

European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition

Organisation



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Keywords

- mass screening
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- organisation
- implementation
- multidisciplinary evidence-based guidelines
- population-based programmes

Multidisciplinary, evidence-based guidelines for quality assurance in colorectal cancer screening and diagnosis have been developed by experts in a project coordinated by the International Agency for Research on Cancer. The full guideline document covers the entire process of population-based screening. It consists of 10 chapters and over 250 recommendations, graded according to the strength of the recommendation and the supporting evidence. The 450-page guidelines and the extensive evidence base have been published by the European Commission. The chapter on

organisation includes 29 graded recommendations. The content of the chapter is presented here to promote international discussion and collaboration by making the principles and standards recommended in the new EU Guidelines known to a wider professional and scientific community. Following these recommendations has the potential to enhance the control of colorectal cancer through improvement in the quality and effectiveness of the screening process, including multi-disciplinary diagnosis and management of the disease.

Background

According to the most recent estimates by the International Agency for Research on Cancer [41] colorectal cancer (CRC) is the most common cancer in Europe with 432 000 new cases in men and women reported annually. It is the second most common cause of cancer deaths in Europe with 212 000 deaths reported in 2008. Worldwide CRC ranks third in incidence and fourth in mortality with an estimated 1.2 million cases and 0.6 million deaths annually. The European Union (EU) recommends population-based screening for breast, cervical and colorectal cancer using evidence-based tests with quality assurance of the entire screening process including diagnosis and management of patients with screen-detected lesions [31]. The EU policy takes into account the principles of cancer screening developed by the World Health Organization [124] and the extensive experience in the EU in piloting and implementing population-based cancer screening programmes [116]. Screening is an important tool in cancer control in countries with a significant burden of CRC, provided the screening services are high quality [117]. The presently reported multidisciplinary, evidence-based guidelines for quality assurance in colorectal cancer screening and

diagnosis have been developed by experts and published by the EU [94].

Methods

The methods used are described in detail elsewhere in this supplement [71]. Briefly a multidisciplinary group of authors and editors experienced in programme implementation and quality assurance in colorectal cancer screening and in guideline development collaborated with a literature group consisting of epidemiologists with special expertise in the field of CRC and in performing systematic literature reviews. The literature group systematically retrieved, evaluated and synthesized relevant publications according to defined clinical questions (modified Patient-Intervention-Comparison-Outcome-Study method). Bibliographic searches for most clinical questions were limited to the years 2000 to 2008 and were performed on Medline, and in many cases also on Embase and The Cochrane Library. Additional searches were conducted without date restrictions or starting before 2000 if the authors or editors who were experts in the field knew that there were relevant articles published before 2000. Articles of adequate quality recommended

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by authors because of their clinical relevance were also included. Only scientific publications in English, Italian, French and Spanish were included. Priority was given to recently published, systematic reviews or clinical guidelines. If systematic reviews of high methodological quality were retrieved, the search for primary studies was limited to those published after the last search date of the most recently published systematic review, i.e. if the systematic review had searched primary studies until February 2006, primary studies published after February 2006 were sought. If no systematic reviews were found, a search for primary studies published since 2000 was performed.

In selected cases references not identified by the above process were included in the evidence base, i.e. when authors of the chapters found relevant articles published after 2008 during the period when chapter manuscripts were drafted and revised prior to publication. The criteria for relevance were: articles concerning new and emerging technologies where the research grows rapidly, high-quality and updated systematic reviews, and large trials giving high contribution to the robustness of the results or allowing upgrading of the level of evidence.

The methodological quality of the retrieved publications was assessed using the criteria obtained from published and validated check lists. Evidence tables were prepared for the selected studies. The evidence tables, clinical questions and bibliographic literature searches are documented elsewhere [70].

In the full guidelines document prepared by the authors and editors [94] over 250 recommendations were formulated according to the level of the evidence and the strength of the recommendation using the following grading scales.

Level of evidence:

- I multiple randomised controlled trials (RCTs) of reasonable sample size, or systematic reviews (SRs) of RCTs
- II one RCT of reasonable sample size, or 3 or less RCTs with small sample size
- III prospective or retrospective cohort studies or SRs of cohort studies; diagnostic cross-sectional accuracy studies
- IV retrospective case-control studies or SRs of case-control studies, time-series analyses
- V case series; before/after studies without control group, cross sectional surveys
- VI expert opinion

Strength of recommendation:

- A intervention strongly recommended for all patients or targeted individuals
- B intervention recommended
- C intervention to be considered but with uncertainty about its impact
- D intervention not recommended
- E intervention strongly not recommended

Some statements of advisory character considered to be good practice but not sufficiently important to warrant formal grading were included in the text.

Results

Several guiding principles for organising a colorectal cancer screening programme and 29 graded recommendations are provided in Chapter 2.

Guiding principles for organising a colorectal cancer screening programme

- ▼
- 1. A colorectal cancer screening programme is a multidisciplinary undertaking. The objective is to reduce mortality from, and possibly incidence of colorectal cancer without adversely affecting the health status of those who participate in screening. The effectiveness is a function of the quality of the individual components of the process.
- 2. The provision of the service must account for the values and preferences of individuals as well as the perspectives of public health.
- 3. The public health perspective in the planning and provision of screening services requires commitment to ensuring equity of access and sustainability of the programme over time.
- 4. Taking into account the perspective of the individual requires commitment to promoting informed participation and to providing a high-quality, safe service.
- 5. Implementation entails more than simply carrying out the screening tests and referring individuals to assessment whenever indicated. Specific protocols must be developed for identifying and subsequently inviting the target population. Protocols are also required for patient management in the diagnosis, treatment, and surveillance phase in order to ensure that all individuals have timely access to the proper diagnostic and treatment options.
- 6. Complete and accurate recording of all relevant data on each individual and every screening test performed, including the test results, the decision made as a consequence, diagnostic and treatment procedures and the subsequent outcome, including cause of death, should be ensured. This monitoring process is of fundamental importance.
- 7. The quality assurance required for screening should also enhance the quality of the service offered to symptomatic patients.
- 8. Appropriate political and financial support are crucial to the successful implementation of any screening programme.

Recommendations and conclusions¹



Organised vs. non-organised screening

- 2.1 In order to maximise the impact of the intervention and ensure high coverage and equity of access, only organised screening programmes should be implemented, as opposed to case-finding or opportunistic screening as only organised programmes can be properly quality assured **(III – A)**.^{Sect 2.2.1; 2.2.2; 2.2.3}
- 2.2 When organising a screening programme, several fundamental aspects should be considered: the legal framework, the availability and accuracy of epidemiological and demographic data, the availability of quality-assured services for diagnosis and treatment, promotional efforts, a working

¹ **Sect** (superscript) after each recommendation in the list refers the reader to the section/s of the Guidelines dealing with the respective recommendation.*

Rec (superscript) throughout the chapter refers to the number of the recommendation dealt with in the preceding text.*

* The first digit of the section numbers and recommendation numbers refers to the respective chapter in the guidelines. For Chapter 1 see: [58]; for Chapters 3 to 10 see: [73,45,112,104,85,103,2,4] respectively.

relationship with the local cancer registry, and follow-up for causes of death at individual level **(VI – A)**.^{Sect 2.2.3}

Implementing the screening programme

- 2.3 A population registry should be implemented for screening if not yet available, combining the most accurate and updated information about the target population **(VI – A)**.^{Sect 2.3.1}
- 2.4 If the screening policy allows for exclusions, the exact definition of the criteria should be given. Exclusions should be carefully and routinely monitored for appropriateness and quality **(VI – A)**.^{Sect 2.3.1.1}
- 2.5 In the absence of hereditary syndromes people with a positive family history should not be excluded from CRC screening programmes **(III – B)**.^{Sect 2.3.1.2}
- 2.6 Subjects belonging to families with hereditary syndromes, identified at the time of screening, should be referred to special surveillance programmes or family cancer clinics, if available **(III – B)**.^{Sect 2.3.1.2}

Participation in screening

- 2.7 Access to screening and any follow-up assessment for people with abnormal test results should not be limited by financial barriers. In principle, screening should be free of charge for the participant **(I – A)**.^{Sect 2.4.2.1}
- 2.8 In the context of an organised program, personal invitation letters, preferably signed by the general practitioner, should be used. A reminder letter mailed to all non-attenders increases attendance rate and is therefore recommended (see also Ch. 10 [4], Rec. 10.7) **(I – A)**.^{Sect 2.4.3.1; 2.4.3.2; 10.4.1.2}
- 2.9 Although more effective than other modalities, phone reminders may not be cost-effective (see also Ch. 10 [4], Rec. 10.8) **(I – B)**.^{Sect 2.4.3.2; 10.4.1.2}
- 2.10 Provision of information is necessary to enable subjects to make an informed choice, but it is not sufficient to enhance participation. Organisational measures enabling people to attend screening should be implemented **(I – A)**.^{Sect 2.4.3.3.1}
- 2.11 Primary health care providers should be involved in the process of conveying information to people invited for screening (see also Ch. 10 [4], Rec. 10.6) **(II – A)**.^{Sect 2.4.3.4; 2.4.3.4.1; 10.4.1.1}
- 2.12 General practitioners or family physicians (or primary health care practitioners, where preventive services are not primarily based on primary care physicians) should be involved in the implementation of organised programmes **(I – A)**.^{Sect 2.4.3.4.2}
- 2.13 Reducing organisational barriers to physicians' advice should be a priority for interventions aimed at promoting GPs' involvement in organised screening programmes **(I – B)**.^{Sect 2.4.3.4.2}

