

## The role of primary care in colorectal cancer screening: Experience from Czech Republic

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Several programmes proven to be effective in the secondary prevention of colorectal cancer (CRC) have already been introduced in Europe, each varying involvement of general practitioners. This paper reviews current screening strategies for CRC from the primary care perspective, looking at the implementation of screening strategies in Europe, focusing on screening programmes based on the faecal occult blood testing (FOBT), and drawing from experiences in the Czech Republic.

We used data on CRC screening from the survey *The Burden of Gastrointestinal Diseases in Europe*, which was undertaken by the Public Affairs Committee of the United European Gastroenterology Federation in 2003. The data were updated by members of European Society for Primary Care Gastroenterology in 2006. For a description of the Czech screening programme, data from General Health Insurance Fund were used. Specific primary care aspects were studied in the research network of 54 general practice settings in the Czech Republic.

National screening programmes have been introduced in several countries, such as Germany, the Czech Republic, Slovakia and Poland. Several important aspects of screening require monitoring: target population adherence, GPs' involvement, assessment of FOBT positive rate, interdisciplinary cooperation, patient compliance and the eligibility of patients for screening. The average population adherence to the screening programmes was low (about 20%). In the Czech Republic, 97 % of GPs participated in the programme, but only 20% of them have been able to screen at least 50 percent of the target population. The eligibility for screening declines with increasing age, co-morbidity and recently performed colonoscopy. In the age group of 50 to 75, approximately 15 % of patients are non-eligible for screening. Finally, the proportion of FOBT positive patients seem higher in established community programmes than the ratio reported from trials.

CRC screening is experiencing a rapid expansion and effective programmes are now available. GPs should play a substantial role in CRC screening either by assessing the risk of their patients, explaining the screening options, or by deciding on the most individually-appropriate strategy within their local health care system. Implications of the population based screening for primary care should be considered and further studied.

**Key words:** colorectal cancer, screening, faecal occult blood testing, primary care, general practitioner

Colorectal Cancer (CRC) is one of the leading causes of cancer deaths in Europe. Tumors of the colon and rectum represent over 300 000 new cases in Europe per year. The Czech Republic, with 76 new CRC cases and 45 deaths per 100,000 inhabitants a year, ranks high among the European countries, together with Slovakia, Hungary and Germany [1]. The CRC incidence rates in 2002 are shown in figure 1. The average 5 year survival rate in Western Europe is 40 %, but only 30% in

Eastern Europe [2]. The factors behind the high incidence of the disease are both endogenous (hereditary) and exogenous (smoking, alcohol intake, lack of exercise, obesity and poor diet). The hereditary based cases represent about 5% of colorectal cancers.

CRC is the most preventable form of visceral cancers. Patients detected in the stage Duke's A, when the cancer is localised within the bowel wall, have the chance for a five-year survival of over 83%; the outlook is worse when the malignancy has spread to lymph nodes (38%), particularly when there are distant metastases (3%). Thus screening and

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early detection of colorectal cancer is important [3]. Several strategies have been proven to be effective in CRC screening.

The incidence data shows that the cancer occurs most often in the age group of 65-75 years, but for adenomas the peak incidence is in a slightly younger age group (55-65 years). Population screening for sporadic colorectal cancer should therefore target age group of those 50 and older. Patients with hereditary syndroms such as familial adenomatous polyps, hereditary non-polyposis colon cancer, those with a long-standing inflammatory bowel disease, or those with first-degree CRC relatives, should all have an individually tailored surveillance program.

