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Editorial Comment

Challenges and pitfalls of mass-screening in the European Union

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Minimal European recommendations for the prevention of the development of four major tumour types by mass screening are proposed by a panel of experts in this issue of the *European Journal of Cancer* (pp. 1473–1478). These recommendations are summarised in Table 1 with additional epidemiological and cost-effectiveness data. Brief reference is also given to the generally neglected aspects of logistics and importantly, as screening is only one means of lowering cancer mortality, competing innovations. Improved 'normal' access to diagnostic care and/or other emerging diagnostic techniques, as well as the large-scale application of medical treatments could also lower mortality rates. The inclusion of some of the experts in these screening projects improves the advice given, but can also limit the focus. Although mass screening for cancer as proposed in the statement offers an important contribution to early detection and cancer control, its effects remain modest. Firstly, the cumulative incidence and, in particular, the mortality rates observed in the unscreened relevant age groups remain low. It is the individual risks that may be high. Moreover, the age-specific relative mortality for each of the four cancer sites described is usually below 5%, with the exception of breast cancer in the age group of 35 to 55 years, where it is approximately 20%, declining to 5% by the age of 70 years. The most effective results appear to be obtained by endoscopy for colorectal cancer, although this has only been examined observationally.

Cervical cancer screening, if carried out systematically (as in Finland [1]), could have a marked effect on both incidence and mortality rates. However, in most European countries to date, either pathologists, gynaecologists or GPs screen in isolation instead of being guided in a collaborative effort with and by epidemiologists. Therefore, although the experts stress the importance of organisation and discipline they are rather unspecific in their recommendations for successful screening procedures that must also remain free from bureaucracy. A successful approach has proved to be a mixture of 'top down' thinking, budgeting, assessment and training with 'bottom up' involvement and commitment. Moreover, in the report in this issue I detected little awareness of all the definition problems and the, partly related, shortage of pathologists in the various countries referred to.

Importantly, not all the advice proposed by the committee of experts is based on solid evidence; for example, the cervical cancer screening that is proposed for ages 20–29 years, unless this is being suggested for high risk individuals only. Breast cancer screening for the age group of 40 to 49 years and the use of sigmoidoscopy for colorectal screening are two other examples where supporting evidence is not yet very strong. Prostate cancer screening was declared experimental for the next 10 years when in reality it is already being implemented by certain urologists in several countries. They also do not put forward arguments of other experts who opposed even research of prostate screening [2] on the basis that it is not possible to distinguish the aggressive from the non-aggressive tumours and address the subsequent problems associated with over-treatment.

If the countries are rated in a league table according to their present mass screening programmes, Finland, Sweden and The Netherlands would top the table while Germany, Spain, Portugal and Belgium would be at the bottom of such a list, the latter group because of too much or too little screening activity. Using such comparative studies, European countries can learn from each other on how to improve their own programmes.

It also becomes obvious from the report that cancer screening is a rather complex set of medical activities. It seems particularly important to screen appropriately, as screening is aimed at a predominantly healthy population who generally perceive screening to be uncontroversial with obvious benefits. Thus, nothing can or should go wrong, i.e. false-positives and negatives should be minimal. This contradiction is not addressed enough in the report. A further description, perhaps as an appendix, of the underlying biological, medical,

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Table 1
Overview of candidate tumour-sites for mass screening in Europe, recommended risk group(s), screening test(s), interval(s) and likely effect(s) and costs