Testing protocol

- 2.14 For FOBT-based screening programmes, the choice of the kit provider should aim to maximise accessibility for the target population **(II – A)**.^{Sect 2.5.1.1}
- 2.15 Mailing of FOBT kits may be a good option, taking into account feasibility issues (such as reliability of the mailing system and test characteristics) as well as factors that might influence cost-effectiveness (such as the expected

effect on the participation rate) (see also Ch. 10 [4], Rec. 10.9) **(II – B)**.^{Sect 2.5.1.1; 10.4.1.3}

- 2.16 Clear and simple instructions should be provided with the kit (see also Ch. 10 [4], Rec. 10.10) **(V – A)**.^{Sect 2.5.1.1; 10.4.1.3}
- 2.17 In order to enhance compliance, testing procedures that require no or only minor dietary restrictions are preferred **(I – A)**.^{Sect 2.5.1.2}
- 2.18 Systematic (preferably automated) check protocols should be implemented in order to ensure correct identification of the screenee's test results and recognition of incomplete or erroneous data **(VI – A)**.^{Sect 2.5.1.3}
- 2.19 Protocols should be in place to ensure standardised and reliable classification of the test results **(VI – A)**.^{Sect 2.5.1.3}
- 2.20 Bowel preparation for screening sigmoidoscopy should preferably involve a single procedure. Cultural factors should be taken into account and population preference should be assessed. **(II – B)**.^{Sect 2.5.2.2}
- 2.21 For screening sigmoidoscopy, several providers should be available that are close to the target population. Organisational options include the possibility of having the enema administered at the endoscopy unit. Clear and simple instructions should be provided with the preparation **(II – B)**.^{Sect 2.5.2.2}
- 2.22 To date no single bowel preparation for colonoscopy has emerged as consistently superior over another in terms of efficacy and safety **(I)** although sodium phosphate may be better tolerated and it has been shown that better results are obtained when the bowel preparation is administered in two steps (the evening before and on the morning of the procedure) **(II)**. It is therefore recommended that there should be colonic cleansing protocols in place and the effectiveness of these should be monitored continuously (see Ch. 5 [112], Rec. 5.22) **(VI – A)**.^{Sect 2.5.2.3; 5.3.3}
- 2.23 For colonoscopy, several providers should be available that are close to the target population. Clear and simple instructions should be provided with the preparation **(VI – B)**.^{Sect 2.5.2.2; 2.5.2.3}

Management of people with positive test results and fail-safe mechanism

- 2.24 In order to ensure timely and appropriate assessment, an active follow-up of people with an abnormal screening test result should be implemented, using reminders and computerised systems for tracking and monitoring management of these patients **(II – A)**.^{Sect 2.5.3}
- 2.25 The cost charged to the participant undergoing assessments should be as low as possible in order to promote equity of access **(II – A)**.^{Sect 2.5.3}

Screening policy within the healthcare system

- 2.26 Gender and age-specific screening schedules deserve careful attention in the design and implementation of screening interventions **(III – C)**.^{Sect 2.6.3.1}
- 2.27 The costs of screening organisation (including infrastructure, information technology, screening promotion, training and quality assurance), the occurrence of adverse effects and the likelihood that patients will actually complete the tests required for any given strategy represent additional important factors to be taken into account in the design and implementation of screening interventions

and in the choice of the screening strategy (III–A).^{Sect 2.6.1–3; 2.6.3.2–5}

Implementation period (step-wise)

2.28 Ideally, any new screening programme should be implemented using individual level randomisation into screening and control groups in the phase in which resources and practical limitations prohibit the full coverage of the target population (VI–A).^{Sect 2.6.4}

Data collection and monitoring

2.29 In order to be able to evaluate the effectiveness of screening, the data must be linked at the individual level to several external data sources including population register, cancer or pathology registries, and registries of cause of death in the target population. Therefore, legal authorisation should be put in place when the screening programme is introduced in order to be able to carry out programme evaluation by linking the above-mentioned data for follow-up (VI–A).^{Sect 2.6.5.1; 2.6.5.2}

2.1 Introduction

National and organised, population-based cancer screening programmes have been in place since the early 1960s, when cervical cancer screening was first implemented in Finland. In fact, the concept of organised screening has largely been built on this experience. The effectiveness of a programme can be measured by the reduction of mortality from the specific cancer site, and this depends on the extent of organisation, i.e. how well different factors in the screening process can be linked together. These factors include the identification of the target population, the performance of the test, and diagnostics and treatment of those who need further assessment or treatment after the primary screening test [56,84].

The effectiveness of screening with regard to its impact on mortality and incidence of CRC is a function of the quality of the individual components of the process, from the organisation and administration up to the assessment, treatment and follow-up of screen-detected lesions.

Fundamental to the success of a screening programme is that people in the target population are actually screened. The uptake rate is a critical determinant of the impact of screening on the reduction of CRC incidence and mortality at the population level. Equity of access to screening is clearly as important a challenge as is high compliance in new screening programmes. Understanding the reasons for non-participation is helpful in the planning phase when considering factors that should be taken into account in the design of the screening programme.

Concerns have been raised about the potential conflict between advocating high uptake rates and the intention to promote informed uptake, i.e. enabling people to make an informed choice about whether or not they want to be screened. The purpose of screening should be to benefit the whole community, while at the same time respecting the individual's autonomy that includes the right to refuse screening. Interventions aimed at increasing uptake should try to identify ways to minimise barriers to participation among those who have understanding of its likely benefits, limitations and harms.

2.2 Organised vs. non-organised screening

The specific policy of a screening programme determines the target age and gender and possibly the geographical area, the screening test and screening interval, and further diagnostics and treatment for those who need them.

The implementation of a population based screening programme is characterised by the definition of a specific population (by target age and geographical area), with eligible subjects being actively invited following an explicit and pre-defined protocol specifying the planned screening interval, as well as the testing and assessment procedures. Screening tests and the related assessments are usually free of charge for the target population in this context.

This policy may be implemented within different organisational contexts, but in all options a pre-defined organised protocol is required that takes into consideration the entire process.

2.2.1 Opportunistic screening or case-finding

Case-finding may take place outside an organised programme in which case it is referred to as opportunistic screening. This type of screening may be the result of a patient request or a recommendation made during routine medical consultation for unrelated conditions, or on the basis of a possible increased risk of developing colorectal cancer (family history or other known risk factors). Opportunistic screening is less efficient and more costly both in terms of resources and harms, and thus it is not recommended as an alternative to organised screening.

2.2.2 Comparison of coverage and effectiveness

Two cross-sectional surveys have assessed the increase in coverage (17% and 23%) resulting from the introduction of organised cervical cancer screening versus the pre-existing opportunistic approach [11,89]. Both in the United Kingdom and Norway the introduction of an organised screening programme was associated with a decrease in the incidence rate of invasive cervical cancer and an increase in the target population coverage, as compared to the period preceding the start of the programme when opportunistic screening was already widespread [78,84]. A decrease in the incidence rate of invasive cervical cancer in women who received organised screening compared to opportunistic screening was also observed in a cohort study [62] and a case control study [77]. A 20% decrease in incidence of invasive cervical cancer was observed in Turin, Italy, among women invited to an organised programme, compared with those not invited, after introduction of the organised programme in an area in which intensive opportunistic screening was already established [88].

Similar findings have been reported by studies conducted in the context of breast cancer screening. Organised screening programmes can ensure better coverage of hard-to-reach populations, as suggested by a recent survey: compared to women undergoing opportunistic screening, participants in an organised programme were more likely to have never been screened, tended to ignore screening efficacy and were at risk of abandoning screening, as a result of their less-favourable attitudes towards prevention [20]. A recent case-control study conducted in Italy showed that the introduction of breast cancer screening programmes was associated with a reduction in breast cancer mortality attributable to the additional impact of the organised programmes over and above the background spontaneous mammography activity. Compared to those not yet invited, women invited to the organised programmes showed a 25% (OR:0.75; 95%

CI:0.62–.92) reduction of the risk of death from breast cancer [83].

