

Within the scope of the measures of comprehensive cancer care, the League also provides continuous support to postgraduate education of primary health care physicians, encourages the acquisition of equipment for the early detection of cancer and founding of cancer patients support groups. In 2002, the League opened its web site to make possible a wide approach to information on cancer prevention, possibilities of its early detection, medical treatment and rehabilitation[23,24].

Early detection of cancer of most common localisations, in the O-B County, has been supplied by the primary health care teams in collaboration with polyclinic-consultation services, although not systematically performed[22]. Subsequent increase in the coverage of the female population after 20 years of age by taking cytological smear at gynaecological examinations resulted in decreasing ratio of invasive to preinvasive cervical cancer forms[25,26]. Under the influence of intense activities of the Osijek League against Cancer, during the past decades, a substantial part of the female 40+ population has undergone mammography, performed at the Osijek University Hospital and the General County Hospital in Našice[22].

In Osijek, first population-based study on the early detection of colorectal cancer by testing for occult faecal bleeding was conducted (from 1981 till 1984), including as many as 11,431 persons. The results showed a high motivation of the population for screening, as 82% of the subjects responded[27]. Test sensitivity was 72.2% for 2-year occurence[28]. Generally, the results confirmed the occult faecal blood testing as the method for the early detection of colon carcinoma, due to its simple application, acceptance by the population, good sensitivity and relatively low costs[27–29]. On the other hand, epidemiological evidence indicated that the implementation of the methods for the early detection of colon cancer is an urgent need. Thus, observed 5-year survival was 35% for the period 1988–1993 and 5-year relative survival was 45% for M and 42% for female[30]. In the period 1973–1989, the Osijek General Hospital recorded the observed 5-year survival of 29.6%, 10-year survival of 21.8% and 15-year survival of 18.2%[31]. Both the incidence and the mortality rate of the colorectal cancer were on a steady increase in Croatia, reaching the values recorded in Western Europe. Between 1968 and 1994, the incidence rate grew up from 13.8 to 37.1 per 100,000 and the mortality rate increased from 8.3 in 1968 to 28.1 in 1997[32]. In the Osijek-Baranja

County, in the 1968–1982 period, the rise in incidence rates of colorectal cancer matched the average for Croatia, while the rise in mortality rates was two times higher, when compared to the corresponding trend for Croatia as a whole[33].

Based on the Osijek experience, suggestion for the implementation of the programme of detection of colorectal carcinoma in the 55+ risk population by testing the occult blood in the faeces in the practice of family physicians, integrated in comprehensive programmes of prevention of chronic and malignant diseases was given and also the idea that the primary health care teams should participate in the programmes for early detection of cancer in women, including education and motivation activities, invitation and follow- up[28].

The Osijek League against Cancer started in 1992 a programme involving the primary health care professionals in cancer prevention and control activities. The programme started in the Slavonia region by a training course for GPs, including final examination and an evaluation of the course at the end of the follow-up period. Printed material provided guidelines with a comprehensive approach, specific for the primary health care setting. The aim of the programme was to emphasize cancer problems as of a high priority, but focused on preventive activities, rational use of resources and efforts concentrated in the primary health care. The initiative was a preparation for the implementation of guidelines at the national level, but in a participatory way and based on the quality-assessment. The results were shown at the International Cancer Congress held in New Delhi, India, in 1994, with the mobilizing title: »New knowledge as a stimulus for action«[34].

Awareness of the health care authorities and the whole community on the social relevance of the early detection of cancer has been growing gradually. In 2006, The Croatian Oncology Society of the Croatian Medical Association initiated the preparation of Proposal for the National Programme of Prevention and Early Detection of Breast Cancer, Uterus Cancer, Colorectal Cancer and Prostate Cancer. The issue was published, in 5,000 copies and distributed to every individual GP across the country, to inform them about the initiatives[35,36]. Soon after that, in 2007, Draft National Programme for Prevention and Early Detection of Cancer in Croatia was introduced[37].

