

Trends in colon cancer incidence in young and older adults in Mačva Region (Serbia)

Tihomir Dugandžija^{1,2}, Marijana Srećković^{1,3}, Vesna Ignjatović⁴, Snežana Panić³, Igor Dragičević³, Nataša Hinić^{1,2}

SUMMARY

Objectives: Our goal was to conduct the first survey and screening of colon cancer incidence trends in the Mačva district, Serbia. **Methods:** Age-specific incidence of colon cancer among the > 20 years old adults that were diagnosed from 2006–2015 was analyzed using data from Cancer Registries of the Šabac Public Health Institute and Public Health Institute of Serbia. Linear model of the incidence rates and annual change in age-standardized incidence rates, by sex and age were presented. Standardized incidence ratio, based on average age-specific incidence rates of colon cancer for Šabac municipality and Central Serbia was calculated. **Results:** Based on the results from our study, colon cancer incidence in Šabac municipality increased in males and females in the last ten years. Risk of developing colon cancer in males and females, calculated by standardized rates ratios was 1.5 and 1.3, respectively. Linear, rising trend for age-standardized incidence rates in the population of Šabac compared to other municipalities in the Mačva district was recorded. Furthermore, standardized incidence ratios for both females and males were higher compared to data from Central Serbia (28% and 22%, respectively). **Conclusion:** Our study revealed increased colon cancer incidence, with a linear increase of colon cancers in young males and also in > 50 years old population.

Keywords: incidence, colon cancer, linear models, standardized incidence ratio, screening

INTRODUCTION

According to GLOBOCAN 2018 data, colorectal cancer (CRC) is the fourth most commonly diagnosed cancer in the world (1) and an increase in the incidence of CRC by the year 2030 is predicted (2). The incidence of CRC differs dramatically from region to region and reflects in risk factors and population demographics (3). The American Cancer Society updated its guideline on May 2018, due to increasing rates of colorectal cancer among young population. It was suggested to lower the age for initial screening from 50 to 45 years of age, among average-risk individuals (4).

Screening studies have reported higher survival rate benefits in screened non-symptomatic populations with known risk factors (5). Ten years ago, the opportunistic National Colorectal Cancer Screening Program that was based on fecal occult blood test (FOBT) and recommended colonoscopy in case of positive outcome was introduced in the Mačva district. Significantly higher incidence of colon cancer was recorded in the municipality of Šabac that led to transition from opportunistic to population- screening program for colorectal cancer (CRC) in 2015.

In our study, we investigated colon cancer incidence trends among adults in Mačva district during a 10-year period. Since screening can lead to reduced cancer incidence, we also evaluated whether an opportunistic colorectal cancer screening program was associated with change in colon cancer incidence trends.

MATERIAL AND METHODS

The colon cancer data were obtained from the Serbian Cancer Incidence and Mortality Data (6) and Regional Cancer Registries of the Public Health Institute (PHI) Šabac. They were grouped by year of diagnosis, 5-year age and gender. Age-standardized incidence rates (ASRs) were calculated and expressed per 100 000 using direct standardization and “world standard population” as proposed by Segi (1960) (7) and Doll, Payne and Waterhouse (1966) (8). We limited the analyses to those aged ≥20 years. Annual incidence rates from year 2006 to 2015 were estimated for eight

age groups (20–39, 40–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75+). The standardized incidence ratio (SIR), based on average age-specific incidence rates of colon cancer for Šabac municipality and Central Serbia were calculated. Linear trend analysis of patients with colon cancer was used to estimate the magnitude of change in age-specific incidence rates. A retrospective data analysis of opportunistic CRC screening coverage of target population for five-year period (2011–2015) was performed using data from PHI Šabac.

RESULTS

Analysis of the incidence rate of colon cancer in the Mačva district

In the observed period, 879 patients with colon cancer were registered on the territory of the Mačva district (500 men and 379 women) and half of all patients lived on the territory of the Šabac municipality. The average ten-year ASRs for colon cancer in the Šabac municipality was higher compared to other municipalities of the Mačva district (Table 1). Slightly higher ASRs for colon cancer were recorded in two rural municipalities with a small population (in males from Ljubovija municipality and in females from Krupanj). On average, the population of Šabac was 1.4 times more likely to get colon cancer than residents of other municipalities in the district (1.3 times men and 1.5 times women; Table 2). No new cases of colon cancer in patients under 20 years of age were registered in municipalities of Mačva district.