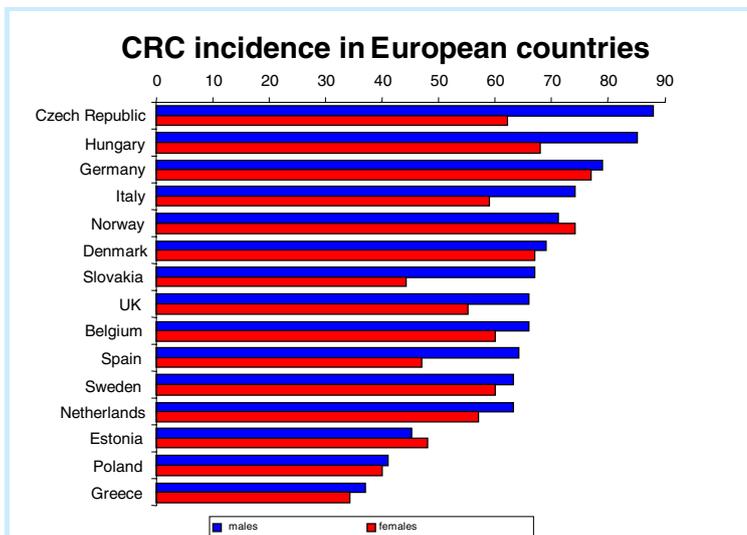
GPs have unique access to their patients, through their medical and family histories. They can play a substantial role in the early prevention and early detection of colorectal cancer. This can be done by providing primary prophylactic recommendations, accurate evaluation of patients with bowel symptoms, and through both the selective screening of high-risk persons and by the screening of the general population. CRC screening has significant implications for primary care physicians.

**Colorectal cancer screening strategies.** The screening strategies for detecting CRC in asymptomatic persons at an early, curable stage include faecal occult blood testing (FOBT), flexible sigmoidoscopy and colonoscopy [4]. *Colonoscopy* is considered to be the most effective screening test, but as a population screening method it is impractical, costly and possibly risky [5]. Colonoscopy remains the only method that combines screening, diagnosis and even prophylactics in the case of polyps removal. It is indicated in a positive result of any other screening methods. It is estimated that regular colonoscopic screening could prevent 76% to 90% of cancers if done every 10 years [6]. Colonoscopy is the screening method of choice for high risk patients.

*Flexible sigmoidoscopy* allows examination of the left side of the colon and rectum, and picks up approximately 75% of all cancers [7]. The role of GP's in programmes based on colonoscopy or sigmoidoscopy is to recruit their patients to specialists. The effectiveness of strategies combining either sigmoidoscopy or colonoscopy (either given once per life or periodically) with FOBT is currently under investigation.

*Faecal occult blood testing (FOBT)* is still considered a reasonable screening strategy [8-12]. Beside the mostly used guaiac tests, there are immunochemical tests and stool-based DNA tests available but they have not been sufficiently evaluated at a large scale. Among FOBT-positive patients, 20-45% will have polyps and 10-15% will have a colorectal cancer at colonoscopy.

The guaiac-based *FOBT* has been the most extensively studied screening test for colorectal cancer [9]. The test is cheap, easy to perform by the patient, and to easy evaluate in the office. Sensitivity of the single test for any FOBT is less than



**Figure 1. Colorectal Cancer Incidence in European countries (per 100,000 person/year)**

**Source: Globocan 2002. International Agency for Research on Cancer, published 2004.**

50%; larger benefit can be obtained if the test is repeated. Although annual testing is likely to result in greater mortality benefits, the cost requirements support a biennial screening, initially. The specificity of a FOBT (rate of negative tests in the absence of CRC) is a principal aspect regarding costs and harm; this is because false-positive tests account for the colonoscopic examinations' overuse. Meta-analysis of mortality results, from the randomised controlled trials (RCT) on FOBT screening [8] shows that those allocated to screening had a reduction in colorectal cancer mortality of 16% (RR 0.84, CI:0.77-0.93). Screening benefits also include possible reductions in cancer incidence, through the detection and removal of colorectal adenomas and potentially through the treatment of early colorectal cancers which would involve less invasive surgery.

Although screening benefits are likely to outweigh harms for population at increased risk of CRC, more information from already established community programmes and responses to them are needed. The aim of this article is to share the experience from the Czech national CRC screening programme, established in 2000.

## Methods

Data on the incidence of colorectal cancer in European countries were taken from Globocan 2002, International Agency for Research on Cancer [1]. Reliable informations on CRC screening strategies were performed according to the results of relevant studies [6,7,8,9,10,11,12]. The description of the status and data concerning the implementation of CRC screening programmes in Europe came from a survey under-

taken by the Public Affairs Committee of the United European Gastroenterology Federation: *The Burden of Gastrointestinal Diseases in Europe*, presented at the Madrid UEGW, 2003 [13]. This information was updated by the member network of European Society for Primary Care Gastroenterology 2006.

