ORIGINAL ARTICLE _____

Discrepancies and misconceptions of perceived colorectal cancer screening barriers between primary health professionals and unscreened population. A comparative study in Greece

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Summary

Purpose: _Our study aimed to compare the views of healthy eligible unscreened adults, to those of primary care providers in Greece, about colorectal cancer (CRC) screening perceived barriers._

Methods: _A sample of 791 unscreened adults (50-75 years) from a recent nationwide health survey in Greece were interviewed about CRC screening barriers, and the main reason for not adhering to colonoscopy and fecal occult blood test (FOBT) was assessed. Results were compared to a concurrent survey of 161 primary care professionals (PCPs) from the same region and the agreement with the general population was assessed with odds ratios (OR) and 95% confidence intervals (CI)._

Results: _General population stated as a primary barrier for colonoscopy, at a significant higher frequency than the PCPs (p<0.001), lack of symptoms (44.5 vs 5.7%), negligence (14.2 vs 3.8%) and lack of PCP recommendation (9.2 vs 2.5%)._

PCPs were more likely to agree for fear of pain of colonoscopy (OR:19.6, 95%CI 9.3-41.4), fear of cancer diagnosis (OR:17.7, 95%CI 10.8-29.1), and embarrassment (OR:13.8, 95%CI 8.1-23.6). Regarding FOBT, the most frequent barrier for the unscreened population compared to PCPs (p<0.001), was lack of symptoms (38.2 vs 3.9%), followed by unawareness of the test (22.9 vs 55.2%) and lack of PCP recommendation (13% vs 12.3%). The only barrier that PCPs agreed at significantly lower frequency was the lack of physician recommendation (OR:0.3; 95%CI 0.2-0.4).

Conclusions: _PCPs do not share the same views as the general population about CRC screening barriers in Greece. PCPs should focus counseling on patient perceived barriers in order to promote adherence._

Key words: _barriers, colonoscopy, colorectal cancer, FOBT, primary care professionals, screening_

Introduction

The significance of early detection and CRC screening is well documented and supported by all international committees and expert groups. International guidelines recommend that all average risk persons aged 50 or older should be screened periodically, with fecal occult blood test (FOBT) and/or colonoscopy or flexible sigmoidoscopy [1-4].

Participation rate is a key indicator of a cancer screening program's acceptance and effectiveness

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[5]. In the case of Greece, participation rates are far from optimal, varying from less than 2% for FOBT for screening purposes [6] to 10% [7]. The most recent survey of general population in Greece (EMENO Health Study) reports similar results (7% for FOBT and 21% for colonoscopy) [8].

As in some other European countries, in Greece CRC screening is still mainly opportunistic [6,9]. Generally, PCPs advice CRC screening tests during routine health checks or after a clinical visit of eligible adults in their practice for some other health issue. It is not uncommon that individuals request the tests on their own initiative, sometimes from a specialist and not a PCP [10]. In an opportunistic screening program, the physicians' role can be seen as a barrier because participation is predominantly dependent on physician's referral [11].

In Greek studies that investigated PCP screening behaviors and recommendation rates, physicians were found not to routinely recommend CRC screening tests (FOBT or colonoscopy) compared to PAP test, mammography and even PSA [10,12].

This was attributed to the physician's perceptions of CRC screening tests not being useful, as well as the unpleasant nature of the tests and the lack of endoscopic facilities [10].

The body of literature about CRC screening barriers consists of reports from different samples of general population, not taking into account the provider perspective. Few studies have addressed provider views about CRC screening barriers and even fewer have compared the perceived barriers both from the provider and the general population perspective [13,14].

