

CancerScope

Oncology Issues in Focus | BY CARRIE PRINTZ



First Person Profile: Leslie Bernstein, PhD

An epidemiologist known for her groundbreaking discoveries about breast cancer, Dr. Bernstein continues to push the field forward

When Leslie Bernstein, PhD, joined the faculty of City of Hope at the age of 67, she told the institution's leaders that she would stay for no more than a decade. After all, she had just spent 25 years at the University of Southern California (USC) in Los Angeles, serving as a professor in the department of preventive medicine, the medical school dean for faculty affairs, and the university vice provost for medical affairs. However, some 13 years after her pronouncement—with a move across the country to be closer to her daughter in New Jersey thrown in—Dr. Bernstein continues to work with the center remotely, publishing research and mentoring younger colleagues. “I’m hoping to retire soon, but so far the answer has been, ‘We’d rather you stay on,’” she says.

It is easy to understand why the leaders of City of Hope, a National Cancer Institute-Designated Comprehensive Cancer Center in Duarte, California, are reluctant to let Dr. Bernstein go. As a professor in its division of biomarkers of early detection and prevention, she has conducted landmark studies

in breast cancer risk and prevention and has been instrumental in leading other key research in cancer epidemiology.

“Very few investigators can point to groundbreaking work that has actually led to changes in practice and impacted the ways that scientists and clinicians think about breast cancer like she can,” says her colleague and former student, Jonine Bernstein, PhD, (no relation), an epidemiologist and coleader of the Population Sciences Research Program at Memorial Sloan Kettering Cancer Center in New York City. “And she’s passionate about every aspect of her work—she’s one of these researchers who’s in it for the people affected as well as for the intellectual challenge.” As a result, many in the oncology world look to involve Dr. Bernstein, in some capacity, with their work, whether it is as a collaborator, advisor, or member of their board or advocacy group. “She sits on every important advisory committee in our field,” Dr. Jonine Bernstein says.

Dr. Jonine Bernstein has long relied on Dr. Leslie Bernstein’s expertise herself. The 2 researchers have worked together for more than 20 years on the Women’s Environmental Cancer and Radiation Epidemiology (WECARE) Study, an international research project funded by the National Institutes of Health that explores genetic susceptibility and the effects of radiation treatment on contralateral breast cancer risk. Together, they designed, conducted, supported, and analyzed the research, which remains the largest study of second primary breast cancer with direct patient interviews, biospecimens, and detailed patient information. “She’s had such an incredible influence on me and my career path,” Dr. Jonine Bernstein says. “She’s an educator, mentor, colleague, and a dear friend.”

The California Teachers Study

Among her many contributions to the field, Dr. Bernstein cofounded the California Teachers Study, along with several cancer epidemiology colleagues. The closed cohort study, launched in 1995, included a total of 133,479 female active or retired public school professionals, primarily teachers and administrators, who completed questionnaires regarding their health behaviors. Participants have been followed in the decades since and monitored for disease development and other health outcomes. Although originally created to study breast cancer, the study also has yielded important findings regarding other cancers and diseases. Indeed, Dr. Bernstein and her colleagues continue to use data from the study, which has led to more than 140 articles, she says.

Because the California Teachers Study did not have biospecimens at its outset, Dr. Bernstein launched a large

case-control study and collected samples from study participants who had been diagnosed with breast cancer after they had enrolled, as well as nonparticipants. Those original 13,000 specimens were supplemented by a focused specimen collection effort that more than doubled the California Teachers Study biospecimen repository, thereby enabling investigators to conduct genetics research.

In addition, pooling data from the California Teachers Study with other cohorts, including those from cancer prevention studies by the American Cancer Society, the Nurses' Health Study, and the USC Multiethnic Cohort Study, has generated more studies with much larger data sets, adding to the strength of their findings. Researchers from these and other large cohort studies are members of the National Cancer Institute Cohort Consortium, which encourages large-scale collaborations to pool data and biospecimens.

