TESTIMONY

HARMON J. EYRE
CHIEF MEDICAL OFFICER
EXCUTIVE VICE PRESIDENT FOR
RESEARCH AND MEDICAL AFFAIRS
AMERICAN CANCER SOCIETY

For

"Making Sense of the Mammography Controversy:
What Women Need to Know About the Benefit of Early Breast Cancer Detection"

Joint Hearing

UNITED STATES SENATE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

SUBCOMMITTEE ON PUBLIC HEALTH

UNITED STATES SENATE

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Contact

Licy Do Canto

American Cancer Society

National Government Relations

202.661.5718 Phone

202.661.5750 Fax

LDOCANTO@cancer.org

Good afternoon, Madam Chairwoman, Mr. Chairman, Senator Frist, Senator Specter, and distinguished m~~m~~embers of both Committees. I am Dr. Harmon Eyre, Chief Medical Officer and National Vice President for Research and Medical Affairs of the American Cancer Society. I am honored to be here today, and I want to thank you on behalf of the more that 28 million volunteers and supporters of the Society for the opportunity to testify ~~before you today~~ about the strong scientific evidence supporting the value of mammography in saving lives from breast cancer~~.~~. The American Cancer Society commends you for conducting this very timely and important hearing.

I respectfully asked that my comments be submitted for the record.

The American Cancer Society is the largest nationwide community-based voluntary health organization dedicated to eliminating cancer as a major health problem by preventing cancer, saving lives and diminishing suffering from cancer through research, education, advocacy and service. ~~Nationwide, more than 28 million volunteers and supporters, including cancer survivors, researchers, healthcare providers and educators, contribute their time and resources to help advance the Society's goals. As the nation's largest cancer-fighting organization, we~~We have set ambitious goals for the year 2015 to reduce the number of people dying from and being diagnosed with breast and other types of cancer, and to significantly improve the quality of life for all cancer patients, survivors, and their families. While we believe that national achievement of these goals is possible, ~~we know that success in this endeavor lies in the continued importance of early detection and prevention in fighting cancer~~increased awareness and utilization of cancer prevention and early detection tools is critical to our success.

Madam Chairwoman and Mr. Chairman, before setting out to explain the American Cancer Society's view on the benefits of mammography, I would like to take a moment ~~and~~ to call attention to the terrible impact that breast cancer is having on women in this

country. This year, 203,500 new invasive cases of breast cancer will be diagnosed, and an estimated 40,000 women will die of the disease~~breast cancer, and 203,500 new invasive cases will be diagnosed~~. On average, a woman dying of breast cancer loses approximately 19 years of life she might otherwise have had ~~if she had not died of breast cancer~~. The human face on those statistics translates into families watching a loved one struggle~~ing~~ with advanced, unsuccessfully treated disease, and a family and community that ultimately ~~is~~are left to mourn her loss. ~~and ache for her dearly. As a~~ As a physician and medical oncologist, I have treated thousands of breast cancer patients in my career and observed first hand the heartbreak this disease visits on families and loved ones. ~~-~~Over the years, I have also witnessed the progress we have made, so that fewer women are dying from breast cancer. I do not wish to see our country lose the ground we have gained.

To this ~~at end~~, ~~,~~ we are hopeful that the recent announcement of the U.S. Preventive Services Task Force's update of their breast cancer screening guidelines and their endorsement of mammography for women ages 40-69, will add to the weight of the wide-scale rejection of the recent mistaken notion that mammography is valueless.

Madam Chairwoman, Mr. Chairman, and members of both committees, the scientific evidence supporting the value of mammography in effectively reducing deaths from breast cancer is solid, and I appreciate having the opportunity today to share with you ~~today~~ the Society's view on this important subject. ~~the value of mammography in effectively saving lives from succumbing to breast cancer.~~

The Origins of Early Detection in Breast Cancer

~~Madam Chairwoman and Mr. Chairman, t~~The importance of detecting localized breast cancer is ~~clearly~~ well established. It was first recognized in the mid-18th century by a French physician who proposed that breast cancer originated as a localized disease that subsequently spread through ~~-~~lymphatic channels to the general circulation. This key concept established the idea that surgery, if performed early, offered the potential to cure breast cancer. Effective means of early detection eluded us, however, until the early 20th century when it was first demonstrated that breast disease could be detected with x-rays, allowing for diagnosis of breast cancer even before symptoms, such as lumps, could be detected by a woman or her physician.