In Greece in particular, there are only a few studies assessing CRC barriers and data from PCPs on barriers are even more limited. To our knowledge, this study is the first to compare the perceived CRC barriers in Greek unscreened population and PCPs. Our study aimed to compare the views of healthy adults, who were never screened or were not up-to-date with current screening recommendations, to those of PCPs, about CRC screening perceived barriers. The rationale is that a compara-
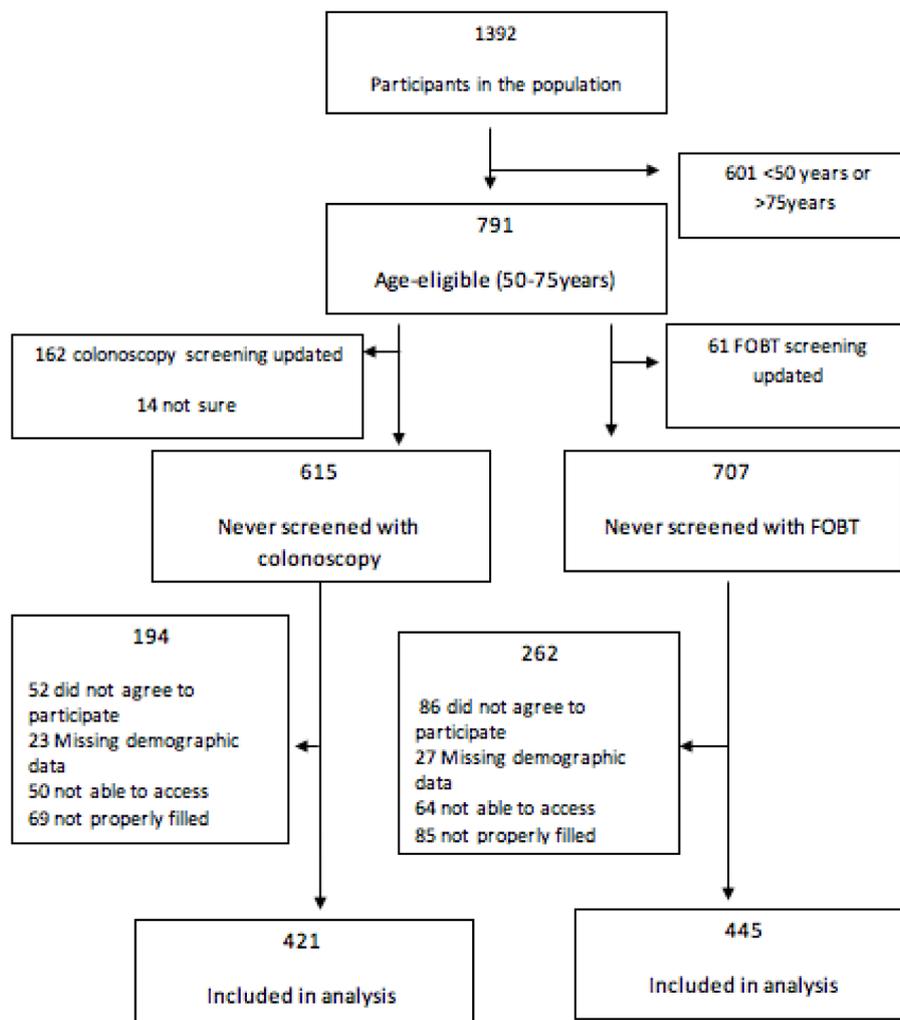

Figure 1. Flow diagram describing participation in the general population sample.

tive study would provide a better understanding of potential discrepancies and may be useful to find common ground in perception of facilitators and barriers. We, therefore, hypothesized that there is a deviation of patient perceived barriers for CRC screening between the general population and primary health care professionals.

Methods

Population based survey

We pooled data from the recent nationwide population-based study EMENO (National Morbidity and Risk Factors Survey) which included 6000 adults in Greece [8]. In the EMENO study, a multistage stratified cluster random sampling method was applied, according to European Health Examination Surveys (EHES) protocols [15] to provide a representative sample of the general population. The field study was conducted from April 2014 to November 2015 and had received permission from the Medical School Ethics Committee of the Kapodistrian University of Athens and from the Hellenic Data Protection Authority. Signed informed consent was obtained from all individual participants included in the study.

Out of this dataset, a subgroup including a total number of 1392 participants in the EMENO study referring to Northern Greece was identified. Eligible participants were asymptomatic, average risk adults 50-75 years old. Adults over 75 years old were not included, because according to the suggested guidelines, they are not eligible, as they may not benefit from CRC screening [16,17]. Additionally, inclusion criteria required that participants should have reported that they had not any CRC screening tests (FOBT and/or colonoscopy/sigmoidoscopy) either ever or for the last six years. The period of six years was chosen on the basis that is a safe interval to declare someone as not screened up-to-date and complies with most guidelines. The participants' flowchart is demonstrated in Figure 1.

All eligible respondents (791 adults) were further interviewed face to face, by trained field researchers, using a specific questionnaire with close and open-ended questions. Data from the EMENO study database, about sociodemographic and other characteristics (age, gender, marital status, education, income, work status, insurance) were also employed.