Physical Activity and Breast Cancer

Another important contribution to the field made by Dr. Bernstein was her 1994 publication of what is believed to be the first definitive research article linking physical activity and breast cancer risk.¹ Prior to that, she had conducted a number of studies concerning the menstrual cycle and hormones, including one study of nuns who had never given birth and their parous sisters that indicated a hormonal link between pregnancy and breast cancer risk.

When Dr. Bernstein and her colleagues began examining the connection between physical activity and breast cancer risk, she says, "we knew that when a woman had her first child and when she had her first and last menstrual periods had an effect on risk, but we had nothing we could tell women they could do to lower their risk." She did, however, have a theory. Having trained as a competitive swimmer (as a teenager, Dr. Bernstein had narrowly missed making the Olympic team), she knew that intense physical activity interfered with the menstrual cycle, which led to reduced exposure to the hormones estradiol and progesterone. Understanding the causal connection between these hormones and breast cancer, she reasoned that exercise could potentially reduce a woman's risk of developing the disease.

For her seminal case-control study, her staff interviewed 545 women aged 40 years or younger who had been newly diagnosed with breast cancer and 545 control subjects. The women were matched based on race, parity, and neighborhood of residence, and were asked about their lifetime physical activity. Dr. Bernstein demonstrated that 3 to 4 hours of exercise each week lowered breast cancer risk by as much as 50%. Since then, more than 60 studies conducted throughout the world have confirmed the link between exercise and a lower risk of breast cancer, according to Dr. Bernstein, although a number of unanswered questions remain, such as whether specific types of exercise (ie, aerobic training versus strength training) are better for reducing risk, she says.

More recently, Dr. Bernstein has explored the role of low-dose aspirin in reducing breast cancer risk. In 2017, she published research that found an overall 16% lower risk

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of breast cancer among women in the California Teachers Study who reported using low-dose aspirin at least 3 times per week.² The risk reduction was even higher, at 20%, for the most common breast cancer subtype, estrogen receptor-positive or progesterone receptor-positive, human epidermal growth factor receptor 2-negative disease.

In 2018, Dr. Bernstein received the American Association for Cancer Research and the American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention. She was only the third woman to receive it.

An Epidemiologist in the Making

Dr. Bernstein's father was diagnosed with metastatic melanoma when she was 11 years old. He even taught her how to drive at that young age so there would be 2 drivers in the family in the event of an emergency ("It was the 1950s, and things were different then," she recalls).

Dr. Bernstein has had a lifelong passion for math, and she says it was her love for the subject that eventually drove her toward epidemiology. She traces the roots of her fascination with numbers back to her father. "My dad played math games with me from the time I was 2," she says.

By age 16, she was a bona fide math whiz and was accepted into the University of California at Los Angeles. She worked full time to afford the tuition. Shortly after, she began dating a fellow competitive swimmer, Saul Bernstein, whom she married when she was 18. "He had always dreamed of being a physician, but he was majoring in physical education in college," she says. No one else in his poor, immigrant family had received a formal education, and "he didn't know how to go about it," she explains.

However, with her help, Saul not only began to excel in his college courses but applied to and was accepted into medical school, eventually becoming a highly regarded pediatric orthopedic surgeon. However, when Dr. Bernstein became pregnant at age 19 years, the couple soon realized that they could only afford 1 education at a time, and she left college. She completed her bachelor's degree in mathematics several years later while her husband was an orthopedic resident.

After Saul Bernstein was drafted during the Vietnam War, he was stationed at US military bases in Kansas and Georgia to care for returning wounded soldiers. Later, the family moved to England, where Saul completed his fellowship. By then a mother of 3, Dr. Bernstein never gave up on her dreams of furthering her education. At age 37, she returned to graduate school at USC, and completed a master's degree

in gerontology in 1978 and a PhD in biometry (biostatistics) in 1981. “I’ve been working ever since,” she says.