Available data from studies conducted in the context of CRC screening indicate that the introduction of organised programmes can have a similar impact, at least on target population coverage. A nationwide observational telephone survey, conducted in France [36], showed that greater compliance with reduced inequalities in the distribution across social groups was achieved in geographical departments where CRC screening was organised by health authorities.

2.2.3 Prerequisites for organised screening

The International Agency for Research on Cancer (IARC) has defined an organised screening programme as one that has the following features: 1) an explicit policy with specified age categories, method and interval for screening; 2) a defined target population; 3) a management team responsible for implementation; 4) a health-care team for decisions and care; 5) a quality assurance structure; and 6) a method for identifying cancer occurrence and death in the population [48].

When organising a new screening programme the following fundamental aspects should therefore be considered:

1. the legal framework for identification and follow-up of the population;
2. the availability and accuracy of the necessary epidemiological data upon which the decision to begin screening is based;
3. the availability and accessibility of essential demographic data to identify the target population and set up an invitation system;
4. the availability and accessibility of quality-assured services for diagnosis and treatment of colorectal cancer and its precursors;
5. promotional efforts to encourage participation in the programme;
6. a working relationship with the local Cancer Registry², if available, and causes of death registry, and maintenance of population and screening registers, to include adjustments to the programme and to ensure evaluation of the effects and follow-up for causes of death at individual level.

The evaluation of outcomes and interpretation of results from the entire screening programme are affected by these aspects, therefore the feasibility of an effectively managed programme should be piloted or built up gradually in the phase in which resources and practical limitations prohibit the full coverage of the target population. It is recognised that the context and logistics of screening programmes will differ by country and even by region. For example the prior existence of a population registry facilitates the issuing of personalised invitations, whereas the absence of a population register may encourage recruitment by open invitation. Many of these contextual differences will explain the differences in outcomes. In opportunistic screening programmes or case-finding, the aforementioned aspects are overlooked and evaluation of the benefits and possible harms will not be possible. The disadvantages also include many unnecessary screenings per person and low coverage of the entire target population, leading to low impact at the public health level. Compared with opportunistic screening, organised screening permits much greater attention to the quality of the screening process including follow-up of participants [68]. Consequently, organised screening pro-

vides greater protection against the harms of screening, including over-screening, poor quality and complications of screening, including poor follow-up of participants with positive test results.

Summary of evidence

- ▶ Organised screening programmes achieve better coverage of the target population including hard-to-reach or disadvantaged groups (IV–V).
- ▶ Organised screening is more effective, and hence likely to be more cost-effective than opportunistic screening or case-finding. The available evidence indicates that organised screening results in a larger reduction of invasive cancer incidence (cervical cancer) or mortality (breast cancer) (III–IV).
- ▶ Organised screening provides greater protection against the harms of screening, including over-screening, poor quality and complications of screening, and poor follow-up of participants with positive test results (III).

Recommendations

- ▶ In order to maximise the impact of the intervention and ensure high coverage and equity of access, only organised screening programmes should be implemented as opposed to case-finding or opportunistic screening as only organised programmes can be properly quality-assured (III–A).^{Rec 2.1}
- ▶ When organising a screening programme several fundamental aspects should be considered: the legal framework, the availability and accuracy of epidemiological and demographic data, the availability of quality-assured services for diagnosis and treatment, promotional efforts, a working relationship with the local Cancer Registry, and follow-up for causes of death at individual level (VI–A).^{Rec 2.2}

2.3 Implementing the screening programme



Organised CRC screening is a multi-step process including:

- ▶ Identification of the target population;
- ▶ Recruitment of eligible subjects;
- ▶ Delivery of screening test;
- ▶ Reporting of screening test results;
- ▶ Reassurance of people with normal results and information on the timing of the next test;
- ▶ Recall of people with unsatisfactory/inadequate screening test
- ▶ Follow-up of people with positive tests, i.e. diagnostic procedures and treatment needed, including a fail-safe system to make sure this actually happens; and
- ▶ Registration, monitoring and evaluation of the entire programme.

Issues related to programme implementation are discussed in Section 2.6.4.

2.3.1 Identifying and defining the target population

Catchment areas and target populations must be clearly defined. The necessary data include unique identification for each person, such as name, date of birth, relevant health insurance or social security numbers, general practitioner (GP) where appropriate, and contact address. Population registers or registries can in general provide such data, but they must be updated regularly to account for population migration, deaths and changes in personal details. In those countries in which population registries are based on administrative areas of small size, communication between registries is essential. Suitable registries might include population, electoral, social security, screening programme, and

² If a cancer registry is lacking, registration of the target cancer should be initiated with the screening programme.

health service registries. Incomplete or inaccurate registries can result in certain groups (such as transients or ethnic minorities) not being invited for screening.

If an accurate, complete and regularly-updated register of the whole target population does not exist, an administrative database that combines information from available registries for all people to be included in screening should be implemented for the purposes of the programme. The legal basis for access to such registries must be set up and all data protection measures should be implemented according to the national and European legislation.

Recommendation

- ▶ A population registry should be implemented for screening if not yet available, combining the most accurate and updated available sources **(VI–A)**.^{Rec 2.3}

2.3.1.1 Inclusion and exclusion criteria

The target population for a CRC screening programme includes all people eligible to attend screening on the basis of age and geographical area of residence. However, each programme may apply additional exclusion/inclusion criteria to identify the population eligible for screening. Potential reasons for excluding a subject from screening might include conditions in which offering the screening test is not appropriate, such as terminal illness (no benefit could be attained through screening), recent (the relevant period should be specified and justified) screening test (the expected benefit achievable by repeating the test might not outweigh the risks associated with the procedure), previous diagnosis of CRC or pre-malignant lesions (these patients should already be followed-up according to specific surveillance protocols, and their inclusion in screening might result in the offer of conflicting management options).

The extent to which such individuals can be identified and excluded from the target population will vary by screening programme: for some programmes it may not be feasible or desirable to identify every category of potential exclusion prior to invitation.

The necessary information may be collected at the first personal contact with the screenee, i.e. at the time of a possible colonoscopy assessment in the case of FOBT programmes, or at the time of the screening exam for FS or colonoscopy programmes.

Exclusion might alternatively be based on the information gathered through the GPs or other primary care providers, who may be requested to check the eligibility of their patients ear-marked for invitation.

If the screening policy allows for exclusions, the exact definition of the respective criteria should be given and exclusions should be carefully and routinely monitored for appropriateness and equity.

Recommendation

- ▶ If the screening policy allows for exclusions, the exact definition of the criteria should be given. Exclusions should be carefully and routinely monitored for appropriateness and equity **(VI–A)**.^{Rec 2.4}

2.3.1.2 Family history

People with a positive family history for CRC are sometimes considered for exclusion from screening programmes targeting average-risk people.

Implementing this option requires the adoption of procedures for identifying people with a positive family history and accurately collecting the information that is relevant to assess an individual's level of risk.

It is also necessary to ensure that an alternative organised programme is in place for this group of people.

Specific surveillance protocols based on colonoscopy at shorter intervals and starting at a younger age have been shown to be effective and are recommended for members of families with hereditary syndromes. However, it is still not clear if more intensive surveillance for people at moderate risk can achieve a favourable cost-benefit ratio [5, 9, 19, 21, 30, 53, 66, 74, 102] **(III)**.

If an alternative option (i.e. access to a specific surveillance protocol) is not available, people with positive family history should not be excluded from a population-based screening programme as screening offers the opportunity of access to an intervention that may ensure protection for people who would not be otherwise covered.

Furthermore, family history, in the absence of hereditary syndromes, does not represent an indication for changing standard surveillance protocols (see Ch. 9 [2], Sect. 9.2.3.2, Rec. 9.13). In a recent study, the characteristics of the neoplasm rather than individual's family history were found to be associated with the risk of recurrence among subjects not fulfilling the Amsterdam criteria. This suggests that these people could be considered at moderate risk of developing CRC and that surveillance intervals of more than five years may be appropriate in these cases [34]. Therefore, family history should not represent a criterion for exclusion from the screening programme, even for patients identified at the time of assessment.

Summary of evidence

Members of families with hereditary syndromes should follow specific surveillance protocols based on colonoscopy at shorter intervals and starting at a younger age **(III)**.

Recommendations

- ▶ In the absence of hereditary syndromes people with a positive family history should not be excluded from CRC screening programmes **(III–B)**.^{Rec 2.5}
- ▶ Subjects belonging to families with hereditary syndromes identified at the time of screening should be referred to special surveillance programmes or family cancer clinics, if available **(III–B)**.^{Rec 2.6}

2.4 Participation in screening



The planning and implementation of screening programmes should take into account cultural, behavioural, economic and organisational factors.