National Programme of the Prevention and Early Detection of Cancer in Croatia[37]

General objectives, set up by the Programme, are: to decrease prevalence of risk factors among the population by promotional and health education activities, to reduce total cancer-related mortality rates in Croatia by 15% within five years after the Programme started, to increase the percentage of diagnosed pre-clinical and localised cancers compared to percentage of advanced stage disease and to increase the early detection coverage of the population.

At the same time taking care to introduce international recommendations, the National Programme tends to be adapting to the national personnel and technical resources. The Croatian Public Health Institute is responsible for the monitoring of the programme implementation and the evaluation of the programme results. Participants in the Programme are: the regional Public Health Institutes, family physicians, health centres and units running specific screening tests. Several preparations are needed to ensure the successful Programme implementation, including: information systems with adequate software for the regional services linked with central coordinators, personal data from the Croatian Health Insurance Institute on population in target groups, electronic application forms for screening tests, informing of the general population on screening and its advantages, an invitation organization, education of medical staff and media campaign. An invitation organization is carried out by the regional Public Health Institutes, in collaboration with the visiting nurse service of health centres and supported by the primary health care teams and the regional nongovernmental organisations.

Target groups, specific aims and screening methods

Breast cancer

Despite an advance in diagnostics and therapy, breast cancer still remains the leading cancer-related cause of death in women worldwide. Both incidence and mortality rates are on the increase in Croatia, with the current crude incidence rate of 100.1/100,000 (2005) and the mortality rate of 40/100,000 (2006)[2] However, it is well proved that over 90% of cases can be cured if cancer is diagnosed at an early stage and adequately treated[9]. Mammography, the recommended screening method, can detect breast cancer two years before the tumour enlarges enough to be palpable[38]. Experience with women included in the screening programmes shows the reduction in the breast cancer mortality[13].

The National Programme for Early Detection of Breast Cancer has been prepared in compliance with the National Strategy for Prevention and Early Detection of Cancer, an integral part of the Health Development Strategy 2006–2011, and according to the principles of WHA 58.22 Cancer Prevention and Control Resolution approved in 2005 by the 58th WHA. High quality mammography, double reading, for women aged 50–69, by 2 yearly examination protocol, is applied as a screening method. BI-RADS classification (stages 0–5) is used for reading of mammograms. Cases are supposed as suspected on cancer if classified as BI-RADS 4 and 5. The short-term aim of the Programme is to reduce breast cancer mortality by 25% within five years from the start of the programme, assuming an optimum coverage of 70%. Clinical examination of breast is also promoted and planned to be a part of periodical medical checks, performed by family physicians every three years for women aged up to 40 and every year for women after that age. Women with family history of first-degree relatives with breast cancer, with previously

determined non-tumour or tumour breast disease and other risks, are included in special, more individually--shaped protocols. Spreading of risk factors among population will be collected according to data obtained from the questionnaires, attached to the invitation letters and asked to be filled[37].

Cervical cancer

Cervical cancer is the second malignant tumour in women worldwide and in Croatia and the Osijek-Baranja County it is on the sixth and the fifth position respectively (2002). Compared to other European countries where an organised cervical screening programme has already been implemented, Croatia has lower morbidity and mortality trends for cervical cancer[2,3]. This may even partially be because the early detection of cervical cancer by cervical cytology (smear) has been performed on all sexually active women, as a part of the primary health care programme for women[22,25,26].

Pap smear cytology test is accepted as »the golden standard« for screening on cervical cancer[9]. According to European quality standards, an optimum testing interval of 3 years is recommended for women with negative tests[39]. As under the best screening programme organisation conditions cervical cancer can be detected in a maximum of 80% of women, implementation of other methods would be desired. Thus, new screening tests, liquid-based cytology and the HPV test, have increasingly been applied[9].

Target groups, included in the National Programme, are women aged 25–64, by 3 yearly examinations. The aim of the Programme is to reduce the incidence of invasive cervical cancer by 60% within 9 years from the Programme onset and to reduce mortality rates by 80% within 13 years from the Programme onset[37].

