Screening should be a program, not just a strategy

To the Editor:

Dans et al. [1,2] discussed the trade-off between benefit and harm in health screening. This dilemma has been succinctly summarized by Gray et al. [3], “All screening programs do harm; some do good as well, and of these, some do more good than harm at reasonable cost,” discussed by others [4,5], and formalized in national screening guidelines (e.g., UK National Screening Committee http://www.library.nhs.uk/screening/ and New Zealand National Health Committee http://www.nhc.health.govt.nz/moh.nsf/indexcm/nhc-screening-improve-health/).

There are important omissions from the tutorials of Dans et al. They described some of the well-known methodological problems that complicate the accurate assessment of the benefits of screening, such as selection bias, lead time bias, and length bias [2]. They do not, however, discuss overdiagnosis. This is an extreme case of length bias. For cancer screening, this refers to the detection, by a screening test, of cancers that would never have caused clinical disease. These cancers result in unnecessary treatment and are a harmful effect of screening, which cannot, at the moment, be determined in the individual case. The extent of overdiagnosis in cancer can be shown from randomized trials where an elevated cancer incidence persists in the screened group, and there is compelling evidence for the existence of overdiagnosis for several cancers [6]. It has been estimated that two to six women screened by mammography and needle biopsy will undergo unnecessary chemotherapy or mastectomy for every 1,000 women screened for a duration of 10 years [7].

Furthermore, the five criteria for evaluating the appropriateness of screening oversimplify the need to consider screening as a program, not as a test (or even a strategy) [8]. Screening can do harm at the population level if it cannot be delivered to all those who need it at a sufficient level of quality to reproduce in ordinary service settings the levels of benefit and harm that were found in the research setting [8]. Local economic analyses are necessary but not sufficient because they do not cover the health care system requirements for implementation of screening as a continuous (rather than a one-off) public health activity and a plan to collate data and monitor outcomes for quality assurance and improvement. Thus, Dans et al. highlight the need to consider the harms of screening, but we recommend more comprehensive, previously published, criteria for appraising the appropriateness of screening.

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On health screening and overdiagnosis

In Reply:

Dr Marcel Zwahlen and Dr Nicola Low have raised very important issues about screening. We thank them for their interest in our article and for the opportunity to discuss their concerns. Two points were raised in their letter, which we would like to respond to.

The first point they had raised is that we have missed discussing the important issue of overdiagnosis, which is the excess number of cases (e.g. cancer) that were detected in the treatment and control arm of a screening trial. Because these cases were “missed” in a nonscreened control group, it is possible that they were clinically unimportant and may...
never have manifested at all. We do allude to this phenomenon in our first article where we state:

“In the natural history of disease, a stage of preclinical disease follows good health (Fig. 1). This stage must be present for screening to work at all. The longer this stage of preclinical disease, the more opportunities there are to detect and treat it. As such, slow benign diseases (with a long preclinical stage) are more easily detected by screening than malignant diseases (with a short preclinical stage). Unfortunately, it is the latter which is our main concern. This is a flaw inherent in most screening strategies. A major criticism against prostate cancer screening, for example, is that it may detect slow indolent forms of the disease preferentially, while often missing the malignant forms” [1].

We mention this again in our second article, when we discuss the limitations of cancer screening:

“Screening tests have a higher chance of detecting slow indolent disease with a relatively benign course, because of long periods of preclinical disease. Rapidly progressive variants, on the other hand, have very short periods of preclinical disease and are less likely to be discovered by screening” [2].

We used the term “indolent” to refer to these relatively “benign” conditions. We hesitated to use the term “overdiagnosis” because it implies absolute knowledge that these conditions will never cause problems or that they will just “melt away” [3]. In truth, we only know that they remained latent for the duration of a trial or posttrial follow-up. Patients who do well even without treatment are fairly common in medicine. That is part of the cost of treatment and the exact reason why we need randomized controlled trials to weigh the costs and benefits. In the future, as biomarkers for prognosis improve [4], we may actually find out that certain screened diseases will never manifest or may actually regress. Until then, we prefer to refer to these cases as “indolent” rather than “overdiagnosed.”

We understand the authors’ point of view that screening should be viewed as public health programs and not just single “strategies.” However, in many poorer countries, such screening programs are of low priority, and decisions often need to be made on an individual basis, considering an individual’s priorities and resources. Furthermore, before we can fully address pragmatic issues, such as adequacy of staffing, opportunity costs, public pressures on eligibility, and quality assurance standards [5], we often need to first address explanatory issues, that is, can the technology work at all? Are the results of the trials valid? This is what we tried to do with the tutorials—give the readers simplified tools to appraise studies evaluating the technology. We do not deny the importance of eventually evaluating screening as a program, but by necessity, such programs will vary from country to country.

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