2.4.1 Barriers

Several factors influencing participation have been identified related to individual's characteristics, the setting and the organisation of the intervention and the knowledge, attitudes and practice of the provider [51, 114]. The findings concerning the relative weight of these factors are not consistent across studies assessing determinants and barriers to participation. However, the variability of the reported findings is probably related to the different conditions under which the examined screening interventions have been implemented.

The organisation of screening within health services appears, in most countries, to be a major determinant of participation rate. Lack of insurance coverage and cost of the test have been identified as the main negative influences on participation for all screening interventions and tests. Also, lack of resources is the

most likely explanation for the negative association of lower socio-economic status with completion of CRC screening tests [24, 33, 65, 101, 107, 120]. Other factors related to service organisation which were fairly consistently related to poor screening attendance are the amount of time required to perform screening, distance from the test provider and lack of physician recommendation (III–V).

Knowledge and perceived benefits of screening, perceived risk of CRC and health motivation were associated with higher participation in most of the studies assessing the influence of these determinants. Worry about pain, discomfort, or embarrassment associated with the test, or fear of test results were also consistently associated with a lower attendance [50, 60, 72, 120, 122] (V).

Gender and age differences in participation to CRC screening have also been reported; most studies have shown a trend to decreased participation among older people, although these findings have not been confirmed by all investigators. It has been reported that participation may be higher among women for FOBT screening and among men for endoscopy screening [33, 50, 60, 65, 67, 95, 101, 120, 122] (V).

Support from a partner probably explains the positive association of marriage with screening uptake. This is more prominent in males. One reason for these findings could be that women have prior experience of screening (breast, cervix) and may therefore need less support to participate [64, 67, 107, 120] (V).

2.4.2 Interventions to promote participation

A systematic review [106], assessed the effectiveness of the following on improving screening participation: regulatory and legislative actions (outside the medical care organisation), financial incentives for providers or patients, organisational change (changes in clinical procedures or facilities and infrastructures), reminders for providers and screenees, provider feedback, education and visual materials. The most effective was the implementation of organisational changes that made delivery of these services a routine part of patient care (establishing separate clinics devoted to screening, involving nursing or clerical staff in the delivery of services, adoption of monitoring and quality improvement approaches), reducing, or eliminating costs for the individual or establishing a system of reminders.

2.4.2.1 Removing financial barriers

Experimental studies conducted in the context of breast cancer screening showed that reduced charges for screening are effective in encouraging uptake among disadvantaged groups [51]. Sending an FOBT with a postage-paid envelope for returning the sample resulted in a significantly higher uptake, compared to non-postage [51]. The return rate was highly significant for medically uninsured people in one of the studies [69]. Offering a free FOBT in addition to educational intervention was superior to the educational intervention alone in promoting completion of screening [82]. Offering financial incentives to subjects invited for screening was not found to have an impact on participation [51].

Summary of evidence

- ▶ Free-of-charge screening is associated with increased participation, including participation of disadvantaged groups (I).
- ▶ The implementation of organisational changes that make delivery of screening a routine part of health care (establishing a system of reminders, establishing separate clinics devoted to screening, involving nursing or clerical staff in the delivery of

services, adoption of monitoring and quality improvement approaches) represent the most effective interventions to enhance participation rate (I).

Recommendation

- ▶ Access to the screening tests and to the follow-up assessment for individuals with abnormal test results should not be limited by financial barriers. In principle access should be free of charge for the participant (I–A).^{Rec 2.7}

2.4.3 Invitation

2.4.3.1 Invitation letter

Strong evidence indicates that receiving a letter signed by the GP increases screening uptake, compared to receiving letters signed by other figures of authority [27, 40, 51].

A personal invitation letter from the GP is also associated with increased participation when the FOBT kit is delivered by mail [27]. It should be considered however that individuals can be encouraged to participate through support provided by other trusted health care professionals. In the Nordic countries, for example, invitation letters are not signed, but refer to the local authorities, and the observed participation rates are very high (70%) [64].

A positive impact on participation due to the offer of a pre-fixed appointment has been reported by several studies of breast and cervical cancer screening (IARC handbook vol 10, [48]) and has also been confirmed among people invited for FS screening. Inviting people to obtain the FOBT kit within a pre-defined time interval, or offering a pre-defined appointment for kit delivery has been adopted in some programmes, but comparative data on the impact of these strategies are lacking.

Data from a recent trial [25] indicate that an advance notification letter significantly increases participation in FOBT screening (from 39.5% to 48.3%). The effect was explained by a population shift in readiness to undertake screening.

2.4.3.2 Reminders

In the English NHS Screening Programme over 50% of participants only respond after receiving a reminder about 28 days after receiving their initial postal invitation. A well-conducted review [49] that assessed the effectiveness of different kinds of reminders (reminder and recall systems delivered by letter; postcard; telephone; auto-dialler; or in person, e.g. a provider gives face-to-face reminder) concluded that all kinds of reminders are effective, with telephone reminders being the most effective, but also the most costly.

Summary of evidence

- ▶ A personalised letter signed by the general practitioner or by another trusted primary health care provider is more effective than an impersonal letter sent by a central screening centre (I).
- ▶ An advance notification letter may increase participation (II).
- ▶ Any kind of reminder is effective in increasing participation, with telephone reminders being the most effective although the most costly option (I).

Recommendations

- ▶ In the context of an organised programme, personal invitation letters, preferably signed by the GP, should be used. A reminder letter should be mailed to all non-attenders to the initial invitation (I–A).^{Rec 2.8}
- ▶ Although more effective than other modalities, phone reminders may not be cost-effective (I–B).^{Rec 2.9}

2.4.3.3 Delivering information about screening

Although the organisation of screening within health services emerges as the most important determinant of uptake, factors related to culture, values and beliefs may still play a role. Also, provision of information is clearly necessary to enable subjects to make an informed choice.

Data from the National Health Interview Survey (NHIS) consistently indicate that lack of awareness of CRC represents one of the main determinants of the underutilisation of screening.

Data from people recruited in the UK sigmoidoscopy trial [119] who were requested to express their intention to attend screening suggest that part of the explanation of the socio-economic status (SES) gradient may be the difference in beliefs and expectations. Lower social groups evaluated the offer of a screening test, which had been publicised identically and was provided free of charge, at a convenient location and time, to all social groups, as being more frightening and less beneficial, than higher social groups. In England, with overall population participation at 60% despite free testing, the uptake rate of the FOBT programme is lower in deprived areas and among ethnic minorities (von Wagner et al 2009). Rural areas were shown to have a lower participation rate than urban areas [42, 59].

Therefore, the way the population is informed about the potential benefits and harms of screening is of particular importance. Strategies aimed at improving population knowledge and awareness of CRC and screening should target health professionals as well as individuals (see also Chapter 10 [4]).

Most programmes provide written information in the form of leaflets to people invited for screening. (see also Chapter 10 [4]). Mass-media campaigns are also implemented, to support enrolment in organised programmes (see also Chapter 10 [4]).

Interventions aimed at promoting health professionals practice and communication with people invited for screening is discussed in Section 2.4.3.4.1 when considering the role of GPs/family physicians (see also Chapter 10 [4]).

2.4.3.3.1 Information conveyed with the invitation (see also Chapter 10 [4])

A systematic review of methods aimed at enhancing screening rates concluded that educational interventions are less effective than organisational changes and should not be the first choice [106]. Findings from more recent studies [29, 46, 61, 87] support such a conclusion. When individuals interested in screening were requested to actively seek further information and a referral to screening from their providers, an information brochure was observed to have no impact, but the number of screening requests increased significantly when the GP delivered an FOBT request form together with the information pamphlet.

The content and format of the information material sent with the invitation may influence a subject's decision to undertake screening (see also Chapter 10 [4]). An individually tailored interactive multimedia programme at the physician's office seemed more efficacious in increasing readiness to undergo screening, as compared to the same intervention not individually tailored [52]. Interventions that use visual instruments to enhance appeal and clarity are more effective: adding illustrations about the polyp-cancer process and the removal of the polyps during FS to written material was associated with a significant increase in knowledge and understanding [16]. Culturally and linguistically appropriate approaches promoting FOBT can enhance screening practice in groups of low-income and less acculturated minority patients [110].

Summary of evidence

- ▶ The impact of information conveyed with the invitation is greater if the invitation is signed by an individual's physician. Involvement of GPs also shows a positive influence on the impact of more tailored and structured information methods (II).

Recommendations

- ▶ Provision of information is necessary to enable subjects to make an informed choice, but it is not sufficient to enhance participation. Organisational measures should be implemented in order to enhance participation in screening (I–A).^{Rec 2.10}

2.4.3.4 The role of primary care providers

Primary health care providers can be effective media for improving awareness of the risk of cancer and of the benefits of screening, for increasing confidence in the screening test method and for countering the reluctance to collect faecal samples. In many European countries this provider is the general practitioner (GP), but other trusted health professionals, such as community nurses for example, may play a similar role.