Madam Chairwoman and Mr. Chairman, aAs you well know, the path toward turning a promising idea into a practical solution can be rather longcan be a time consuming journey in the scientific world, becausein light of the high standards of scientific evidence that are required.guard this path. Promising work in breast imaging continued through the first half of the 20th century, eventually leading to a turning point in the early 1960s when Dr. Philp Strax, a radiologist in one of the Health Insurance Plan of Greater New York medical groups, proposed a large-scale study to rigorously evaluate the potential of mammography and clinical breast examination to reduce deaths from breast cancer mortality. Professor Sam Shapiro, Director of Research and Statistics at the Health Insurance Plan, and Dr. Louis Venet, a surgeon with experience in clinical breast examination screening programs, later joined him as co-investigators. This study became Tthe Health Insurance Plan of Greater New York Project, historically known as the HIP Study, and was initiated in

December 1963. It was the first randomized, controlled trial to evaluate the efficacy of breast cancer screening with clinical breast examination (CBE) and mammography. Approximately 62,000 women aged 40-64 were randomly assigned to two groups: the study group was offered annual clinical breast examination and two-view mammography for four years, and the control group received usual care.

The fact that this study was a randomized controlled trial is important because, with respect to cancer screening, it is critical to know whether the actual act of screening is the factor making the difference in saving women's lives. The ideal study would be one in which you had two identical groups of people, with the only difference between them being whether they weregot screened. Obviously, a study like that is impossible. Therefore, the next best thing is to randomly assign a large group of individuals to either the group that is offered screening orand the group that receives usual care. If our randomization has succeeded, and the study is well organized to maintain the integrity of equality between the study group and the control group, then we come very close to the theoretical ideal of two identical groups. Randomization of the women in the study controls for the factors we know about and the factors we don't know about that could bias our findings. If scientists simply looked at breast cancer death rates among women who have been screened versus not screened, it would not account for the fact that women, mindful of their health, would tend to seek screening and women less health conscious, might not. Therefore, without randomization, the difference in breast cancer death rates could be attributed to factors other than screening. That is, randomization tries to control for these and other differences among the study participants It helps us to truly demonstrate whether or not that screening, and not some other factor, is the factorreason that reduces death rates are reduced.

The HIP study was a dramatic turning point. It offered hope for the first time that through intervention was possible – we could reduce the number of women who died from breast cancer. The randomized HIP study demonstrated that there were approximately 30% fewer breast cancer deaths in the study group compared with the control group. Without question, the results of the HIP study ushered in a new era in breast cancer control, one in which there would be increasing emphasis on detecting and treating breast cancer before the onset of symptoms. However, scientists are rarely willing to recommend wholesale change in health policy based on one study.. Before recommending screening to the general population, we would have to not only know that it works, but that it was possible to implement a screening program at the community level.

The Logic Behind Early Detection

Before I talk about the next series of studies, I want to quickly discuss the logic The logic behind early detection and the relationship to the is based on the underlying biology of breast cancer. Breast cancer is a progressive and systemic disease, in which our ability to treat and cure a small tumor is much greater than our ability to treat and cure a larger tumor once it becomes larger. Treatment is easier and the outcomes are better, when the cancer is caught before there is lymph node involvement and before the cancerit has

metastasized, or spread, to distant organs. There is no more consistent and straightforward measure of a breast cancer patient's prognosis than the size of theherthe tumor. A few statistics to put this in perspective: When breast cancer is still localized – meaning that it has not spread to other organs --, 97% of patients survive for five years or more. Once the disease has spread to other organs, however, prognosis is bleak, with 79% of patients dying within five years. Our goal is survival – and scientific evidence ~~in its totality~~ demonstrates that screening ~~is a critically effective tool in achieving this objective~~can help us achieve the goal of lives saveds. Indeed, the important role screening plays in reducing breast cancer deaths has been demonstrated repeatedly., and it is etched in the mind of every physician that treats breast cancer patients.

Promising Concept to Promising Solution: The Importance of Routine Breast Cancer Screening

As I mentioned, above, the HIP study was not enough on its own to recommend screening to the general population. Before recommending screening to the general population, we would have to not only know that screening works, but that it was possible to implement an effective screening program in the community. The results of the landmark HIP study led the American Cancer Society and the National Cancer Institute to collaborate on a larger project to determine the practicality of bringing mammography screening to women at the community level. This project, known as the Breast Cancer Detection Demonstration Project, or BCDDP, screened over 280,000 women at 29 centers between 1973 and 1980. Participation rates were high over the course of the study and final analysis underscored the importance of mammography screening – nearly half of all breast cancers in this study were found by mammography alone.

