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DIETARY INTAKE OF VITAMIN B_{12} IN RELATION TO DIET AND LIFESTYLE CHARACTERISTICS IN A POPULATION AT HIGH RISK FOR COLORECTAL CANCER

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SUMMARY

Objective: Besides irreplaceable role in health, vitamin B_{12} is proposed to have cytoprotective role in colorectal cancer (CRC). So far, studies are inconclusive on the role dietary intake of vitamin B_{12} has in CRC. The aim of this study was to determine whether total dietary intake of vitamin B_{12} and contribution from its food sources relates to a low-risk diet and lifestyle in a population at high risk for CRC.

Methods: An observational study on 200 healthy adults from Eastern Croatia was conducted during April–May 2013. A typical diet of this population in this region is characterized with all known major dietary risk factors for CRC placing the population at high risk for CRC, yet the incidence of CRC remains relatively low.

Results: Diet and lifestyle characteristics of 52.2% of participants can be classified as the high-risk for CRC. Women, people in lower BMI category, and urban residents have significantly lower risk of the high-risk diet and lifestyle. Higher intake of vitamin B_{12} shows positive association with the low-risk diet and lifestyle. Intake of vitamin B_{12} from milk, dairy and fish represent independent factors for the low-risk diet and lifestyle in this population at high-risk for CRC.

Conclusions: Higher intake of vitamin B_{12}, especially intake from milk, dairy and fish are associated with the low-risk diet and lifestyle in a population at high risk for CRC. Further studies should focus on interplay between vitamin B_{12} and other nutrients that share the same food sources to elucidate their role in the aetiology and pathology of CRC.

Key words: colorectal cancer, dietary vitamin B_{12}, population at high-risk for CRC, diet and lifestyle characteristics, high-risk diet and lifestyle

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INTRODUCTION

Colorectal Cancer – Epidemiology and Recent Insights

Colorectal cancer (CRC) is distinctive for its strikingly high correlation with diet (1). Incidence rates have changed significantly (2) but it remains the third most common cancer globally, with high mortality if diagnosed in later stages and immense impact on public health (3, 4). In Croatia, CRC is the third most common cancer in men and the second in women (5). Incidence of CRC drastically increased between 1990 and 2013; 175% for males and 125% for females (6), with mortality rate of around 66%, regardless of gender (5). Still, large variations in CRC incidence across Croatian regions (5, 6) are attributed to large differences in dietary patterns across Croatia (7).

Dietary and lifestyle risk factors for CRC are well known (8). Currently, the strongest positive association with CRC risk was found for intake of red and processed meat (2). However, omitting meat and meat products from diet means eliminating highly valuable sources of protein, iron and vitamin B_{12} (9).

Vitamin B_{12} – Body Homeostasis and Dietary Sources

As the largest and most complex vitamins of all, vitamin B_{12} plays an irreplaceable role in human health; from one carbon (C-1) metabolism, through epigenetic alterations related to gene expression and related risk of cancer, neurodevelopment and cognition, and foetal programming via maternal nutrition, to metabolism (including hyperhomocysteinemia, adiposity and insulin resistance) (10–12).

Along with other B complex vitamins (folate, vitamin B_6 and B_2), vitamin B_{12} acts as a co-enzyme in a network of interrelated biochemical pathways that donate and regenerate C-1 units, affecting folate-dependant reactions and mitochondrial energy and lipid metabolic pathways (10). Normal C-1 metabolism enables DNA replication, DNA repair, and regulation of gene expression (12), which is why vitamin B_{12} started to raise interest within the scientific community in the area of cancer research. Vitamin B_{12} is often compared with folate and considered to have positive effect in C-1 cancer-related alterations, like in CRC (13–15).

Naturally, vitamin B_{12} can be found only in foods of animal origin, such as meat, poultry, fish (including shellfish), and to a lesser extent in milk and dairy (16, 17). Importantly, vitamin B_{12}

from these dietary sources has the highest bioavailability (between 40% and 89%) (7). Besides vitamin B_{12}, meat, especially red meat, is a valuable source of other B complex vitamins like niacin, thiamine, riboflavin, and pyridoxine (9), which can also be found in high amounts in fish and milk and dairy products. All of these B vitamins have immense importance in maintaining a normal C-1 metabolism (12–14).

