ELSEVIER

European Journal of Cancer 40 (2004) 638–642

European Journal of Cancer

www.ejconline.com

Editorial

Colorectal cancer screening in Europe: first things first

Colorectal cancer screening is advocated increasingly by a variety of doctors and experts across the industrialised world. The main reasons proposed for its use include the relatively high frequency and mortality from the disease observed for males and females [1], its early detectability (through occult bleeding and even non-bleeding polyps) and potential curability of Dukes' stages A and B. Furthermore, the suffering of those who die slowly from their disease (that could in some cases be avoided) generates awareness among their doctors, especially if the patients are of the same age .

In most countries, there are, or have been, rising trends in incidence, and to a lesser extent in mortality, especially in males, resulting in a marked increase in 5-year survival of almost 1% annually during the 1980s in central northwest Europe [2]. The relatively high mortality from colorectal cancer among the middle aged provides another argument for screening, although the absolute incidence and mortality are still low for those aged below 65 years (Fig. 1). Indeed, the absolute lifetime risk of developing colorectal cancer remains below 3–5% across Europe and below 2–3% for dying. For a 60-year old person without familial risk who assesses his risk 10–15 years ahead, the chances of dying from colorectal cancer remains far below 1.5% (Fig. 2a, b), and this would be even lower for a 50-year old. From a lifestyle perspective, many other and obvious risks, that are also related to colorectal cancer occurrence such as a lack of exercise, threaten a person of the same age. It is therefore not surprising that the—by definition—'low-risk' public does not have strong feelings about mass screening of the middle aged; at older ages when most cases occur (Fig. 3) many people or patients also suffer from other chronic diseases and the proportion of patients with serious co-morbidities is above 50% [3]. Nevertheless, and despite controversies on the interpretation of mass screening discussed in this journal some years ago [4], a sound 'technical' case can be made for colorectal cancer screening. This argument could even be strengthened when comparisons of effectiveness and costs are made with the expensive (although they are free) breast and cervical cancer screening programmes.

Continuous improvements in the sensitivity and specificity of Faecal Occult Blood Testing (FOBT) and the various types of endoscopy also support a move towards use of these tests and investigations on a larger scale, as well as to development of even more sensitive and specific methods that could replace them, such as proteomics of the faeces and non-invasive virtual colonosocopy. The result is an interesting chaotic situation with heated discussions within many congress halls.

The European Union has become more active in the area of cancer screening and the commission has now recommended to the various member states that colorectal cancer screening should be introduced, but without specifying the type or its frequency.

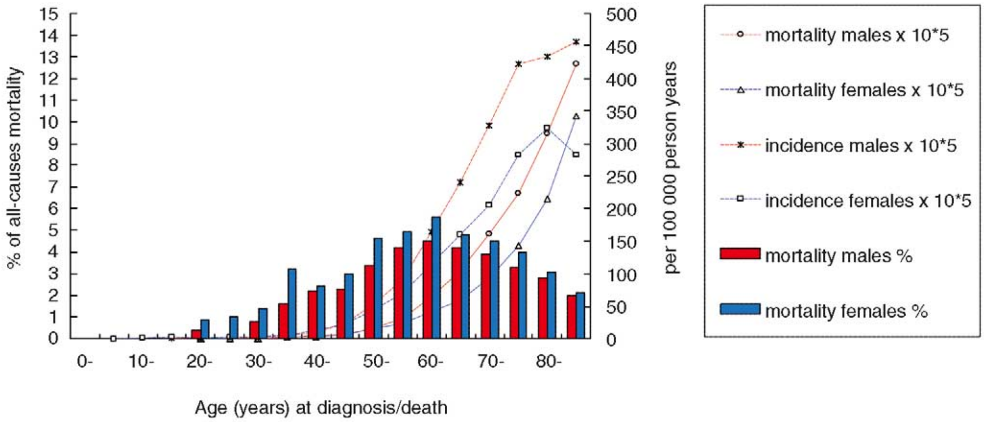
So, why not start the actual implementation? Herein, I give some arguments for a somewhat hesitant or even 'no-unless' view that I usually have towards mass screening for cancer. Its complexity and the irresistible tendency of the experts driven by the distorted risk perception of the public drift into medical perfection (laws of diminishing return are also ignored), thereby resulting in screening dominating other priorities in cancer care. In these processes, the healthy 'worried well', including many policy-makers, often become more vocal than the sick.