Furthermore, among study participants, breast cancers were diagnosed at more favorable, early stages when compared with breast cancer cases among women nationwide during the same period. Most importantly, overall long-term survival has been much better among participants in the screening study. The bottom line is that, based on these two studies, we now had enough scientific evidence to say that mammography was an effective tool to detect breast cancer early, and breast cancer deaths would be reduced if we detected the disease before it had spread. Mammography was a tool that could make a difference.~~could detect the disease in its earlier stages, before it had spread, and that mammography was an effective tool in achieving this goal. this study mirrored the findings of the HIP study in that the reduction in breast cancer deaths is due to the shift from detecting the disease at advanced stage to detecting it before it has spread.~~

Thanks to the groundbreaking results of the BCDDP and the HIP study, the Society determined that there was sufficient evidence to promote routine breast cancer screening in the U.S. as a public health initiative in 1980. As the largest national health organization devoted to reducing cancer incidence and deaths, the American Cancer Society is well recognized as a primary resource for cancer screening guidelines. Our screening guidelines are ~~set based on~~established through a rigorous scientific review process and are re-evaluated at least every five years. ~~Based on the groundbreaking results of the Breast Cancer Detection Demonstration Project and the HIP study, the Society first determined~~

~~that there was sufficient evidence to promote routine breast cancer screening in the U.S. as a public health initiative in 19XX.~~ We have reviewed the scientific evidence relating to mammography repeatedly since 1980, and we have continuously concluded that while improvements in technology are certainly welcome, mammography remains~~is~~ the best tool we currently have to detect breast cancer ~~in its~~ early. In fact, as the Institute of Medicine recently concluded, mammography presently is the gold standard by which breast cancer is detected early. ~~stages. To be certain, iIt~~

As I mentioned, evaluation of mammography has continued. Between 1976 and 1982, six additional randomized controlled trials were initiated in ~~the~~ Edinburgh, Sweden, and in Canada. While there are ~~some~~ differences in the ~~results~~ results,~~–~~ all of these studies~~,~~ (with the exception of the Canadian studies)~~—~~ show a ~~favorable~~ benefit from breast cancer screening with mammography, both with and without clinical breast examination. In fact, the trials show a statistically significant reduction in breast cancer death by about 25-30% for women aged ~~forty~~ 40 and older and similar benefits for women in their forties compared with women aged 50~~fifty~~ ~~50~~ and older.

The accumulation of evidence from randomized trials over the years has strengthened the science behind breast cancer screening. In fact, one remarkable observation from the trials is that in the group offered screening, the observed reductions in the mortality rate in each trial are ~~uniformly~~ consistent with ~~the reduced rate of~~reductions in the rate of advanced breast cancer when compared with the control group. Put simply, the studies ~~unequivocally~~ showed that detecting breast cancers early increases the chances of survival.

~~In other words - bBreast cancerEarly detection through screening works.~~

It is important to note that trial results derive from controlled environments~~,~~. It is also necessary to demonstrate~~-~~ ~~and now that they are behind us, we must it is important to demonstrate , if the effects of a screening program are to be truly understood,~~ whether true benefits are being achieved under real-life circumstances. In Sweden where screening is a national health priority, those women receiving regular screening have been shown to reduce their risk of dying from breast cancer by over 40% compared with women who do not get regular screening ~~--~~, a fact that should not be ignored.

Revisiting Complex Questions: Reports from Cornell University and Cochrane

Madam Chairwoman and Mr. Chairman, as you know, in spite of the overwhelming evidence, mammography has not been without its detractors. Recently, two of these detractors have been able to gain widespread media attention and cause great ~~—in much of the scientific community's view— unnecessary and regrettable~~ confusion among the ~~general population~~public about the value of mammography. I am speaking of course about the Cochrane Review on Screening for Breast Cancer as published in *the Lancet* ~~in 2000~~. In my view, this current confusion is a regrettable development that is harmful to women. Given the weight of evidence from the trials and the reductions in breast cancer death rates observed in real life instances, ~~however,~~ the conclusions of the Cochrane Review ~~on~~

~~Screening for Breast Cancer, as published in *the Lancet* in 2000,~~ are quite ~~startling~~ frustrating to many in the scientific community. Indeed, the Cochrane conclusions are at odds with the most fundamental understanding of breast cancer as a progressive disease. Moreover, these conclusions run contrary to decades of supporting scientific evidence from the individual trials, meta-analyses, observational studies and case series, national trends, and confirmatory, independent expert reviews conducted by medical and scientific groups in North American and Europe.

