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Report on the Dutch consensus development meeting for implementation and further development of population screening for colorectal cancer based on FOBT [1]

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Abstract. A consensus development meeting was held to evaluate whether or not in the Netherlands all requirements were fulfilled for implementation of population screening with FOBT for colorectal cancer, or whether consensus was present that fulfilment by additional research or organisational actions could be obtained within 2–3 years. There was consensus that all classical Wilson and Jungner (1968) criteria, and six additional ones added more recently, had already been fulfilled or could be fulfilled within 2–3 years. Consequently, it was concluded that a national population screening for colorectal cancer should be implemented and carried out in the Netherlands in line with current national and European cancer screening programmes. A list of organisational actions to be taken was established. Research that is needed before the actual national launch of the screening within 2–3 years has been defined. Priorities have to be set for research and organisational actions for the coming 2–3 years for the implementation of population screening. In addition, research suggestions have been defined for the next 10–15 years for evaluation and/or improvement of implemented FOBT screening, and for future screening methodology. It was considered essential that infrastructure for future research would be embedded in the screening programme. A project group to arrange this should be formed.

Keywords: Colorectal cancer, adenoma, screening, FOBT, consensus

List of abbreviations

AMC:	Academic Medical Center Amsterdam;
CBO:	Kwaliteitsinstituut voor de gezondheidszorg CBO [Dutch Institute for Healthcare Improvement];
CDP:	Consensus development procedure;
CRC:	Colorectal cancer;
CVZ:	College voor zorgverzekeringen [Health Care Insurance Board];
FOBT:	Faecal occult blood test;
GE:	Gastroenterologist;
GG&GD:	Gemeentelijke Geneeskundige en Gezondheidsdienst [Municipal Health Service];
GP:	General practitioner;
IK:	Integraal Kankercentrum [Comprehensive Cancer Center];
MC:	Medical center;
NVVR:	Nederlandse Vereniging voor Radiologie [Radiological Society of the Netherlands];
PALGA:	Pathologisch-Anatomisch Landelijk Geautomatiseerd Archief [pathological anatomy national automated archive];
QA:	Quality assurance;
QC:	Quality control;
UEGF:	United European Gastroenterology Federation;

[1] Commissioned by the Netherlands Organisation for Health Research and Development [ZonMw] and the Dutch Cancer Society [KWF Kankerbestrijding].

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UMC: University Medical Center;
VSOP: Vereniging Samenwerkende Ouder- en Patiëntenorganisaties [Dutch Genetic Alliance];
ZN: Zorgverzekeraars Nederland (sector organisation representing the providers of care insurance in the Netherlands).

General introduction

The debate on the introduction of population screening for colorectal cancer (CRC) in the Netherlands has been going on for some time. As yet, no political decision to introduce population screening for CRC has been taken. The Ministry of Health, Welfare and Sport however has shown interest and investigates the possibilities for the introduction of population screening.

ZonMw had already commissioned a project in preparation for the design of a large feasibility study on population screening for CRC. This resulted in the publication of the Cocast report in 2003 [1]. Since then, ZonMw has received several grant applications for further development of population screening for CRC and research into the possibility of population screening using methods other than FOBT in the future. It was obvious that in the absence of a clear agenda, grant applications were very diverse and a divergent rather than convergent situation was emerging. It was concluded that in order to facilitate programming at ZonMw, goals for research and development studies need to be defined.

This has resulted in a timely plan to arrange a consensus development procedure, starting mid 2004, to discuss and define a road map for future developments and investments. The choice of FOBT for population screening appeared most obvious as was supported by international publications [2,4,6,7,9,13] and in the Netherlands by recommendations of the Health Council of the Netherlands [5], the Dutch Cancer Society [8], the Cocast group [1], and the 'Nationaal Programma Kankerbestrijding' (the Dutch programme for cancer control) [11].

Hence, the choice for FOBT was a pre-consensus issue and this has guided decisions on grant priorities. Accordingly, ZonMw's Prevention Programme has approved a grant application for a FOBT implementation study of screening using the FOBT method (Amsterdam–Nijmegen trial). The results of this implementation project are expected in the year 2007 and should help to define a protocol for population screening that is tailored to the situation in the Netherlands.

In September 2004 the Dutch Cancer Society published a Signalling Report entitled 'Early detection of CRC: reduction in mortality by population-based screening' [8]. The report lists the techniques available for population screening for CRC, and the results of population screening in other countries. Using this information, it provides recommendations for the implementation of population screening for CRC in the Netherlands. Its main recommendation is that population screening for CRC should be introduced in the Netherlands in the near future in several trial centres. For population screening to commence there must be agreement between all parties. A meeting at which the problems and priorities can be identified from various perspectives would accelerate and improve the introduction of population screening.

On November 4th, 2004, the report of the 'Nationaal Programma Kankerbestrijding' [11] was presented to the minister of Health, Welfare and Sport, Hans Hoogervorst. The report recommends that the Ministry of Health, Welfare and Sport takes control of matters and initiates a decision-making process on the introduction of population screening for CRC before the end of the year, according to a step-by-step plan setting out clear deadlines. In his speech, the minister announced that his Ministry is studying the possibility of introducing population screening for CRC.