Incidence rates of colon cancer in Šabac municipality

Age-standardized incidence rates (ASRs) of colon cancer among males and females was higher in Šabac compared to other municipalities of Mačva district (Figures 1 and 2). Among males colon cancer increased by 10.8% per year ($R^2=0.8$), and the observed trend can be considered statistically significant during the ten-year observation period (Figure 1a.), which was not the case with other investigated municipalities. Among females in Šabac, colon cancer incidence increased by 1.7% per year in 2006 - 2015 period (Figure 2a).

Arch Oncol 2023; 29(1):11-5

Published Online
June 10th, 2022
<https://doi.org/10.2298/AO0210205005D>

¹ Faculty of Medicine, University of Novi Sad, Hajduk Veljkova 3, 21000 Novi Sad, Serbia

² Oncology Institute of Vojvodina, Put dr Goldmana 4, 21204 Sremska Kamenica, Serbia

³ Public Health Institute Šabac, Jovana Cvijića 1, 15000 Šabac, Serbia

⁴ Department for Nuclear Medicine, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovića 69, 34000 Kragujevac, Serbia

Correspondence to:
Marijana Srećković
dsrecekovicmaja@gmail.com

Received 2021-02-05
Received in revised form 2022-03-09
Accepted 2022-04-29



This work is licensed under a Creative Commons Attribution 4.0 license

Municipality	Gender	Number	Crude rate	ASR	Male to female ratio
Bogatic (M1)	male	50	31.9	18.1	1.8
	female	30	18.8	10.2	
Koceljeva (M2)	male	13	17.4	9.6	0.8
	female	17	23.1	12.9	
Krupanj (M3)	male	20	20.7	11.9	0.8
	female	29	30.9	15.6	
Ljubovija (M4)	male	29	36.0	23.4	3.5
	female	10	14.6	6.8	
Mali Zvornik (M5)	male	14	20.7	14.4	1.1
	female	13	19.3	13.4	
Vladimirci (M6)	male	29	29.4	16.8	1.3
	female	29	30.3	13.2	
Loznica (M7)	male	127	30.5	18.4	1.6
	female	88	20.4	11.4	
Šabac (M8)	male	218	37.0	22.3	1.6
	female	163	26.4	14.3	

M - Municipality

Table 1: Average number, crude rate and ASRs of colon cancer cases in different municipalities from Mačva district in 2006-2015 period

SRR	M8 vs. M1	M8 vs. M2	M8 vs. M3	M8 vs. M4	M8 vs. M5	M8 vs. M6	M8 vs. M7
Males	1.2	2.3	1.9	0.9	1.5	1.3	1.2
Females	1.4	1.1	0.9	2.1	1.1	1.1	1.3

M - Municipality

M1 = Bogatic; M2 = Koceljeva; M3 = Krupanj; M4 = Ljubovija; M5 = Mali Zvornik; M6 = Vladimirci; M7 = Loznica; M8 = Šabac

Table 2: Standardized rates ratio (SRR) for colon cancer in Šabac municipality compared to other municipalities from the Mačva district in 2006-2015 period

Population under 50 years of age

For males aged 20 to 39 years, colon cancer incidence rose by 22% per year between 2006 and 2015. In the age group 40 to 49 years, the increase was 15% per year from 2006 to 2015. In females under 50 years, colon cancer incidence rates were falling during the ten consecutive years of observation (2006-2015). In contrast trend to males, for women aged 20 to 39 years and 40-49 years, colon cancer rates have been decreasing were 14.5% and 8.9% per year, respectively (Figures 3 and 4).