As you are probably aware, the Cochrane report ~~view~~ rejected ~~5~~ five of ~~7~~ the seven major mammography trials as ~~too~~ flawed ~~to provide credible evidence leaving~~. The researchers then ~~only 2~~ two ~~trials,~~ claimed~~ing~~ that these two remaining trials ~~each of which~~ showed that mammography was not beneficial. ~~no benefit for mammography.~~ Inexplicably, one of the reports they selected~~,~~ was an early report of the Malmö study. The early report was made before there had been sufficient time for follow up and therefore did not show a difference in ~~, was an early report that showed no benefit and no difference in~~ breast cancer deaths between the study group and control group when all deaths in each group were compared. For some unknown reason, the Cochrane review ~~completely~~ ignored ~~that there was~~ a second later report of this study that had allowed sufficient time for follow up. This later report did indeed show that mammography was beneficial. In fact, it showed that there were ~~, whereas a later report with a longer period of follow up showed~~ 19% fewer deaths in the group offered screening.

Because most breast cancer deaths do not occur rapidly after diagnosis, experts in the evaluation of screening have known for years that a lengthy period of follow up in a screening study is necessary to observe a lower mortality rate if ~~indeed~~ there is one. In fact, this very point was strongly made in a ~~recent~~ report in *the Lancet* only a few weeks ago by investigators from Cornell University. T~~, which demonstrated that the Cochrane analysis, by showing no benefit to mammography from the data from the 1st Malmo report, was wholly misguided. The~~ he Cornell ~~Investigators~~ investigators demonstrated that once a sufficient amount of follow up was allowed, even the first Malmo study ~~does indeed~~ shows a ~~clear benefit of mammography – there was a~~ clear reduction in breast cancer deaths. ~~concluded that if the analysis allowed for a sufficient period of follow up after breast cancer diagnosis, the 1st Malmo indeed clearly does demonstrate a clear benefit of mammography.~~ In other words, ~~one of the very studies that the Cochrane analysis highlighted as showing no effect, did in fact decrease deaths from breast cancer when followed long enough~~the Cochrane analysis used incomplete ~~the wrong~~ data, making ~~and therefore~~ their conclusions ~~are unsubstantiated and highly~~ suspect. ~~.~~

Knowing that the results of a scientific study can have a great impact on many aspects of health care and health policy, standards for conducting these types of studies are set high and are adhered to by most of the scientific community. Unfortunately, on close examination, it is evident that the ~~-~~Cochrane review does not adhere to some of these standards and is deeply flawed. Indeed, it appears that the review's investigators failed to perform a careful examination of the published literature – for example, missing the second Malmo report – and made arbitrary and inconsistent judgments about study quality. ~~| Further, they used what can only be described as an indefensible methodology –~~

~~rejecting the majority of the world's trial data and only accepting the studies that proved the point they wished to make.~~ ~~I think this sentence is too shrill. Can we delete it?]~~ Moreover~~, – and this was perhaps the most egregious problem –~~ the Cochrane analysis concluded that the only reliable endpoint for comparison was not death from breast cancer, but death from all causes.

Using death from all causes as the means for evaluating mammography effectiveness is far-fetched in the extreme. The trials were designed to demonstrate a difference in breast cancer deaths – not deaths from all causes. To demonstrate a difference in deaths from all causes, an enormous number of people would need to be enrolled in any~~in the~~ trial. These trials were too small to individually demonstrate a difference in all cause mortality and were never intended to do so. Moreover, breast cancer screening cannot logically be expected to reduce deaths from hip fractures, diabetes, trauma, or other causes of death.

Furthermore, the Cochrane analysis alleges that some of the trials should be ignored because of possible~~they feel that there was~~ bias and error in determining the cause of death. This assertion is simply wrong~~, degree of bias and error that occurs in the determination of cause of death, which is alleged by the Cochrane investigators, is specious,~~ since the level of error, due to dishonesty or incompetence on the part of blinded and non-blinded expert panels, would have had to be entirely habitual to ~~bias~~ change the results so completely. All told, the claims made by the Cochrane review ~~of the data from the 1st Malmo study~~ are based more on conjecture ~~-~~than an actual demonstration of errors.

The authors of the Cochrane analysis ~~felt that all-cause mortality is important because they~~ are part of a group in the scientific community who hold that studies should look only at all-cause mortality, not on mortality from breast cancer alone. ~~because breast cancer deaths represent a relatively small percentage of all deaths in women. a lower percentage of all deaths occurring in women are caused by breast cancer. Therefore, according to this group, thinking behind this rationale is that because a woman participating in screening would only reduce her risk of dying from any cause by only a relatively small percentage, breast cancer screening is not an important part of preventive health care.~~ This ~~estimate~~ train of thought ~~conclusion~~is quite misleading, because the goal of any preventive health program is not to prevent death, which will occur eventually~~ no matter what we do~~, but to reduce our chances of dying prematurely~~. Thus, a woman~~Breast cancer screening makes sense for women between the ages of 40 and 70 ~~has the potential to significantly reduce her risk of dying early~~ because breast cancer is a leading cause of death in that age group – it offers women the chance to save those 19 years of life that I mentioned at the beginning of my remarks.