In the Netherlands, we thus find ourselves at the beginning of a process that might eventually lead to the introduction of population screening for CRC. It is fortunate that almost without exception all organisations are in favour of and suggest introducing screening for CRC. ZonMw and The Dutch Cancer Society joined forces and took the lead in organising a consensus development meeting. The consensus development meeting is instrumental in defining research (or decisions) (a) in the short term that are necessary to finalise a protocol for FOBT-screening, and (b) in the longer term for the further development of the screening programme, either concerning improvement of the present approach and/or concerning new technologies. In addition, the participation of most, if not all, parties involved in screening and future research will stimulate communication, identification of hurdles, commitment and effective implementation. Hopefully it will result in clear understanding of future research priorities and provide indications for sources of programme funding.

Overview of the consensus procedure

ZonMw and The Dutch Cancer Society have opted for a consensus development procedure (CDP) according to a structure described before [12] because the parties involved in the introduction of population screening for CRC are diverse in terms of organisation, financing, responsibilities, and may have conflicting interests. A CDP is a systematic approach to gaining awareness of each other's interests, and obtaining clarity on each other's intentions and efforts and on the possibilities for introducing population screening. The idea is for parties to agree as much as possible and to expose any differences of opinion.

The CDP discussed all issues on which agreement (consensus) must be reached in order for population screening to be introduced, according to a structured approach for which extended criteria of Wilson and Jungner [3,10,14] for population screening have been used as a checklist.

First, in the spring of 2004, representatives from many parties were interviewed in order to define topics and specific questions to be answered and additional parties needed to reach a consensus. The CDP was finalised by bringing together all the stakeholders at a meeting in February 2005 to discuss the topics and assess the degree of consensus that exists among them.

During the CDP, issues have been discussed that might hamper the introduction of population screening for CRC, and ways of ensuring that it will run smoothly. The outcome of these discussions will guide ZonMw in its decision regarding what type of research it should support for the purpose of introducing population screening in the coming 2–3 years. Both ZonMw and the Dutch Cancer Society are keen on solving any practical and organisational problems connected with population screening for CRC. An organisation for CRC screening using FOBT needs to be set up. It is of paramount importance that the results from ZonMw-financed research can be implemented. For the Dutch Cancer Society, the organisation of CRC screening is important in view of its position that population screening should commence as soon as possible.

The CDP has additionally identified research issues that may accompany screening implementation, research focusing on aspects of the screening that might be improved and finally, research to evaluate additional or new screening technologies that may be added to the FOBT infrastructure or replace it on the long run. The planning of the infrastructure of the screening was also discussed. The requirements for the databases and biobanks to enable a cost-effective and time-effective infrastructure for the mentioned research were defined.

The CDP has produced four products:

(1) An assessment of the extended Wilson and Jungner criteria in relation to CRC screening.
(2) An inventory of existing knowledge and gaps in the knowledge, and in existing organisational infrastructure.
(3) Solutions for unresolved questions (decisions or dedicated research) and a list of organisational actions to be taken.
(4) Forecast and infrastructure of future research for screening and possible improvements.

Together, these products constitute a road map towards a nationwide CRC screening programme in the Netherlands and its continuous improvement.

The expected timelines are as follows:

- 2005: Political decision on the introduction of population screening for CRC.
- Up to 2007: Trial implementation and implementation study of screening using the FOBT method (Amsterdam–Nijmegen trial).
- Up to 2007: Further research and organisation for the purpose of the introduction of population screening.
- Short-medium term: Research for the purpose of improving the quality of the population-screening programme.
- Short-long term: Research for the purpose of future changes/improvements to the screening method.

The Consensus development meeting

Procedure

The meeting comprised the following groups of participants: A consensus committee (Appendix 1)[1], responsible for the conduct and reporting of the consensus meeting, expert speakers providing background information (Appendix 2)[1], and an audience of professionals representing all relevant parties (Appendix 3). In addition, foreign experts in the field of CRC screening participated in the discussions.

The consensus questions were defined in advance on the basis of interviews with different representatives or stakeholders of the government, the Health Coun-

[1] Conflicts of interest were recorded and filed.