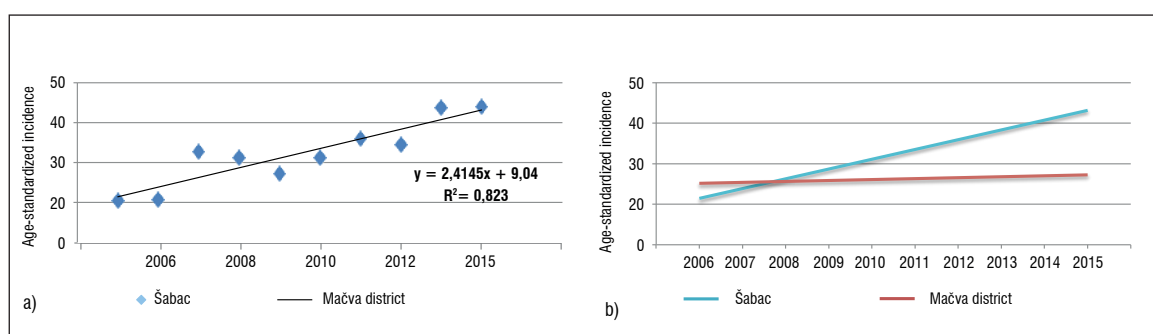
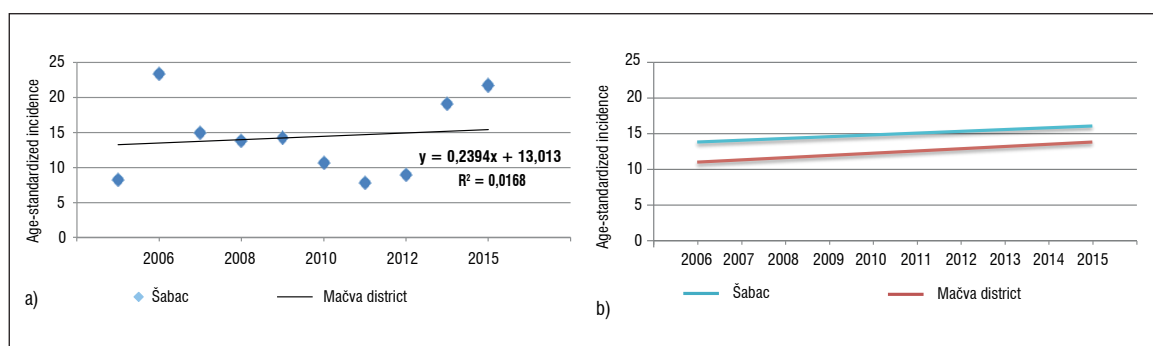
Population at and over 50 years of age

For males in their 50s and 60s, colon cancer incidence increased by 4.5% and 10.7% per year, respectively. For females, colon cancer incidence increased by 12.6% (for aged 50-59 years) and by 1.6% (for aged 60-69 years) per year in 2006 – 2015 period. For those aged 70 years and older incidence increase was at a rate of 10.9% per year over the entire 10-year period. For females in their 70s and older, an increase of 2.9% per year was observed over the entire 10-year period. Colon cancer incidence for males aged 70 years and older, were higher compared to females (10.9% per year) over the same period (Figures 3 and 4).

Results suggest that ten-year incidence of colon cancer among females and males in municipality of Šabac was 28% and 22%, respectively. This was higher than expected based on average age-specific incidence rates for Central Serbia (Tables 3 and 4).

Colorectal Cancer Screening

We conducted an analysis of the coverage obtained by the opportunistic screening program in the five-year period (from 2011 to 2015). Prior to 2011, the coverage of the target population with the screening program for colorectal cancer in health centers in Mačva district was not monitored.

**Figure 1.** Trends of age-standardized incidence rates of colon cancer among males (a) in Šabac municipality and (b) compared to Mačva district data**Figure 2.** Trends of age-standardized incidence rates of colon cancer among females in (a) Šabac municipality and (b) compared to Mačva district data