At an operational level, several questions need to be addressed with regard to the context and care implications of mass screening, the benefit in absolute terms and the side-effects. If specific diagnostic care services are to be extended to the public 'at risk', should this not be done in addition to the delivery of care to the sick and 'high-risk', based on symptomatic and/or genetic features? Should we not be more aware of the strong cultural changes that have taken place in many medical firms and hospitals (from places to suffer and die to places that protect) to deliver care for the many healthy instead of for the few sick. In other words, we should be aware of the potential frictions between the everyday opportunistic care situation and the industrial logistics of mass screening. But even if you opt for the industrial approach of mass screening, in-born conflicts remain

0959-8049/$ - see front matter
doi:10.1016/j.ejca.2003.12.015

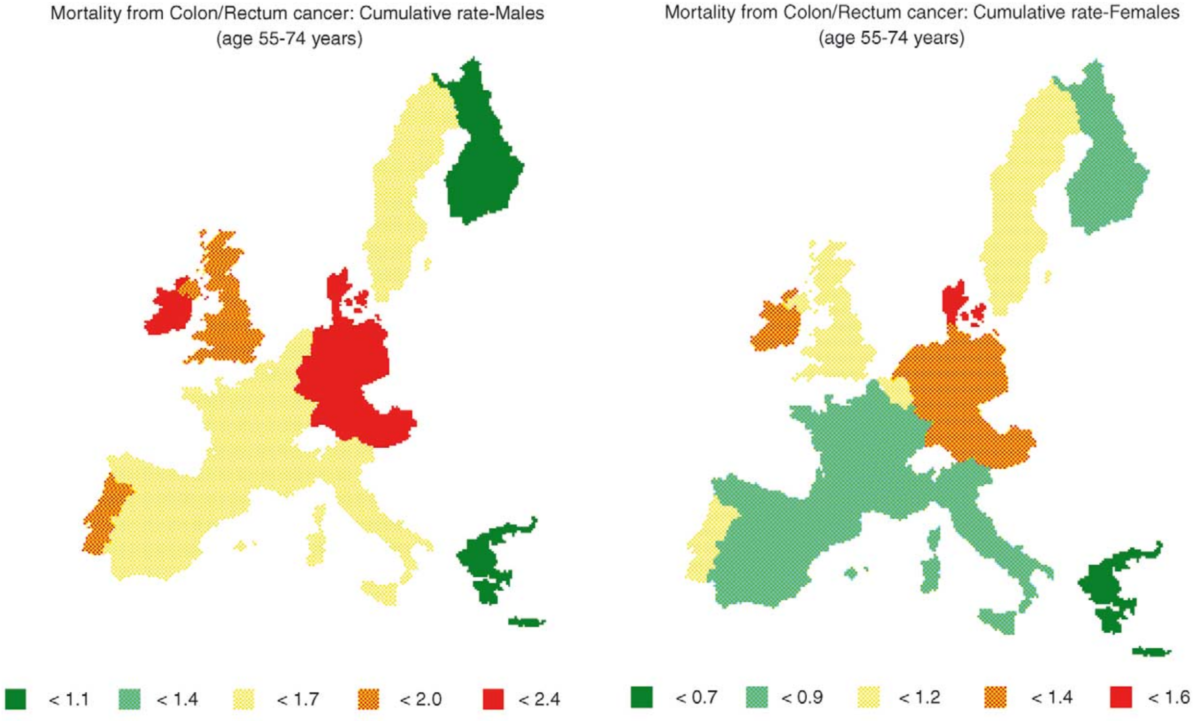
between the necessary long-term investments in manpower, equipment, logistics and risk communication (on absolute death risks please) on the one hand and competing innovation (in fact the only competition that works in health-care) in the development of new technologies on the other hand. As Schumpeter would say: the latter have the potential for creative destruction of former investments. Let *us be so prudent as to not to put* ‘*all our eggs in one basket*’. *My view would be that in this potentially chaotic situation of permanently changing care provision, (far preferable to stagnation) the priorities for the distribution of the available resources and care should go to the sick first, then to the ‘high-risk’ and finally to the ‘low-risk’ and not vice versa. Or, put another way, investments for mass screening should never hamper the early detection of the cancer in those needing endoscopy because of symptoms or familial risk.*

Therefore, a short description of the context of early detection is important.



source: Netherlands Cancer Registry & Statistics Netherlands

Fig. 1. Incidence of and mortality from (relative % and per 10*5) colorectal cancer in The Netherlands, 1998.