Primary health care providers should be trained to deliver evidence-based information on screening and there should be a consensus on the programme protocol before starting the programme.

1.4.3.4.1 Role of GPs/family physicians

The involvement of GPs in screening can be very effective in improving compliance, according to the findings of several studies from different countries [12, 39, 44, 59, 97, 100, 108], but the effect is dependent upon the GP's own willingness to get involved. The findings of studies conducted in the context of opportunistic screening showed that the probability of not receiving a GP recommendation for CRC screening was highest among those with a low socioeconomic status (SES) [12, 55, 92, 121]. These findings suggest that inadequate provider counselling represents an important determinant of the SES gradient in screening uptake. Compliance was shown to be closely linked to practitioner motivation also in the context of organised programmes [39, 59].

Knowledge of GP attitudes and preferences is therefore crucial in enhancing participation. A study based on semi-structured questionnaires addressed to 32 GPs in England [125] indicated that for GPs to effectively promote screening they must have adequate information prior to the start of a screening programme. The evidence should be based specifically on the effectiveness of the screening programme, and information on the proportion of false negatives and the proportion of false positives.

Summary of Evidence

- ▶ The implementation of organisational measures aimed at facilitating participation in screening is required in order to achieve the expected impact of educational interventions (II).

Recommendation

- ▶ Primary health care providers should be involved in the process of conveying information to people invited for screening (II–A).^{Rec 2.11}

2.4.3.4.2 Interventions aimed to promote provider involvement (See also Chapter 10 [4])

Provider education has been identified as a potentially effective intervention to promote CRC screening utilisation, even if the implementation of organisational measures may be necessary to achieve an impact of educational efforts [106]. This conclusion is supported by the results of recent experimental studies: educational seminars offered to physicians did not show an effect on

rates of CRC screening [118], while a reminder note to the physician to direct his patients to perform an FOBT was more effective than a mail reminder and as effective as a phone reminder for the patients.

Even if GPs are not delivering kits, or not collecting or reading the test cards, they should be aware of how the programme, and in particular the invitation scheme, is structured. They can advise non-compliers about screening, which is important for older people, or for those with lower socio-economic status, and they can offer counselling for patients with positive tests. To facilitate this task, GPs should receive the results of screening and assessment tests performed by their patients.

Summary of evidence

- ▶ Primary health care providers appear to be effective media for improving awareness of the risk of cancer and the benefits of screening, and increasing confidence in and countering the reluctance to take the screening test (I).
- ▶ Educational interventions are less effective than organisational changes in improving the impact of physicians' counselling on their patients' screening rates (I).

Recommendations

- ▶ GPs or family physicians (or primary health care practitioners where preventive services are not primarily based on primary care physicians) should be involved in the implementation of organised screening programmes (I–A).^{Rec 2.12}
- ▶ Reducing organisational barriers to physician's advice should be a priority for interventions aimed at promoting GP involvement in organised screening programmes (I–B).^{Rec 2.13}

2.5 Testing protocol



2.5.1 FOBT

2.5.1.1 Delivery of kits and collection of stool samples (see also Chapter 4 [45])

The test kit may be delivered by mail, at GPs' offices or outpatient clinics, by pharmacists, or in other community facilities, and in some cases with the support of volunteers. There is no evidence that any of these strategies may have an impact on the proportion of inadequate samples, provided that clear and simple instruction sheets are included with the kit [32, 111, 129].

The choice of the provider should aim to maximise accessibility, taking into account local conditions, settings and cultural factors. Mailing of the FOBT kit with instructions, together with the invitation letter and the information leaflet, is effective in increasing participation rates [22, 95]. These results are consistent with previous reports indicating that the GP's letter and mailing of FOBT kits represent the most important factors for improving compliance [54]. Mailing of the FOBT kit might not always represent a cost-effective strategy, if the baseline participation rate and the expected increase in participation are low. Compared to mailing a second FOBT kit to all non-responders, mailing a recall letter with a test order coupon resulted in a substantial decrease in the programme costs, but also in a significant decrease in participation [109]. The authors of the trial suggested, however, that the spared costs might be allocated more efficiently to communication interventions that might have a higher impact on compliance.

Several test providers close to the target population should be available when the subject is required to reach health or community facilities to get the kit. A recent study [39] showed that the

time required to reach the test provider was the strongest determinant of compliance: OR (<15 minutes versus 15–30 or >30 minutes): 0.8 (0.5–1.3) and 0.3 (0.2–0.7) respectively.

Volunteers or non-health professionals may also be involved in the distribution and collection of kits. Delivery of kits may represent in this case an additional opportunity for counselling, for conveying information about the programme and for providing instructions for test utilisation. Subjects contacted at home by a trained non-health professional who delivered the kit and collected the sample from the participant's home showed a substantially higher completion rate of iFOBT, as compared to the group who received the kit by mail with an invitation from their primary care physician [32].

Community volunteers, who have received some general training by the programme staff, have been involved in the kit distribution in the context of ongoing organised programmes and their involvement has been consistently associated with high participation rates [129]. As no randomised comparison is available, it is difficult to dissociate their specific effect from other characteristics of the communities or target populations involved. Sustainability over time represents an important issue to be taken into account when planning to use volunteer support.

The modalities adopted for stool collection, storage and shipping of the sample to the laboratory are mainly dependent on the characteristics of the test adopted, i.e. its stability at environment temperature. Based on these considerations mailing of the samples may be an option that can be implemented more easily for guaiac than for immunochemical tests, which need to be processed faster. Accessibility of the collection facilities remains an important goal, but the logistics of the sample handling may promote reducing the number of collection facilities in order to ensure an appropriate storage or timely shipping to the laboratories. See also Chapter 4 [45] for tests characteristics and storage requirements.

Summary of evidence

- ▶ There is no evidence that the proportion of inadequate samples may be affected by the provider used to deliver the kit, if clear and simple instruction sheets are provided with the kit (II–V).
- ▶ The time required to reach the test provider represents a strong determinant of compliance (II).
- ▶ Sending the FOBT kit together with the invitation letter may be more effective than sending a letter alone, but this strategy may not be cost-effective (II).

Recommendations

- ▶ The choice of the kit provider should aim to maximise accessibility of the target population (II–A).^{Rec 2.14}
- ▶ Mailing of FOBT kit may be a good option, taking into account feasibility issues (such as reliability of the mailing system and test characteristics), as well as factors that might influence cost-effectiveness (such as the expected impact on participation rate) (II–B).^{Rec 2.15}
- ▶ Clear and simple instruction sheets should be provided with the kit (V–A).^{Rec 2.16}

2.5.1.2 Performing the test: dietary restrictions and number of samples

In order to reduce the probability of a false positive result, dietary restrictions are usually recommended when guaiac-based tests are used. Retesting of subjects with a positive test (possibly with dietary restrictions being recommended) represents an alternative option adopted in some programmes to deal with this prob-

lem. A review of 5 trials (10 359 participants overall) comparing Guaiac FOBT with and without dietary restriction found a significant difference in compliance in favour of testing without dietary restrictions only in the trial where restrictions were particularly extensive. Authors concluded that advice to restrict the diet and avoid NSAIDs and vitamin C does not substantially reduce completion rate except perhaps when the dietary restrictions are particularly extensive [80]. More recent randomised trials [28,40,113] have demonstrated that better compliance can be achieved using iFOBT compared to a guaiac-based test. These results are not explained by the nature of the test but by lack of dietary and drug restrictions and easier and more pleasant sampling methods. Indeed, dietary restriction was associated with a significant decrease in participation also among people offered iFOBT test, compared to controls receiving the same test who were not advised to control their diet [26].

Summary of evidence

- ▶ Compliance is affected by dietary restriction and number of stool samples to be collected. Compliance is found to be consistently higher when the test adopted does not require modification of a subject's diet and sampling is limited to one bowel movement (I).

Recommendation

- ▶ In order to enhance compliance, testing procedures that require no or only minor dietary restrictions are to be preferred (I–A).^{Rec 2.17}

2.5.1.3 Examination of the samples, test interpretation and reporting

Detailed protocols on handling the stool samples must be available and followed. Identification and tracing of the sample through the entire process should be ensured by adopting appropriate labelling allowing the sample and patient's ID code to be linked. Automated check protocols should be implemented in order to avoid mismatching of the results. All data, including test results, should have a regular backup system.

Guidelines for the equipment, organisation, quality assurance (within and between laboratories) to be adopted for different FOB tests, as well as the professional requirements for the staff, are described in Chapters 4 [45] and 6 [104].

An operational definition for an inadequate screening test should be made explicit in the programme protocol, taking into account the characteristics of the test (i.e. the stability and the storage requirements of the tests) as well as the testing procedure adopted (i.e. the number of samples or of cards required) (see Sect. 2.5.4.2.1 and 2.5.4.2.2).