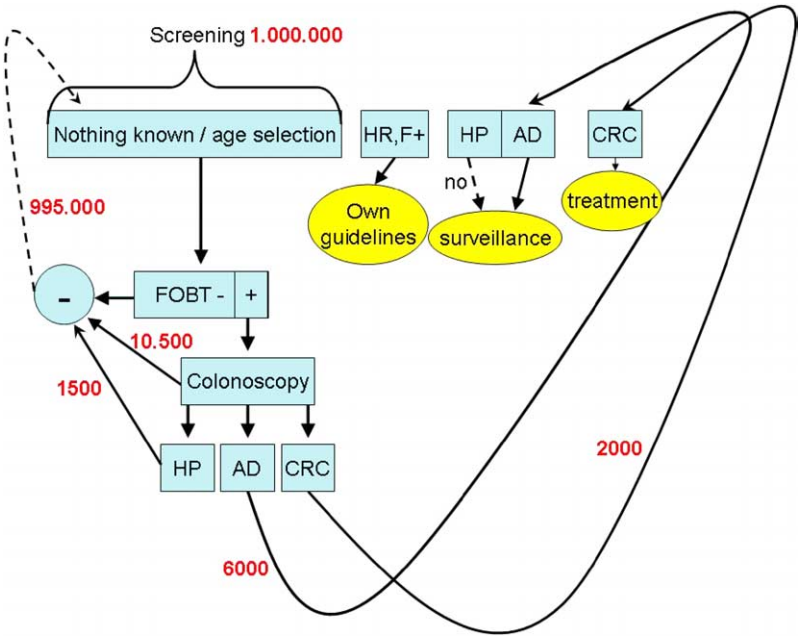

Fig. 1. Approximate cohort composition for 1 million individuals. Abbreviations in the figure: HR = high risk; F+ = positive family history; CRC = colorectal cancer; HP = hyperplastic polyp; AD = adenoma. Numbers are approximates taken from European literature.

cil of the Netherlands, screening organisations, health insurance companies, with ethical, screening, economical and biobank experts, radiologists, pathologists, gastroenterologists and general practitioners organisations. A pre-consensus was established in favour of the introduction of population screening using FOBT. This was used as a starting point to define questions on implementation and future research.

In order to investigate the essential requirements for implementation of population screening using FOBT, an extended list of criteria for population screening initially issued by Wilson and Jungner has been assessed. Invited expert speakers were assigned to answer questions about fulfilment of criteria, gaps in knowledge and potential improvements of FOBT screening in a structured lecture during the meeting.

A set of questions was divided over a number of experts in sessions dedicated to "Organisation Aspects" and "Medical and Technical Aspects" and "Future Developments".

To guide the discussions, a diagram was prepared concerning cohort composition per million individuals (Fig. 1) and an organisation flow chart was provided (Fig. 2).

The outcomes of the workshop sessions were summarised in draft documents that were reported in a plenary session and the conclusions reached were subjected to the consensus procedure. Voting instruments were available, but their use was not necessary.

A writing committee has finalised this report.

General questions

1. What are the data from international investigations that indicate that FOBT screening for CRC fulfils the (extended) criteria of Wilson and Jungner?
2. Which aspects would be a serious threat to start a nation-wide FOBT screening in the Netherlands in 2–3 years?
   (a) Specific national aspects preventing extrapolation of international research?
   (b) Rate limiting steps (beyond 2–3 years) in organisation?
3. Which aspects form an opportunity for a quick/smooth introduction of nation-wide FOBT screening?
   (a) Existing organisations/screening facilities/harmonisation of all cancer screening;
   (b) Already available protocols/experiences; e.g. from other screening programmes.

