HOFF, G.; BRETTHAUER, M.; SKOVLUND, E.; GROTMOL, T.:
Re: Baseline findings of the Italian multicenter randomized controlled trial of "once-only sigmoidoscopy"--SCORE

Re: Baseline Findings of the Italian Multicenter Randomized Controlled Trial of "Once-Only Sigmoidoscopy"—SCORE

We have just finished a colorectal screening trial in Norway *(1)* and therefore read the baseline findings from the Italian large-scale flexible sigmoidoscopy screening study (the SCORE study) *(2)* with great interest. However, we wish to comment on some aspects of this study.

Study population. The initial approach of asking for interest in participation was done in three different ways, either by direct draw from the population register or by asking all general practitioners or a random sample of practitioners in one region to provide candidate screenees. There may have been practical reasons for this approach, which should not influence the primary outcome (reduction in colorectal cancer incidence and mortality) after randomization of respondents to screening/no screening, but the overall population coverage may have been influenced. In addition, the threshold chosen for the actual invitation to flexible sigmoidoscopy screening differed between regions (e.g., in one area, only those initially reporting a definite willingness to attend if offered an examination were actually invited). Thus, we are presented with baseline findings from three or more separate recruitment protocols, making it difficult to interpret compliance, and consequently cost-effectiveness, and to make the results applicable to the general population.

Exclusions. We were surprised that any past history of colorectal polyps was an exclusion criterion. In the age group (55–64 years) studied by Segnan et al. *(2)*, one would expect to find polyps in approximately 50% of the population [36%–65%, depending on the endoscopist *(3)*]. The total percentage of exclusions reported by Segnan et al. was 11%, but larger percentages of people were probably excluded in areas where endoscopy was freely available and where polyps had consequently been diagnosed more frequently. Excluding up to 50% of the population in a study testing the potential benefit of a national endoscopy screening program seems inappropriate, particularly because Segnan et al. do not suggest that there is or should be a surveillance program for individuals other than those who present with high-risk adenomas.

Random assignment to screening or control group. Again, three separate methods were used, which may influence not only population coverage but also, as Segnan et al. point out, outcome. In one region, cluster randomization was used, with the physician being the unit of randomization. This was evidently done to reduce the probability of contamination (spontaneous endoscopy in the control group) in areas in which open-access endoscopy was practiced. After stratification of primary response rates of patients from each practice, the practices were randomized 1:1 for recruitment to the screening or control group. We are a bit uncertain how reduced endoscopy contamination is achieved by this method. The best method to reduce contamination would have been to not include any area with open-access endoscopy. In another location, ordinary random assignment on an individual basis was used. The use of the first two methods is especially surprising because a more appropriate method, household randomization, was used in another area. This "household randomization" is usually done exactly to reduce the risk of contamination, as in the large-scale British flexible sigmoidoscopy study *(4)*. Why was this not done for the whole study population? In addition, the recent contentious debate on mammography screening, in which cluster versus individual randomization has been a key issue *(5)*, makes it even more difficult to understand why three different randomization approaches were used.

We are, however, pleased to see that the authors have pointed out the large variation between the centers regarding detection rates for adenomas. We fully agree that there is a great need for implementing quality-control procedures for endoscopy performance in population-based screening programs.

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