Mortality from Colon/Rectum cancer: Cumulative rate-Males (age 55-74 years)

Mortality from Colon/Rectum cancer: Cumulative rate-Females (age 55-74 years)

Cancer in the European Union (1995). IARC, 1999

Cancer in the European Union (1995). IARC, 1999

Fig. 2. (a) Mortality from colon/rectum cancer: cumulative rate—males (age 55–74 years); (b) mortality from colon/rectum cancer: cumulative rate—females (age 55–74 years). Source: EUROCAN.

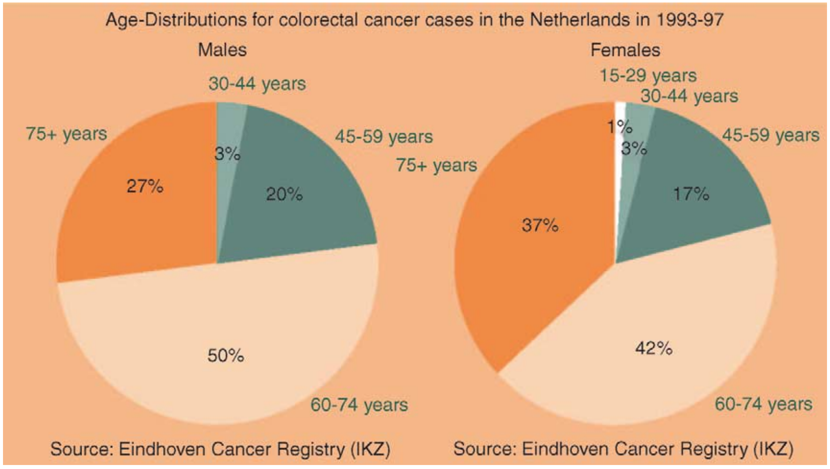


Fig. 3. Age distributions for colorectal cancer cases in The Netherlands in 1993–1997.

1. The context of mass screening

Screening for cancer is in fact a marked extension of the normal, but often complex and ambiguous, diagnostic (endoscopic and pathological) process, which is primarily aimed at detecting those with signs and symptoms who are at a 'low-risk' of developing the disease. Here, we should take into account that, depending on the nature of and access to the medical practice, one third or more of newly diagnosed subjects experience such delay that their situation became so clear that they could also be recognised and referred by lay people. However, we should all agree that general practitioners (GP's) or general office-based specialists must **always** be able to easily refer for endoscopy patients with some (always arbitrary) level of suspicion of cancer. The chances of finding a cancer are usually below 10%, but accurate practice is possible. Such patients can be seen up to once a week by a full-time GP and more often by a general specialist. Guidelines that include 'watchful waiting' and some patient education [5] may be an appropriate instrument to counteract the potential overuse of endoscopy in cases that have a very low level of suspicion. After one or more polyps have been found, modest surveillance practices have been developed [6], although there is large variation in these practices across Europe and within countries and social groups. Clinical research and guidelines should be a better answer to overuse than a screening programme. We also have to assume that in the last two decades most improvements in colorectal cancer survival documented in the literature have been the result of improved care and early diagnostics [2,7]. In the area of my cancer registry, where low barrier endoscopy has been offered since the 1980s, 5-year relative survival from colon cancer has increased from 45 to 60% in the late 1990s [8]. With respect to rectal carcinoma, a similar increase was observed, but this occurred somewhat later and was largely affected by more complex, multimodal treatments [9]. The study from Norway reported in this issue of the *European Journal of Cancer* is a very good example of this progress [10]. Does this not also imply that the past efficacy of randomised trials of mass screening in Denmark and the UK will be less than the future effectiveness of similar activities?

2. Surveillance of familial cancer

Screening and surveillance for familial cancer should be the second priority (where the first priority should be to treat and care for the sick). Guidelines and criteria have been developed over the last ten years [11] that do not yet appear to be well implemented in and within many countries. It would concern about 0.5% of the population. The 'experts' tell us improvements are still possible in the process of recognition, which is a question of clinical and personal awareness and pathological activity, both of which are always amenable to innovation. These persons and patients are mostly middle aged when relative mortality is highest (Fig. 1), and therefore the number of life-years saved is greatest. The maximum benefit on colorectal mortality would be between 10 and 15%.