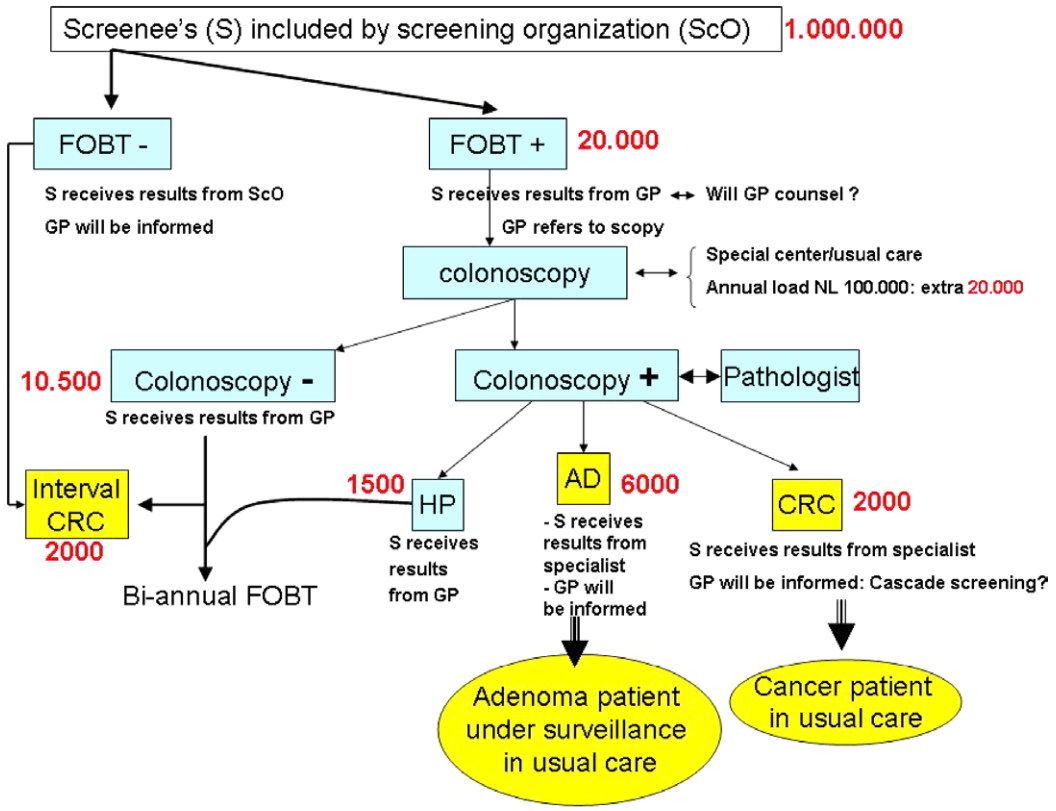

Fig. 2. Concept flow chart. Abbreviations in the figure: ScO = screening organisation; GP = general practitioner; S = screening individual; HP = hyperplastic polyp; CRC = colorectal cancer; AD = adenoma.

4. To obtain the best protocol for evidence-based screening and best practice for follow-up, which aspects
   (a) should be further investigated in 1–2 years;
   (b) require a decision by experts based on presently available evidence;
   (c) should be subject of flanking research during screening for continued improvement.
5. How should future research on new methods be organised in relation to the planned national screening?
   (a) National or regional data- and bio-banking;
   (b) Regional centres of excellence.
6. For each consensus topic an underlying question is: "What is the role of ZonMw and other research organisations such as The Dutch Cancer Society, CVZ, etc. in addressing the research topics", or more in general "what needs to be done, and who is responsible".
7. Which working parties or project groups should be defined to prepare a consensus on specific topics in the coming 2–3 years?

General screening criteria

As criteria for implementation of screening we used an extended list based on Wilson and Jungner's (1968) [14] original and WHO criteria, and additional criteria on ethical (National Council for Public Health, 1994) [10] and practical (Hanselaar, 2002) [3] issues.

The general screening criteria listed below were supplied to all participants. The numbers refer to criteria numbering in the text.

1. The condition sought should be an important health problem for the individual and community.
2. There should be an accepted treatment or useful intervention for patients with the disease.
3. The natural history of the disease should be adequately understood.

4. There should be a latent or early symptomatic stage.
5. There should be a suitable and acceptable screening test or examination. (The test must be acceptable for the target population.)
6. Facilities for diagnosis and treatment should be available.
7. There should be an agreed policy for referring for further examination and whom to treat as patients.
8. Treatment started at an early stage should be of more benefit than treatment started later.
9. The cost should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be a continuing process and not a once only project.
11. The time between test and result and between result and treatment must be as short as possible.
12. The recruitment procedure should not limit people in their freedom to participate or not in the screening programme.
13. Potential participants should receive adequate information about pro and cons of participation. Benefits and risks should also be well known to health care providers.
14. Public education should promote a broad accessibility of the programme. It should however not include a moral pressure effect.
15. There should be quality assurance (QA) and quality control (QC) procedures for the whole screening programme.
16. Screening programmes are concerted actions meeting organisational and managerial requirements.

Consensus statements about the extended Wilson and Jungner (W&J) criteria[2]

W&J 1. The condition sought should be an important health problem for the individual and community.

Consensus: CRC is an important health problem for the individual and community. In 2001, 9206 cases were diagnosed with CRC and this number is expected to increase to 13835 in 2015. In 2003, 4.429 died from CRC and this number is expected to increase in 2015 to 5305 in 2015. Overall five years survival is 55%. It is of equal importance in both genders [8].

[2]The meeting was recorded: both presentations and discussion. The records are kept by ZonMw.

W&J 2: There should be an accepted treatment or useful intervention for patients with the disease.

Consensus: There are accepted treatments/interventions for patients with malignancies and adenomas. Active surveillance after treatment is defined, but not based on extensive evidence. It is proposed to decide to initially follow guidelines as they are. Further interventions after removal of hyperplastic polyps are not generally indicated at present.

W&J 3: The natural history of the disease should be adequately understood.

Consensus: The natural history of the disease is adequately understood for invasive CRCs and for adenomas, but not completely.

W&J 4: There should be a latent or early symptomatic stage.

Consensus: There is an early stage that can only be detected by screening.

W&J 5: There should be a suitable and acceptable screening test or examination. (The test must be acceptable for the target population.)

Consensus: FOBT screening is a suitable and acceptable method for population screening for the near future (<2–3 years). Based on experience in other European countries, a compliance rate of at least 60% can be expected.

W&J 6: Facilities for diagnosis and treatment should be available.

Consensus: A nationwide screening programme is expected to generate at least 15,000 extra colonoscopies per year. The necessary adaptation of the capacity and quality of diagnostic and therapeutic interventions within 2–3 years is feasible provided adequate funding is made available.

W&J 7: There should be an agreed policy for referring for further examination and whom to treat as patients.

Consensus: All individuals with a positive FOBT will be offered colonoscopy. There are agreed treatment and surveillance protocols for patients with adenomas/CRCs.

W&J 8: Treatment started at an early stage should be of more benefit than treatment started later.

