We thank Dr. Keen for responding to our article [1]. Much of his response is about cost, which is beyond the scope of our article and is not discussed in any of the national organization screening guidelines. We agree that more screening results in more direct financial expenditures for screening if the number of screening mammograms is used as a surrogate for cost. We also agree that more aggressive screening regimens result in more life-years gained and more breast cancer deaths averted. Dr. Keen's cost analysis, however, is limited. Cost analysis of a screening program is complex and should not be restricted to insurer direct costs but include the financial costs and burdens of not screening or screening less aggressively-- that is costs of alternative managements. These costs include lost productivity from increased morbidity and mortality (a major opportunity cost), incremental costs of treating later stage cancer, cost of treating more metastatic breast cancer, and costs associated with symptomatic assessments of unscreened women. The economic cost due to lost productivity alone secondary to the (avoidable) death of a single woman in her 40s is $1.4 million which equates to $1.4 billion per 1000 lives saved [2]. Medical insurers do not cover these large costs. Treatment of metastatic breast cancer is estimated as $250,000 per woman [3]. More difficult costs to estimate are those related to excess morbidity such as treatment-related cardiomyopathy, peripheral neuropathy and lymphedema.

Another focus of Dr. Keen's letter is overdiagnosis. We explicitly stated in our Methods section why our article did not discuss overdiagnosis: "Because both CISNET modelers and the USPSTF acknowledge that "methods for estimating overdiagnosis at a population level are not well established" [references 12,14,17 of reference 1] and "Existing science does not allow for the ability to determine precisely what proportion of cancer diagnosed by mammography today reflects overdiagnosis and estimates vary widely depending on the data source and method of calculation used," [reference 11 of reference 1] the decision was made not to include overdiagnosis in this study's risk assessment." [1] However, since Dr. Keen raises the issue, we would like to stress that overdiagnosis is not reduced by screening less frequently or by starting screening at later ages. There is now strong evidence that all cases of screen-detected invasive cancer and DCIS, if untreated, remain suspicious and are detected at next screening -- meaning that less intensive screening may delay but does not reduce overdiagnosis [4]. Therefore, overdiagnosis should not be used as rationale for starting screening after age 40 or for screening biennially instead of annually. Furthermore, Johns et al recently reported only 0.3% overdiagnosis in a large screening study from the UK after an appropriate follow –up period. [5].

In conclusion, women considering screening mammography should be aware that the greatest reduction in breast cancer specific mortality is achieved with annual screening mammography starting at age 40, with CISNET computer models demonstrating a nearly 40% reduction in breast cancer specific mortality, compared with only a 23% reduction in breast cancer specific mortality associated with biennial screening of women 50-74 [1]. Screening mammography decisions should be made by women, not for women.

References:

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