Nowadays, vitamin B_{12} can be found in a wide variety of fortified foods, especially in cereal products (e.g. breakfast cereals). With numerous pros (and cons), fortification with vitamin B_{12} remains to be voluntary in most countries around the world (Croatia is among countries that do not have mandatory fortification with vitamin B_{12}). However, even in countries with such measures in force, vitamin B_{12} deficiency prevalence is high (16, 17). Supplements also need to be considered when estimating total intake of vitamin B_{12} (16, 18). Population groups at risk of low intake of vitamin B_{12} include elderly, children and infants, and vegetarians and vegans (10).

In food, vitamin B_{12} is bound to protein, and its absorption asks for a normal gastric activity i.e. production of gastric pepsin and acid. Three proteins have the ability to bind vitamin B_{12} and will ensure its optimal absorption: haptocorrin, intrinsic factor (IF) and transcobalamin (1, 10). Any disturbance in the gastrointestinal system (due to medications, acute or chronic inflammations, etc.) can impair vitamin B_{12} status of an individual (11).

Vitamin B_{12} and Carcinogenesis

Vitamin B_{12} has been proposed as a potential cytoprotector in terms of neoplasms of the bowel (19). They analysed separate segments of the bowel and found that vitamin B_{12} is the only nutrient unavailable for absorption in the segments with the highest incidence of neoplasms (19). This hypothesis has been extended to interplay between vitamin B_{12} and iron, especially from the aspect of their bioavailability from food groups that are rich sources of both nutrients (7).

The majority of studies that looked at the role of B complex vitamins, primarily folate in oncogenesis were focused on C-1 metabolism (20, 21). So far, studies are inconclusive on the role dietary intake of vitamin B_{12} has in CRC (13–15, 22–24). Some studies showed positive relation between intake of vitamin B_{12} and lower risk of CRC (13–15), while others showed no effect for other forms of gastric cancers (24).

Increased plasma vitamin B_{12} concentrations were found in oncology patients, with established positive correlation with the state of disease (25). On the other hand, *in vitro* and *in vivo* studies found that vitamin B_{12} in higher doses inhibits proliferation of the cancer cells (26). The Master Key Effect hypothesis set by Volkov (27) suggest that treating an oncological patient with high doses of vitamin B_{12} could help body to recover under the stress of such severe pathology.

MATERIALS AND METHODS

Study Hypothesis and Aims

Based on the available literature on the role vitamin B_{12} has in CRC (13–15) and current understanding of major risk factors for CRC (2) we hypothesize that dietary intake of vitamin B_{12} and contribution from its food sources is an important characteristic of a low-risk CRC diet and lifestyle.

The aim was to determine whether total dietary intake of vitamin B_{12} and contribution from separate food groups can be related to a healthier diet and lifestyle profile, i.e. a low-risk CRC diet and lifestyle.

Study Protocol

An observational study was conducted on adult population from Eastern Croatia, encompassing areas of the city of Osijek and Baranja region. The region was selected because a typical diet in this region is characterized with major dietary risk factors for CRC, from high intake of meat (especially red meat) and processed meat (smoked sausages, ham, bacon etc.), high preference towards salty and spicy food (especially hot), and foods with high fat content (saturated fats). According to the Croatian National Cancer Registry, CRC incidence in 2013 in the study region was below the national average for both genders, and lower than in some coastal regions of Croatia (6) with a diet generally considered as healthier, more similar to the Mediterranean diet (7).

Inclusion criteria were age between 18 and 75 years, participants had to be omnivores (vegetarians and vegans were excluded), without any serious medical diagnosis (including CRC), and with no regular use of medications or supplements.

In 2013, for the study region the incidence of colon cancer was 27.9 per 100,000 and 18.4 per 100,000 for rectal cancer, while the number of new cases of colon and rectal cancer was 141 in total, 78 in men and 63 in women (6).