Colorectal cancer

On a global scale, colorectal cancer is on the third position by incidence and forth position by mortality rate among the malignant diseases[3]. In Croatia, colorectal cancer is ranking second in both men (after lungs) and women (after breast)[2]. However, its incidence in the group aged 60 years and more largely extents that of the younger age group (78.3%, compared to 7.9% in the group up to 50 years of age)[2]. Other known high-risk population groups are: patients with a history of colorectal adenoma and cancer and inflammatory bowl diseases, as well as individuals with a positive family history of colorectal cancer and polyposis syndromes. Patients with a history of earlier stomach, breast, ovarian, bladder, kidney, cervical, lung and prostate cancer, are also at increased risk[9,40,41].

Considering results in five-year survival rates after the disease is detected, colorectal cancer is on the second favourable position, immediately after breast cancer. However, the data is much worse for the Eastern European countries, then for the developed countries (34% of cases, compared to 54% and 65% in the West European countries and the USA, respectively)[3,6]. By taking into account the fact that a 10–35 years long-lasting period is needed for the transformation of benign adenomas to cancer, it seems reasonable to expect that the systematic implementation of the programme of active seeking for persons with localised cancer or pre-cancer colorectal lesions could substantially reduce colorectal cancer mortality rate in the population. Under such conditions, colorectal cancer could reach a high cure rate of 80% and more[42,43].

Experiences on using the conventional screening method for the early detection of colorectal cancer, the Faecal Occult Blood Test (FOBT), applied in asymptomatic population at average risk, show that 3–5% persons with positive results are to be expected. They are referred to further diagnostic procedures, including colonoscopy or proctosigmoidoscopy and double-contrast irrigography. By following up such protocol, it is possible to achieve the reduction in mortality rate 18% to 33%[42,44–46]. A recently introduced screening test, the Faecal Immunochemical Test (FIT), has been shown as simpler for use and of a better specificity, then the conventional one. Its disadvantage is a higher price and still insufficient results of effectiveness analyses[41,47].

According to the National Programme, the screening protocol include men and women aged 50–74, in every second year a check-up by the FOBT and the coverage of at least 60%. Test-positive individuals are referred to colonoscopy to determine the cause of occult bleeding. Individuals from the high-risk groups are managed following the special protocols[37]. The main Programme aim is to reduce colorectal cancer mortality rates. Specific aims are oriented towards improvements in diagnostics and treatment and standardization of protocols[37].

Prostate cancer

Prostate cancer is one of the three major cancer sites in men. However, it is rare in males under 50 years of age, while its incidence rates increase rapidly in each decade after that age[3]. Males with family history of disease (at least one blood relative: father, grandfather, or brother, with prostate cancer) are at a higher risk even in an age before 50[9,10].

Prostate cancer tests include digitorectal examination and the PSA (the prostate-specific antigen) level determination. If it is possible, the free prostate-specific antigen (FPSA) level, or the FPSA/PSA ratio can be determined[9,10, 48]. Persons with positive tests have to be referred to further examination by transrectal ultrasound of the prostate (TRUS) and biopsy.

Up to date there is not enough evidence that systematically performed screening methods would render a considerable reduction in prostate cancer mortality. For that reason, early detection of prostate cancer is generally recommended for men with increased risk and men aged 50 and over, however, only on their demand[9,10].

According to the National Programme, the target group will be made up of men aged 40–50 at increased risk, men aged 50 and over with symptoms of prostatism

and of those who have no symptoms, but require examination. The aims of the programme are: to cut off prostate cancer mortality for 15% by five years after the programme onset and to increase the ratio of cases with localised cancer to those with advanced stage[37].

An early attendance on implementation of the Programme for screening on breast cancer

Health care authorities who initiated the inauguration of the National Programme for Prevention and Early Detection of Cancer of the most frequent sites were aware that the immediate implementation of the entire Programme would not be possible[4,36,37]. In 2006, funds were gained for the realization of the part of the Programme. According to the conclusion of the Croatian Government, the National Programme for Early Detection of Breast Cancer has started first, on 2 October 2006[49]. Until end of May 2008, a total number of 554 860 women were invited to mammography, with the average responding-rate of 55.8% (varying among counties from 42% to 83.6%). There were 760 newly diagnosed breast cancer cases, with the caution that many cases suspected on cancer were still under evaluation[50].