In reflecting on the state of the cancer research field, Dr. Bernstein says she and other colleagues have felt that too much focus has been placed on genome-wide association type studies and too little on understanding mechanisms that will lead to prevention efforts. “For example, we’ve never done a clinical trial of exercise and breast cancer risk, because it’s really difficult to do,” she says. “What we need instead are smaller studies to nail down the mechanisms involved so we can answer questions like what type of exercise is best and at which ages during a woman’s lifetime is it most important to exercise.”

In addition to her work, Dr. Bernstein is the proud grandmother of 11 grandchildren, whose list of accomplishments is growing, with one about to receive her PhD, another conducting HIV research in South Africa,

and a third applying to medical school. The remaining grandchildren are still in college. “I spend a lot of time with them—guiding them and answering their questions,” she says.

She offers those in the field a similar gift, Dr. Jonine Bernstein says. “She’s so thoughtful and incredibly humble—she takes great joy in having people around her succeed. Everyone should be so lucky as to work with and be supported by a Leslie Bernstein in their life.”

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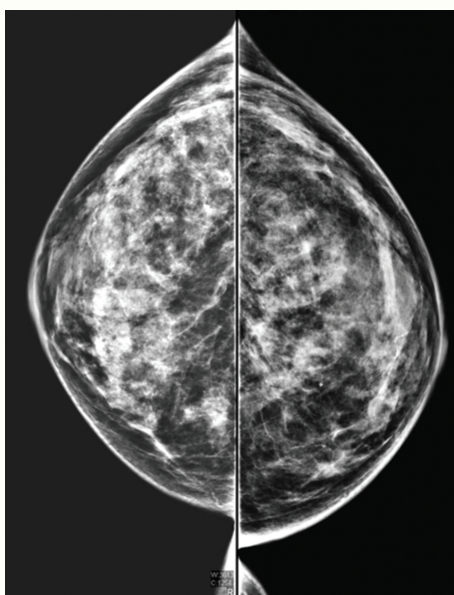
State Laws That Require Breast Density Notification Modestly Increase Screening and Detection

State laws that require health care providers to notify women with dense breasts about their additional risks of breast cancer can lead to further screening, as well as a modest increase in detection, according to a Yale University study published in the *American Journal of Public Health*.¹

Dense breast tissue, which occurs in approximately one-half of women aged in their 40s and 50s in the United States, can increase the risk of breast cancer and also make it harder to detect the disease on a mammogram. As a result, many states have enacted laws requiring providers to notify women about breast density after they undergo a mammogram. In addition, some states now mandate that such notifications encourage these women to consider further screening tests such as an ultrasound and magnetic resonance imaging.

For the study, researchers from Yale’s schools of public health and medicine sought to determine whether these varying laws affect screening patterns. To do so, they analyzed data from more than 1 million mammograms given to privately insured women aged in their 40s and 50s who lived in states with one of the following: no notification law, a law that requires only notification of breast density, and a law that requires mention of supplemental tests.

Their findings demonstrated that women in states with laws requiring recommendations for supplemental screening



tests had higher rates of both receiving ultrasounds and cancer detection after implementation of the law. Conversely, they found no changes in states that only required notifications regarding breast density. The increase in ultrasound and detection rates was small: a predicted 10.5 ultrasounds per 1000 mammograms and less than 1 additional breast cancer found per 1000 mammograms.

Corresponding author Susan Busch, PhD, a professor of public health at Yale, notes that the language in state notification laws appears to make a difference in changing clinical practice. To have an impact, the legislation should include detailed information regarding specific, additional testing options, she says.

Dr. Busch and coauthor, Cary Gross, MD, a professor of general medicine and epidemiology and the director of the National Clinician Scholars Program at Yale, add that further study is still needed to determine whether these more aggressive screening efforts actually detect advanced cancers and translate into a reduction in breast cancer mortality.

Reference

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