Anonymous, study-specific questionnaires were randomly given to a total of 200 potential participants, between April and May 2013. After completion, total of 22 participants were excluded due to incomplete reporting. Attrition rate was 11.0%.

The questionnaire consisted of questions that assessed participant's general and socioeconomic characteristics (age, gender, residence, number of household members, education, employment status, income, etc.), questions that assessed participant's diet and lifestyle characteristics and a semi-quantitative food frequency questionnaire that assessed intake of vitamin B_{12}.

Questions that assessed participant's diet and lifestyle characteristics were prepared according to our current knowledge on risk factors for CRC (2), and also covered protective characteristics, many that are in line with the current recommendations for a healthy balanced diet and lifestyle (28). The same questionnaire was previously used on a student population from the same region (29). Questions were scored on a scale from 1 to 5, where 1 point was given for the worst and 5 points for the best response. For example, if a person never eats breakfast, he/she would get 1 point, and if a person eats breakfast every day, he/she would get 5 points. Minimum number of points was 19, and maximum 105 where higher score correlate with a diet and lifestyle related to a lower risk for CRC (low-risk CRC diet and lifestyle). Based on the difference between minimum and maximum scores achieved, participants were categorized as the high-risk CRC diet and lifestyle group (score ≤ 74) or the low-risk CRC diet and lifestyle group (score ≥ 75). Self-reported height and weight were used to calculate body mass index (BMI) which was then used to categorize participants as underweight, normal weight, overweight or obese according to WHO's recommendations (30).

Semi-quantitative food frequency questionnaire (SQFFQ) was used to assess vitamin B_{12} intake. The following food sources were covered: meat and meat products, fish, milk and dairy, and eggs. The method was chosen because it is practical and shows the lowest level of error in terms of underestimating or overestimating dietary intake (31), especially if the emphasis is on micronutrient assessment (32), like in this case. This was also a method of choice for several other studies that dealt with vitamin B_{12} intake in different population groups (33). Also, participants were asked about consumption of breakfast cereals (on Croatian market breakfast cereals for children and imported ones are frequently fortified with vitamin B_{12}). If a participant was consuming this group of products, they were asked to indicate a manufacturer. Computer program NutriPro (Faculty of Food Technology Osijek, Osijek, Croatia) which uses the National Composition Tables (34) was used to calculate the intake of vitamin B_{12}.

Statistical Analyses

Data were analysed with software tool Statistica 13.3 (StatSoft, Tulsa, Oklahoma, USA), at significance level $p = 0.05$. Normality of data distribution was tested by the nonparametric Kolmogorov-Smirnov test for the comparison of medians and arithmetic mean, and histograms plotting. Categorical data are presented as absolute and relative frequencies, and numerical data with median and interquartile range. Mann-Whitney U test was used to test two independent variable groups, and for several independent variable groups Kruskal-Wallis test was used, since the overall data did not show normal distribution. Spearman's test was used to calculate correlations for numerical data.

By inferential statistics the association of a number of independent variables with the score for diet and lifestyle characteristics as a binary dependent variable was tested with a univariate logistic regression. Independent variables tested were age, gender, BMI (numerical and categorical), residence, total vitamin B_{12}, and separate intake of vitamin B_{12} from all food groups. Independent factors that were found significant in a univariate logistic regression were included in the multiple logistic regression model. If the probability of alpha error was less than 0.05, we considered the relationship significant.

Table 1. *Participants' general characteristics, diet and lifestyle score and total vitamin B_{12} intake and contribution from separate food groups, with Spearman's correlation coefficient ($N = 178$)*