This raises another point. Screening is an undertaking in which we test the many to find the few. No screening test is 100 percent accurate. In some cases, cancer will be missed during screening. In other cases, women will be told they need additional tests for abnormalities that ultimately turn out not be cancer. Providers must handle each step of the screening process with great sensitivity. Likewise, more education can be done to assure women that "false positives" are part of the pathway to a normal interpretation. A group of investigators at Dartmouth found that women are highly accepting of false

positives as part of the process of saving lives from breast cancer. This does not mean we should not devote more attention to reducing the avoidable false positive rate, but it is important to note that many women understand the inevitability of false positives and accept them as part of the process of early detection.

Another criticism of mammography is that it detects ductal carcinoma in situ, or DCIS, a non-invasive cancer. In the course of screening for invasive breast cancer, we will detect DCIS. Since not all DCIS will progress to invasive disease, screening has been criticized for over treating DCIS.

Madam Chairwoman and Mr. Chairman, approximately a third of DCIS may progress to invasive disease and we do not know which will or will not progress. The notion that detection of DCIS should be avoided, or that screening should be postponed until DCIS progresses to invasive disease betrays a fundamental misunderstanding about the biology of breast cancer and the interplay between disease progression and early detection. The intent of breast cancer screening is the detection of small invasive cancers in order to give women an advantage in fighting their disease. The challenge today and in the future is tailoring the treatment of DCIS to ensure that it is treated appropriately and that a woman is not put through a greater treatment ordeal than is necessary – but that's a treatment issue not a screening issue. The only option for avoiding the diagnosis of DCIS is not being screened for breast cancer, which would make no sense at all since the incidence rate of invasive breast cancer is many times greater than the chance of a diagnosis of DCIS.

All told, in addition to numerous critiques of the Cochrane Review in published literature by well-known experts ~~in the evaluation of~~on screening ~~studies~~, no national or professional body has ~~concluded~~ found that this review's conclusions are ~~even remotely~~ convincing. As additional reviews are published, and as additional national groups reject the review's ~~deeply~~ flawed interpretation of the data, it is our hope that policymakers and others will devote ~~the~~ more attention toward setting the record straight. Mammography, while not a perfect tool, is ~~the~~ currently the best tool we have to catch breast cancer early and to reduce deaths from the disease. ~~cornerstone of our current pubic health strategy to control breast cancer.~~

Next Steps

Madam Chairwoman, Mr. Chairman, and m~~M~~members of the C~~c~~ommittee, we have made incredible progress towards reducing deaths from breast cancer in North America and Europe. Here in the U.S., after nearly two decades of a public-private partnership in health promotion, a majority of women aged 40 and older are receiving mammograms. The efforts to improve the quality of mammography, and in particular the importance of the landmark Mammography Quality Standards Act of 1992, which the Chairwoman authored, have assured every woman in this country of ~~a~~ higher quality breast imaging. These efforts have produced results. The death rate from breast cancer has declined by over 20% in the last decade. According to the American Cancer Society, progress in the U.S. in breast cancer screening, improved therapy, and increased awareness means that

there will be many thousands fewer women who will be expected to die this year from breast cancer than would have died if mortality rates were the same today as they were in 1989. Furthermore, new technology, such as digital mammography, computer-aided detection, and potentially MRI hold the promise for even more successful breast imaging technology – but at this time, mammography is the best tool we have.

~~**Madam Chairwoman and Mr. Chairman, we are hopeful that the recent announcement of the U.S. Preventive Services Task Force's update of their breast cancer screening guidelines and their endorsement of mammography, will add to the weight of the wide-scale rejection of the Cochrane Review. [I think we may want to move this up toward the front of the testimony, as it is the most recent news.]**~~

The American Cancer Society will continue to provide information designed to inform women of the benefits and limitations of mammography screening. We are confident that, armed with information, women and their health care providers will continue to see mammography as the best current strategy to reduce death from this disease, and that those whose confidence was shaken by the recent media attention will regain their confidence as the authoritative and credible interpretation of the scientific data on mammography prevails. To this end, we urge women 40 and older to continue to follow the advice of their physician and be screened for breast cancer annually.

Madam Chairwoman, Mr. Chairman, and members of the Ceommittee, thank you again for the opportunity to speak to you today.