This paper used the six years experience of the national screening programme in the Czech Republic [14,21,23,24,25]. For a quantitative description of the Czech screening programme, data from the General Health Insurance Fund (GHIF) and from the National Health Statistics Institute were used. Clients of GHIF amount to 7 million people from which 1,75 million belong to the target group (above the age of 50 years) for screening.

Several aspects important for FOBT based population screening in primary care settings were reviewed drawing from the experience in the Czech Republic. Screening programme monitoring and data collection were performed in a network of 54 general practice settings. These aspects are adherence to screening and compliance, eligibility for screening, FOBT-positive rate and the impact of screening on primary care setting.

## Results

*Colorectal cancer screening programmes in Europe.* There is a widespread interest in colorectal cancer screening in Europe. National screening programmes have been introduced in several countries, such as Germany, the Czech Republic, Slovakia and Poland, and it have been seriously considered in other countries, such as Hungary, Austria, Italy, UK, France and The Netherlands (Table 1). The involvement of GPs varies according to the chosen screening strategy. Screening must be accepted and implemented by the central government but the GP's and primary care staffs' commitment and accep-

tance of the programme is crucial. Primary care's contribution to population-based screening includes explanation, encouraging participation in screening and active involvement in media campaigns to raise public awareness for colorectal cancer screening. In countries such as the Czech Republic and Slovakia, concerning FOBT based programmes, general practitioners are actually doing the systematic screening in their offices, and have a crucial role in the programme.

*National screening programme in the Czech Republic 2000-2006.* The FOBT has become a part of the regular, preventive check for asymptomatic people over the age of fifty; it has been provided by GPs every two years, since the year 2000 in the Czech Republic. GPs buy the FOBT kits for themselves, distribute them to patients and then analyse them in their office upon completion. Upon FOBT completion, the practice is reimbursed. In case of FOBT-positive result, patients are referred to outpatient or inpatient departments of gastroenterology, accredited for screening colonoscopy. The Czech Republic has 10,5 million inhabitants.

### 1) Adherence to the screening programme

The global data after six years demonstrate that about 20% of the target population participated in the programme. 97 % of 5000 GPs in the country joined the screening programme, but only 20 % of them reached 50 % FOBT coverage of the target population of those over fifty. GPs with higher rates of FOBTs performed have had higher costs and workload using a system of repeated interventions and reminders.

### 2) Workload of GPs and specialists

In absolute numbers, 650 000 FOBTs were performed in a primary care settings within a two year period (2004-2005). GPs who achieved 50% participation of the target population in screening performed 150 FOBTs a year in average. A distinct increase in the number of total colonoscopies (up to 40 %) and endoscopic polypectomies (up to 80 %) com-

**Table 1. Implementation of CRC screening in Europe. Data from *The Burden of Gastrointestinal Diseases in Europe* undertaken by the Public Affairs Committee of the United European Gastroenterology Federation, 2003. Updated by European Society for Primary Care Gastroenterology (ESPCG) in 2006.**

Countries	Incidence (per 100,000 persons) (M/F)	National CRC screening programme	Method
CZECH REP.	88 / 62	national programme established in 2000	FOBT/colonoscopy
HUNGARY	85 / 68	national programme prepared	FOBT/colonoscopy
GERMANY	79 / 77	established in 1977, adapted in 2002	FOBT/colonoscopy
ITALY	74 / 59	different options of screening since 2000	Sigmoido/colonoscopy
NORWAY	71 / 74	decision process started	Not decided yet
DENMARK	69 / 67	national screening studies	Not decided yet
SLOVAKIA	67 / 44	national programme established in	FOBT/colonoscopy
UK	66 / 55	programme prepared and planned for 2007	FOBT/colonoscopy
BELGIUM	66 / 60	national screening studies	Not decided yet
SPAIN	64 / 47	new topic	
NETHERLANDS	63 / 57	discussed, programme postponed 4 years	
POLAND	41 / 40	national programme established in 2000	Colonoscopy
ESTONIA	45 / 48	new topic	