Characteristic		n (%)	r
Age (years)*		35 (28–48)	
Gender	Men	70 (39.3)	
	Women	108 (60.7)	
Residence	Urban	115 (64.6)	
	Rural	63 (35.4)	
BMI (kg/m^2)*		24.7 (21.8–28.0)	
BMI category	Underweight	2 (1.2)	
	Normal weight	89 (50.0)	
	Overweight	59 (33.1)	
	Obese	28 (15.7)	
Diet and lifestyle score*		74 (68–80)	0.20
Diet and lifestyle characteristics	High-risk	93 (52.2)	
	Low-risk	85 (47.8)	
Total vitamin B_{12} (µg)*		3.76 (2.57–5.92)	
Contributing food groups	Meat (%)	28.9 (15.0–45.4)	0.66
	Fish (%)	20.1 (3.7–39.9)	0.58
	Milk and dairy (%)	28.8 (14.7–49.7)	0.43
	Eggs (%)	5.8 (1.2–13.2)	0.31

BMI – body mass index; *values are given as median and 25–75% range. Values of median daily intake and contribution are given. Values in parentheses represent a range of 25–75% of daily intake, i.e. percentage of contribution. Spearman's correlation coefficients between total dietary intake of vitamin B_{12} intake, contribution from separate food groups and diet and lifestyle characteristics score. All coefficients are significant at $p < 0.001$ level.

RESULTS

Participant's general characteristics are shown in Table 1. Mean age of participants was 35 years, with a higher proportion of women (60.7%), and participants from urban areas (64.6%).

Table 2. *Total dietary intake of vitamin B_{12}, and separately from contributing food groups in relation to gender and place of residence ($N = 178$)*

	Men	Women	p-value	Urban	Rural	p-value	High-risk group	Low-risk group	p-value
	n = 70	n = 108		n = 115	n = 63		n = 93	n = 85	
Total vitamin B_{12} (µg)	4.01 (2.77–7.29)	3.56 (2.41–5.59)	0.170	3.86 (2.61–5.76)	3.59 (2.38–6.17)	0.739	3.29 (2.12–4.66)	4.35 (2.91–6.34)	0.008*
Meat (µg)	1.07 (0.48–2.93)	0.77 (0.33–1.69)	0.115	0.84 (0.33–2.10)	0.85 (0.49–2.21)	0.606	0.81 (0.48–2.10)	1.05 (0.38–2.49)	0.641
Fish (µg)	0.64 (0.00–1.79)	0.60 (0.22–1.46)	0.629	0.56 (0.14–1.46)	0.88 (0.24–1.79)	0.200	0.58 (0.00–1.40)	0.75 (0.25–2.12)	0.054
Milk and dairy (µg)]	0.83 (0.48–1.43)	1.25 (0.74–2.11)	0.023*	1.26 (0.68–1.87)	0.83 (0.51–1.43)	0.028*	0.90 (0.52–1.36)	1.34 (0.73–2.35)	0.004*
Eggs (µg)	0.37 (0.14–0.83)	0.16 (0.05–0.28)	< 0.001*	0.18 (0.07–0.55)	0.21 (0.09–0.55)	0.591	0.18 (0.07–0.55)	0.18 (0.07–0.55)	0.271

Mann-Whitney U test. Values of median daily intake are given. Values in parentheses represent a range of 25–75% of daily intake. *Statistical difference at $p < 0.05$ level.

Table 3. Odds ratio for diet and lifestyle characteristics score in relation to participants' characteristics and intake of vitamin B_{12} (univariate logistic regression) (N = 178)

Factor	Odds ratio (OR)	95% Confidence interval for OR		p-value
		Lower	Upper	
Age (years)	0.995	0.972	1.019	0.681
Gender (men = 1, woman = 2)	1.847	1.002	3.407	0.049
BMI (kg/m^2)	0.940	0.877	1.008	0.083
BMI category (underweight = 1, normal weight = 2, overweight = 3, obese = 4)	0.657	0.436	0.991	0.045
Residence (urban = 1, rural = 2)	0.443	0.235	0.836	0.012
Total vitamin B_{12} (μg/day)	1.073	0.993	1.160	0.074
Meat (μg/day)	0.983	0.890	1.086	0.737
Fish (μg/day)	1.220	1.006	1.479	0.044
Milk and dairy (μg/day)	1.700	1.217	2.375	0.002
Eggs (μg/day)	1.796	0.908	3.552	0.092