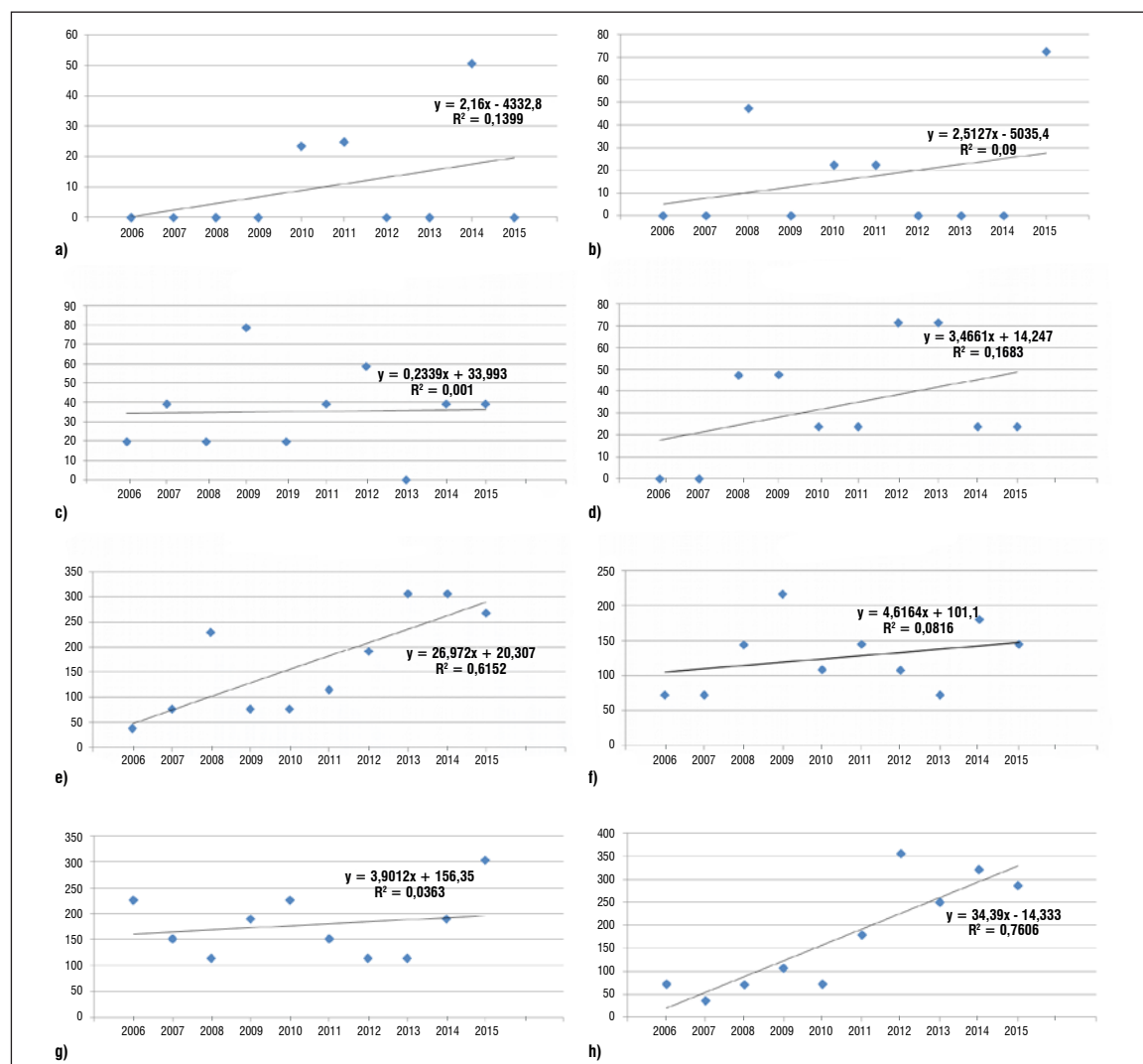


Figure 3. Age-specific colon cancer incidence rates in the Šabac municipality in 2006 - 2015 year period for males aged: a) 20-39 years, b) 40-49 years, c) 50-54 years, d) 55-59 years, e) 60-64 years, f) 65-69 years, g) 70-74 years, h) 75+ years

Year	Age-specific incidence rates		SIR	95% CI	p-value
	Šabac	Central Serbia			
2006	428.8	496.9	86.3	78.3-94.9	0.99
2007	375.3	580.4	64.7	58.3-71.6	1
2008	672.6	629.6	106.8	98.9-115.2	0.05
2009	716	659.3	108.6	101.0-116.9	0.02
2010	572.9	619	92.6	85.1-100.5	0.97
2011	699.9	606.2	115.5	107.1-124.3	0.001
2012	898.7	652.6	137.7	128.9-147.0	0.000
2013	814.2	594	137.1	127.8-146.8	0.000
2014	1111.8	580.4	191.6	180.5-203.2	0.000
2015	1136.9	661.9	171.8	161.9-182.1	0.000
Total (2006-2015)	7427.1	6080.3	122.15	119.5-125.0	0.000