The questionnaire included open-ended questions about the principal reason for not participating in colonoscopy/sigmoidoscopy and FOBT separately, as both tests are used currently interchangeably for CRC screening in Greece [6]. At this point, there were no probes for specific answers and participants were encouraged to express freely only the most influential reason for not having colonoscopy and/or FOBT separately. Responses, in the stage of analysis, were entered in an Excel worksheet and reviewed independently by two members of the research team and coded using content analysis. The coded data were again reviewed, until a consensus was reached, resulting in the final categories of principal barriers. These categories were then treated as quantitative data and expressed as frequencies.

Participants were also asked to state their level of agreement, in a 4-level Likert scale, in a statement inquiring about the most frequently cited barriers for each screening test. This list was formed after extensive literature research on the published papers on CRC screening perceived barriers and after cultural and conceptual moderation for the Greek context [13,14,18-23]. The 4-level scale (I agree-I somewhat agree- I somewhat disagree- I disagree) was chosen in order to force opinion and avoid neutral responses. The full CRC screening perceived barriers questionnaire we developed and used is presented in the Appendix.

PCP survey

To test the hypothesis that there is a deviation of perception of CRC barriers between PCPs and the general population, we conducted a concurrent survey that included a sample of PCPs from the same district in Northern Greece, approached during a regional scientific venue for primary health care. This sample, although conveniently selected, was from the same region as the general population sample.

A total number of 161 out of 213 administered questionnaires were properly filled and analyzed, resulting in a 75% response rate. A modified version of the same questionnaire as the general population survey was used to depict their perspective towards the principal reason health service users did not participate in CRC screening tests. Respectively, they also stated in the same 4-level Likert scale the level of agreement in the exactly same list of common cited patient perceived barriers as previously reported in the general population study.

Questionnaires were specifically designed for the study, piloted firstly in a group of ten volunteer PCPs and finally evaluated by a group of primary health care and research methodology experts of the Medical School of Aristotle's University of Thessaloniki.

Statistics

Quantitative data were summarized with means and standard deviations (SD) whenever normally distributed or else with medians and interquartile ranges (IQR). Qualitative variables were described with frequencies and percentages. In order to assess agreement between PCPs and general population about the perceived CRC screening barriers, we compared the computed "agree" variable (sum of agree-somewhat agree) for each barrier. Moreover, to better comprehend the magnitude of the diversion is responses between PCPs and general population, we calculated the likelihood to agree on each barrier, undertaking a series of logistic regressions (LR). Odds ratios (OR) with the respective 95% confidence intervals (CI) were presented. An OR>1 denoted that PCPs agreed more often than the general population on the specific perceived barrier, while an OR<1 denoted that PCP agreed less often than the general population on the specific perceived barrier. P values were two-tailed at a significance level of 5%. All analyses were conducted using the statistical package IBM/SPSS version 24.0.

Table 1. Sociodemographic characteristics of CRC unscreened individuals with either or both methods (FOBT, colonoscopy)

Characteristics	n/N (%)
Gender	
Male	202/445 (45.4)
Female	243/445 (54.6)
Marital status	
Single	23/445 (5.2)
Married	322/445 (72.4)
Divorced	23/445 (5.2)
Widowed	77/445 (17.3)
Education	
No school	45/445 (10.1)
Elementary	194/445 (43.6)
High school (3 years)	58/445 (13.0)
High school graduate (6 years)	77/445 (17.3)
University/ College graduate	71/445 (15.9)
Employment	
Unemployed	32/445 (7.2)
Employed	117/445 (26.3)
Retired	223/445 (50.1)
Domestic employment/Other	73/445 (16.4)
Residence	
Urban	147/445 (33.0)
Rural	298/445 (67.0)
Health insurance	
Yes	414/445 (93.0)
No	5/445 (1.2)
Unknown	26/445 (5.8)
Private health insurance	
Yes	12/445 (2.7)
No	429/445 (96.4)
Unknown	4/445 (0.9)
Citizenship (Greek)	
Yes	427/445 (96.0)
No	18/445 (4.0)
Family income (€/month)	
<350	43/445 (9.7)
351-700	98/445 (22.0)
701-900	53/445 (11.9)
901-1150	65/445 (14.6)
1151-1400	39/445 (8.8)
1401-1700	31/445 (7.0)
1701-2100	22/445 (4.9)
>2100	28/445 (6.3)
I do not know/wish to answer	66/445 (14.8)
Mean age, years (SD)	64.6 (10.8)
Median school, years (IQR)	6.0 (6.0, 12.0)