3. The rising demand for endoscopy

Referral by a GP and general specialist and surveillance, especially for familial cancer, may result in an annual increase in demand for endoscopy of between 4 and 6%; 2–3% for epidemiological and demographic reasons and another 2–3% due to the extension in the indications in cases of familial risk and their surveillance and also related to the generally increasing public awareness about colorectal cancer. This would imply a doubling of demand in most countries within the next 15 to 20 years with of course substantial inter- and intra-country variations. Some curbing of demand (or supply by overenthusiastic gastroenterologists, here and there) must be made possible through the development of evidence-based guidelines and self-regulation.

The third (and not the first) health-care priority should be mass screening directed at, by definition, 'low-risk' people, certainly if the surveillance work directed at people with a familial risk has been implemented well. Mass screening would increase the demand for endoscopy substantially, depending on the type of screening and the interpretation of the various risks following the detection and classification of polyps. Of course, there will always be the usual discrepancies between epidemiologists who (from their desks) know what is good enough for a 'low-risk' population and gastro-enterologists who feel that they are screening patients instead of symptom-free people and do not want to miss polyps. Endless discussions can be foreseen regarding the quality of tests and endoscopy in relation to the sensitivity of the screening method and to pathological ingenuity in defining the aggressiveness of polyps. Moreover, let us not forget to include in the various cost-calculations the extra pathologists that will be needed for all this work.

All in all, mortality from colorectal cancer in the screened group (where another endless discussion on age limits can be foreseen) could be lowered by 15% due to FOBT [12,13] and even more ($>50\%$?) due to endoscopic screening [14]. However, compliance with the latter is still modest at the population-level, usually below 30% in trials and there is no country in the world where this level has become higher than 20%. The discussion on the benefits and costs of screening usually becomes endless: we are—in fact—looking at efficacy data that has been collected by dedicated doctors in the past (sometimes with obsolete methods) in populations with less favourable stage distributions. This is reflected in the modest relative survival rates for colon cancer in England and Denmark, below the European average, when the trials were performed (Fig. 4, source: Eurocare study, [15]). Thus, the effect of FOBT on mortality is likely to be less than the 15% observed in the past for these two countries. Given the favourable changes in stage distribution and endoscopic care provision in many countries, and also for familial screening, one wonders what the future effectiveness of FOBT screening will be?

The effects of screening must finally be measured in terms of future decreases in mortality, and possibly also in incidence. It is remarkable that the former trends are rather favourable in many countries, particularly given the rising trends in incidence observed in many of these countries.

In conclusion, my view would be to strengthen our current diagnostic capabilities as a first priority, expand with demand and, if necessary, restrict endoscopy here and there, by developing guidelines. In this rapidly evolving field, further efficacy and feasibility research projects should be carried out on the various approaches to early detection and screening, in 'high-risk' populations (the second priority) and also in 'standard' and 'low-risk' groups. Such research takes at least 10 years to observe any real effects. When countries are involved in such studies, a knowledge base is built and we can competitively learn from each other. In the

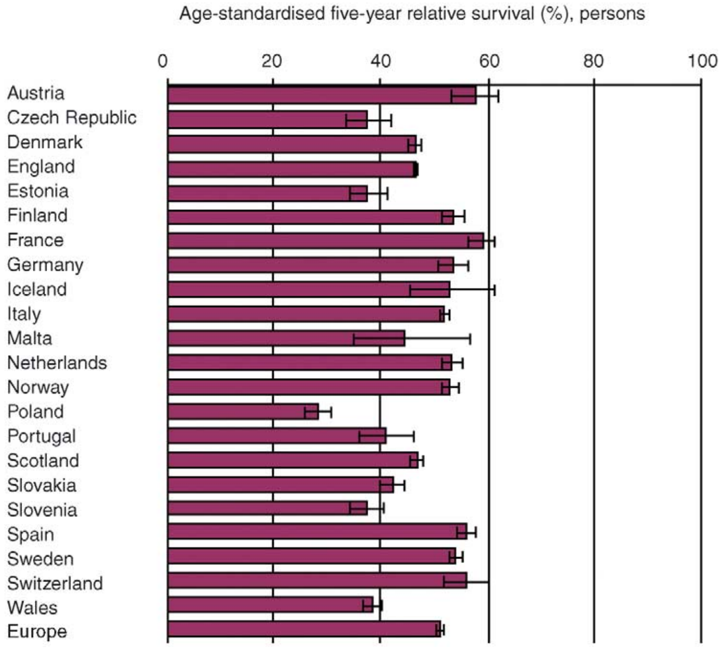


Fig. 4. Relative 5-year survival from colon cancer in Europe, 1990–1994 (source: Eurocare III). EUR, European average. Source: [15].

meantime, the gradual expansion of adequate endoscopic care should continue with possibly monitoring of quality control than we have used in the past.