Protocols should be in place to define the appropriate test and the algorithm used to classify a test result (as negative or positive). For quantitative or semi-quantitative iFOBTs, an explicit definition of cut-off levels for haemoglobin concentration should be defined. Protocols or rules for combining results when using multiple samples, the number of samples that are needed to evaluate the test result, etc. must be in place. When using a quantitative test, provision should be made to record the information concerning the actual amount of haemoglobin, both for tests classified as negative and for those classified as positive.

Some people may present with clinical conditions such as inflammatory bowel disease (Crohn's disease or haemorrhagic recto-colitis), which may explain a positive FOBT result. In such cases, if no cancers were detected, then the screening result should be classified as negative for the purposes of the screening

programme. These patients should then be referred for treatment in the appropriate clinical setting.

See Chapter 10 [4] for a discussion of information about negative test results.

Recommendations

- ▶ Systematic (preferably automated) check protocols should be implemented in order to ensure correct identification of the screenee's test results and recognition of incomplete or erroneous data (VI–A).^{Rec 2.18}
- ▶ Protocols should be in place to ensure standardised and reliable classification of the test results (VI–A).^{Rec 2.19}

2.5.2 Endoscopy

2.5.2.1 Obtaining bowel preparation for endoscopy screening

The bowel preparation may be obtained from the office of the primary health care provider (e.g. GP), from endoscopy units or other screening facilities, or from pharmacists. There is no evidence concerning the impact of any of these strategies on participation rate, or on the proportion of inadequate exams. The aim should be to maximise accessibility taking into account local conditions, setting and culture. Several providers close to the target population should be available. The bowel preparation should be provided with clear and simple instruction sheets (see also Chapter 5 [112]).

2.5.2.2 Bowel preparation for sigmoidoscopy (see also Chapter 5 [112])

The acceptability of different types of preparations is influenced by cultural factors, which should be considered together with the evidence concerning the effect of the preparation, when choosing among different options. No difference in the proportion of inadequate exams was observed when comparing a single enema regimen to a preparation using two enemas or to oral preparation [3,99].

Summary of evidence

- ▶ A bowel preparation regimen using a single enema self-administered at home two hours before the endoscopy has been reported as the most acceptable option (II).
- ▶ Using two enemas may not decrease participation, while a preparation using both oral preparation and enema has a negative effect on compliance (II).

Recommendations

- ▶ Bowel preparation for screening sigmoidoscopy should involve a single procedure, either enema or oral preparation. A single self-administered enema seems to be the preferred option, but cultural factors should be taken into account, and population preference should be assessed (II–B).^{Rec 2.20}
- ▶ Several providers of bowel preparation close to the target population should be available when the subject is required to reach health or community facilities to get the preparation. Organisational options include the possibility of having the enema administered at the endoscopy unit. Clear and simple instruction sheets should be provided with the preparation (II–B).^{Rec 2.21}

2.5.2.3 Bowel preparation for colonoscopy (see also Chapter 5 [112])

Data on the impact of different preparation regimens in the context of population screening with colonoscopy are lacking. A recent systematic review [8] concluded that no single bowel preparation emerged as consistently superior, but sodium phosphate was better tolerated. The authors identified a need for rigorous study design to enable unequivocal conclusions to be drawn on the safety and efficacy of bowel preparations (see Ch. 5 [112], Sect. 5.3.3).

Timing of administration of the recommended dose appears important, as it has been established that split dosing (the administration of at least a portion of the laxative on the morning of the examination) is superior to dosing all the preparation the day before the test, both for sodium-phosphate and polyethylene glycol [1, 23, 79, 90] (II)

Summary of evidence

- ▶ To date no single bowel preparation for colonoscopy has emerged as consistently superior over another in terms of efficacy and safety (I) although sodium phosphate may be better tolerated and it has been shown that better results are obtained when the bowel preparation is administered in two steps (the evening before and on the morning of the procedure) (II).

Recommendations

- ▶ Preparation regimes used for colonoscopy seem equivalent in terms of efficacy and safety, although sodium phosphate may be better tolerated (I) and it has been shown that better results are obtained when the bowel preparation is administered in two steps (the evening before and on the morning of the procedure) (II). It is therefore recommended that there should be colonic cleansing protocols in place and the effectiveness of these should be monitored continuously (see also Ch. 5 [112], Rec. 5.22, Sect. 5.3.3) (VI–A).^{Rec 2.22}
- ▶ Several providers close to the target population should be available when the subject is required to reach health or community facilities to obtain the preparation. Clear and simple instruction sheets should be provided with the preparation (VI–B).^{Rec 2.23}

2.5.2.4 Test interpretation and reporting

2.5.2.4.1 Inadequate test

As mentioned above (Sect. 2.5.1.3), an operational definition for an inadequate screening test should be made explicit in the programme protocol, taking into account the characteristics of the test as well as the testing procedure adopted.

2.5.2.4.2 Defining a negative test and episode result

An explicit protocol defining the conditions for classifying a test as negative should be adopted, specifying the criteria for referral to colonoscopy assessment (in FS-based programmes) or surveillance (TC-based programmes).

Also, an operational definition for a negative screening episode should be made explicit in the programme protocol. A screening episode should be classified as negative when, based on the results of the primary test or of the recommended assessments (if any), the subject is referred again to the standard screening protocol. The rationale for having such pragmatic definition is to avoid the risk of labelling people detected with lesions that do not have clinical and prognostic significance (see also Chapter 10 [4]). This approach allows concomitant measurement of the

detection rates for various types of lesions that are included among the performance indicators listed in Chapter 3 [73]. See Chapter 10 [4] for details on how to communicate information about negative and positive test results.

2.5.3 Management of people with positive test results and fail-safe mechanisms

The potential reduction of mortality through cancer screening can only be achieved if subjects with abnormal findings receive timely and appropriate follow-up for detected abnormalities.

The findings of a recent US survey indicated that less than 15% of health plans monitor receipt of appropriate follow-up care by patients with abnormal results. This lack of organised tracking systems probably explains the low proportion of people with abnormal screening findings who receive adequate follow-up [126]. In particular, among patients receiving FOBT screening in the Veterans health administration, 41% of those with a positive test failed to receive appropriate assessment [38]. The negative implications of follow-up failures are substantial, including at the population level. A previous analysis of the screening history of invasive cervical cancers identified by a population-based cancer registry showed that about 20–25% of women with invasive cancer had been recommended for an early repeat smear, but had not received adequate follow-up [17].

Effective interventions targeting the screen-positive individuals include [6]: reducing financial and other barriers for further investigations or eliminating the costs for the patients, mail or telephone reminders, and providing written information material or telephone counselling addressing fears related to abnormal findings. All these interventions were found to be successful in increasing the proportion of people receiving timely follow-up. Few interventions have been assessed at the practice/provider level. The offer of same-day follow-up on-site colposcopy for abnormal Pap-smears [47] or an on-site colonoscopy following a positive sigmoidoscopy [105], has led to improved patient compliance. In a predominantly minority and indigent population targeted for cervical cancer screening, subjects managed through a specialised clinic, including nurse case manager, tracking system, reminder calls, rescheduling of missed appointments and clinical staffing with on-site colposcopy, achieved a significantly increased follow-up compared to a randomly assigned control group [37]. The implementation of infrastructure (computerised systems for tracking and monitoring of screening abnormalities) and organisational changes (multidisciplinary team work) are required to ensure sustainability over time of effective interventions.

Treatment and after-care service following evidence-based guidelines should be offered to all patients detected with cancer or pre-invasive lesions at the time of assessment of abnormal screening findings.

Summary of evidence

- ▶ Reducing the financial barriers for further investigations, utilisation of mail or telephone reminders, written information material or telephone counselling addressing fears related to abnormal findings, implementation of computerised systems for tracking and monitoring of screening abnormalities and organisational changes (multidisciplinary team work) were found to be successful in increasing timely follow-up (II).

Recommendations

- ▶ In order to ensure timely and appropriate assessment, active follow-up of people with screening abnormalities should be

implemented, using reminders and computerised systems for tracking and monitoring management of these patients
(II – A).^{Rec 2.24}

- ▶ The cost to the participant undergoing assessments should be as low as possible in order to promote equity of access
(II – A).^{Rec 2.25}

2.5.4 Follow-up of population and interval cancers (see also Chapter 3 [73])

The ascertainment of interval cancers represents a key component of the evaluation of a screening programme. The documentation and evaluation process requires forward planning and linkage between screening registries and cancer registries, including data on causes of death, with no losses to follow-up. Data collection and reporting should cover all cancers appearing in the target population.

Methods of ascertainment and follow-up may differ across countries and screening programmes depending on the availability and accessibility of data and of existing data sources: cancer/pathology registries, clinical or pathology records or death records/registries. See Chapter 3 [73] for a description of the indicators and the data requirements.