n: the number of responses, N: the total number of subjects

Results

Population survey

From the EMENO study database for this region, 791 adults from an original sample of 1392 were eligible (between 50 and 75 years of age). Among those, 615 (78%) were never screened with colonoscopy/sigmoidoscopy, 707 (89%) were never screened with FOBT, while 585 (74%) were not screened with neither. Four hundred twenty one were included in the analysis for colonoscopy/sigmoidoscopy and 445 for FOBT (Figure 1).

The main sociodemographic characteristics of the unscreened sample are depicted in Table 1. The majority of the respondents were female (54.6%), married (72.4%), with elementary education (43.6%). Most were retired pensioners (50.1%),

Table 2. Sociodemographic and work characteristics of PCPs

Characteristics	n/N (%)
Gender	
Male	47/161 (29.2)
Female	114/161 (70.8)
Profession	
Physician	114/161 (70.8)
Non physician	47/161 (29.2)
Physician specialty	
General practitioner	97/114 (85.1)
Other specialties	17/114 (14.9)
Postgraduate degree	
Yes	30/159 (18.9)
No	129/159 (81.1)
PhD degree	
Yes	7/158 (4.4)
No	151/158 (95.6)
Position	
Intern	35/149 (23.5)
Specialist	79/149 (53.0)
Nurse	20/149 (13.4)
Other	16/149 (10.7)
Practice	
Public provider	139/159 (87.4)
Private practice	17/156 (12.6)
Practice location	
Urban	82/137 (59.8)
Rural	55/137 (40.2)
Mean age in years	43.6 (7.7)
Median years of Work Experience (IQR)	10.0 (5.3, 20.0)

n: the number of responses, N: the total number of subjects

only 26.3% were employed, while unemployment rate in this sample was 7.2%. The mean age of the sample was 64.6 (SD:10.8) years.

PCP survey

Most primary care providers in this sample were female (70.8%), specialists (52.3%) and general practitioners (85.1%). The median work experience was 10 years (range 0-35) and the majority practised in urban areas (60%), in public primary care facilities (76%). In Table 2 the main sociodemographic and work characteristics of the PCP sample are demonstrated.

CRC barriers and comparison

In Table 3, the results of the answers of the unscreened population and PCPs about the most important barrier for colonoscopy and FOBT are presented. The most frequent barriers that the general population stated, at a significant higher frequency than the PCPs, for colonoscopy were the lack of symptoms (44.5 vs 5.7%), negligence (14.2 vs 3.8%) and lack of PCP recommendation (9.2 vs 2.5%). On the other hand, PCPs reported more frequently, as primary barrier, the fear of pain (22.8 vs 5.3%), the unawareness of the test (22.2 vs 10.8%), the difficulty of the test (14.6 vs 0.3%) and embarrassment (13.9 vs 0.5%). Remarkably, all other barriers were reported at a very low frequency

for both groups. All differences were significant (p<0.001).

Regarding FOBT, the results seem to be quite similar and also differed significantly between the two groups; the most frequent barrier for the unscreened population was again the lack of symptoms (38.2 vs 3.9%), followed by unawareness of the test (22.9 vs 55.2%), lack of PCP recommendation (13 vs 12.3%), negligence (10.5 vs 7.1%) and not being necessary (6.7 vs 7.8%). Several other barriers were reported by a rate less than 3% by both the general population and PCPs.

Significant differences in agreement were observed between PCPs and the general population for almost all barriers for colonoscopy, with the exception of lack of symptoms (82.1% PCP vs 84.7% general population, p=0.492) and having more important things to do (40% PCP vs 33.3% general population, p=0.181). In fact, PCPs agreed more often than the general population in the specified perceived barriers for colonoscopy/sigmoidoscopy. Specifically, PCPs were almost 20 times more likely than asymptomatic adults to agree for fear of pain of colonoscopy (OR:19.6, 95%CI 9.3-41.4), 18 times for fear of cancer diagnosis (OR:17.7, 95%CI 10.8-29.1), 14 times for embarassment (OR:13.8, 95%CI 8.1-23.6), 10 times for test preparation (OR:10.4, 95%CI 5.5-19.7). The only barrier that PCPs agreed on, at significantly lower frequency than

