

# National Program of Colorectal Carcinoma Early Detection in Brod-Posavina County (East Croatia)

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## ABSTRACT

*Colorectal carcinoma (CRC) is a major public health problem as the third leading malignant tumor in men and fourth in women in Croatia. Prognosis and treatment greatly depend on tumor stage at the time of detection. Therefore, the National Program of Colorectal Carcinoma Early Detection has been performed since 2007. The aim is to present the response rate, colonoscopy findings and number of newly detected CRC cases in Brod-Posavina County. During five years of the National Program performance, 28 CRC cases were detected in Brod-Posavina County, with the 3.3‰ rate of carcinoma detection. The majority of CRC cases were found in the 50–64 age group. The response rate in the County was low (20.4%), corresponding to the national rate but far from the recommended one. Such a result could be attributed to the low level of awareness in the population at large, complex testing technique for general population, fear from disease detection and from colonoscopy as a diagnostic procedure. Note should be made of the underestimated role of family physicians; their involvement in the National Program should certainly result in better response rate in our County as well as at the national level.*

**Key words:** colorectal carcinoma, screening, fecal occult blood test, incidence

## Introduction

Colorectal cancer (CRC) is the third most prevalent type of cancer in the world<sup>1</sup>. It is the third most common malignant tumour in males and the fourth most common malignancy in women in the Republic of Croatia<sup>2</sup>. Its prognosis is closely related to the disease stage at the time of diagnosis<sup>1</sup>. Clinical trials have demonstrated that it is possible to reduce the incidence or improve cancer survival through prevention and early detection<sup>3</sup>.

The European Union (2003) extended the recommendation of implanting colorectal cancer screening using the fecal occult blood test (FOBT) in the population aged between 50 and 74 years<sup>4</sup>. Four randomized clinical trials have shown that annual or biannual screening with guaiac-based tests (C-FOBT) reduces overall mortality due to CRC by 16% and CRC incidence by 20% and 17% respectively<sup>5</sup>. Colorectal cancer mortality has been declining over the last two decades in Europe, particularly in women, the trends being, however, different across countries and age groups. In the European Union (EU), between 1997 and 2007 mortality from colorectal cancer declined by around 2% per year, from 19.7 to 17.4/100,000 men (world standardized rates) and from 12.5 to

10.5/100,000 women. Persisting favorable trends were observed in countries of western and northern Europe, while there were more recent declines in several countries of Eastern Europe, including the Czech Republic, Hungary and Slovakia particularly in women (but not Romania and the Russian Federation). In 2007, a substantial excess in colorectal cancer mortality was still observed in Slovakia, Hungary, Croatia, the Czech Republic and Slovenia in men (rates over 25/100,000), and in Hungary, Norway, Denmark and Slovakia in women (rates over 14/100,000)<sup>6</sup>. Colorectal cancer (CRC) was the second leading cause of cancer mortality in men (N=1063, 49.77/100,000), as well as women (N=803, 34.89/100,000) in Croatia in 2009<sup>7,8</sup>. The Croatian National CRC Screening Program was established by the Ministry of Health and Social Welfare, and its implementation started in September, 2007<sup>9</sup>. CRC is a good candidate for screening, because it is a disease with high prevalence, has recognised precursors, and early treatment is beneficial<sup>10</sup>. Benefits of screening include a modest reduction in colorectal cancer mortality, a possible reduction in cancer incidence through the detection and removal of colorectal

adenomas, and potentially, the less invasive surgery that earlier treatment of colorectal cancers may involve<sup>11</sup>.

The aim is to present the response rate, colonoscopy findings and colorectal carcinoma (CRC) cases detected during the first cycle of the National Program of Colorectal Carcinoma Early Detection (Program) in the Brod-Posavina County 2007–2012.

