that screening can reduce mortality in colorectal cancer with up to 30% and also attractive to health care providers when they are told that it is cost/effective.

But, it is not that simple. There are many sources of error and bias in studies performed. This varies as in breast cancer screening where doubt now has been pronounced concerning the scientific validity of the studies, which are the basis for current recommendations (P Gøtzsche, The Lancet 2000; 355: 129–34).

Today much is focused on evidence based medicine. A firm base is especially important when you are introducing a new treatment of – as in this case – will introduce a population screening.

According to my opinion we do not have scientific data enough to advice those responsible for health care (i.e. politicians) that screening should be introduced. Especially if drawbacks ate not considered in a balanced view.

In the debate I will point out that:

(1) A relative decrease in mortality of 15–30% corresponds to an absolute reduction of less of than 0.1% and that the NNT is high (650–1250).
(2) Performed studies do not inform about number of years gained due to screening.
(3) Performed studies very seldom report, or discuss, any harm caused by screening.
(4) Cost/effectiveness is only estimated.
(5) In concluding I will claim that not only the scientific analysis must be validated but that ethical and economical considerations must be done, not at least taking the harm/benefit ratio into account

1357

Follow-up in colon cancer

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Regular follow-up programs for colorectal cancer patients are time-consuming and require a highly skilled staff. Therefore the question is often raised whether an aggressive follow-up actually helps to improve the overall results and the individual prognosis. There is no doubt that the slow growth rate of large bowel carcinomas provides a fair chance for effective surgery of a recurrent tumor. However, an intensive, varied diagnostic program, repeated at short intervals, is necessary for the detection of recurrent disease in time to permit another attempt at radical cure. In our hospital an out-patient clinic for follow-up patients was initiated. The results of aggressive follow-up were studied to assess:1) patient compliance, 2) early diagnosis of recurrent disease, 3) incidence of curative surgery for recurrence, 4) life expectancy after radical surgery for recurrence. Results of a computer-aided follow-up program for patients with colorectal cancer were analyzed. In a 10 year period 1293 patients underwent this program, the drop-out rate was 17%. 299 recurrences in 168 patients were discovered (40% local recurrence, 29% liver metastases and 31% others). 51% of patients with local recurrence and 47% with liver metastases were symptomfree. Radical surgery could be performed in 50% of local recurrences and in 26% of liver metastases. The 3 year survival rate after radical surgery was 35% for local recurrences and 33% for liver metastases, the five-year-survival rate 23% and 15%, respectively.

1358

Against follow-up after curative surgery for colorectal cancer

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Vast amounts of resources, human as well as economic have been utilized over many years to detect recurrence at an early stage, making it suitable for surgical removal and thereby possible prolongation of life. Five RCT's have been published since 1995, all of these being incapable of reaching a valuable conclusion.

Overall, prospective as well as retrospective data suggest a 1% survival gain by intensive follow-up.

In recent years, a prolongation of life has been demonstrated after palliative chemotherapy for recurrent colorectal cancer, when the recurrence is detected in an asymptomatic stage.

Multicenter, multinational RCT's have been suggested to assess the best follow-up, but cost calculations based on the Danish RCT show, that a small benefit from intensive follow-up (1–2% increase in long-term survival) will be at least 4 times as expensive as that obtained by initial screening of persons with average risk for colorectal cancer.

Colonoscopy should not be used for detection of recurrence, but repeated colonoscopy with polypectomy may reduce incidens as well as mortality from metachronous colorectal cancer.

References

[1] Kjeldsen BJ, Thorsen H, Whalley D, Kronborg O. Influence of follow-up on health-related quality of life after radical surgery for colorectal cancer. Scand J Gastroenterol 1999; 34: 509–15

1359

Decrease in prostate cancer mortality following introduction of prostate specific antigen (PSA) screening in the Federal State of Tyrol, Austria, 1993–99

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Introduction and Objectives: Several factors support the use of screening tests for early detection of prostate cancer. First, patients do not experience symptoms in the early stages, and are unlikely to seek medical attention until the disease has progressed. Second, improvements in detection methods have increased the prospect for identifying the disease at an early stage when the lesion is still organ-confined, more easily treated, and often curable.

Methods: In 1993 PSA testing was made freely available to males aged 45–75 years in the federal state of Tyrol, Austria, and a mass screening project was launched. The Tyrol is an Alpine region in the western part of Austria with 331.410 inhibitants (65.123 males between 45 and 75). Previously (1990–1993) both PSA and digital rectal examination had been used as screening tools but not within an organised programme. The screening project was performed in collaboration with general practitioners, medical examiners, urologists, and medical laboratories in the Tyrol Blood Bank of the Red Cross. Informed consent was obtained from all volunteers participating in the program. In case of elevated PSA levels the volunteers were advised to undergo further urological evaluation, while men with normal PSA levels were invited to have a repeat PSA test twelve months later. The mass screening program was provided free of charge by the health and social security services of the Federal State of Tyrol and the University Hospital of Innsbruck.