The implementation of the Programme on the regional level is carried out by the county Public Health Institute in collaboration with family physicians, health centres and radiological units. The nongovernmental organisations are also involved, as partners. The campaign is supported by the media and through promotional publications[37,51,52].

In the Osijek-Baranja County, the available equipment includes 7 mammography units in total. The main mammography unit has taken its place in the Osijek Health Centre[53]. A preliminary attendance of the Health Centre Osijek shows that up to 12 December 2007 (during a 14-month survey), a total of 7,826 women have undergone mammography with the responding rate of 51.29%. Among them, a total of 140 cases (1.76%) were referred for further diagnostics as suspected on cancer [54,55].

Launching of the National Programme for Early Detection of Colorectal Cancer

The National Programme for Early Detection of Colorectal Cancer has started on 1st November 2007[56]. The necessity for its urgent launching is illustrated by the fact that, in Croatia, high mortality-rates have been recorded (40.6/100,000, 2006), probably due to a low percent (less than 10%) of newly diagnosed colorectal cancer cases with localised lesions[2,7,56].

The implementation of the Programme is carried out by laboratory workers and physicians employed at the county Public Health Institutes and specialists colonoscopists. Family physicians are included, participating in education and motivation activities. The Croatian Public Health Institute and its counties public health institutes departments coordinate and monitor the action, taking care also of invitation organisation, collecting and evaluation of data[37,52,56].

Invitation letters are sent by mail, addressed to citizens aged 50–74 years. In envelope there are three testing-cards together with instructions for their use, questionnaire about risk factors and educational brochure ensuring the invited persons are informed on the screening. The invited persons are asked to mail testing-cards back together with the filled questionnaire. Subjects with positive tests are invited for further diagnostics. The questionnaire about risk factors, including: nutrition, alcohol consuming, low physical activity, overweight, as well as history of colon diseases and family history of colorectal tumorous diseases, will allow insight into the spreading of the risk factors across the target population[56].

Estimations of the cost, personnel and equipment, required for the realization of the Programme, have been done on the basis of the results of similar actions already performed in other countries. According to this, the screening response is not expected to exceed 50–60%, at least in the first year of the Programme implementation. About 3–4% of tested individuals will be FOBT positive and 80% of them will respond to the invitation for colonoscopy. Endoscopic service is going to be organised on the basis of such estimation. Furthermore, 10% of FOBT positive patients will be diagnosed as cancer and 40% – as benign adenomas[22,40,46].

Until end of May 2008, a total number of 93,000 invitation letters were sent. The preliminary results indicate very low responding rates (36.8% maximum, average 23.8%). The percent of FOBT positive tests widely varies across the counties (from 3.8% to 32.9%). Until now, there were 58 cases diagnosed as cancer[57].

Project: »Model of Early Cancer detection Integrated in a Practice of a Family Physician«

Family physicians are in a position to cooperate with the population which enables them to implement many preventive measures in a planned and systematic manner, such as: health education activities, counselling, recognizing the early symptoms and signs of a disease and performing screening tests in high risk groups. Considering these facts, we have proposed that screening and early diagnosis of cancer of most frequent sites could be more efficient if integrated in a practice of family physicians, compared to the existing models, either one based on the user's request, or the other centrally directed and supplied mostly by the public services (e.g. the National Programme)[58].

The Project: »Model of early cancer detection integrated in a practice of family physician«, approved by the Ministry of Science, Education and Sport, and carried out by the Department of Family Medicine of the Osijek University School of Medicine, was planned to promote the pro-active or patient-oriented approach[8,59,60]. That means that the doctor encourages preventive actions, in

contrary to the health care where the doctor generally responds to the patient's requests. The doctor recognizes medical needs of the groups and individuals, makes a decision upon the priorities, manages the screening protocol and plays a role in adequate treatment, prevention of complications and the early death onset and takes efforts to support improvements in all aspects of the patient's quality of life[59,60].