Table 3. Frequencies of responses to the question [a] for the principal barrier for colonoscopy and FOBT*

Primary reason	Colonoscopy		FOBT	
	Unscreened population	*PCP*	*Unscreened population*	*PCP*
	% (n/N)	*% (n/N)*	*% (n/N)*	*% (n/N)*
Lack of symptoms	44.5 (169/380)	5.7 (9/158)	38.2(153/401)	3.9 (6/154)
Negligence	14.2 (54/380)	3.8 (6/158)	10.5(42/401)	7.1(11/154)
Do not know what the test is about	10.8 (41/380)	22.2 (35/158)	22.9 (92/401)	55.2 (85/154)
Lack of PCP recommendation	9.2 (35/380)	2.5 (4/158)	13.0 (52/401)	12.3 (19/154)
Fear of pain	5.3 (20/380)	22.8 (36/158)	0	0
Not necessary	5.8 (22/380)	3.2 (5/158)	6.7 (27/401)	7.8 (12/154)
Financial issues	1.8 (7/380)	4.4 (7/158)	0.5 (2/401)	0.6 (1/154)
Difficulty of access	0.5 (2/380)	1.3 (2/158)	0.2 (1/401)	0.6 (1/154)
Other priorities	2.1 (8/380)	0.6 (1/158)	3.2 (13/401)	1.3 (2/154)
Long waiting list	0.3 (1/380)	1.9 (3/158)	0	0
Difficulty of the test	0.3 (1/380)	14.6 (23/158)	0	3.9 (6/154)
Embarrassment	0.5 (2/380)	13.9 (22/158)	0.2 (1/401)	3.2 (5/154)
Relationship with PCP	1.3 (5/380)	0.6 (1/158)	0.5 (2/401)	0
Fear of diagnosis	1.1 (4/380)	0.6 (1/158)	1.7 (7/401)	0.6 (1/154)
Other	2.4 (9/380)	1.9 (3/158)	1.0 (4/401)	3.2 (5/154)

[a] "What do you believe was the most significant reason for not having this screening test? Please state only the primary reason"
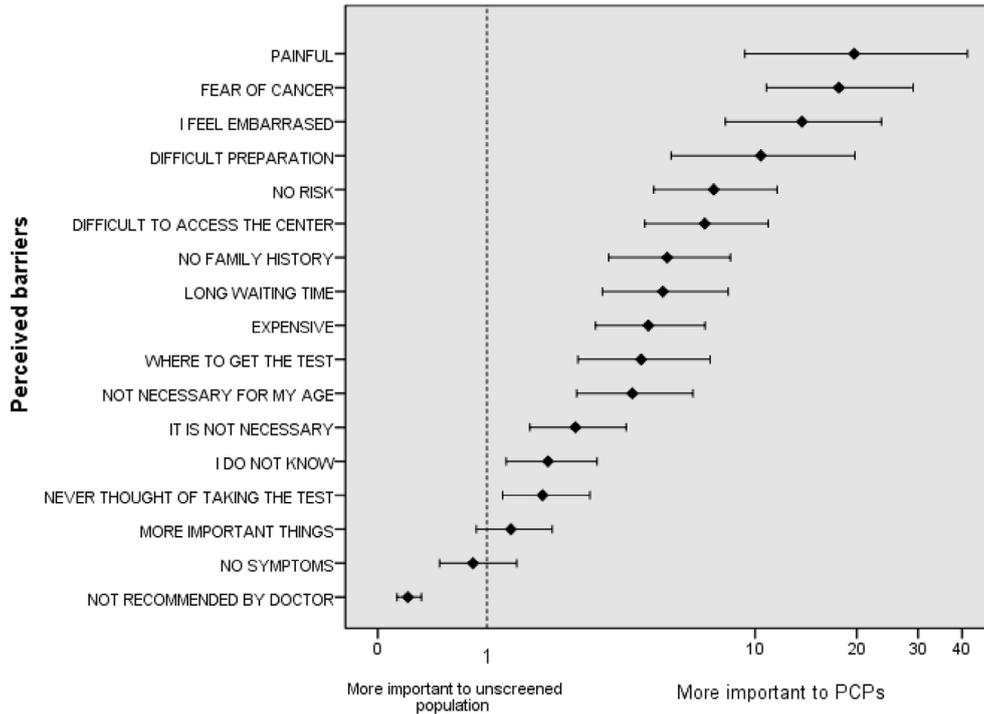*Fisher's exact test, p<0.001