## Material and Methods

The Ministry of Health and Social Welfare launched the National Program in September 2007. Public health teams at county Institutes of Public Health were appointed local Program coordinators. In addition, Laboratory of Microbiology, County Institute of Public Health, Department of Internal Medicine and Department of Pathology, Forensic Medicine and Clinical Cytology, General Hospital »Dr. Josip Benčević« from Slavonski Brod were involved in Program implementation in the Brod-Posavina County. During the 5-year period (2007–2012), a total of 49,855 planned calls for fecal occult blood test (FOBT) were distributed in the County, according to instructions issued by the Ministry of Health and national coordinators from the National Institute of Public Health. The target population included all individuals aged 50–74 of both sexes. They all received informative material, questionnaire and three FOBT sets to their home address and asked to send the completed tests and filled in questionnaires by mail to the Laboratory of Microbiology, County Institute of Public Health. The guaiac test consisting of the specially prepared stabilized paper impregnated with natural guaiac resin and a reagent containing hydrogen peroxide (<6%) and 75% denatured ethyl alcohol in aqueous solution is analyzed at Laboratory of Microbiology by specialist in medical laboratory diagnosis and microbiologist. Reliability of test result mainly depends on proper preparation of the subject tested. Test procedure is explained in test insert and requires delay of testing during hemorrhoidal hemorrhage, diarrhea, urinary tract hemorrhage or menstruation, and avoiding taking more than 250 mg citrus fruits daily (one orange contains 7–75 mg of vitamin C) for three days before testing. Laboratory testing is performed by use of a detection reagent applied onto test fields. Test result is positive if blue color appears on the test field

upon adding the reagent. Test is read within 30 seconds to 3 minutes. According to the manufacturer's information, sensitivity of the method is 96%; however, guaiac test positivity in the population of asymptomatic subjects is only 1–2%. Test results and questionnaires are then forwarded from microbiology to public health workers to be entered in the Ministry of Health software. In case of positive FOBT, the public health team makes an appointment for colonoscopy at Department of Internal Medicine, General Hospital »Dr. Josip Benčević« in Slavonski Brod, in order to detect the cause of bleeding. The notice and instructions on preparation for colonoscopy are sent to the positive subject's home address, while respective information on the examination is also sent to the subject's general practitioner. On colonoscopy, material is obtained for analysis and referred for histopathology to verify the diagnosis. The rate of carcinoma detection was calculated as the number of carcinoma detected *per* 1000 FOBT. Data on the response rate, colonoscopy findings and CRC cases detected were analyzed by descriptive methods using all monthly reports on the public health team activities.

## Results

A total of 49,855 persons born between 1937 and 1957 were invited for screening in Brod-Posavina County; 10,168 (20.4%) envelopes were returned, however, only 8443 (16.9%) of these with the test completed. Out of 8382 FOBTs received (there were 6 incorrect tests), 602 (7.2%) were positive. Of these 602 persons called for colonoscopy, 478 persons presented for examination. Twenty-eight CRC cases were confirmed by colonoscopy (5.9% of subjects submitted to colonoscopy, 4.7% of FOBT positive cases, or 0.33% of all subjects examined), yielding a 3.3% rate of CRC detection. The number of invited and responsive persons and the number of CRC detected according to age groups are shown in Table 1, and colonoscopy findings in Table 2.

## Discussion

All individuals aged 50–74 at an average risk of developing CRC are recommended to undergo FOBT (guaiac

**TABLE 1**  
THE NUMBER OF INVITED AND RESPONSIVE PERSONS AND NUMBER OF COLORECTAL CARCINOMA DETECTED  
ACCORDING TO AGE GROUPS

Age groups	Invited	Responsive persons	Completed FOBT	FOBT (+)	(–)	CRC
50–54	13019	2344 (18.0%)	2206	108	2092	7
55–59	9128	2066 (22.6%)	1908	64	1798	7
60–64	8876	1961 (22.1%)	1539	92	1442	7
65–69	9573	2183 (22.8%)	1596	188	1404	5
70–74	9259	1614 (17.4%)	1194	150	1044	2
Total	49855	10168 (20.4%)	8443	602	7780	28