The central role of family medicine in the implementation of preventive programmes has been recognized as an advantage from the organisational aspects and by means of decreased expenditure, compared to the programmes with strict formal control centred to the public institutions[8,46,59,60]. In some European countries, e.g. Great Britain, family physicians partially participate in the national programme implementation by means of conducting the screening tests, performing health awareness actions and ensuring adequate diagnostic and therapeutic procedures for patients with positive results of screening tests to be done[61]. Health care authorities in collaboration with professional associations developed quality indicators for the programme implementation surveillance. These indicators serve as the basis for the payment and are included in the additional Contract concluded between the doctors and the National Health Insurance[61].

The Project was originally conceived as a »pure« integrated model. The expected outcomes, planned by the Project, were: to considerably increase the number of early diagnosed and cured patients, to increase the 5--year survival rate and in the long term to decrease total and specific mortality. Answers were expected on the main issues: 1. How to increase the coverage of the risk groups significantly? 2. Whether family physicians are motivated and educated sufficiently for the implementation of an integrated model for the early cancer detection and by which methods that can be improved? 3. Which prerequisites (including the personnel, time, material, equipment) are needed for the implementation of this model into the official health care system? 4. How to achieve an efficient collaboration and coordination among those participating in the programme, including: family physicians, specialists, public health services, local government and the community? 5. How to implement the Programme in practice, not exceeding much the present resources?[58]

The research sample was planned to include from 10,000 to 15,000 subjects at increased risk for the development of breast, cervical, colorectal or prostate cancer (out of total of about 45,000 insured persons, recorded in 15–20 family medicine teams). Target groups for these four cancer sites, recorded on the lists of other family medicine teams in the Osijek Region, not included in the Project, will be used as a control. Family physicians will play a central role in all stages of the research protocol, taking responsibility for the selection of patients, encouraging them to participate in the research and informing them on screening, its advantages, as well as potential risks of further diagnostic procedures, necessary for cases tested positivelly[58].

A simulated model of the early detection of colorectal cancer – estimation of time and cost required

A simulated model, performed in representative primary health care surgery with approximately 2,200 patients on the list, showed that total of 928 persons aged 50 years and more have to be subjected to the screening by FOBT, according to the recommendations of the National Programme[62]. In addition, there were 66 individuals at increased risk for colorectal cancer, including: persons with the history of colorectal adenoma or cancer, ulcerative colitis and Crohn's disease, carcinoma of other sites and a family history of polyposis and non-polyposis colorectal cancer. In the next 4 years of the Project, 208 more patients, who will reach their fifty, will be included in the programme. Taken together, in the first 5 years, the total of 1202 persons will be covered by one round of screening. On the basis of the two-year screening protocol, during 5 years of research, a maximum of 3,304 persons will apply FOBT. Taking into account the commercial price of FOBT and personnel time spent in screening and administrative work, multiplied by up-dated points determined by the Croatian Health Insurance Institute norms, expected expenditure should not exceed 20,000 HKN per year of research. Considering the current patients burden, 2 or 3 patients should be added per day,

TABLE 3
A SIMULATED MODEL OF EARLY DETECTION OF THE COLORECTAL CANCER (A PRIMARY HEALTH CARE TEAM – A BASIC UNIT FOR THE ESTIMATION OF TIME AND COST REQUIRED)

Year Of Research	Number Of Patients Included Per Year	FOBT/kn	Time Cost Per A Physician 10 min/kn	Time Cost Per An AssistenT 10 min/kn	Additional Time Cost For Fobt Positive Patients	Total Cost kn
2007	526	7,890	7,174.64	4,523.6	523.84	20,112.08
2008	526	7,850	7,174.64	4,523.6	523.84	20,112.08
2009	554	8,310	7,556.56	4,764.4	556.58	21,187.54
2010	552	8,280	7,529.28	4,747.2	556.58	21,113.06
2011	573	8,595	7,815.72	4,927.8	556.58	21,895.10
		40,965	37,250.84	23,486.6	2,717.42	104,419.86

FOBT – Faecal Occult Blood Test

which takes 20–50 minutes extra time, depending on whether it is the first examination or a follow-up of cases with positive results.