Figure 2. Comparison of reported barriers to colonoscopy/sigmoidoscopy by general population adults >50 years, who had not been ever tested or in the last six years and PCPs, with odds ratios (OR-black diamonds) and 95% confidence intervals (horizontal lines). Vertical line indicates no difference in the agreement between PCPs and general population. An OR>1 denoted that PCPs agreed more often than general population on the specific perceived barrier, while an OR<1 denoted that PCP agreed less often than general population on the specific perceived barrier.
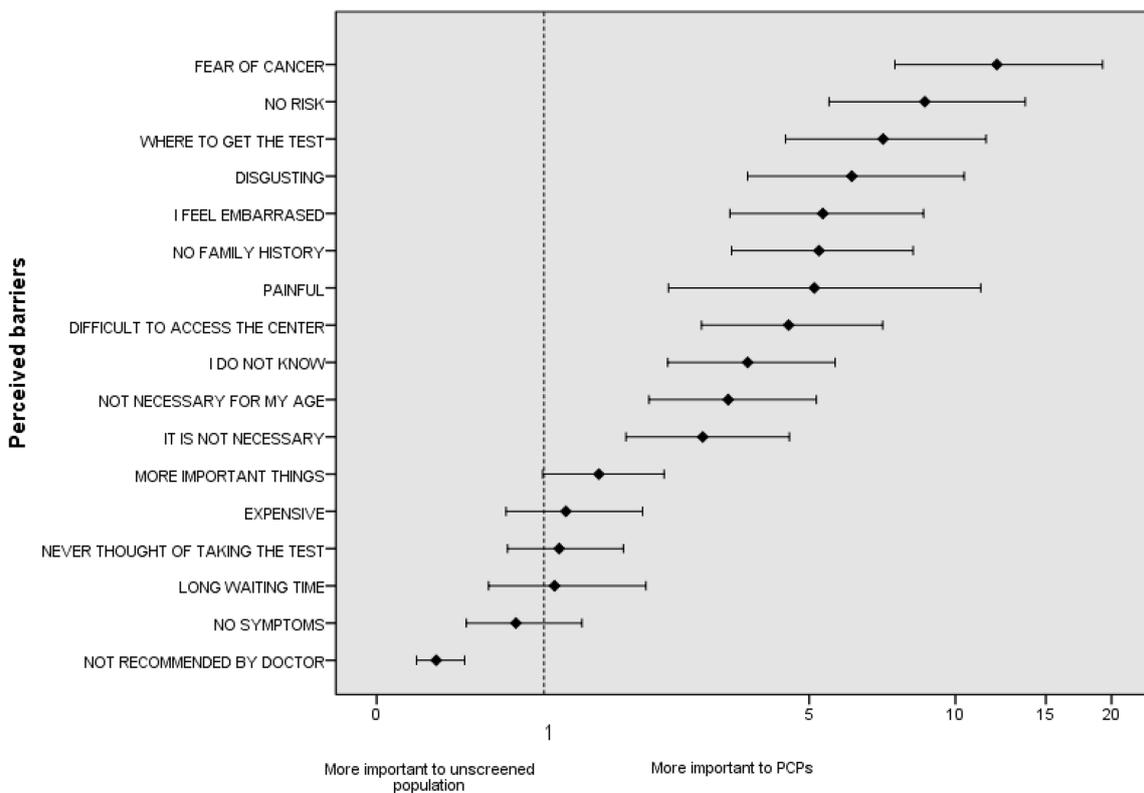

Figure 3. Comparison of reported barriers to FOBT by general population adults >50 years, who had not been ever tested or in the last six years and PCPs, with odds ratios (OR -black diamonds) and 95% confidence intervals (horizontal lines). Vertical line indicates no difference in the agreement between PCPs and general population. An OR>1 denoted that PCPs agreed more often than general population on the specific perceived barrier, while an OR<1 denoted that PCP agreed less often than general population on the specific perceived barrier.

the general population was the lack of physician recommendation (OR: 0.2; 95%CI 0.1-0.3; p<0.001; Figure 2).