Tumour site (% of all new cancers by gender)	High risk group Age-range (years)	Cumulative rate (%) in age-range of high risk groups. Incidence	mortality[b]	Proposed evidence-based mass-screening test (verifying procedures)	Interval between 2 tests	Maximum effect on incidence or mortality according to no. of tests	Costs per inhabitant[b] and per life-year saved (€)	Issues, competing technologies, remarks[c] (Always: manpower shortages)
Cervix (3–6)	30–60	< 0.4	< 0.2	Pap-smear (colposcopy)	Every 5 years (3?)	< 90% incidence (OB)	3–5[c]	Ever changing terminology
	20–29 (if high risk)	< 0.05	< 0.002			< 70% mortality (OB)		Value of computerised cytology
	60+ (if no previous screens)	< 0.5	< 0.4		Prolonged in women with negative tests?	(3–5000 smears for 1 death)	10 000–20 000	Follow-up of low-grade lesions? HrHPV-screening in near future?
Breast (25–35)	50–69	< 5	< 2	Mammography:	Every 2 years	< 30% mortality (RCT) (1000 mammographies for 1 death)	4–6[c]	Need for multidisciplinary aftercare by 'dedicated' breast teams.
	70–75[a]	< 1.5	< 0.5	Two-view double reading	(> 2 years)		5000–8000	Digital mammography.
	40–49[a]	< 1.5	< 0.5	(Cytology, biopsy) Breast — (self) examination?	12–18 months every month (cumulative)	Up to 20% (OB, RCT) Small (rather psychological value)		Adjuvant systemic therapy. Familial cancer screening.
Colorectal (10–15)	50–74	M < 5	< 3	Faecal occult blood test (FOBT) (colonoscopy and polypectomy)	Every 2 years	Up to 16% (RCT) (3000 to 5000 FOBTs for 1 death or 500 sigmoidoscopies)	Approx. 5[c]	Virtual colonoscopy. Distinction of high-risk tissue? Chemoprevention?
		F < 4	< 2	Sigmoidoscopy (colonoscopy and polypectomy)	Once or every 5 years (discontinued after negative screen)	Up to 70% on incidence (OB); < on mortality	< 5000	Role of familial screening?
Prostate (10–25)	55–74	< 6	< 3	PSA-test Biopsy at > 3–4 ngr/ml	Not yet known	Up to 20%? (> 1000 biopsies)	Unknown > 10 000	Adequate treatment of localised disease?

M, male; F, female; PSA, prostate specific antigen; RCT, randomised trial; OB, observational; ngr, nanogram; HPV, human papilloma virus; Hr, high risk.

[a] Only with adequate coverage of group 50–69 years.

[b] Age-range of mortality 5 years later than incidence.

[c] Rough estimates per annum.

psychological and logistical aspects of screening would have enriched this report. And why have no critical opinions, such as those recently described in the controversies section of this journal with regard to breast cancer [3] and colorectal screening [4], been put forward? In fact, differences between the mass screening "yes, unless" view of the screeners versus the more sceptical "no, unless" approach of many, usually more experienced, members of the medical profession can become smaller when opinions are exchanged. Compromises must be made.

If the aforementioned criticism largely deals with the question of how to make the past perfect, there will be new problems or challenges in the future for other tumour sites that are amenable to screening such as skin melanoma, lung and ovarian cancer.

Mass skin melanoma screening has been carried out occasionally as it is considered cheap and easy by dermatologists. However, despite the rising incidence and mortality rates, it is generally not deemed worthwhile; the lifetime cumulative incidence approaches 1% whereas the mortality remains below 0.3%. Moreover, the false-positive and negative rates would only be reasonable if the screening was carried out by trained dermatologists. However, dermatologists are usually in short supply and do not like to spend much time examining healthy skins. Increased melanoma awareness in the general population, among general practitioners and dermatologists can lead to timely referral and curative resection of up to 80% of skin melanomas in females and slightly less in males. This is especially so in males above the age of 50 years who tend not to attend screening campaigns. The melanoma epidemic may be subsiding in those born after 1950 owing to better education with respect to the harmful effects of intermittent sunshine, especially in childhood. Risk groups such as skin type, eye colour, presence of atypical moles and familial occurrence affect less than 10% of the population, although their distinction will remain fairly arbitrary. Randomised trials of screening would be almost impossible from a practical point of view as they would need large numbers of people followed-up for long periods of time and any effects of screening would probably be diluted by crossovers due to the unavoidable publicity. The current policy in many countries is to raise awareness, in addition to assessing trends in mortality and incidence. Breslow thickness could function as an indicator of success.

Lung cancer screening by means of spiral computed tomography (CT)-scanning in former smokers had a high sensitivity in a recent pilot study. It seems more promising than the largely unsuccessful and invalid attempts using chest X-rays as a screening modality in the late 1970s. This technique had a low sensitivity and too little contrast to accurately be used as a screening tool. Hopefully spiral CT-scanning is as accurate as it is expensive. In addition, further studies are needed to assess the validity of morphology obtained at a bronchoscopy [5]. This should be considered in former as well as current smokers.