Consensus: Scientific evidence clearly shows that, in the case of CRC, early detection and treatment leads to more benefit than treatment that has started later.

W&J 9: The cost should be economically balanced in relation to possible expenditure on medical care as a whole.

Consensus: Extrapolations of cost-effectiveness ratios of other European countries indicate that it is economically sensible to perform FOBT screening in the Netherlands. This favourable cost effectiveness ratio remains present down to a participation level of approximately 25% of the approached target population.

W&J 10: Case finding should be a continuing process and not a once only project.

Consensus: FOBT screening should be nationwide and bi-annual. The infrastructure will be maintained for a period of at least 10 years.

W&J 11: The time between test and result and between result and treatment must be as short as possible.

Consensus: The time between test and result will be in the order of days (1 week). In case of a positive FOBT, there should be timely access to colonoscopy (preferably within three weeks). This is essential for acceptance of screening among target populations. The waiting time between result of colonoscopy and treatment/further intervention should be in accordance with the standards for regular care.

W&J 12: The recruitment procedure should not limit people in their freedom to participate or not in the screening programme.

Consensus: The recruitment procedure is organised by the national screening management according to established legal and ethical standards ensuring free choice of individuals.

W&J 13: Potential participants should receive adequate information about pro and cons of participation. Benefits and risks should also be well known to health care providers.

Consensus: The information procedure for individuals is the responsibility of the national screening organisation and will be carried out in line with current national and European screening programmes, and will be performed according to established ethical standards ensuring free choice of individuals. People will be empowered to make an informed choice.

W&J 14: Public education should promote a broad accessibility of the programme. It should however not include a moral pressure effect.

Consensus: Public education is the responsibility of the national screening organisation and will be carried out according to established ethical standards.

W&J 15: There should be quality assurance (QA) and quality control (QC) procedures for the whole screening programme.

Consensus: It is the responsibility of the national screening management to complete the set-up of a quality system including both quality assurance and quality control before the screening starts.

W&J 16: Screening programmes are concerted actions meeting organisational and managerial requirements.

Consensus: Yes, this is accomplished by having a national screening management.

General conclusion: All criteria from the extended list of Wilson and Jungner have already been fulfilled or could be fulfilled within 2–3 years. Consequently, a national population screening should be implemented and carried out in line with current national and European cancer screening programmes.

Start of FOBT population screening after 2–3 years

General advise

It is advised, based on all available evidence, to perform population screening bi-annually and with a lower age limit of 50 and an upper age limit of 74 (the exact age range to be decided within 2–3 years based upon further research on cost-effectiveness, feasibility and resources).

Action lists or agenda's (<2–3 years)

The first action to be taken is instalment of a 'national screening management' by the Minister of Health. In addition, CVZ, ZonMw, and the Dutch Cancer Society will establish an expert committee to work out the action list, and to set priorities for research and organisation for the coming 2–3 years for the implementation of population screening.

(A) Organisational agenda (<2–3 years)

The organisational actions that have to be taken to implement FOBT screening are listed in Table 1.

For reference purposes a concept organogram of a national screening organisation is given in Fig. 3.

Table 1
List of organisational actions

Action	By whom	Remarks
Rapid identification of who will be the national screening management and assurance of smooth transition process	Minister of Health, Welfare and Sport	
Funding and long term estimates of screening costs	CVZ	
Draft implementation programme set-up	National screening management*	Use experiences from national and international screening programmes, and the results of the Dutch implementation study.
Set-up of specialised colonoscopy centres for the follow-up of screening. The funding for this should come out of the regular health care funds.	CBO	
Preparation of screening organisations under supervision of the national screening managements	National screening management	Feedback needed by professional organisations (GPs, GEs, budget makers, patients, individuals participating in screening, general public).
		Process control
Communication to the general public, the media, and to health care professionals	National screening management	Develop communication plans to effectively bring the message about screening across, and empower the public to make an informed choice.**
	ZonMw for research projects	
		Information and guidelines for health care professionals
		Inform insurers in order to obtain guarantee of reimbursement for treatment.
Monitoring of programme, and management of information	Expert committee (CVZ, ZonMw, The Dutch Cancer Society)	Monitor side effects of the programme. Find characteristics of non-compliant group
Establishment of research goals for the next 2–3 years	Expert committee (CVZ, ZonMw, The Dutch Cancer Society)	
Working out of logistics of the primary process of screening	Screening organisations	Define the maximum intervals between screening and colonoscopy, without interfering with the regular care of CRC patients.
		Define and set up reporting procedures.
Quality Working group set-up	National screening management in collaboration with screening organisations.	Quality programme for other screening programmes needed as well
Design of Database (all data from people to be invited)	Pilot project	Develop (bioinformatics) research tools as add-ons to regular screening programme.
		Decide on whether database is part of or linked to the biobank
		Can it be paid out of the diagnosis treatment code?
		Biobank should be part of the research programme, is not prerequisite for screening programme.