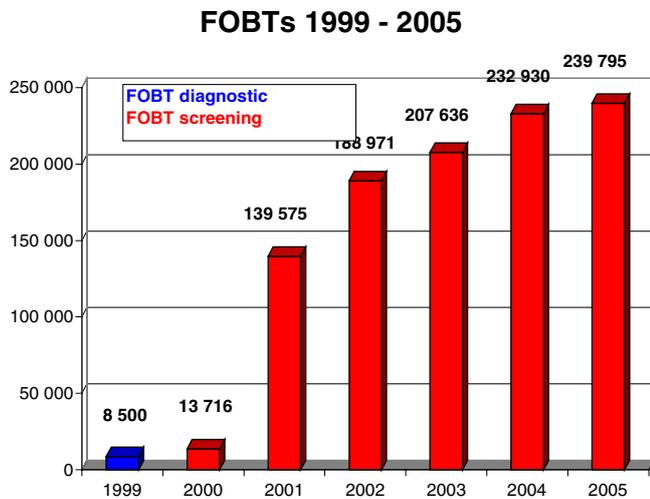


Figure 2. Number of FOBTs performed in general practice during years 1999 – 2005 in General Health Insurance Fund clients. GHIF covers 7 million people, 1,75 million in age over 50.

pare to situation in 2000 was registered, as well as a trend of increase in curative resections. In 2005, out of all 98 134 total colonoscopies performed, 11% were based on a positive FOBT (Figures 2 and 3). The waiting times for colonoscopy for persons screened FOBT-positive did not exceed 3 weeks anywhere in the country. Another finding, from GP settings in the Czech Republic, showed that 10-20 % of persons subsequently refused colonoscopy after testing FOBT-positive.

3) Eligibility for colorectal cancer screening in patients registered in general practice

Not all patients over fifty are eligible for screening due to different clinical reasons. The eligibility for screening of persons over fifty, who were registered to GPs, was thus a subject of a separate study.

General practitioners were asked to register their patients who were non-eligible for screening, due to age, serious comorbidity, follow up programmes or due to a recent colonoscopy based on symptoms. Patients who were addressed and strictly refused screening, were also registered. Data from 9 general practices, registering a total of 7309 persons over fifty, were analysed. 1681 persons (23%) were found non-eligible for screening. 212 persons (3%; 66% of them were men) strictly refused FOBT. In the age group 50-75 (5704 persons), 742 persons (13%) were determined to be non-eligible. In the age group over 75 (1605 persons), 915 persons (57%) were found to be clinically non-eligible for screening. 32 patients (2%) were undergoing anticoagulation therapy. The study concluded that one quarter of persons over fifty registered in a general practice, were non-eligible for FOBT screening. The better rate was found in persons of age group 50-75, but the non-eligibility rate was still 13-17%. The non-clinical reasons for when FOBT was not appropriate included the strong negative personal attitudes some people had.

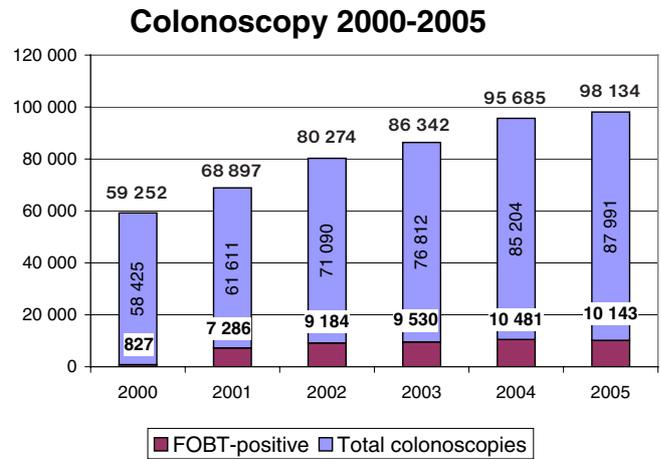


Figure 3. Number of all colonoscopies and colonoscopies performed on the basis of positive FOBT in GHIF clients in the period 2000-2005.