Table 4. Odds ratio for diet and lifestyle characteristics score in relation to participants' characteristics and intake of vitamin B_{12} (multiple logistic regression) (N = 178)

Factor	Odds ratio (OR)	95% Confidence interval for OR		p-value
		Lower	Upper	
Gender (men = 1, woman = 2)	1.548	0.782	3.062	0.209
BMI category (underweight = 1, normal weight = 2, overweight = 3, obese = 4)	0.776	0.490	1.229	0.280
Residence (urban = 1, rural = 2)	0.520	0.260	1.041	0.065
Fish (μg/day)	1.261	1.019	1.562	0.033
Milk and dairy (μg/day)	1.536	1.092	2.159	0.014
Constant	0.900			0.918

High prevalence of overweight (33.1%) and obesity (15.7) was found, but BMI did not correlate with diet and lifestyle score or total vitamin B_{12} intake (results are not shown). Still, a 34% lower risk of having a high-risk CRC diet and lifestyle was found for people in lower BMI category (Table 3).

Intake of vitamin B_{12} was 3.76 μg/day (2.57–5.92 μg/day), with the highest contribution from meat (28.9%) and milk and dairy (28.8%). Dietary intake of vitamin B_{12} showed significant correlation with all separate food groups and diet and lifestyle score, but the strongest correlation was found for meat (r = 0.66), fish (r = 0.58), and milk and dairy (r = 0.43) (Table 1).

For men meat is the main contributing food group (1.07 μg/day), and milk and dairy for women (1.25 μg/day). Men and women significantly differ in contribution of milk and dairy ($p = 0.023$), and eggs ($p < 0.001$) to daily intake of vitamin B_{12} (Table 2). Women have a 15% lower risk of having a high-risk CRC diet and lifestyle in comparison to men (Table 3).

According to participant's residence, those living in urban areas have slightly higher vitamin B_{12} intake (3.86 vs. 3.59 μg/day) (Table 2), but the only significant difference was found for milk and dairy (1.26 μg/day in urban vs. 0.83 μg/day in rural, $p = 0.028$). However, people living in urban areas have a 56% lower risk of having a high-risk CRC diet and lifestyle (Table 3).

According to participant's score for diet and lifestyle characteristics, 52.2% (93/178) fall into the high-risk group, and the remaining 47.8% (85/178) in the low-risk group (Table 1). Participants in the low-risk group have significantly higher intake of vitamin B_{12} (4.35 vs. 3.29 μg/day, $p = 0.008$) and intake of vitamin B_{12} from milk and dairy (1.34 vs. 0.90 μg/day, $p = 0.004$) (Table 2).

Logistic regression analysis revealed that higher contribution of fish (OR = 1.261, 95% CI: 1.019–1.562, $p = 0.033$) and milk and dairy (OR = 1.536, 95% CI: 1.092–2.159, $p = 0.014$) to intake of vitamin B_{12} represent independent factors related to the low-risk CRC diet and lifestyle (Table 3 and 4).

DISCUSSION

Dietary Intake of Vitamin B_{12}

Meat is the lead dietary source of vitamin B_{12} in the study group, followed by milk and dairy. These findings are in accordance with the Framingham Offspring Study (18), and other studies showing that meat and meat products contribute around 30% to the total dietary intake of vitamin B_{12} (7).

Tucker et al. (18) found that despite similar dietary intakes, plasma concentrations of vitamin B_{12} were significantly lower in the meat group than in the cereal and milk groups. Also, the highest risk of low plasma vitamin B_{12} concentration (<185 pmol/L) was found for those in the meat group, i.e. among subjects with the highest contribution to intake of vitamin B_{12} through meat and meat products (OR = 2.4, 95% CI: 1.7–3.4). The highest impact on plasma vitamin B_{12} concentration among non-supplement users had dairy, followed by cereals and meat, poultry and fish (regression coefficients 56.4, 35.2 and 16.7, respectively) (18).