Table 1
(Continued)

Action	By whom	Remarks
Provision of sufficient facilities for colonoscopy for FOBT positive individuals.	Ministry of Health, Welfare and Sport, CVZ, ZN, Dutch Society of Gastroenterologists	Set up training facilities for nurse endoscopists Nurse Practitioner Training Institutes to be involved.
Exploration of legal issues concerning screening programme.	National screening management	
Exploration of the role of the GP in the screening process	National screening management	
Evaluation	Independent organisation	Outcome: Can one improve the whole system? Continuous evaluation programme

*National screening management has until now been done by CVZ. This will change in the near future, therefore in the 'by whom' list, 'National Screening Management' is mentioned next to CVZ.
**This may involve reconsideration and possible adjustment of (standard) informed consent norms, in case 'full informed consent' appears unattainable.

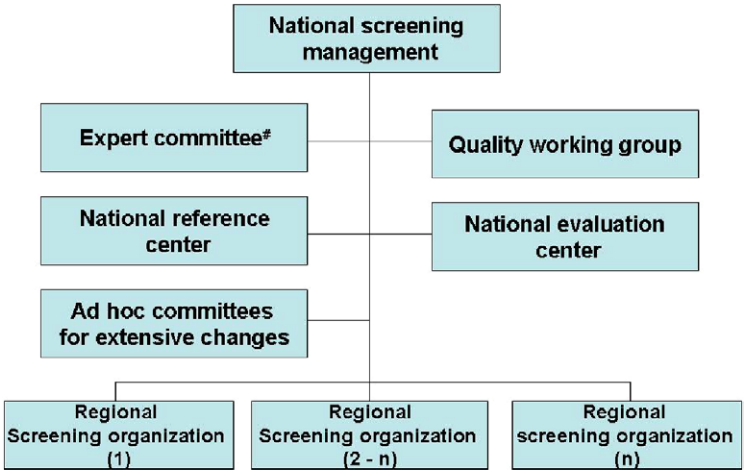

Fig. 3. Concept organogram of a national screening management. #It is proposed to form the expert committee as soon as possible to work on the organisational and research agendas.

(B) Research agenda (<2–3 years)

The research agenda, without priorities, for the coming 2–3 years before implementation of FOBT screening is listed below.

- Studies on different FOBT methods to address: (a) acceptance by the individual; (b) possible differences in sensitivity and specificity; (c) simplicity and costs of the screening method (automation?); (d) possibilities to adjust cut-off values for positive scores to temporarily reduce inflow in follow-up procedures (issuing from the Amsterdam–Nijmegen implementation study).
  The Erasmus MC is already dealing with cost effectiveness calculations for the various tests, including cut-off values.
- Feasibility studies with respect to adaptation of the capacity and quality of diagnostic and therapeutic intervention facilities.
- Communication studies (effectiveness of different messages and tools) to explore whether people are really empowered to make an independent choice, and whether messages are understandable and acceptable for different population groups.
- CRC awareness studies and campaign among general public and health care professionals.
- Comparison of models aiming at improvement of compliance.
- For the purpose of bio- and databanking, establishing in advance whether additional tests will affect compliance.

– Study on whether or not to include the age group of 50–55 yrs in population screening in the future.

Research agenda for continued improvement of the FOBT-based screening

The question was put forward whether or not and how, in a time span of 10–15 years, efforts should be made to improve faeces-based population screening. It was suggested to evaluate and discuss improvements and procedures in cooperation with all stakeholders, including patient representatives.

Firstly, it was proposed to explore the performance and cost effectiveness of faecal tests additional to FOBT, such as tests for DNA hypermethylation, multiple point mutations or specific proteins. An important strategy in establishing new tests is gain of knowledge of tumours, which lack mutations by faecal DNA testing. New tests should be compared with results of screening in different age groups with FOBT only.

Enhancement of the specificity with new methods, for instance a CD44 (protein) test or imaging techniques may improve the definition of negative results preceding colonoscopy.

Secondly, new tests and combinations have to be compared with the 'gold standard' (colonoscopy) aimed at reduction of the number of false positive FOBTs. As colonoscopy is a taxing procedure, a comparison of CT colonography with standard colonoscopy in FOBT positives, could yield an alternative reference standard.

Thirdly, to maximize the effectiveness of screening it should be identified why some cancers are missed by colonoscopy. The understanding of the contribution of flat adenoma to the development of carcinoma is important in this regard. In addition, an improved understanding of the biology of colorectal carcinogenesis is required including model studies. Identification of adenomas with a high risk of progressing to cancer can increase specificity. Methods to detect these high-risk adenomas either with imaging or biomarkers are desired. Study into the difference in the sensitivity of colonoscopy to detect CRC in the left or the right part of the colon, might lead to improvements.

Fourthly, research and training needs to be focused on quality assurance and quality control of existing procedures. Aspects include: (a) Training of endoscopist specialists; (b) Introduction of nurse endoscopists; (c) Evaluation of the training programme; (d) Development of protocols for performance of endoscopies; and (e) Development of a task force that sets standards.

Fifthly, the screening enables identification of factors for future risk profiling, e.g. environmental and genetic factors.