SIR - Standardized incidence ratio

CI - Confidence Interval

Table 3: Age-specific incidence rates and standardized incidence ratios (SIRs) for colon cancer among males in the Šabac municipality and Central Serbia in the 2006-2015 period

Year	Age-specific incidence rates		SIR	95% CI	p-value
	Šabac	Central Serbia			
2006	238.2	284.3	83.8	73.5-95.1	0.99
2007	652.6	366.5	178.1	164.7-192.3	0.000
2008	439.8	301	146.1	132.8-160.4	0.000
2009	478	331.8	144.1	131.4-157.6	0.000
2010	383.9	383.7	100.1	90.3-110.6	0.5
2011	407.5	373.1	109.2	98.9-120.4	0.04
2012	236.9	322.3	73.4	64.4-83.41	0.99
2013	284	320.6	88.6	78.6-99.5	0.98
2014	567.3	335.4	169.1	155.5-183.6	0.000
2015	660.9	386.1	171.2	158.4-184.7	0.000
Total (2006-2015)	4349.1	3404.8	127.7	124.0-131.6	0.000

SIR - Standardized incidence ratio

CI - Confidence Interval

Table 4: Age-specific incidence rates and standardized incidence ratios (SIRs) for colon cancer among females in the Šabac municipality and Central Serbia in 2006-2015 period