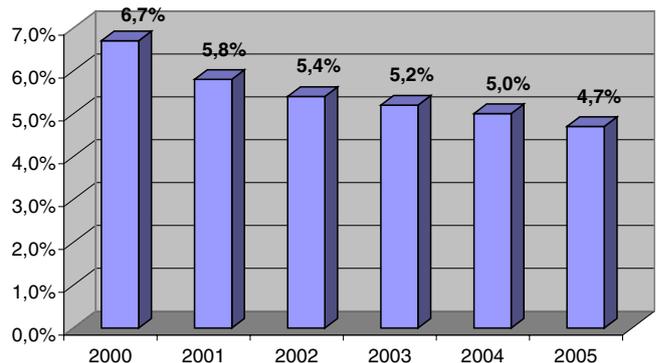


Figure 4. FOBT-positive rate (percentage) in subjects screened in the period of 2000-2006

4) FOBT- positive rate

The ratio of positive FOBT in the first year of Czech national screening programme (2000) was 6,7 %, then 5,6 % in 2002, and finally 4,8 % in 2005 (Figure 4).

These are indirect data, relating programme effectiveness, while the direct data (mortality, tumor staging) are expected in a few years time.

5) Other aspects

The establishment of the Czech screening programme for colorectal cancer involves even some other aspects. There were regional variations in cooperation between GPs and gastroenterologists. Some GPs expressed concerns in relation to the resultant increase in their workload, possible harm to asymptomatic patients, and possibility of ungrounded reassurance for patients following a negative FOBT result. This could result in the underestimation of the significance of CRC

symptoms, which occurred later on. Other concerns included low reimbursement rates, an increase in health costs as a result of the screening programme, and possible litigation as a result of participation in the programme. Also frequent questions have been asked in relation to patient inclusion and exclusion criteria.

Strategies for change were implemented in cooperation of both Czech Society of General Practice and Czech Society of Gastroenterology. Interdisciplinary seminars were organized throughout the whole country to discuss topics and to explore avenues for improvement. Regional CME activities for physicians and nurses have been organised including both theoretical and practical training in FOBT.

## Discussion

Despite recent development, there has been no real improvement for the treatment outcomes in colorectal cancer. Therefore, screening and early detection will continue to be vital in the future. Colorectal cancer screening is experiencing a rapid expansion, and effective programmes are now available.

FOBT is considered a reasonable screening strategy, while colonoscopy is the method of choice for high risk patients. It is not yet clear which simple method or which combination of methods will prevail.

The task for GPs is to assess the risk of patients, explain the screening options and then to decide on the most individually appropriate method possible within the boundaries of their respective health care system. The involvement of primary care staff is crucial for population adherence and compliance.

The adherence to CRC screening is a key factor on determining its effectiveness to reduce mortality. There are different strategies, both used and suggested to enhance participation, such as a national or local media campaign, reminder letters, and through telephoning. The general social context of the screening is important, and includes involvement of state administration, sick funds, and support of both patients and physicians. The compliance for FOBT screening varied between 50-60% in European randomised trials.

Regional trials had previously demonstrated the feasibility of FOBT programmes in general practices in the Czech Republic, and also the potential compliance of the Czech population [21]. In terms of professional capacity, the conditions for a screening programme have been favourable. 90 % of the population are registered with GPs, and there are more than four hundred specialists in gastroenterology employed in the health system.

There has been confusion between patient compliance compared to population adherence of the programme. In both, large prospective studies performed in the Czech Republic in 1985-1991 and 1997-1998 83-89 %, of probands, have produced the Haemocult slides [21,22]. A study from the French region showed a 29% return rate in tests sent to patients by

mail [23]. Data from Czech practices demonstrate that 80-90 % of patients who obtained a test in the practice returned it within three months. These make up the compliance of the data. The overall adherence of the target population to the screening programme is much lower, however (less than 20%). The results with regards to adherence, are comparable to the German experience, where a CRC screening programme has been established since 1976. Similar adherence has been reported from Slovakia.