2.6 Screening policy within the healthcare system

There should be a national and governmental context for planning of CRC screening. The programme needs political support with sustainable funding to succeed. If appropriate structures in the healthcare system are lacking, screening should not be implemented until they are developed, for example using the implementation phase to build up the needed structures.

It is essential that the programme is integrated into the healthcare system and is accepted by both the population and health professionals involved in the diagnostic process for CRC. Organisation of the screening programme should integrate the structures of the entire health care system appropriately and it should comply with national guidelines and protocols. Within the organisational framework of the programme, the target population should be defined as well as the frequency of screening. Provisions should be made for the financing of the programme, including evaluation costs.

The professional and organisational managers of a screening programme must have sufficient authority and autonomy, including an identified budget and sufficient control over the use of resources to effectively control the quality, effectiveness and cost-effectiveness of the programme and the screening service. The institutional structure must facilitate effective management of quality and performance.

Process and outcome indicators should be constantly evaluated to serve the needs of the individual and the health service.

Adequate protection of all data should be ensured, following requirements set by European directives concerning data protection and national privacy legislation.

2.6.1 Local conditions at the start of a programme

Before implementation of a screening programme, an inventory of baseline conditions including information on opportunistic screening rates, background CRC incidence rates and availability of endoscopic resources should be made.

In order to run a successful programme, adequate resources, in terms of both staff and facilities must be available, and an adequate infrastructure must be in place.

Colonoscopy is the final common denominator of all the CRC screening strategies. Therefore, as the implementation of any form of population screening for CRC will place greater demands on colonoscopy resources, the feasibility of CRC screening also depends on the availability of colonoscopy services. There may also be limitations to access for subjects in rural or remote areas and in the public health sector. Clearly, CRC screening is only feasible if access can be guaranteed to individuals who participate in screening.

In many European countries, CRC early detection activity exists in some form, e.g. testing personally initiated by patients, or as a component of private health care. According to the findings of a recent survey conducted in 10 European countries and in Canada, about 10% of colonoscopies are performed for screening [18]. However a wide variation was found in the occurrence and in the appropriateness of the exams. The inappropriateness rates ranged between 0% and 50%. Similarly the proportion of colonoscopies performed following clinical indications which were judged to be inappropriate was about 25%, suggesting overuse of the exam. Even if screening exams should be delivered within dedicated sessions (see also Chapter 5 [112]), promoting a more appropriate use of colonoscopy might therefore increase quality of care and favour an efficient use of available resources. As suggested by simulations conducted in the US [93] a more efficient use of colonoscopy resources may result in an increase in the capacity to meet the demand of screening-induced colonoscopies.

It is unlikely, however, that simply providing funds to increase existing activity will enable the programme or screening policy to be successful. In parallel with introducing the general principles of organised screening, governments should consider the introduction of administrative measures (i.e. not paying for unnecessary exams) and implementing educational interventions aimed at enhancing appropriateness of colonoscopy referrals. In some countries, re-allocation of resources already used for opportunistic screening activities will be sufficient to cover the entire target population within a defined screening interval.

2.6.2 Defining the relevant healthcare professional and facilities

Depending on each country's health system and culture, different health professionals can be involved in kit delivery and stool sampling collection or in delivering bowel preparation for endoscopy screening (i.e. GPs, nurses, paramedics, pharmacists, volunteers from no-profit organisations, etc.), as well as in performing sigmoidoscopy when offered as a screening test (i.e. GPs, nurses gastroenterologists,). Each country should follow quality assurance standards for the facilities and establish minimum training requirements for each type of professional, fulfilling the present guidelines (see Chapter 6 [104]).

2.6.2.1 Diagnostic and treatment centres

Screening will be neither effective nor efficient if patients with a positive FOBT or FS are not followed up with a proper evaluation of the entire colon and appropriate management, if needed. Trained endoscopists are essential, and each programme should establish and monitor validated training for colonoscopy, following the guidelines in Chapter 6 [104]. To help in the planning of location of endoscopic services for screening, five levels of com-

petency are proposed in Chapter 5 [112] (see 5.3.1). The definitions of the proposed levels take into account the facilities and the level of competency which are necessary to remove screen-detected lesions, and consequently how often the patients should be referred elsewhere in order to have the detected lesions safely and expertly removed. If all resources are not available in a given area, large centres, particularly for diagnosis and treatment, can serve more than one area, provided that adequate communication is established.

2.6.2.2 Public health specialists

Considering the different healthcare environments, public health specialists with adequate epidemiological knowledge or equivalent expertise are recommended. These professionals are needed from the onset, to ensure that the programme includes a population-based information system that monitors each step of the screening process. They will then be responsible for gathering data and for ongoing monitoring in order to identify problems that need intervention. These public health specialists can be based at a national or regional level, whereas the other health professionals who are providing screening services are needed in each area. Public health specialists should have training in, and an understanding of basic epidemiology, statistics and communication. A European training programme on monitoring and evaluation of screening programmes would be desirable (see also Chapter 6 [104]).

2.6.3 What factors should be considered when deciding which primary test to use?

According to the findings of a survey of the International Colorectal Cancer Screening Network (ICRCNS) describing CRC screening protocols adopted in various countries, a number of diverse screening initiatives have been implemented with a wide variation in various aspects of programme implementation including the tests used for primary screening. Currently FOBT is the only primary test recommended by the EU for CRC screening [31], (see Ch. 1 [58], Sect. 1.1.4) [10].

Today there is a range of options for CRC screening in the average-risk population. The tests commonly adopted in screening interventions include tests for occult blood (either guaiac or immunochemical), sigmoidoscopy (FS) and total colonoscopy (TC). Whether one method is superior to the other is not clear from several analyses [81, 128]. Although clear experimental evidence is available only for FOBT, FS and TC are commonly considered as reasonable alternatives (see Chapter 1 [58]). It has been suggested that a country's screening initiative should be adapted to suit population size, healthcare system and methods of funding, and should be individualised to practice settings and if possible to people [10, 123]. Thus, when deciding which primary test to use, several factors should be considered. Some of them are connected with country-specific conditions.

2.6.3.1 Gender and age differences (see also Chapter 1 [58])

CRC incidence and mortality are consistently lower among women than among men, and they show an increasing trend with age, although age-specific CRC incidence and mortality vary strongly within Europe. Comparative analyses of age- and gender specific CRC incidence and mortality in 38 European countries indicate that the differences across countries translate to wide age ranges at which comparable levels of risk are reached. The risk advancement attributable to these geographical differences in age-specific

incidence and mortality rates across Europe has been estimated to be up to 10 years or more, while the lower incidence and mortality among women quite consistently translates to an age difference of approximately 4–8 years at which comparable levels of risk are reached [14, 15, 86]. CRC incidence and mortality represent important parameters affecting potential benefits of screening, which must be weighed against costs and potential adverse side effects when choosing the age of screening initiation.

Cost-effectiveness modelling of different strategies was generally consistent in evaluating as efficient to begin screening between 50 and 60 [35, 75]; decreasing the stop age from 85 to 75 yielded a small reduction in life-years gained with a large reduction in the number of tests. Another important factor when assessing the age at which to stop screening is the remaining life expectancy.

2.6.3.2 Participation

Acceptability of the proposed strategy and test represents a critical determinant of the impact of an organised programme. It influences the cost-effectiveness of the most commonly recommended tests due to different levels of participation [128]. The effectiveness of an intervention is therefore influenced by the compliance level that can be achieved, and ultimately the best option for a patient is the one he or she will attend. It has been suggested that the relevant information when comparing different strategies should be the estimate of the level of relative adherence to different tests which provide comparable levels of life-years gained per number of colonoscopies. More acceptable tests would pick up a higher proportion of prevalent lesions, even if their sensitivity were low, because more people would attend screening [96].

Differences in exclusion criteria, if any, should be taken into account.

Thus the availability of different screening methods that would allow individuals in the target population to choose their preferred strategy based on their preferences and values does not seem to be an effective option. The offer of a choice between two tests was not associated with increased coverage in a recent trial [95]. Offering an alternative test to people refusing the main screening strategy of a screening programme might represent a feasible option [129]. However, the sustainability and the organisational impact of such strategy should be assessed at the local level.

2.6.3.3 Screening interval and neoplasia detection rates according to the site distribution (see also Chapter 1 [58])

Evidence from randomised trials indicates that annual guaiac FOBT is associated with a higher mortality reduction compared to biennial screening. Observational studies [91, 127] support the indication of biennial screening with iFOBT (see also Chapter 4 [45]). The recommended interval for colonoscopy screening is usually 10 years, although evidence from observational studies would indicate that the protective effect may be longer. A five-year interval is usually recommended for FS screening, although available evidence does not support such a recommendation: observational studies have indeed suggested that the protective effect of the exam for CRC arising in the distal colon may last for more than 10 years and it would justify the adoption of a protocol offering the test once in a lifetime [76, 98].