High intake of meat is confirmed as one of the main diet characteristics of people from the study region, which is a well-known high-risk factor for CRC (2). These findings are in line with our previous research conducted on student population from the same region (29). Student's diet characteristics showed high consumption of meat and meat products (42.4% eat meat and meat products several times per day, and 41.3% up to 5 times per week), high preference for salty and spicy food, and low intake of fish, fruits and vegetables (29). These characteristics reflect a diet that increases the risk for CRC (2, 11, 13). Even more importantly, diet of students with positive family history of CRC was the worst (according to diet and lifestyle score) (29).

Sun et al. (22) in their meta-analysis show that high total intake of vitamin B_{12} (from diet and supplements combined) has an inverse relation with CRC risk if the intake is >12 μg/day.

Also, the association is stronger than if only dietary vitamin B_{12} is considered. A matched-pair study on CRC patients by Ravasco et al. (23) found significant difference in diet quality (macro and micronutrient). Healthy subjects had a mean intake of vitamin B_{12} of 2.1 µg while CRC patients had a mean intake of 6.0 µg (23). They concluded that increased weekly intake of vitamin B_{12} (and dietary iron) increases relative risk for CRC (23). In our study, mean intake of vitamin B_{12} was 3.76 µg/day, which is above the recommended 2.4 µg/day (28). This is much lower than reported by Tucker et al. (18) with an average intake of 6.2 ± 0.2 µg/day for non-supplement users, and 5.5 ± 0.3 µg/day for non-cereal consumption (i.e. fortified cereals). As previously mentioned, unlike in the United States, food fortification (referring to cereals and products) with vitamin B_{12} or other micronutrients is not an obligatory measure in Croatia (16, 17). The consumption of cereals in our study population was very low (0.5% of participants consumed breakfast cereals on a monthly basis), and participants noted consuming non-fortified cereals. Therefore, this food group was excluded from the analysis.

Subanalysis of Participants' Characteristics – Gender, State of Nourishment and Residence

Gender differences in relation to dietary and lifestyle habits have been extensively researched. From the aspect of CRC risks, women tend to have better dietary as well as lifestyle habits (35), while men in general have higher intake of meat and meat products (36), well-known CRC dietary risk factors (8). Our results confirm the trend; women have higher intake of vitamin B_{12} from milk and dairy, while for men, meat and meat products are the principal source of vitamin B_{12}. Additionally, logistic regression analysis showed that women have a 15% lower risk of having a high-risk CRC diet and lifestyle. Our findings are in line with our previous research (29) and the study conducted by Nikolić et al. (37). They conducted an observational survey on healthy adult population from the city of Niš, Serbia, by using a questionnaire with the risk score method (37). Also, they found that women reported better dietary and lifestyle habits (including lower intake of meat) i.e. have lower risk of cancer than men, regardless of age (37).

Women are more aware of the importance diet has on the overall health and wellbeing (1, 29, 38), with age, education, incomes, residence, number of household members and state of nourishment (observed as BMI) being the important additional determinants for their dietary behaviour (39–41).

Body fatness observed as BMI shows strong positive association with increased risk of CRC (2), and the link is especially strong in men (1, 42). For every 5 kg/m^2 increase in BMI the risk of CRC increases by 9% in men (42). Also, obesity and weight gain seem to be associated with more-aggressive CRC and higher mortality (1, 42). We found that participants in the lower BMI category have a 34% lower risk of having a diet and lifestyle characteristics known to significantly increase the risk of CRC.

Due to industrialization, once large differences in food accessibility and variety between urban and rural areas begin to fade (38, 41). Our findings confirm slight variations between participants from urban and rural areas. However, the only difference was found for intake of vitamin B_{12} from milk and dairy which is much higher among urban residents ($p = 0.028$). In rural areas, people still heavily rely on food they produce, and their diet is under a higher influence of season (38, 41). On the other hand, milk and dairy are considered as a more affordable (cost wise) source of highly valuable proteins in comparison to meat (38, 43). Diet of people living in urban areas is more influenced by socioeconomic characteristics, especially employment status and incomes. Still, high contribution of milk and dairy can mean that people from urban areas are more informed about nutrition and try to compensate for sedentary lifestyle or consumption of fast foods, which are characteristic for urban populations (41). Regardless of the underlying reason for higher consumption of milk and dairy, we found a 56% lower risk of a high-risk CRC diet and lifestyle among urban residents.