References

1. Bray F, Sankila R, Parkin DM. Estimates of cancer incidence and mortality in Europe, 1995. *Eur J Cancer* 2002, **38**, 99–166.
2. Sant M, Capocaccia R, Coleman MP, *et al.* Cancer survival increases in Europe, but international differences remain wide. *Eur J Cancer* 2001, **37**, 1659–1667.
3. Marco de MF, Janssen-Heijnen MLG, Heijden van der LH, Coebergh JWW. Co-morbidity and colorectal cancer according to subsite and stage: a population-based study. *Eur J Cancer* 2000, **36**, 95–99.
4. Faivre J, Tazi MA, Autier Ph, Bleiberg H. Should there be mass screening using faecal occult bleeding tests for colorectal cancer? (Current controversies in cancer). *Eur J Cancer* 1998, **34**, 773–780.
5. Thompson MR, Heath I, Ellis BG, Swarbrick ET, Faulds Wood I, Atkin WS. Identifying and managing patients at low-risk of bowel cancer in general practice. *Br Med J* 2003, **327**, 263–265.
6. Atkin WS, Saunders BP, British Society for Gastroenterology; Association of Coloproctology for Great Britain and Ireland. Surveillance guidelines after removal of colorectal adenomatous polyps. *Gut* 2002, **51**(Suppl. 5), V6–9.
7. Faivre-Finn C, Bouvier-Benhamiche AM, Phelip JM, Manfredi S, Dancourt V, Faivre J. Colon cancer in France: evidence for improvement in management and survival. *Gut* 2002, **51**, 60–64.
8. Coebergh JW, Janssen M, Louwman M, Voogd AC, eds. *Cancer Incidence, Care and Survival in the South of The Netherlands, 1955–1999: A Report From the Eindhoven Cancer Registry with Cross-border Implications*. Eindhoven, Integraal Kankercentrum Zuid, 2001 (ISBN 905001-009-1).
9. Martijn H, Voogd AC, van de Poll-Franse LH, Rutten H, Repelaer van Driel OJ, Coebergh JWW. Improved survival of patients with rectal carcinoma since 1980; a population-based study. *Eur J Cancer* 2003, **39**, 2073–2079.
10. Angell-Andersen E, Tretli S, Coleman MP, Langmark F, Grotmol T. Colorectal cancer survival trends in Norway 1958 to 1997. *Eur J Cancer* 2004, **40**, in press (doi: 10.1016/j.ejca.2003.09.034).
11. Dunlop MG. Guidance on large bowel surveillance for people with two first degree relatives with colorectal cancer or one first degree relative diagnosed with colorectal cancer under 45 years. *Gut* 2002, **51**(suppl. V), v17–v20.
12. Scholefield JH, Moss S, Sufi F, Mangham CM, Hardcastle JD. Effect of faecal occult blood screening on mortality from colorectal cancer: results from a randomised controlled trial. *Gut* 2002, **50**, 840–844.
13. Jorgensen OD, Kronborg O, Fenger C. A randomised study of screening for colorectal cancer using faecal occult blood testing: results after 13 years and seven biennial screening rounds. *Gut* 2002, **50**, 29–32.
14. Atkin WS. UK flexible sigmoidoscopy screening trial investigators. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomized trial. *Lancet* 2002, **359**, 1291–1300.
15. Sant M, Aareleid T, Berrino F, *et al.* EUROCARE-3: survival of cancer patients diagnosed 1990–94—results and commentary. *Ann Oncol* 2003, **14**(Suppl. 5), V61–V118.

J.W.W. Coebergh
Comprehensive Cancer Centre South, Eindhoven Cancer Registry and Department of Public Health, Erasmus University Medical Centre Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands
E-mail address: j.coebergh@erasmusmc.nl