Baines says Kopans omits facts in attack on critics; he replies

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For purposes of analyzing screening trial results, would not the cutoff of subgroups below age 50 and 50 and over make more sense to the reader were it pointed out that most women under age 50 are premenopausal and most over age 50 are postmenopausal? Isn't the natural history of breast cancer somewhat influenced by these two stages of life? The cutoff is not as arbitrarily irrational as Dr. Kopans suggests.

While I disagree with much of what Dr. Kopans writes, I will respond only to his remarks about the Canadian National Breast Screening Study (CNBSS) which he has been attacking for 25 years. He is particularly critical of the design of the study. Ironically, the design was the direct outcome of recommendations by a (U.S.) National Cancer Institute/American Cancer Society Working Group.2 In spite of Dr. Kopans' opinion to the contrary, the CNBSS was meticulously conducted.

Compared with the Swedish Two-County Study (2-CS):

- Women were individually randomized in the CNBSS and complete demographic and risk factor data are available for the controls. This is unlike the 2-CS, in which only subjects' age at time of cluster-randomization is known.
- The CNBSS was able to document, in both the mammography group and the controls over 50, demographic and risk factor variables (such as age at menstruation, age at first birth, menopausal status). The proportions were virtually identical in both groups, thus validating the randomization procedure. In contrast, the 2-CS study had no information about controls other than age at entry.
- Cause of death, in particular death from breast cancer, was determined by an external panel in the CNBSS, whereas it has been said that in the 2-CS the principle investigator was involved.
- Numbers of deaths, breast cancer diagnoses, and breast cancer deaths have been consistently reported in the CNBSS. In the 2-CS, these numbers fluctuate wildly in successive publications.
- Breast cancer detection rates were higher in the CNBSS at Screen-1 (2.53/1000 and 5.48/1000 at ages 40 to 49 and 50 to 59, respectively, versus 2.09 and 4.67 in the 2-CS) and tumor sizes were smaller (1.6 cm versus 2.2 cm in the 2-CS), hardly evidence of flawed mammography.3

There is only one site where the entire story of the CNBSS is told, including examples of the ridiculous misinformation that has circulated in the U.S.: www.radcliffe-oxford.com/medicalspending/ .

As deputy-director of the Canadian National Breast Screening Study, I, like Dr. Kopans, have long been involved in breast screening and the associated controversy. The controversy reveals much about human behavior in general. It boils down to what I now call the American disease: a total inability by too many to respect those who have beliefs other than their own. Dr. Kopans, I do not distort data, I do not rely on weak science, and the literature is replete with responses to your challenges.

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References

Kopans' response

There are no ungrouped data that support Dr. Baines contention that the age of 50 has any meaning. It is fine to speculate that menopause may have an effect, but ungrouped data do not support this. Speculating about menopause is what led to data grouping, which is what makes changes that actually take place gradually with increasing age appear to occur suddenly at the age of 50. If we asked when the hairs on our heads turn gray and compared everyone age 44 and younger, as a single group, with everyone 45 and over, as a single group, then it would appear that we suddenly turn gray at age 45.

Dr. Baines is also well aware that retrospective, subgroup analysis of trials that were not designed and powered to permit age stratification should not be used to make medical recommendations, yet this is the basis for separating women ages 40 to 49 from other women. These are not my rules. They are in textbooks and paper after paper.

Dr. Baines raised issues that I did not address in my article. I did not compare her results with any other trial. I only pointed out that the results in the CNBSS 1 were compromised. She did not refute any of the problems with the CNBSS1 because they are irrefutable. Their own power calculation (published in 1980) showed that they only had the power to detect a 40% or higher mortality reduction when a 25% to 30% reduction was expected. That the quality of the mammography was indefensibly poor for a trial of mammography screening was even shown in their own review, and affirmed by their own physicist.

That the CNBSS violated fundamental rules for randomized, controlled trials is also indisputable. Dr. Baines did not deny the published fact that the randomization was unblinded and all women had a clinical breast examination before they were allocated to the screened or unscreened control groups. Women with lumps and palpable axillary lymph nodes were identified by the examination and allowed to participate in the trial. The allocation was on open lists so lines could be skipped, permitting more women with advanced cancers to be placed in the screening group. The fact that there were, statistically, significantly more women with advanced cancers allocated to the screening group is also indisputable.

Why the CNBSS 1 is defended and even held up as a well-done trial when it violated the fundamental rules of randomized controlled trials is incomprehensible. As Dr. Baines well knows, shifting 10 to as many as 100 women in her trial of 10s of thousands would have no impact on the demographics, but could completely bias the results.

It seems clear that this is what happened, rendering the results highly questionable. There can be no argument that these are major violations of the fundamental rules for randomized controlled trials. The methodology would not be permitted in a trial today for exactly the reasons given. It remains unclear and incomprehensible as to why "experts" who oppose screening defend this unblinded, imbalanced, biased trial.

With regard to "the American disease: a total inability by too many to respect those who have beliefs other than their own," I would only say that breast cancer screening should not be a matter of "belief." I have always argued based only on the facts, which can be examined by anyone, and not on my beliefs.

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