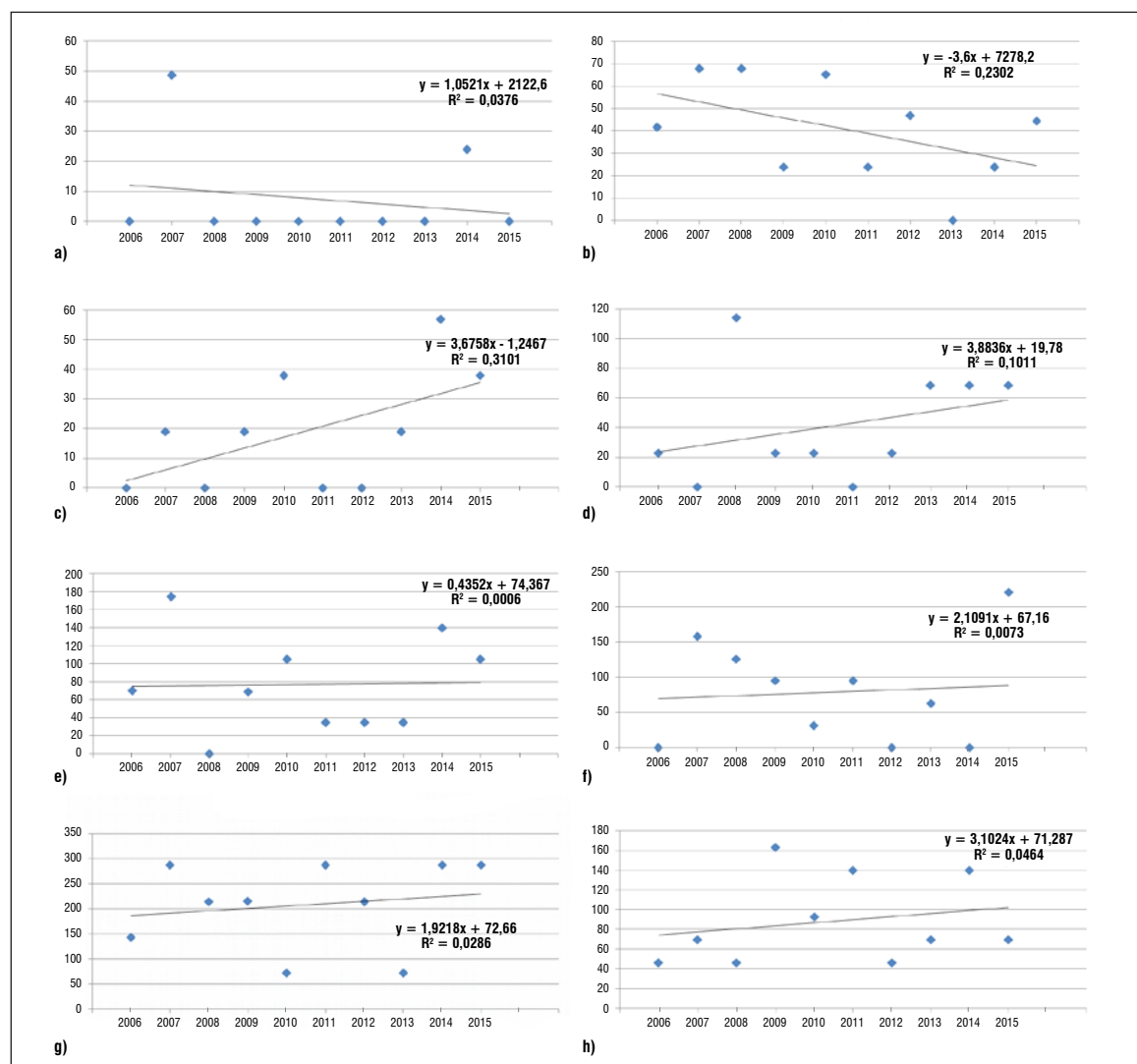


Figure 4. Age-specific colon cancer incidence rates in the Šabac municipality in 2006 - 2015 period for females aged: a) 20–39 years, b) 40–49 years, c) 50–54 years, d) 55–59 years, e) 60–64 years, f) 65–69 years, g) 70–74 years, h) 75+ years

In the observed five-year period, the percentage of performed FOBT in the screening group of participants was only 6.00% ($6.00 \pm 4.80\%$). During 2016, newly introduced population-based program covered 17.95% of the target population.

DISCUSSION

Risk factors for colorectal cancer are an important public health problem worldwide. Evidence of unequal distribution both in the world and within the territorial units of a country, suggests the influence of geographical factors, environmental factors and lifestyles in some regions.

In our study, age group < 50 years was defined as young, taking into account the ages of starting CRC screening for individuals at average risk. It is important to note that different studies use different age cutoffs (age < 55 in some and < 40 in others) (9, 10). Based on the average ten-year ASRs values for colon cancer, the highest ASRs were observed in municipality of Šabac compared to the other municipalities in the Mačva district. Among residents of Šabac municipality, we found increased risks of developing colon cancer in males and females, with SRRs of 1.5 and 1.3, respectively. During the ten-year observation period linear, rising trend

of ASR was observed in Šabac municipality population, when compared to other municipalities from Mačva district. Standardized incidence ratios (SIRs) for females and males were 28% and 22% respectively, and they were higher compared to data from Central Serbia. Our analysis of incidence trends over time has found out that in population of males below 50 years of age the incidence of colon cancer increased, and that for females aged 20 to 59 years colon cancer rates decreased in the 2006 - 2015 period. The reason for the decrease of colon cancer incidence in young females is not entirely clear.

The risk factors for the increase of cases of colon cancer in young males have not been fully elucidated in previously conducted research but clinicians should be aware of this trend in order to identify patients at risk (11). Hereditary factors were thought to be the most probable cause of CRC in young patients (12). In large number of recent studies some risk factors, such as alcohol, smoking, red meat and overweight/obesity (13, 14) have been found to be related to colon cancer. Previous research in the US reported that younger people are not regularly screened for CRC, which exposes them to an increased risk of being diagnosed at late stage of the disease (15).

In our study age-specific incidence increased rapidly for both genders after the age of 50. This finding does not correlate with recent studies in the United States, Israel and Japan, that show decrease in incidence among older age groups (countries where organised screening has been initiated since the 1990s) (16, 17), which may be associated with low participation in opportunistic screening program that was found in our study. A previous study analyzed incidence rates in Australia during recent period, showed that they stagnated or decreased in older age groups, most possibly due to the expanded screening and high-risk monitoring (5). This was not observed in our study most probably due to low participation in opportunistic screening program (average percent was 1.8% in 2011 – 2015 period). The reduction of the colorectal cancer incidence in the United States was attributed to mass screening, reduced risk factors, as well as improved diagnosis and treatment (18-20). According to the American Cancer Society colorectal cancer incidence for the average risk population should be decreased by 75% (21), which is also the goal of the National screening program for colorectal cancer in Serbia (22). Colorectal cancer screening as organized program has been implemented in Serbia since 2012, while primary health center of Šabac municipality performs screening program since 2015. Screening test used for colorectal cancer are immunochemical test for occult blood in the stool (iFOB test) and colonoscopy. Screening is performed in 50-74 years age group (23), but public health may largely benefit from national mass screening program.