Similarly, the agreement between PCPs and the general population seemed to be followed for most barriers for FOBT; however in addition to the lack of symptoms (82.1% PCPs vs 85.5% general population, p=0.368) and having more important things to do (41% PCPs vs 31.6% general population, p=0.056), no differences were found for the barriers cost of the test (19% PCPs vs 16.5% general population, p=0.518), never thought of taking the test (72.1% PCPs vs 69.5% general population, p=0.585) and long waiting time (14.4% PCPs vs 13.3% general population, p=0.775; Figure 3.

PCPs were also more likely to agree than the general population in many perceived barriers for FOBT, although in most cases the difference between PCP and general population was not as substantial as in the case of colonoscopy. However, on the barrier of test unawareness and on the barrier "I do not know where to get the test" the differences between PCPs and general population were greater than for colonoscopy (OR:3.6 vs OR:1.9 and OR:7.1 vs OR:4.3, respectively). Again, the only barrier that PCPs agreed at significantly lower frequency than the general population was the lack of physician recommendation (OR: 0.3; 95%CI 0.2-0.4; p<0.001).

Discussion

To the best of our knowledge this is the first study that attempted to compare the beliefs of perceived CRC barriers, between a representative sample of the general population and PCPs in Greece. We hypothesized that a substantial deviation of perceived barriers for CRC screening between general population and PCP exists in Greece and this seems to be supported by our findings, which are quite consistent for both colonoscopy and, the less invasive, FOBT.

Notably, PCPs in our study tended to agree more than the unscreened population in most "traditionally" patient reported barriers in literature (such as fear of pain or embarrassment); either on patient-related barriers (unawareness, fear of pain, embarrassment, fear of cancer diagnosis, lack of time) or on organizational issues (cost of the test, access to the diagnostic center, waiting time). These findings are also consistent with prior research. In a large comparative study in the USA, both PCPs and unscreened healthy individuals identified more often patient-related than system-related factors; however the majority of PCPs reported patient-motivational issues (such as embarrassment), while the general population reported

lack of knowledge and awareness as major barriers. They did, however, coincide with PCPs' perceptions about the lack of physician recommendation [14].

In another comparative study of PCPs and general population, physicians identified more often patient-related barriers, such as embarrassment/anxiety about the test, lack of awareness and fear of cancer diagnosis. On the contrary, only 1% of the general population reported pain or embarrassment as barriers. They were, however, much more likely to report the lack of recommendation and the lack of symptoms as important barriers [13]. On the other hand, there are studies of the general population, where fear of pain is highly reported by almost half of the respondents [20], as well as embarrassment from the test by one third of the sample [24].

Nevertheless, one of our primary findings is the divergence of views about the physician recommendation. As may be expected, PCPs were found to significantly agree less than the unscreened population about this barrier and the fact that the general population was five times more likely to report it as a significant barrier, requires further explanation and investigation. PCPs in our study did, however, cite it at almost the same frequency (13%) as a barrier for FOBT while not for colonoscopy, indicating probably their limited contribution in promoting FOBT screening. This is not a unique finding; in many physician surveys, PCPs do not list recommendation as a significant barrier. In a mixed-methods study though, physicians admit that "the barrier actually is more the PCP, not mentioning the test to the patient rather than the patient not accepting it" and they offer some explanation, including treating more acute conditions and limited visit time [25].

Some physicians may not recommend CRC screening because of competing priorities, both their own and the patient [26]. Being able to know their patients' history, their social and family status and problems (as this is the case in many instances in primary care), may affect their decision to suggest a screening test. It is like they decide for their patients, considering their priorities. Moreover, in a qualitative study in a community health center in USA, discrepancies of patient reports were also found; some patients cited lack of doctor recommendation, although a cross-check of their records found that in some cases their doctors actually recommended the test. This finding was attributed to a communication gap [23] and this might also be the case in our comparative study.

Why PCPs underestimated the lack of recommendation as a barrier? Whereas it is true that European guidelines have been long adopted as

official policy in Greece, it is unclear if they are actually implemented in everyday practice. Although our purpose was not to examine or crosscheck if PCPs actually prescribe regularly CRC screening tests, literature about PCP awareness and recommendation of screening tests revealed PCPs' suboptimal recommendations from Greek primary care physicians [6,10,12]. This, according to the authors, was attributed to limited guidelines awareness and the fact that PCPs were not convinced about the necessity of the tests (especially FOBT), in contrast to other suggested cancer screening tests (PAP test, mammography etc). In the opportunistic CRC screening context, which is the case in Greece, recommendation relies greatly on PCP involvement; if the PCP is not committed to the concept or the guidelines of CRC screening he is not likely to promote it to the population.