Estimations were done of a total cost in the first year of the Project, on the basis of the research sample, accounting for about 15,000 subjects. Only extra working burden of family medicine teams and the price of standard screening tests were used in estimation (Table 3).

Based on such analyses, we considered that the implementation of the programme of the early detection of colorectal cancer is possible, not exceeding much the present cost and time burden of family physician's teams. The suggested model has some additional advantages, including possibilities for opportunistic approach. That means that family physician is in the favourable position, having opportunities to perform educational sessions, interviews, or screening activities at the time of patient's visits because of other reasons. This may contribute to the rational use of all resources.

Purpose, aims and expectations

Direct aim of this research is to considerably increase the coverage of the risk population with screening of most frequent cancer sites, compared with the present state, to increase the percentage of diagnosed pre-clinical and localised cancers compared to percentage of advanced stage disease, to decrease the specific and overall mortality and to improve the 5-year survival rate and cancer-related quality of life. Another aim is to assess the acceptability and the applicability of an integrated model of the early cancer diagnosis, based on the active approach and systematic preventive work of family physicians. A further aim is to approximate the personnel and time normatives and to estimate the material and total cost required for systematic implementation of the early cancer detection programme in official health care. Finally, cost-effectiveness analyses will be done. An integrated model of the early cancer detection will be compared with the approach inaugurated by the National Programme, mostly conducted by the public health services. Selective advantages of integrated model as well as potential obstacles when it is implemented in routine practice will be pointed out. The data collected until the Project is closed will be used for the estimation of the 5-year cancer-related survival rates[58].

Additional positive outcomes are expected, e.g. family physicians to acquire knowledge of methods of the early cancer detection and the skills to apply them in practice. They will be able to develop their capabilities of how to motivate and encourage the population to participate in the screening protocols and the skills of how to communicate with the community when implementing preventive health care measures. An indirect aim of this research, which the Project participants are keeping in mind, is to promote preventive health care measures, especially by means of primary prevention and health-education activities, as priorities in the family physician's work. Simultaneously, this research tends to point out the importance of good collaboration within the health care system, including clearly separated duties between primary health care doctors and specialists in their coordinated action to decrease the frequency of the main diseases in the population, especially those with the highest impact on premature mortality[58].

The integrated model of prevention and the early cancer detection should become a part of the community health policy, integrated into the overall chronic disease prevention and control framework. Therefore, it must have realistic dimensions, with standardised and clearly defined programme stages. The final goal is to improve the well-being of individuals, families and the whole community.

Implementation of the Osijek-Baranja County Project in the National Programme

A permanent dilemma is running through debates about strategies for implementing measures in primary care. That is: whether it is better to regulate technical issues by strict central control or to integrate the new programme within the existing working framework, based on partnership, stepwise approach and patient-oriented approach?

The Chair for Family Medicine of the Osijek University School of Medicine and the manager of this Project has actively participated in the creation of the National Programme for Prevention and Early Detection of Cancer in Croatia. As the preparations for the Project go in parallel with the launching of the National Programme, some propositions, genuinely arising from the Project, have subsequently been incorporated in the Draft National Programme. In reverse, the original intention, founded by the Project, to develop a model for cancer prevention and the early detection centred to family physician's teams, was later modified, in order to avoid the interruption of the National programme implementation. The original model is now tending to be, not only an alternative for, but also a part of the National Programme. It may serve as a pilot project, showing advantages of active participation of family physicians in implementation of the National Programme of Early Cancer Detection, beyond the scope of the organisation form carried out solely by the public institutions.

According to such modifications, the role of family physicians in the Project, with the respect to the particular cancer site, was defined as follows:[63]

Breast cancer

The role of family physicians is to complete the National Programme by making contact, in collaboration with the visiting nurse service, with women who did not respond to mammography invitation letters, sent by the regional Public Health Institute. These women will be additionally motivated for the screening. For women who in any case reject to participate in the screening, family physicians organize a clinical examination of breasts

once a year and refer suspected patients to mammography[63].

