

# HIP Randomized Breast Cancer Screening Trial (1963–1982)

From 1963 to 1982, researchers in New York City, New York, carried out a randomized trial of mammography screening. Mammography is the use of X-ray technology to find breast cancer at early stages. The private insurance company Health Insurance Plan of Greater New York, or HIP, collaborated with researchers Sam Shapiro, Philip Strax, and Louis Venet on the trial. The researchers' goal was to determine whether mammography screening reduced breast cancer mortality in women. The study included sixty thousand women aged forty to sixty-four. Half of the women received two annual breast examinations that involved mammography, a breast exam, and an interview. The rest of the women were not invited for annual examinations. After follow up, the researchers found that of the women who received the examinations, thirty percent fewer died from breast cancer than the women who did not receive any examinations. The HIP trial was one of the first large-scale clinical trials to provide evidence that mammography screenings helped prevent breast cancer deaths in women.

The main researchers in charge of the randomized trial were Shapiro, Strax, and Venet. Shapiro worked as the research director at the Health Insurance Plan of Greater New York in New York City. The HIP was a private insurance company that provided healthcare coverage for people in New York, Massachusetts, and Connecticut. Shapiro analyzed statistical data for the trial. According to obituary in Washington Post, Shapiro instigated the clinical trial, as he was interested in possible benefits of mammography. Strax was a medical doctor in Manhattan, New York, whose wife died of breast cancer prior to the start of the clinical trial. He served as the chief radiologist, reviewing all mammograms that showed breast cancer. Venet, the chief clinician, worked with the surgeons to coordinate recommendations for biopsy, a procedure in which tissue sample of the breast is surgically removed and examined to determine the presence of cancer.

By the mid-twentieth century, researchers had begun investigating the use of mammography as a tool for screening breast cancer. In 1930, US physician Stafford L. Warren reported using mammography as a diagnostic tool for breast cancer and other abnormalities of breasts. Later in 1961, US physician Jacob Gershon-Cohen showed that mammography could be used to screen healthy women for breast cancer. However, at that time researchers had yet to perform any large-scale clinical trial.

In 1963, researchers began the HIP randomized trial, which aimed to determine whether or not regular mammography screening could lower the mortality rate of breast cancer. As part of the study, Shapiro, Strax, and Venet investigated how frequently breast cancer could be diagnosed by mammography, by a clinical examination, or by a combination of the two. That gave researchers a measure of how useful mammography was compared to a clinical examination in diagnosing breast cancer. The researchers also aimed to include information on the race, age, religion, marital status, education level, and other demographic variables of the participants, which could provide insight into factors that may affect breast cancer. To accomplish that, the researchers invited a wide variety of women from New York City to participate in the study.

The researchers conducted the randomized clinical trial over the span of twenty years. Between 1966 and 1982, Shapiro and his colleagues published their results in three separate articles. The first article was published in 1966 in the Journal of American Medical Association and described the objectives, methods, and preliminary results of the trial. In that article, the researchers reported that mammography appeared to reduce breast cancer deaths. The second article was published by the same journal in 1971 and updated the study results, reinforcing the idea that mammography was

useful in preventing breast cancer deaths due to early diagnosis possibilities, yet the researchers concluded that the effect could have been short-term and thus continued the study to include long-term results. In 1982, the Journal of National Cancer Institute published their third article on the final ten to fourteen-year follow up. That article included evidence that thirty percent less deaths occurred in the experimental group than the control group.

In the first article, Shapiro, Strax, and Venet describe how they selected women for the study. The researchers randomly selected 60,000 women who were between the ages of forty and sixty-four, lived within the New York City area, and were insured by the HIP. The researchers then separated the women into two groups, with each woman in the experimental group corresponding to a demographically similar woman in the control group. During the very first appointment, the researchers gave women in both groups a clinical breast examination that included a physician touching the breasts to feel presence of any lumps. Shapiro and his colleagues did that to eliminate any participants with existing or prior breast cancer from both groups.

Next, Shapiro and his colleagues outlined the methodological differences between the control and the experimental groups. They called the women in the experimental group for an examination that included mammography, clinical examination, and an interview twice a year. Mammography is a procedure in which a woman's breasts are pressed down and scanned with an X-ray. During the clinical breast examination, physicians physically checked the woman's breasts for lumps. In the interview portion, the researchers asked the woman about her demographic information and family health history. The women in the control group did not receive any examinations from the researchers, though they were not stopped from receiving examinations on their own. Shapiro and his colleagues state in the first article that sixty-four percent of the women who were invited came to the first examination. Of those women, eighty-three percent came for the first follow up examination.