In comparison to distributing test by post, delivering test by GP or nurse directly in practice is more effective [23].

The data on incidence of sporadic CRC, suggest a starting age of 50 years. With age increase, the cancer becomes prevalent, but potential years of life saved through screening decrease. The screening should stop at the age when the potential to prolong a life is low. The results of eligibility study support seventy five as an appropriate upper age limit for screening interventions. On the other hand half of patients over seventy five was found eligible for screening. There should be an individual approach in this age group [25].

The other concern is the workload involved and the capability of GPs to evaluate the tests in their office. Mortality reduction demonstrated in clinical trials may not be achieved in community practices because of inappropriate tests, techniques, and the inappropriate follow up of positive results [19]. Another concern is screening costs and feasibility of screening for different health care systems. The cost-benefit study which was performed in nineties in the Czech Republic showed that the costs was balanced against benefit [20].

Another aspect of screening is its potential harm for asymptomatic people. Diet restrictions increase the test accuracy but make the test more complicated. Handling with faecal material can be perceived as inconvenient and unpleasant. The harmful effects of screening include the physical complications of colonoscopy, disruption of lifestyle, the stress and discomfort of testing, and the anxiety caused by false-positive screening results [15]. Also, false negativity can bring ungrounded reassurance and diagnostic delay for persons with cancer or a pre-malignant condition. False positivity, however, will lead to unnecessary procedures and stress as was mentioned earlier. In some people screening generates fear and anxiety about the possible results, the procedures, and the potential loss of their socioeconomic position, etc. In previous Czech studies, the FOBT positivity rate was 2,9 % and 3,9 % respectively. It corresponded with the results of major RCTs [9], where false-positive rates for FOBT ranged from 2,1 % [16]. to 5 % [17]. A higher FOBT-positive rate found in the Czech programme thus means a higher number of false positive tests resulting in anxiety and redundant colonoscopies with possible risk of complications. Higher rates were reported even from the first years of the CRC screening FOBT-based programme, established in Slovakia.

The higher FOBT positivity may be due to:

- limited experience of GPs and nurses in analysing samples in practice
- use of different types of FOBT
- including symptomatic patients in screening (using FOBT as a diagnostic tool).

FOBT screening as a reimbursed and evaluated performance measure, in general practice, can result in inappropriate screening in order to improve screening rates. In one study FOBT was found inappropriate in a third of the sample, most commonly because of a documented life-limiting comorbidity, and its use for diagnosis instead of screening [18].

Programme itself has brought several added values. It has contributed significantly to the CRC awareness among GPs and public and possibly helped to improve early diagnosis of the cancer. As a result of many central and regional round tables between gastroenterologists and GPs the interdisciplinary cooperation has improved with the benefit for patient (bowel preparation, explanation of procedure, waiting times).

And finally campagne for CRC screening has attracted people to other preventive oncological or cardiovascular interventions provided by GPs.

The Czech experience contributes to questions about the community's responses to screening and feasibility for different health care systems:

- FOBT screening is feasible and fits well to systematic preventive activities in general practice.
- The appropriate age range for screening is 50 to 75, with approximately 15 % of patients non-eligible for screening
- To increase the adherence to the screening a system of repeated interventions and reminders should be established within the practice
- The FOBT positivity rate must be watched carefully and analysed similarly to colonoscopy results
- The programme must be supported by an ongoing media campaign
- CRC screening requires close and effective interdisciplinary cooperation, in both education and organization, at a central and regional level