Results: In the first year (1993) 32.3% of the 65,123 males aged 45–75 years underwent screening; 68% of all men in this age range were tested at least once in the first five years of the study. The incidence of prostate cancer in the Tyrol reached a peak in 1994 and has declined since. Significant migration to lower stages and an increase in the number of organ-confined, potentially curable prostate cancers have been observed since the introduction of this screening program. However, the percentage of clinically insignificant lesions in the screened group did not increase. Morality from prostate cancer among Tyrolean men aged 40–79, which had remained constant from 1970 to 1993, has now declined, whereas in other parts of Austria the mortality rates for males in this age range have changed much less. Based on the age specific prostate cancer mortality rates in Tyrol between 1986 and 1990 there were 17 fewer prostate cancer deaths in 1997 (32% decrease), 22 deaths fewer in 1998 (42% decrease) and 18 deaths fewer in 1999 (33% decrease) than were expected. This decrease in mortality is statistically significant ($p < 0.05$).

Conclusion: The present study shows that the policy of making PSA screening freely available to the Tyrolean population and participation of a high percentage of males aged 45–75 have led to an increase in the number of organ-confined, potentially curable cancers detected as well as to a reduction in prostate cancer mortality.

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Screening may not decrease prostate cancer mortality – policy making should be delayed (until evidence from randomised studies is available)

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Screening for prostate cancer remains a controversial issue around the world. Even in the United States where screening is highly prevalent important organisations advising on the patterns of medical care have taken contrary positions. In Europe, a statement of the committee against cancer of the European Union has adopted the view given in the title of this presentation.

Fortunately, there is evidence coming from important databases in the United States and from preliminary results of studies conducted in Europe and in Canada that screening may be effective in terms of decreasing prostate cancer mortality. This evidence however is heavily debated in the epidemiological and urological community. Even if, as is also hoped

and expected by those investigators who are engaged in the ongoing randomised screening studies in Europe and in the United States, screening will be shown to have an effect on prostate cancer mortality, this will not be the complete answer. Obviously, the most important question is: Does early diagnosis and aggressive management decrease prostate cancer mortality? The answer to this question alone however will not qualify screening as a health care policy in the critical judgement of most care providers around the world. The degree of over diagnosis, the impact on quality of life after treatment in relation to the risk of the untreated disease, the side-effects of treatment, the role of ageing and related chronic disease and life expectancy in decision taking, a better definition of the watchful waiting in prostate cancer management are all issues that are tightly connected to the question of whether prostate cancer screening can become a health care policy. Obviously, only the availability of such data will at the end allow a complete risk benefit and cost analysis. It is hoped that all these questions can be answered positively so that finally a preventive measure can be introduced into one of the most important disease entities of the male population.

In the meantime the powerful available early diagnostic capabilities cannot be withheld from well informed men. The accent here however has to be **well informed.** Standardised procedures for proper information prior to carrying out a PSA test are under development in various countries. To carry out testing without providing this information must be considered unethical.

1361

Immediate endocrine treatment is preferable and prolongs survival

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Trial data suggests that in men with advanced prostate cancer, immediate endocrine therapy improves disease specific survival, whether used as sole treatment (MRC PR03) or as an adjuvant treatment with radiotherapy (EORTC 22863). No trial data suggests an adverse effect of immediate treatment. The outcome is less clear when overall survival (death from all causes) is considered. In older men, with conflicting morbidity, prolongation of cancer survival will increase the opportunity of death occurring from other causes first. The possibility of a treatment induced mortality resulting from hormonal treatment has also been invoked, although the suggestion that hormone treatment may cause cardiovascular deaths has not been observed in PR03. Translation from the comparatively small number of patients studied in even the largest trials to the population as a whole is likely to translate the observed improvement of disease specific survival into an overall benefit. In addition, in PR03, clear benefits in reduction in complications such as spinal cord compression and control of the local tumour were seen, differences which have persisted as the trial data have matured. While quality of life data is not available from the quoted trials, it is as likely that patients will gain in benefit from control of their cancer as much as they lose from the side effects of treatment.