Data collection in the follow-up of FOBT screening could provide additional evidence for the degree of effectiveness of the present surveillance for various situations and experimental protocols may (regionally) evaluate other modalities.

Interval cancers provide an opportunity for retrospective analysis of risk elements recorded in the screening. It may reveal the relative incidence of rapidly developing adenomas as well as other factors. This would require additional information, including family history.

The aforementioned potential improvements in scenarios should be modelled and selected for experimental evaluation. Similarly, such procedures can be used for:

– Assessment of changes in cost effectiveness due to expected changes in cohort composition, cumulatively increasing surveillance after each screening round, increase of registration of high-risk groups circumventing screening.
– Assessment of the effects of e.g. over-the-counter FOBT tests, or open access of screening.
– Assessment of effects of combinations of FOBT with infrequent endoscopic/imaging screening.

Consensus: Repeated FOBT screening shows sufficient specificity ($\sim$*98%) and limited sensitivity (*$\sim$*50%) and leaves room for improvement. This improvement is not to be expected from the FOBT itself. New faecal tests with high sensitivity are being developed.*

Research agenda/questions for possible future (10–15 years) replacement of FOBT screening

The question was put forward whether or not and how, in a time span of 10–15 years, efforts should be made to evaluate replacement of the FOBT test. The following topics were considered of relevance for further evaluation:

(A) Multi-biological-variables testing on faeces

Other faecal tests can detect the presence of adenomas and malignancies with DNA/RNA and/or protein-analysis. In view of the multiformity of biological deviations, a panel of tests will be needed to achieve sub-

stantial coverage of the phenotypes. The performance of the following tests should be compared with FOBT: (a) DNA hypermethylation test; (b) Multiple point mutation tests; (c) Protein tests (Note that this list is not comprehensive).

An important strategy in establishing new tests is further research for additional mutations linked to colorectal cancer.

(B) Endoscopic procedures

New endoscopic developments should be tested. These include:

- Magnetic markers for colonoscope guidance;
- Wide-angle colonoscopy for improved adenoma detection;
- Self-propulsion colonoscope;
- Video capsule colonoscopy;
- Fluorescence endoscopy;
- Magnification endoscopy;
- Colouring techniques to enhance diagnostic sensitivity (chromendoscopy).

(Note that this list is not comprehensive.)

(C) Virtual imaging procedures

The most promising virtual imaging method is CT colonography, as moderate to good sensitivity and good specificity have been reported in low-prevalence populations. Further research is needed into radiation dose in relation to bowel preparation.

Computer-assisted detection is a promising development with regard to test characteristics and cost effectiveness.

Molecular tagging may in the future further enhance the performance of virtual imaging.

Consensus: Replacement of the FOBT should be evaluated in case its future improvements (see previous agenda) are unsatisfactory, and/or in case more acceptable methods for the screening of the target population are developed and could be implemented in population screening.

Research infrastructure

The availability of screening data and biological specimens in banks and the possibility of the coupling of these with follow-up data would create a research infrastructure.

The following topics were raised:

- In the forthcoming two years, a study should be performed to evaluate the possibility of the development of a modified faeces collection device that allows additional tests on faeces as well as biobanking of this material.
- Arrangements can be made to store biological material for prolonged periods of time (>10 years) to cover follow-up periods.
- The *exact* questions that can be asked and answered should be identified beforehand (within 2 years) to define the database- and biobank-characteristics.
- Access to and ownership of database- and biobank should be defined beforehand.
- A biobank should contain additional biological material other than faeces.
- A biobank should be a national organisation, probably with regional storage facilities.
- Attention should be paid to ways to obtain a structured report (including pathology) for subjects with positive FOBT test results.
- Communication with different countries should be intensified:
  - Harmonize agendas with respect to research issues;
  - Improve compatibility of different 'banks'.

Consensus: A project group should be formed to define the infrastructure (linking, extra data) and potential research (and patient care) questions within two years.

Appendices

Appendix 1: Consensus committee

M. de Visser (Gezondheidsraad [Health Council of the Netherlands]) (Chair),
M. van Ballegooijen (Erasmus MC),
S.J.H. van Deventer (AMC),
J.B.M.J. Jansen (UMC St. Radboud),
G.A. Meijer (VU University Medical Center),
J. Stoker (AMC),
G.A. de Valk (College voor zorgverzekeringen [Health Care Insurance Board]),
M.F. Verweij (University Utrecht).

Appendix 2: Expert speakers

J.H. Kleibeuker (UMC Groningen),
M.F. Verweij (University Utrecht),
G.A. de Valk (CVZ),
A.M. van Peppen (IK Amsterdam),

R.J.C. Steele (Dundee, UK),
F.M. Nagengast (UMC St. Radboud),
P. Fockens (AMC),
M. van Ballegooijen (Erasmus MC),
W. Hameeteman (Academisch Ziekenhuis Maastricht),
S.J.H. van Deventer (AMC),
J.C. Hardwick (AMC),
J. Stoker (AMC),
R. Reij (CVZ),
G.A. Meijer (VU University Medical Center),
N. Malila (Cancer Society of Finland),
J. Faivre (France),
A. Laghi (Italy).