The expected impact of endoscopic tests is also related to the site distribution of the neoplastic lesions in the colon and on their natural history (see also Chapter 1 [58]).

According to the results of a population-based case-control study, about 75–80% of colorectal cancer cases could be prevented by colonoscopy, with stronger effect for distal than for proximal CRCs [13]. Recent cohort studies of people examined with colonoscopy confirm a protective effect of colonoscopy but suggest that the protective effect for proximal lesions might be overestimated [7, 57].

2.6.3.4 Cost-effectiveness (see also Chapter 1 [58])

Available evidence from cost-effectiveness analysis suggests that all commonly considered CRC screening strategies (FOBT, Flexi-Sig, TC total colonoscopy) are nearly equivalent for prevention of colorectal cancer mortality (assuming 100% adherence) [128] and they therefore represent reasonable alternatives. Compared with no screening, nearly all analyses found that any of the common screening strategies for adults 50 years of age or older will reduce mortality from colorectal cancer. The cost per life-year saved for colorectal cancer screening (US\$ 10 000 to US\$ 25 000 for most strategies compared with no screening) compares favourably with other commonly endorsed preventive health care interventions, such as screening mammography for women older than 50 years of age or treatment of moderate hypertension.

The costs of a screening programme are strongly affected by the organisation of screening, including the costs of infrastructure, information technology, screening promotion, training and quality assurance, and by the characteristics of the health system. These same factors represent the main determinants of the cost of the screening test, which influences the estimates of the relative costs of different strategies. The timing of the costs and benefits should be considered as well: for example, endoscopy costs are met at the beginning, while those of FOBT spread over 10 years.

Also, the advantage in terms of risk reduction must be weighed not only against the programme costs, but also against the inconvenience for the patient and the adverse effects (some of them causing death, potentially, thus mortality evaluation is also key in cost-effectiveness) associated with each strategy. These factors will influence the likelihood that patients will actually complete the tests required for any given strategy and therefore these factors also have a strong impact on the costs of the tests.

2.6.3.5 Resources and sustainability of the programme

A recent resources-use analysis of the strategies considered for the UK bowel cancer screening programmes found considerable differences between screening strategies in terms of endoscopy staffing and capital requirements. Limited availability of endoscopy services would favour the adoption of strategies using highly specific tests targeting older age groups, while a sigmoidoscopy-based strategy would be preferred if the financial resources are constrained. Also, the high number of cases detected when adopting a strategy using biennial FOBT for people aged 50 to 69 would have a significant impact on surgical services. Resource constraints, mainly related to availability of highly qualified personnel [115] represent a strong barrier to the adoption of colonoscopy as a primary screening tool.

Summary of evidence

- ▶ The balance in favour of screening is likely to be reached at rather different ages in the various European countries, and several years later among women than among men (III).
- ▶ Offering people the option to choose a preferred strategy based on individual preferences and values does not result in increased coverage (II). Offering an alternative test to people

refusing the main screening strategy adopted by a screening programme might represent a feasible and effective option (V).

- ▶ The relative effectiveness in terms of incidence and mortality reduction of TC compared to FS might be overestimated (IV).
- ▶ The costs of a screening programme are strongly affected by the organisation of screening, by the characteristics of the health system. Different strategies involve different timing of the expected costs and of the achievable benefits (III).
- ▶ The impact of each specific strategy is strongly affected by its acceptability in the target population (III).

Recommendations

- ▶ Gender- and age-specific screening schedules deserve careful attention in the design and implementation of screening interventions (III–C),^{Rec 2.26}
- ▶ The costs of screening organisation (including infrastructure, information technology, screening promotion, training and quality assurance), the incidence of adverse effects and the likelihood that patients will actually complete the tests required for any given strategy represent additional important factors to be taken into account in the design and implementation of screening interventions and in the choice of the screening strategy (III–A),^{Rec 2.27}

2.6.4 Implementation period (step-wise)

From an epidemiological perspective implementation entails more than simply carrying out the screening process and onward referral for assessment whenever required. The particular epidemiological concerns at the early, implementation phase focus on the complete and accurate recording of all individual data pertaining to every participant, the screening test, its result, the decisions made as a consequence and their eventual outcome in terms of diagnosis and treatment and monitoring the causes of death.

Pilot demonstration projects have been carried out in some European countries to assess the feasibility of national programmes and their impact on routine services and to test whether the short-term outcomes of RCTs could be achieved in a context of routine care by a programme covering the whole target population [43, 111].

A new screening programme should be implemented in such a way that effectiveness can be evaluated. This can be achieved using individual-level randomisation into screening and control groups at the phase when the programme is new and resources and practical limitations prohibit the full coverage of the target population. This step-wise implementation, in which the target population is gradually taken into the programme as available resources expand, is both feasible and accepted when the available resources are used to their full extent.

A randomised screening design is helpful in the start-up phase when all the healthcare services and the infrastructure have not been evaluated within the screening programme, and since there cannot be certainty that the desired outcome and quality will be reached in that particular programme. In the first years of screening, an invitation scheme that gradually expands to cover more regions and age groups over the years can be used. Individuals in the control group will be offered screening later after the first years. This provides an unbiased comparison group.

A model from Finland is based on individual-level randomisation over the first six years [63]. For a six-year implementation phase it was expected that the number of colorectal cancer deaths will accumulate during 10 years from launching the programme in a population of around 3 million and a colorectal cancer mortality

rate of approximately 15/100 000. Meanwhile, feasibility can be studied and the programme monitored with various process indicators such as attendance rates, proportion of test positives, detection rates, and positive predictive values.

A randomised screening design can also be used to assess the impact of alternative policies, such as different methods of invitation, or different target age groups. The randomised approach may also represent an acceptable and feasible alternative to assess the impact of a new screening test or to compare cost-effectiveness of different screening strategies, when a clinical randomised trial to evaluate the reduction in cancer occurrence or mortality is deemed impractical.

For other aspects relevant to implementation of screening programmes, see Sect. 2.3.1.

Recommendation

- ▶ Ideally, any new screening programme should be implemented using individual-level randomisation into screening and control groups in the phase when resources and practical limitations prohibit the full coverage of the target population (VI – A).^{Rec 2.28}

2.6.5 Data collection and monitoring (see also Chapter 3 [73])

2.6.5.1 Data sources

To determine whether a programme has been effective with respect to its impact on mortality and morbidity requires continuous follow-up of the target population over an extended period of time, and ascertainment and recording of the outcomes of the screening process and of the indicators of programme impact.

There is a special need to monitor performance of programmes using new tests.

The monitoring and evaluation of the programme therefore require that adequate provision be made in the planning process for the complete and accurate recording of all the relevant data. Achieving this goal is dependent on the development of comprehensive systems for documentation of the screening process, monitoring of data acquisition and quality, and accurate compilation and reporting of the results.

The information system should be designed to support the implementation of the different steps of screening, to record screening findings of each individual, to identify those detected with abnormalities, to monitor that the recommended action has been taken and to collect information about assessments and treatment.

For the purposes of impact evaluation this information should be linked to several external data sources, and legal authorisation to be able to achieve this should be secured: population registries, for estimating population coverage and to identify people in the target population in relation to their screening history; cancer or pathology registries, for cancer follow-up and for quality assurance purposes and feed-back to clinicians; and cause of death register for individuals in addition to population statistics, for assessing vital status and cause of death for final effectiveness evaluation.

2.6.5.2 How to respond to outcomes of monitoring

The design of the information system should take into account the views and data requirements of all groups involved in the screening programme. A wide range of consultation and participatory planning is important to improve programme evaluation, through common definition of data elements, indicators and

standards. The programme should ensure that professionals involved in screening receive timely feedback on programme and individual performance. Rapid publication of the monitoring results is important as screening units and other actors need the information to run their activity and to implement quality assurance and training efforts. (See also Chapter 6 [104]).

In order to achieve these aims it is recommended to identify a co-ordination board that is responsible for regularly auditing the programme and taking necessary actions (including indications about the specific organisational changes which are necessary to meet the desired quality standards).

Recommendation

- ▶ In order to be able to evaluate effectiveness of screening, the data must be linked to several external data sources including population registries, cancer or pathology registries, and registers of the cause of death at the individual level in the target population. Therefore, legal authorisation should be put in place in order to be able to link the aforementioned data for follow-up when screening is introduced (VI – A).^{Rec 2.29}

Conclusions



In a multidisciplinary process, wide consensus has been achieved on a comprehensive package of evidence-based recommendations for quality assurance in organisation of colorectal cancer screening. Following these recommendations has the potential to enhance the control of colorectal cancer in Europe and elsewhere through improvement in the quality and effectiveness of the screening process that extends from systematic invitation to management of screen-detected cases.

Disclaimer



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