High vs. Low-Risk CRC Diet and Lifestyle

Participants were almost equally distributed between the high-risk (52.2%) and the low-risk (47.8%) CRC diet and lifestyle group. Participants in the low-risk group have significantly higher intake of vitamin B_{12} ($p = 0.008$), with the highest contribution from milk and dairy ($p = 0.004$), which have been confirmed to correlate with a diet of better quality (44, 45). In our study intake of vitamin B_{12} from milk and dairy and fish were confirmed as independent factors related with a low-risk CRC diet and lifestyle.

While studies are still inconclusive regarding dietary intake of vitamin B_{12} (13–15, 22–24), high contribution from milk and dairy can be observed as a potential modulator of CRC risk, probably attributable to its high content of calcium (8, 45). Strong inverse correlation was found between intake of calcium (dietary and supplemental) and total cancer risk, and risk of cancers of digestive system, especially CRC (46, 47). Both, dietary and supplemental calcium are considered as probably protective on the risk of CRC (2).

Fish is important source of proteins and unsaturated fatty acids. While inverse association between fish consumption (more than 80 g/day) and CRC risk was found in the EPIC study (48), no association was found in a large prospective study in the United States (49). Recent systematic review by Sala-Vila and Calder (50) concluded that the current evidence does not support increased intake of fish to reduce the risk of cancer.

Strengths and Limitations of the Study

This is an observational study on adult population who live in the region where a typical diet reflects all known major risk factors for CRC. Still, the incidence of CRC in the region, according to the Croatian National Cancer Registry (5, 6) is lower than in other regions characterized with a more Mediterranean-like diet (e.g. coastal regions, Dalmatia).

The study was designed to test the relevance of dietary intake of vitamin B_{12}, total and from major food sources for CRC risk observed as diet and lifestyle characteristics which have been shown to either increase or reduce the risk of CRC (1, 2, 8). Hypothesis presented by Kurbel et al. (19) and inconclusive findings on the role vitamin B_{12} has in CRC (13–15, 22–24) were the reason why focus was put on vitamin B_{12}.

Data presented in the manuscript add up to existing data and support high intake of vitamin B_{12} as one of protective factors for the risk of CRC. Also, women and people in lower BMI category were found to have lower risk of having diets and lifestyle related to a higher risk of CRC. The same was found for urban population. The most important results are identification of vitamin B_{12} intake from milk and dairy and fish as independent factors for a diet and lifestyle characterized with a low-risk of CRC.

However, due to its design, the study does not have the appropriate strength to draw conclusions in terms of reduced risk of developing CRC. We can only speculate that for this population at high risk for CRC, high intake of vitamin B_{12} and especially high contribution from milk and dairy could be one of the underlying reasons of a relatively low CRC incidence.

Presented findings support the need for further analysis on possible interplay between vitamin B_{12} and other nutrients highly abundant in identified food groups, i.e. calcium from milk and polyunsaturated fatty acids from fish. Another nutrient with immense importance in the aetiology of CRC, which shares the same food sources as vitamin B_{12} and calcium is iron. Their interplay seems plausible enough to be analysed further (7).

CONCLUSION

Our results support positive association between higher dietary intake of vitamin B_{12} and a diet and lifestyle characterized with a low-risk of CRC. Women, people from urban areas and those in lower BMI category have significantly lower risk of having a diet and lifestyle with a high-risk of CRC. Confirmed independent protective factors include intake of vitamin B_{12} from milk and dairy and fish.

While no conclusion can be drawn in terms of reduced risk of developing CRC, the results strongly support intake of vitamin B_{12} and contribution from its food sources with a positive, low-risk diet and lifestyle in a population with an increased risk of CRC. Still, further analysis is needed to assess interplay with other nutrients (iron, calcium, polyunsaturated fatty acids) that share the same food sources with vitamin B_{12}.

Conflict of Interests

None declared

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