Appendix 3: Experts in the audience present during the whole meeting

The expertise was distributed over participants as follows: (A) Screening, cancer and organisational expertise (23%); (B) Medical/technical expertise (42%); (C) Patients, institutes, organisations, government (35%).

W.J.J. Assendelft	Leiden UMC,
M. van Ballegooijen	Erasmus MC,
J.F.W. Bartelmans	AMC,
A.C. van Bellen	VSOP en St. Bloedlink,
S.M. Bloemers	ZonMw,
P.A. Bolhuis	Gezondheidsraad,
E. Borst	Nederlandse Federatie van Kankerpatientenverenigingen,
L. Boomsma	Nederlands Huisartsen Genootschap,
J.A. Bovenberg	Leiden UMC/Rechten Faculteit,
A.P. de Bruine	Academisch Ziekenhuis Maastricht,
J.W.W. Coebergh	Erasmus MC,
E. Dekker	AMC,
S.J.H.van Deventer	AMC,
L.C.J. Dorssers	Erasmus MC, Josephine Nefkens Instituut,
A.J.M. Drenthen	Nederlands Huisartsen Genootschap,
A. Durrani	ZonMw,
T. Elemans	Stichting Doorgang,
M. van Engeland	Universiteit Maastricht,
J. Faivre	Burgundy Cancer Registry, France,
J. Gore-Booth	Colon Cancer Concern, UK,
J.D.F. Habbema	Erasmus MC,
T. Hanselaar	Dutch Cancer Society,
J.C. Hardwick	AMC,
G.J. den Heeten	AMC,
W. Heijbroek-deClercq	IK Amsterdam,
M.H. Hemrika	Zorgverzekeraars Nederland,
F.J. Hes	LUMC,
K.Y. Ho	NVVR,
R. Holland	UMC St. Radboud/LRCB,
C. Honing	Dutch Cancer Society,
N. Hoogerbrugge	UMC St. Radboud,
P.P.C.W. Huijbregts	Nederlandse Federatie van Kankerpatientenverenigingen,
J.B.M.J. Jansen	UMC St. Radboud,
L.W.M. Janssen	UMC Utrecht,
M.B.J.A. Janssens	ZonMw,
J. Jesperson	Ribe County Hospital, Denmark,
D.M.A.E. Jonkers	Academisch Ziekenhuis Maastricht,
J.H. Kleibeuker	UMC Groningen,
C. Kluft	TNO,
H.J. de Koning	Erasmus MC,
O. Kronborg	Odense University Hospital, Denmark,
E.J. Kuipers	Erasmus MC,
A. Laghi	Universita degli Studi di Roma La Sapienza, Italy,
J.S. Laméris	AMC,
C.A.L.M. Lennards	IK Oost,
A.J.J. Lock	College voor Zorgverzekeringen,
J. van Londen	ZonMw,
N. Malila	Cancer Society of Finland,
G.A. Meijer	VU University Medical Center,
C.J.J. Mulder	VU University Medical Center,
F.M. Nagengast	UMC St. Radboud,
S. Nevenzeel	GG &GD Amsterdam,
C. O'Morain	UEGF, Ireland,
M. Oudkerk	UMC Groningen,
J. Paulides	IK Rotterdam,
P.H.M. Peeters	UMC Utrecht,
A.M. van Peppen	IK Amsterdam,
A.M. van de Pol	PALGA,
I.J.S. Poortman	VSOP,
R. Reij	College voor Zorgverzekeringen,
M. Samson	UMC Utrecht,

H.J. Smeijers	Nederlandse Stomavereniging 'Harry Bacon',
H.J. Smid	ZonMw,
P. Snel	Slotervaartziekenhuis,
R.J.C. Steele	Ninewells Hospital and Medical School, Dundee, UK,
R.W. Stockbrügger	Academisch Ziekenhuis Maastricht,
J. Stoker	AMC,
S. Thomas	Erasmus MC,
E. Thunnissen	Canisius Wilhelmina Ziekenhuis,
R.A.E.M. Tollenaar	Leiden UMC,
C.M.J. Tops	Leiden UMC,
R. Truyen	Philips Medical Systems Nederland B.V.,
G.A. de Valk	College voor Zorgverzekeringen,
W.A. van Veen	Gezondheidsraad,
A.L.M. Verbeek	UMC St. Radboud,
M.F. Verweij	Universiteit Utrecht,
M. de Visser	Gezondheidsraad,
F. Vlems	Dutch Cancer Society,
J. van Vliet	Ministerie van VWS,
J.M.L. Vroom	Maag Lever Darm Stichting,
T. van Wezel	Leiden UMC,
J.T.H. Wijnen	Leiden UMC,
N. de Wind	Leiden UMC,
H. Wollersheim	UMC St. Radboud,
J.P. de Zoete	Catharina Ziekenhuis Eindhoven.

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