The researchers further describe how they gathered data from all participants. Shapiro and his colleagues conducted extensive follow-ups with any woman who was diagnosed with breast cancer during the study, whether by the researchers or by outside physicians. To determine the differences in survival rates between the experimental and the control groups, the researchers used their own records, hospital records, state death records, cancer registries, and direct communication with the women. They used that information to identify women that were initially diagnosed with breast cancer and to identify causes of death of women in the trial.

In 1966, the researchers published their first preliminary results of the randomized trial, despite having screened less than one third of the women from the experimental group. They advised 202 women in the experimental group to get a biopsy, or a removal of sample breast tissue, as there was suspicion of breast cancer. Of those women, the researchers advised ninety-seven women to get a biopsy solely based on mammography, ninety-five women to get a biopsy based on the clinical examination only, and ten women to get a biopsy based on both methods. They confirmed breast cancers in twelve of the women in the mammography subgroup, eight in the clinical examination subgroup, and three in the mammography and clinical examination subgroup. According to the researchers, those results meant that mammography was useful in finding more cases of breast cancer than a clinical examination. Shapiro and his colleagues indicated that mammography was a useful tool for detecting early cases of breast cancer and aiding women to seek treatment. However, the researchers were cautious about the results, as those were the short-term results only, which meant that not enough time has passed since the beginning of the study to analyze true effects of mammography on breast cancer death rates.

Five years later, Shapiro and his colleagues published their second article, which included information about first cases of breast cancer mortality in both groups. By 1969, thirty-one women had died from breast cancer in the experimental group, as opposed to fifty-two women in the control group. The mortality rates for the experimental and the control groups were similar for the first two years of the experiment. However, after those two years and after women in the experimental group had received multiple mammograms, the mortality rate for the experimental group significantly decreased. According to Shapiro and his colleagues, those results indicated that screening for breast cancer with mammography helped detect early breast tumors and reduced breast cancer mortality.

Next, Shapiro and his colleagues compared death probability for both groups to predict the life expectancy of women in both groups. The researchers calculated the probability of death for the women in the control and the experimental group within three and a half years after diagnosis with breast cancer. The probability of death for women diagnosed with breast cancer in the control group was 33.7 percent, and it was 15.3 percent in the experimental group. According to Shapiro and his colleagues, those results meant that women who received mammograms twice a year were twice as likely to live longer than three and a half years after diagnosis than those who did not receive regular mammograms. Shapiro, Strax, and Venet noted that the follow up information was significant, but they still had reservations about long-term usefulness of mammography.

In 1982, Shapiro and his colleagues published their third article on the HIP randomized trial, in which they focused on the long-term results of the trial. The researchers reported that after ten years of follow up after the first screening, thirty percent more women died of breast cancer in the control group than in the experimental group. They reported that the difference lowered after fourteen years of follow up, but that their results showed that significantly more women survived breast cancer in the experimental group due to the possibility of early diagnosis. Also, there was a significantly lower mortality from breast cancer for women forty to forty-nine in the experimental group, which the researchers attributed to their age group. However, most of those women were diagnosed with breast cancer after they reached fifty years old, which led Shapiro and his colleagues to question whether regular mammography was useful for women under fifty. Shapiro and his colleagues did not conclude whether or not mammography was necessary for women younger than fifty years old and said that more research was needed to test that.

The HIP randomized trial provided evidence for the utility of mammography screenings for detection of early breast cancer. The researchers concluded that women who received mammograms regularly were less likely to die from breast cancer, compared to women who did not get regular mammograms. Shapiro and his colleagues used their long-term results to confirm that regular mammograms were useful in early diagnosis of breast cancer, even though it was not clear whether women under fifty years old should obtain regular mammograms. The articles on the HIP trial provided the first clinical evidence of mass mammography usefulness and was later included in a Cochrane systematic review on mammography.

Following the results of the HIP randomized trial, the American Cancer Society, US Preventative Task Force, World Health Organization, and National Cancer Institute published guidelines about screening women for breast cancer using mammography.

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