Ovarian cancer is rather aggressive in its course affecting approximately 1% of women aged 40 to 70 years. Regular screening by means of Ca-125 and echography appeared to reduce mortality by up to 50% [6]. However, further testing in field studies is necessary before its introduction in mass screening can be seriously considered.

With regard to the screening advice given by the committee, I am not persuaded that the advice to screen for colorectal cancers by the faecal occult blood test (FOBT) is the correct one for most of the countries. Moreover, Autier [4] suggest that the modest effects from some of the RCTs (approximately 20%) were also affected by the more intensive follow-up in the screened patients. These effects have been observed in Denmark and Britain, two European countries with a high incidence and poor survival [7], which to a large extent is due to the unfavourable stage at diagnosis and poor access to endoscopy. Furthermore, the prognosis of rectal carcinoma has greatly improved over the last 20 years due to improved surgical techniques and preoperative radiotherapy and this improvement is likely to continue following the current large-scale introduction of mesorectal surgery. Fortunately, adequate treatment can also, in some cases, be an additional way of reducing the mortality rates due to cancer. The use of endoscopy as a screening tool looks promising, which is supported by some very recent, but perhaps a bit optimistic, model calculations. These are based on American studies that suggest a relatively low cost for this modality compared with the high cost of treatment for colorectal cancer needed with FOBT-screening, which should be largely avoided upon endoscopic screening [8]. In light of the continuously changing technologies and promising chemoprevention strategies, several small demonstration projects of short duration (not necessarily trials) seem warranted in the near future in various countries. These would be preferable to a few big trials of longer duration whose outcome may be outdated by the time of the appearance of the results. Logistics and manpower are also extremely important considerations here.

With respect to cervical cancer to implement the advice of the committee in sticking to the 5-year interval and decreasing the intensity of follow-up smears seems likely to be an uphill struggle. And debate will increasingly focus on HPV testing which is now also being explored. Whether that will be used as an adjunct to current screening programmes or replace them is presently unclear. More emphasis would be warranted on better education of women and their partners as to the nature and natural history of the disease as they are presently kept in the dark.

Mass screening of women aged 40 to 49 years is also an area of great controversy. There are plans for a large European screening trial, but I wonder whether we should wait so long (at least 10 years) for results which will undoubtedly be diluted (by more familial screening) or superseded by new developments in treatment. Based on an interpretation of work already completed, I would advocate a gradual lowering of the screening age from 50 to 49 years and so on down to 45 years when the rise in incidence starts slowing down (and a screening interval of 1.5 years which may need to be maintained until the age of 54 years). I would, however, only advocate this where there is already a 'good' screening programme in place for women over 50 years of age. Moreover, I would advocate in women over 65 years of age to lengthen the screening interval to 3 years.

To conclude, mass screening implies at the same time an enormous commitment of various professionals in the public health sector and the medical profession. If this can not be provided by a generous commitment of various public or third party payers, then it is irresponsible to start. The understanding of the complexities and advantages of these programmes by the general public is low and should be improved. Moreover, the medical profession itself is often divided over its benefits and also confused over the clinical relevance of the new biology and thus, is or should be afraid of over-treating patients. The medical profession generally has a demand-orientated, individual approach whereas screening is supply-orientated and has a mass-industrial approach and yet needs the same medical profession for a proper performance.

In a nutshell, screening is about selecting people with pre-malignant or localised disease for early treatment. The report in this issue has tried to discuss some of the complexities and grey areas and pleads for a centralised organisation and quality control based on the successful examples of the relatively small Scandinavian countries. However, it does not clearly describe the actual problems of introducing mass screening which implies implementation of standardisation and industrial procedures in a medical environment that largely consists of individualised, tailor-made procedures and passive, on-demand, patient education. The paper implies that there are pitfalls but these are not addressed openly.

These recommendations are targeted at politicians in various parliaments, health ministers and a range of advisory boards on the one hand and various segments of the medical profession on the other. Both groups have difficulties in understanding the paradoxical complexities of the early detection of cancer, as well as the problems of false-negatives and false-positives. They also underestimate the far-reaching logistics. All of these aspects need to be considered when implementing mass screening programmes.

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