1362

Endocrine treatment should be delayed (until clinical evidence of progression)

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The widespread use of prostate-specific antigen (PSA) has induced a dramatic shift in the prostate cancer population: patients are now diagnosed with prostate cancer much earlier and failure of radical therapy is also detected at a very early stage. An ever increasing cohort of asymptomatic patients present threfore with minimal disease and prolonged expected survival. In addition significant advances in medical care have allowed correction of previously redhibitory comorbidities, thereby increasing the likelihood of longer survival. Should all these patients receive immediate endocrine treatment? In my view, there are compelling arguments in favor of delaying treatment: (1) Since endocrine therapy is only palliative and asymptomatic patients have no symptoms to palliate, delaying treatment avoids androgen ablation and its poorly tolerated side effects. When symptomatic progression occurs – and it will inevitably if the patient lives long enough – effective treatment is still available. (2) Observation means watchful waiting and not neglect: rapid progression and complications can be detected early by PSA based follow-up and modern imaging technology; treatment can therefore be started early enough to prevent catastrophic complications that inevitably occur when treatment is started too late. (3) Well-differentiated prostate cancer progresses slowly and many such patients will die of other causes, with cancer rather than from cancer. (4) Cost is reduced.

Admittedly, the timing of endocrine therapy in low-risk prostate cancer remains controversial because of the unpredictability of the two main variables: the evolution of a particular tumor cannot be reliably anticipated and the precise survival of a particular prostate cancer patient is unknown. Solid data however exist that can help the Urologist to individualize treatment, and his patient to make an informed choice. Patients with well differentiated tumors, low initial PSA, prolonged PSA doubling-time clearly do not need immediate therapy, local or general. Patients with severe comorbidities limiting foreseeable survival also can be observed expectantly. By contrast, patients with high-grade cancers, high initial PSA, symptomatic and/or rapidly progressing disease should be treated immediately. For the intermediate cohort of patients, strict watchful waiting is an option with initiation of therapy at early signs of progression. Unfortunately no strict clinical or biological criteria exist to trigger a change in therapeutic attitude.

Early treatment offers advantages in time to progression and disease specific survival, but there is no convincing evidence that it provides a clinically significant survival advantage counterbalancing its well-known side effects, especially in low-risk low-volume disease. Until now, in my view, no study has convincingly demonstrated a definitive benefit when androgen suppression was given early in low-risk low-volume prostate cancer, and watchful waiting therefore is a preferred – albeit temporary – option.

1363

Neo-adjuvant therapy for localized NSLC

E.F. Smit. *Vrije Universiteit Amsterdam, Pulmonary Diseases, Amsterdam, The Netherlands*

Neo-adjuvant or induction therapy for localized NSCLC (stage I-III) denotes the use of cytoreductive therapy before local-regional therapy. Its rationale is provided by the findings that survival after localized therapy leaves room for improvement, recurrences after surgery and/or radiotherapy are mainly at distant sites (+ 75%) and occult metastatic disease can be found in many 'early stage'patients (pts). Postoperative chemotherapy has been shown not to improve on survival in randomized controlled trials (RCT) mainly due to the inability to deliver the intended chemotherapy dose. Small RCT's of neoadjuvant chemotherapy in operable NSCLC pts demonstrated a survival benefit for those receiving chemotherapy, especially when complete resections could be performed. The survival benefit is retained at long term follow up. Most investigators agree that induction chemotherapy has acceptable toxicity and overall mortality/morbidity is low, although especially right pneumonectomy after induction therapy carries a considerable risk for postoperative mortality. Induction chemotherapy before radiotherapy in stage III pts improves survival. RCT of induction vs concomitant chemoradiotherapy have yielded conflicting results. A Japanese study did show a survival benefit for concomitant as opposed to sequential chemoradiotherapy but others failed to confirm these results. Toxicity of concomitant chemoradiation strategies is considerable (esophagitis) and should be reduced before it can be applied in routine clinical practice. Pivotal questions include the 'best' induction strategy (regimen?, chemotherapy alone vs chemoradiation for operable patients), restaging and 'best' local treatment (surgery vs radiotherapy) after induction therapy and management of patients with persistent nodal disease. These and other questions are the subject of large clinical trials which are underway. In conclusion: the use of neoadjuvant therapy is backed by data, is feasible and is promising for stage I-III NSCLC pts.

1364

Concomitant radiotherapy-chemotherapy for the treatment of lung cancer

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Synchronous use of chemotherapy and irradiation has become the standard of care for limited disease Small Cell Lung Cancer (SCLC) and increasingly the treatment of choice for locally advanced Non Small- Cell Lung Cancer (NSCLC). This approach has been adopted on the basis of limited clinical evidence and often without clarity for the basis on which an improvement in therapeutic index could be based. The fundamental aim of using common exposure time to chemotherapy and irradiation is the enhancement of the rate of local control from what can be achieved by radiotherapy alone. The effects on metastatic disease are secondary and determined by the effectiveness of the tolerable dose of the chosen chemotherapy regimen. Many of the old and new drugs with proven activity in lung cancer have radiosensitising properties in vitro and in vivo and need dose reductions when given with synchronous irradiation. The exception is the classical Platinum/Etoposide schedule in SCLC which in full doses with radiotherapy