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LETTER TO THE EDITOR

Population screening for colorectal cancer – how strong is the evidence?

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To The Editor

Hakama et al. [1] have presented a well written paper in this journal—an Acta Oncologica Expert Report. The authors are most familiar with problems in screening for colorectal cancer. They are apparently positive to screening and conclude with a recommendation that a screening programme should be started with a feasibility study. The authors refer to the two well known screening studies, from England and Denmark respectively [2–5] and build their discussion on them. These studies report a reduced mortality in colorectal cancer after screening with 15% and 18% respectively. The authors also refer to a report from a UK pilot study of screening for colorectal cancer [6], which states that population screening within the NHS in UK is feasible and should lead to reduction in deaths from colorectal cancer, if performed. In fact Hakama et al., like others who are in favour of screening, all refer to the same two studies [2–5].

How strong is the evidence that screening reduces colorectal cancer mortality, in these studies? Let us look at that. The English and Danish studies are randomized controlled trials (RCT), consequently any difference found should be attributed to the single differing variable in the studies, e.g. screening or no screening. Thus any reduced mortality found in the intervention group should be reflected in a corresponding reduced mortality due to all causes. That was however not the case. This fact then raises questions about the validity of defining diagnoses of death in the trials. Even if admittedly, in these ambitious studies, major efforts to minimize errors were done, the authors consistently use relative figures to report their results. Had absolute figures instead been reported the reduction should have been presented from 0.08% to 0.16% [2–5]. Not even have the original authors used the more easily understood NNT (Number Needed to Treat, or here, to screen). This number can however be calculated and in the English study the numbers needed to invite for screening every second year during 10 years to avoid one death with the diagnosis of colorectal cancer is 1 250 [2].

According to our opinion, the referred studies [2–5] have shown, with reservation for the above discussion on validity, that in the screening groups there was a reduction in deaths with a diagnosis of colorectal cancer but it has not been shown that mortality, during the period studied, has been reduced. Then any discussion on life years, or QALYs, gained or even on deaths prevented is not justified. Hakama et al. neither refer to comments in the updated online Cochrane review [7] but only to the original report, double published in 1998 [8], nor do they refer to authors who have challenged the whole concept of screening [9,10]

Hakama et al. further discuss the translation of results of intervention from a scientific study to the effect if used as routine in a population and they proceed to advocate feasibility studies. Normally this is the correct way to go if one wants to see if results achieved in a study can also be achieved when in routine use. But there is no possibility that results from a feasibility study can be better than in scientific RCTs! Like in the UK pilot study [6)] you can find how high the compliance rate is and more specific, in various age groups. But you cannot add scientific proof concerning the effect of screening. So, whether screening reduces mortality in colorectal cancer or not is only supported by the fragile data from the English and Danish studies.

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The tables (VI and VII) at the end of the paper by Hakama et al. [1] may be regarded as seductive. They are based on an assumption that the effectiveness is 20%-that is even higher than the efficacy in the European screening studies referred to. Hakama et al. state that data from the European studies can be extrapolated to the Nordic countries and then showing that approximately 1 500 deaths in colorectal cancer per year could be prevented by screening [1]. Such extrapolation can according to our knowledge not be done correctly without knowing the incidence of colorectal cancer in the various age groups in the referred studies!

So, in summary, in spite of the fact that the English and Danish studies [2–5] are very good—and the best we have—we must accept that there are some scientific shortcomings. This cannot be improved by feasibility studies. It is an enormous responsibility, for the medical profession to take, if existing evidence is presented in a way that leads health authorities to start mass screening without having further proof of the effect of screening for colorectal cancer.

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In response

MATTI HAKAMA, GEIR HOFF, OLE KRONBORG & LARS PÅHLMAN

Our points of view [1] mainly deviate from those in the letter by Ekelund and Janzon as to the degree of evidence and magnitude of effect in screening for colorectal cancer.

First the evidence. Ekelund and Janzon call for absolute effects (their percentages are still measures of relative effect). Take an example in absolute figures, if an expected number of 100 colorectal cancer deaths can be reduced to 80, there is a 20% and statistically significant reduction in mortality. At the same time about a total of 2 500 deaths will take place in that population. However, because of statistical random variation, the range of deaths we observe is between 2 400 and 2 600. The effect of 20 deaths can not be distinguished from the random noise of 200 deaths. The observation of Ekelund and Janzon of no statistically significant reduction in total mortality is correct but their inference or conclusion is simply wrong. The disappearance of statistical significance is not necessarily because of disappear-

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