Family physicians also keep records on the results of mammography (BI-RADS 0, 1, 2, 3, 4, 5), performed according to the National Programme schedule, on used diagnostic and treatment procedures for the women suspected on breast cancer, as well as on the 5-year survival data[63].

Colorectal cancer

In order to avoid the interruption of the National Programme implementation, individuals for the target groups were selected in this way to be in the lower (45–50 years) and the upper (75–80) age group, compared to the criteria defined in the National Programme (50–74 years of age). The implementation of the Project is planned to be completely under the responsibility of family physicians. They would take care about organising the invitation and registration of persons from the target groups, keep records on performed screening, read tests and refer patients with positive FOBTs for the follow-up. They would keep records on all interventions, done, determined diagnoses and all other relevant data in a 5-year follow-up[63].

Cervical cancer

The early detection of cervical cancer is already a part of the primary health care programme for women and its implementation is opportunistic – Pap smear test is performed annually on all sexually active women who visit a gynaecologist.

The role of family physicians, in the Project, will be to invite women aged 25–64, from their patients' lists, who have not been checked up by the Pap test in the last three years. Family physicians should increase the awareness of these women of the advantages of regular gynaecological examinations and refer them to their primary gynaecologists. For that purpose, an on-line link was installed between the central Pap test register in the department of cytology at the Clinical Hospital Osijek and PC of every family doctor included in the Project[63].

Family physicians will keep the evidence on the results of Pap tests, further diagnostic and treatment procedures if they are needed, determined diagnoses and the 5-year survival data[63].

Prostate cancer

The whole protocol is conducted by family physicians. They keep registration of male patients at higher risk for the development of prostate cancer, according to the recommendations defined in the National Programme (aged 50 years and more with the symptoms of prostatism). As a part of this procedure, they perform interviews with male patients aged 40–50 years, to find out if their family history indicates the higher risk for prostate cancer. They suggest patients diagnosed with prostate cancer to inform their male relatives about the necessity of the screening[63].

The screening methods include digitorectal examination and referral of patients to PSA testing. Family physicians keep evidence of the screening and refer patients with suspected conditions to the urologist and keep records on the results of diagnostic procedures and treatments as well as on survival[63].

The First Year of Research – Preparations for the Screening

During the first research year, the defined target population was informed on preventive measures, risk factors, first signs of most frequent malignant diseases and methods of the early cancer diagnosis. For that purpose, lectures were held in local communities and health centres and health education brochures were issued[64–66]. The head of the Project, and a founder of the National Programme, was a co-author of the book »How to prevent and detect cancer early?«, published in 2007 in as many as 50.000 copies and distributed to all family doctors in Croatia[67]. Citizens and people from target groups can inform themselves on cancer-related issues by using the web site www.prevencijaraka.org.

A total of twenty family medicine teams gave their consent to be joined to the Project. A half of them have a practice in the Health Centre Osijek and the others are dispersed in smaller towns and rural settlements across the Slavonia Region. Patients from their lists, if belong to any of target groups, defined in the Project, will be included in the research. Currently, the available pool amounts around 27,000 of patients (Table 4 and 5).

Family physicians, included in the research, were interviewed in order to find out their attitudes on many aspects of the early cancer detection. Based on this analy-

TABLE 4
CURRENT POOL OF WOMEN ENTERING PARTICULAR CANCER SITE

Cancer Site	Target Group	Estimated Number Of Patients Included
Breast	50–69	3,746
Cervix Uteri	25–64	7,578
Colon	45–49	1,078
Colon	75–80	835