## References

- [1] FERLAY J, BRAY F, PISANI P, PARKIN DM. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No. 5, version 2.0., Lyon: IARC Press 2004.
- [2] BERRINO F, CAPOCACCIA R, ESTEVE J et al. Survival of Cancer Patients in Europe: the EURO-CARE-2 study. IARC Scientific Publications No 151, Lyon, France 1999.
- [3] LIGNINE M, RICH M, TEUTECH S et al. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the US preventive services task force. *Ann Intern Med* 2002; 137: p.132–141.
- [4] RANSHOFF DF. Colon cancer screening in 2005: status and challenges. *Gastroenterology* 2005; 128: p.1685–1695.
- [5] ARAGHIZADEH FY, TIMMCKE AE, OPELAK FG et al. Colonoscopic perforations. *Dis Colon rectum* 2001; 44: 713–716.
- [6] LIEBERMANN DA, WEISS DG, BOND JH et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380, *N Engl J Med* 2000; 343: 162–166.
- [7] ATKIN WS, COOK CF, CUZICK J et al. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial. *Lancet* 2002; 359: p.1291–1300.
- [8] TOWLER BP, IRWIG L, GLASZIOU P et al. Screening for colorectal cancer using the faecal occult blood test, Hemocult. *BMJ* 1998; 317: 559–565.
- [9] BOND J. fecal occult blood test screening for colorectal cancer. *Gastrointest Endosc Clin North America* 2002; 12: p.11–21.
- [10] BOND J. The place of Fecal Occult Blood Test in Colorectal Cancer Screening in 2006: The U.S. perspective. *Am J Gastroenterol* 2006; 101: 219–221.
- [11] STEELE JC. Fecal Occult Blood Test Screening in the United Kingdom. *Am J Gastroenterol* 2006; 101: 216–218.
- [12] SUNG J. Does Fecal Occult Blood test Have a Place for Colorectal Cancer Screening in China in 2006? *Am J Gastroenterol* 2006; 101: 213–215.
- [13] *Gastrointestinal Cancers in Europe in: The Burden of Gastrointestinal Diseases in Europe*, Public Affairs Committee, UEGF, 2003.
- [14] SPICAK J, WOHL P, PETRYL J et al. The national screening programme based on FOBT: the yield of colonoscopy. *Endoscopy*, in press.
- [15] ROBINSON MHE, HARDCASTLE JD, MOSS SM et al. The risks of screening: data from Nottingham randomised controlled trial of faecal occult blood screening for colorectal cancer. *Gut* 1999; 45: 588–589.
- [16] COLOMBOL, CORTIG, MAGRIF et al. Results of a pilot study of endoscopic screening of first degree relatives of colorectal patients in Italy. *J Epidem Comm Hlth* 1997; 51: 423–58.
- [17] LINDHOLM E, BERGLUND B, KEWENTER J et al. Worry associated with screening of colorectal carcinomas. *Scand J Gastroenterol* 1997; 32: 238–45.
- [18] FISHER DA, JUDD L, SANFORD NS. Inappropriate colorectal cancer screening: findings and implications. *Am J Gastroenterol* 2005; 100: 2526–30.
- [19] NADEL MR, SHAPIRO JA, KLABUNDE et al. A national survey of primary care physicians' methods for faecal occult blood. *Ann Intern Med* 2005; 142: 86–94.
- [20] FRIC P, ZAVORAL M, DVORAKOVA et al. An adapted programme of colorectal cancer screening – 7 years experience and cost-benefit analysis. *Hepatogastroenterol* 1994; 41: 413–416.
- [21] ZAVORAL M., ZAVADA F, FRIC P. The Czech national programme of secondary prevention of colorectal cancer. (in Czech, English summary) *Ces a Slov.Gastroent Hepatol* 2005; 59: s.7–12 (In Czech).
- [22] ZAVORAL M, ZÁVADA F, ŠÁLEK C, FRIČ P. Czech Society of Gastroenterology: Colorectal Cancer Screening in the Czech Republic. *Endoscopy* 2006; 38: 550–551.

- [23] DENIS B, PERRIN P, BELIN J et al. First results of a pilot population-based faecal occult blood colorectal cancer screening programme. UEGW 2005. Gut 2005; 54 (Suppl VII): p.A246.
- [24] SEIFERT B, HERBER O. The role of General practitioners in colorectal cancer screening. In: Improving patient care in primary care in Europe, EQuIP, NHG 2004, ISBN 90-5793-175-3, p. 44–49.
- [25] SEIFERT B. Eligibility for colorectal cancer screening with fecal occult blood testing in patients registered in general practice (in Czech, summary in English) Čes a Slov Gastroent a Hepatol 2005; 59), 105–107 (In Czech).