Another concerning finding was that most participants viewed the lack of symptoms as a critical CRC barrier. In fact, having no symptoms was by far the top rated barrier by the general population, when participants were asked to describe the principal barrier. This obviously indicates that there is a serious misunderstanding of the purpose of screening and secondary prevention in general. On the other hand, although there was no significant difference in agreement for this barrier from the PCP's perspective, only approximately 5% of them believed this is the principal reason for not adhering to CRC screening tests. Moreover, PCPs were much more likely to agree on test unawareness as a barrier, especially in the case of FOBT, as more than 55% cited it as the primary reason for noncompliance. These findings combined suggest a serious deficit in health literacy, a well-known predictor of CRC screening compliance [11,27-29]. It is important to actively engage PCPs in the process of conveying information to people eligible for screening, conforming to the European guidelines for quality assurance in CRC screening (Level of Evidence II – Grade A recommendation) [3].

Appendix. Full CRC perceived barriers questionnaire

Below is a list of reasons people refer to as barriers for not participating in screening tests for colorectal cancer (CRC). There is no correct or wrong answer. We just wish to record in what extend these reported barriers obstructed you personally from taking the advised test, besides the principal reason you already have stated earlier

Please indicate your level of agreement as below, marking with the number which represents you the most, for each test you did not have.	Colonoscopy/ sigmoidoscopy	FOBT

I did not have the screening test (or did not have it the last six years) because:
I agree (4) - I somewhat agree (3) - I somewhat disagree(2) - I disagree(1) - I do not answer (N/A)

1. I do not know what exactly is the test for
2. I fear it will be painful
3. I feel embarrassed to take the test
4. My doctor did not recommend it
5. I have more important things to do
6. I do not experience any symptoms and therefore I do not need it
7. I do not feel I am at risk for CRC
8. I do not have a family history for CRC
9. I fear the test will find I have CRC
10. I am not convinced it is necessary
11. It is expensive
12. I do not know where to get the test
13. It is difficult to access the test center
14. It is not necessary for my age
15. Never thought of taking the test
16. There is long waiting time
17. Difficult/unpleasant preparation
18. I think it is disgusting

Offering informed screening test choice is also documented to promote CRC screening adherence [30].

These findings could find theoretical ground to the popular Health Belief Model (HBM), which has been proposed by many authors as a theoretical model to explain cancer screening behavior [18,20,31]. According to HBM, the lack of symptoms, the unawareness of the test and the non-recommendation can be considered perceived barriers, while the PCP recommendation is a cue to action, a motivator that triggers action. The lack of symptoms can also be viewed as a lack of perceived threat. More barriers, low perceived threat and fewer cues to action are well-documented determinants of poor adherence [18,20,32].

Conclusions

The differences we have found in perceived barriers clearly indicate the need for more focused work in this area. Nevertheless, PCPs should at least keep in mind that their concerns may not coincide with those of their patients, even when they recommend a CRC screening test. This means that there must be a shift in PCP comprehension and attitude on patient perceived barriers, taking into account the general population actual needs and views about CRC screening, being unbiased by personal assumptions. Any interventions should be specifically tailored to address the patient perceived barriers, in the concept of patient-centered health promotion, identifying the barriers and facilitators to informed decision-making [3,33]. Taking into account patient views and expectations, could be the first decisive step to increase the potential for CRC screening uptake.

Authors' contribution

- Athanasios Mastrokostas: conceived and designed the study, retrieved, analyzed and interpreted data, drafted the manuscript. Magda Gavana: designed the study, interpreted data and critically reviewed the manuscript. Maria Gkrizioti: analyzed data and critically reviewed the manuscript.
- Emmanouil Smyrnakis: contributed to interpretation and edited the draft report.
- Evangelos Cholongitas: contributed to interpretation and edited the draft report.
- Alexis Benos: contributed to interpretation and edited the draft report.
- Anna-Bettina Haidich: supervised the study, analyzed and interpreted data, critically reviewed the manuscript.

Conflict of interests

The authors declare no conflict of interests.

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