TABLE 5
CURRENT POOL OF MEN ENTERING PARTICULAR CANCER SITE EARLY DETECTION PROTOCOL

Cancer Site	Target Group	Estimated Number Of Patients Included
Colon	45–49	1,255
Colon	75–80	497
Prostate	40–49	2,357
Prostate	≥50	4,747

sis, it could be concluded that family physicians possess a good formal knowledge on these issues and already perform many preventive activities in their routine practice, mostly in the form of the counselling about healthy life styles and empowerment of the patients at higher risk for checking up. Their attitudes are that the prevention and the early detection of cancer is useful and necessary and still insufficiently implemented in a practice. However, they suppose that all activities should be clearly defined in advance, in the form of the Preventive Programme. Moreover, preventive activities should become a centre of their occupation. In order to implement preventive programmes successfully in the routine practice, certain organisational prerequisites should be done, in terms of decreasing the number of patients on their lists and more precisely defined aims and tasks of the family medicine as an independent medical profession, by turning the efforts towards the prevention. In general, initiatives, presented in the Project, are welcome and meet the secret need of family doctors to work better and improve their competences. Also, they expect to be engaged in the research and professional activities more actively.

For those doctors who gave their consent to participate in the Project, educational sessions have been prepared. A special course was organised to improve their skills in examination methods they have to perform independently, by themselves, such as: Hemoccult test, digitorectal and clinical breast examination. One of two planned education sessions has already been organized with information about the Project and software that will be used for data collecting.

Firstly, we had planned special electronic forms to be formed and linked to the basic information system, reently installed for the application in the primary health care, to allow keeping the records on data. However, because of the substantial financial and organisaional difficulties in solving the task, we had simple, independently installed software made. It is formed as a register of surveillance for any of four cancer sites of interest. Continuous recruitment of new patients in register will be possible automatically, using personal data on sex and age.

Instead of conclusions: bridging cancer prevention from the past to the future

The Project: »Model of early cancer detection integrated in a practice of a family physician«, carried out by the Department of Family Medicine of the Osijek University School of Medicine, is a logical continuation of a long-term experience on primary prevention and the early detection of cancer in the Osijek-Baranja County and collaborated work of the Health Centre Osijek and the City of Osijek League against Cancer. The final aim of the Project is modelling the programmed approach in cancer control which is also the global trend in preventive medicine in general.

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NAPORI U BORBI PROTIV RAKA U HRVATSKOJ MORAJU BITI USMJERENI KA PRIMARNOJ ZDRAVSTVENOJ ZAŠTITI

S A Ž E T A K

Ovaj rad predstavlja cjeloviti pregled dugotrajne tradicije i sadašnjeg stanja prevencije i ranog otkrivanja raka u Hrvatskoj. U usporedbi s drugim europskim zemljama, Hrvatska se nalazi na nezavidnom visokom mjestu u morbiditetu i mortalitetu od raka. Svjetska iskustva u implementaciji nacionalnih programa za rano otkrivanje raka jasno pokazuju da je takav pristup najuspješniji i dugoročno gledajući najjeftiniji način borbe protiv raka. U Hrvatskoj su poduzimane brojne pojedinačne akcije u zaštiti od raka, ali nikada sustavno, niti uključene u zdravstvenu politiku. Nacionalni Program prevencije i ranog otkrivanja raka čestih lokalizacija za koje postoje učinkoviti *screening* testovi (dojke, grlića maternice, debelog crijeva i prostate) je nedavno započeo. Dugogodišnje lokalno iskustvo u implementaciji programa zaštite od raka, u Osječko-baranjskoj županiji, je značajno pridonijelo tim inicijativama. U ovom preglednom radu je ukratko prikazan Nacionalni Program i rani rezultati njegove implementacije. Osim toga, opisane su i pripreme

za znanstveni projekt: »Model ranog otkrivanja raka integriran u praksu liječnika obiteljske medicine«, koji je nedavno pokrenula Katedra za obiteljsku medicinu Medicinskog fakulteta Sveučilišta u Osijeku. U tom projektu se predlaže program ranog otkrivanja raka u kojemu bi liječnici obiteljske medicine snosili odgovornost za implementaciju programa. Ističu se prednosti takvog modela, u usporedbi s modelom koji se predlaže u Nacionalnom Programu, a koji je upravljan odozgo i kojega u najvećoj mjeri provode javne službe.