Our study showed the rising incidence of colon cancer, with a linear rise found in young males. This finding is in line with a recent update of the guideline for CRC screening by the American Cancer Society. Also, our study indicated rising trends in colon cancer in people aged over 50.

Declaration of Interests

Authors declare no conflicts of interest.

REFERENCES

- Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A, Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2018;0:1–31.
- Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008-2030): a population-based study. *Lancet Oncol* 2012; 13: 790–801.
- Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. *Prz Gastroenterol* 2019; 14(2):89-103.
- Wolf AMD, Fontham ETH, Church TR, Flowers CR, Guerra CE, LaMonte SJ, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin* 2018; 68:250-281.
- Young JP, Win AK, Rosty C, Flight I, Roder D, Young GP, et al. Rising incidence of early-onset colorectal cancer in Australia over two decades: report and review. *J Gastroenterol Hepatol* 2015;30:6–13.
- Institute of Public Health of Serbia „Dr Milan Jovanović Batut“. Cancer incidence and mortality in central Serbia. 2006-2015. Retrieved from: <http://www.batut.org.rs/index.php?content=185>.
- Segi M. Cancer mortality for selected sites in 24 countries (1950-1957) Sendai, Department of Public Health, Tohoku University of Medicine; 1960.
- Doll R, Payne P, Waterhouse JAH, ed. Cancer Incidence in Five Continents, Vol. I: UICC: Switzerland: Springer-Verlag; 1966.
- Troeng L, Sodhi-Berry N, Martini A, Malacova E, Ee H, O'Leary P, et al. Increasing incidence of colorectal cancer in adolescents and young adults aged 15-39 years in Western Australia, 1982-2007: examination of colonoscopy history. *Front Public Health* 2017; 5:179.
- Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS, Jemal A. Colorectal cancer incidence patterns in the United States, 1974-2013. *J Natl Cancer Inst* 2017;109.
- Vuik FE, Nieuwenburg SA, Bardou M, Lansdorp-Vogelaar I, Dinis-Ribeiro M, Bento MJ, et al. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. *Gut* 2019;68:1820-1826.
- Losi L, Di Gregorio C, Pedroni M, Ponti G, Roncucci L, Scarselli A, et al. Molecular genetic alterations and clinical features in early-onset colorectal carcinomas and their role for the recognition of hereditary cancer syndromes. *Am J Gastroenterol* 2005; 100:2280-7.
- Fardet A, Druet-Pecollet N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. *Crit Rev Oncol Hematol* 2017; 119:94-112.
- Walter V, Jansen L, Hoffmeister M, Brenner H. Smoking and survival of colorectal cancer patients: systematic review and meta-analysis. *Ann Oncol* 2014; 25:1517-25.
- Kasi PM, Shahjehan F, Cochuyt JJ, Li Z, Colibaseanu DT, Merchea A. Rising Proportion of Young Individuals With Rectal and Colon Cancer. *Clin Colorectal Cancer* 2019; 18(1):e87-e95.
- Schreuders EH, Ruco A, Rabeneck L, et al. Colorectal cancer screening: a global overview of existing programmes. *Gut* 2015;64:1637–49.
- Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut* 2017; 66(4):683-691.
- Kohler BA, Ward E, Mc Carthy BJ, Schymura MJ, Ries LA, Ehemann C, et al. Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. *J Natl Cancer Inst* 2011;103(9):714-36.
- Edwards BK, Ward E, Kohler BA, Ehemann C, Zuber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer* 2010;116(3):544-73.
- Siegel RL, Jemal A, Ward EM. Increase in incidence of colorectal cancer among young men and women in the United States. *Cancer Epidemiol Biomarkers Prev* 2009;18(6):1695-8.
- American Cancer Society. Cancer Facts & Figures 2011-2012. Atlanta, GA: American Cancer Society; 2012. Available at: www.cancer.org/research/cancer-factsfigures/acspc-031941.
- National Programme of Early Detection of Colorectal Cancer, Official Gazette of RS, No 73/13.
- National Cancer Screening Office. Available at: <http://www.skriningsrbija.rs/eng/colorectal-cancer-screening/>.