FOBT – fecal occult blood test, CRC – colorectal carcinoma

**TABLE 2**  
COLONOSCOPY FINDINGS

Age groups	Orderly	Polyps	Hemorrhoids	Diverticula	CRC	Others
50–54	36	31	7	13	7	3
55–59	5	21	8	3	7	1
60–64	14	32	6	16	7	5
65–69	26	51	19	33	5	3
70–74	12	58	22	25	2	0
Total	93	193	62	90	28	12

test) screening over 3-year cycle<sup>9,12</sup>. The anticipated cycle length of 3 years was considerably prolonged, with the initial invitation to testing completed by the end of 2012, i.e. more than 5 years. A total of 49,855 persons were invited for testing in Brod-Posavina County. Discrepancy between the number of test envelopes returned and the number of tests performed occurred because some persons had died, moved elsewhere, lived abroad, etc. The response rate of 20.4% was consistent with the average national response rate of 19.9% reported in 2007 and 2011<sup>13,14</sup>. A rate of 28.1% exceeding the national average rate was recorded in Međimurje County<sup>15</sup>. All these response rates are by far lower than those recommended by EU guidelines of 65% and even from the minimal acceptable rate of 45%. In our County, there was no significant age related difference in response (Table 1). Such a low response rate may be ascribed to inadequate understanding of the screening test instructions (how to perform stool sampling, how to apply it onto the test card, how to send it, and how to properly store the test during sampling period), fear from positive finding and fear from colonoscopy that follows testing, and general unawareness of the CRC prevalence. In the County, 602 (7.2%) positive tests have been identified to date, which is consistent with EU guidelines for the first cycle of screening (1.5–8.5%)<sup>12</sup> (Table 1). We received 0.1% of incorrect tests, which is also in line with EU guidelines (less than 1% desirable)<sup>12</sup>.

Development of CRC can be prevented by screening programs in a population at a higher risk, in this case individuals of both sexes aged 50–74. The test used on screening detects the majority of early CRC cases and advanced adenomas. Implementation of screening tests in the target population reduces the incidence and mortality of the disease<sup>5</sup>. An increase in the incidence of carcinoma is expected to be recorded in the first years of National Program implementation. In Brod-Posavina County, the incidence of CRC in 2006 was 52.61/100,000; in 2007, 2008 and 2009 it was similar (58.84/100,000, 58.27/100,000 and 58.84/100,000, respectively), showing an increasing tendency compared with 2006. It continued increasing in 2010 (64.49/100,000), as expected.

The screening test is available, acceptable by price, noninvasive and simply applicable by the majority of general population<sup>5</sup>. Considering the low response rate, the question is whether it really is so simple. As mentioned above, the target population may in part have

quite a low level of literacy and education, thus they cannot fully understand and follow the insert instructions, and do not respond to the invitation for screening.

Testing for occult bleeding once a year combined with occasional colonoscopy is a successful method of CRC prevention<sup>16</sup>. According to the manufacturer's instructions, the method sensitivity is high (96%); however, in the population of asymptomatic individuals, guaiac test shows positivity of only 2–5% (in our study 7.1%) and 1–2% of false-positive results. Test limitations in terms of lower sensitivity generally refer to small size polyps and early lesions, whereas some studies also pointed to low sensitivity in detecting carcinomas located on distal colon and higher sensitivity for carcinomas located on left colon<sup>16</sup>. The specificity of guaiac test is low because only 5–10% (in our study 4.9%) of tested subjects have carcinoma related lesions, whereas all others are false-positive. Such a great number of false-positive subjects is one of the test drawbacks and increases the price of screening, since colonoscopy is regularly performed in test positive subjects<sup>17,18</sup>. In spite of all these test shortcomings, controlled clinical trials have found periodical testing for occult bleeding to lead to low but significant reduction in CRC mortality by 15–18%. Due to the low specificity of guaiac test, new tests for detection of occult bleeding have been marketed, e.g., immunologic and hemoporphyrin tests characterized by high sensitivity, while low specificity remains a problem; therefore, guaiac test is still most frequently used on screening<sup>18</sup>.

As recommended, public health workers make an appointment for colonoscopy for all FOBT positive persons, which can take up to one month due to the limited capacity of Department of Internal Medicine, General Hospital »Dr. Josip Benčević« in Slavonski Brod. Our colleagues from Međimurje County are faced with a similar problem<sup>15</sup>. Colonoscopy was performed in 478 persons, although appointment was made for 602 persons, yielding a colonoscopy response rate of 79.4%, which is below the acceptable rate according to EU guidelines<sup>12</sup>. Screening confirmed 28 CRC cases (5.9% of those submitted to colonoscopy, 4.7% of FOBT positive individuals and 0.3% of all individuals included in the National Program). The rate of CRC detection was 3.3‰, which falls within the recommended range (1.2–9.5‰)<sup>12</sup>. Pathologic findings accounted for 80.5% of all colonoscopy findings, predominated by polyps and diverticula (50.1% and 23.4%, respectively) (Table 2).

At the national level, colonoscopy verified 77.5% of pathologic findings, with colon polyps accounting for 38.5% of the findings<sup>13</sup>. Family physicians have not been adequately involved in the screening, although they should play a key role in motivating target population, thus increasing the response rate. Our colleagues from Osijek have demonstrated that a higher response rate can be achieved with family physicians taking the central role in the screening<sup>19</sup>. Dutch authors also report on the higher response rate in the countries where family physicians have been actively included in the National Programs<sup>20</sup>. The inadequate role of family physicians in our country has also been described by the authors from Medimurje County. Screening can only prove efficient if associated with an appropriately high rate of response<sup>1</sup>; therefore, it is of paramount importance to undertake due measures at the national level, which will lead to such a result (promotion, health education, and involvement of family physicians and visiting nurses). The countries where such national programs have not yet been introduced point to the role and need of mass screening<sup>21</sup>

due to continuously rising incidence<sup>22,23</sup>, mortality and detection of advanced stage carcinomas<sup>24</sup>, associated with reduced therapeutic options and poorer disease prognosis. Screening with retesting has a major role in the detection of polyps with a high rate of malignant alteration, as well as of earlier stages of disease, as malignant transformation may take even more than 10 years<sup>25</sup>.

## Conclusion

The National Program of Colorectal Carcinoma Early Detection is of major public health importance; however, improvements are required at both local and national level. It should be backed up by more aggressive mass media promotion, health education of the population at large, and inclusion of family physicians and visiting nurses in order to ensure optimal response rate in the target population. The Program software should also be improved for better data evaluation and faster Program performance. Satisfactory results can only be expected when all the preset guidelines are fully met.

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## **NACIONALNI PROGRAM RANOG OTKRIVANJA RAKA DEBELOG CRIJEVA U BRODSKO-POSAVSKOJ ŽUPANIJI (ISTOK HRVATSKE)**

### **S A Ž E T A K**

Kolorektalni karcinom (CRC) predstavlja veliki javno zdravstveni problem, budući da je na 3. mjestu po zastupljenosti malignih tumor kod muškaraca, a na 4. mjestu kod žena u Hrvatskoj. Prognoza i liječenje uvelike ovise o stadiju u kojem je tumor otkriven. Stoga se u Hrvatskoj od 2007. godine provodi Nacionalni program ranog otkrivanja raka debelog crijeva i naš cilj je u ovom radu prikazati odaziv, nalaze kolonoskopije i broj otkrivenih CRC u Brodsko-posavskoj županiji. Tijekom 5 godina provođenja Nacionalnog programa u Brodsko-posavskoj županiji je otkriven 28 karcinom. Najveći broj karcinoma je u dobnoj skupini od 50–64 godine. Stopa detekcije karcinoma je 3,3 ‰. Odaziv na razini županije je nizak i iznosi 20,4% što odgovara prosjeku u Hrvatskoj, ali je daleko od preporučenog. Takav rezultat možemo tumačiti slabom prosvjećenosti populacije, kompliciranosti testa za opću populaciju, strahom od bolesti i kolonoskopije kao pretrage. Naglasili bi da je uloga liječnika obiteljske medicine neadekvatna, te da bi se njihovim uključivanjem u Nacionalni program mogli postići bolji rezultati na nivo naše županije, a i Hrvatske.