



Breast Cancer Screenings

FOR WOMEN WITH DOWN SYNDROME

DOWN SYNDROME EXPERTS AND CLINICIANS, DR. BRIAN CHICOINE AND DR. BARRY MARTIN, EXPLORE THE BENEFITS AND HARMS OF BREAST CANCER SCREENINGS FOR THIS LOW-RISK POPULATION

THE US PREVENTIVE SERVICES TASK FORCE recommends biennial screenings for breast cancer for the typical female population between the ages of 50-74, while noting that screening decisions in ages prior to 50 should be made on an individual risk basis. Do these recommendations still apply to women with Down syndrome who have a much lower risk of solid tumors and lower life expectancy? According to the Centers for Disease Control and Prevention (CDC), the average life expectancy for a typical woman in the United States is 78.6 years, compared to 57.5 years for a woman with Down syndrome. While breast cancer screenings for high-risk women are very practical, are there similar benefits for women with Down syndrome, and do these potential benefits outweigh the potential harms of screenings, such as physical harm and mental trauma?

Dr. Brian Chicoine, Medical Director of the Advocate Medical Group Adult Down Syndrome Center in Chicago, Illinois, and Dr. Barry Martin, primary care physician at the Adult Down syndrome clinic at Denver Health in Denver, Colorado, set out to answer these questions. Both are lead authors of the legacy publication, *GLOBAL Medical Care Guidelines for Adults with Down Syndrome*°, the first evidence-based guidelines for adults with Down syndrome, which was recently published in *JAMA, the Journal of the American Medical Association*.

With only sparse and outdated resources available for adults with Down syndrome, doctors often have little choice but to follow breast cancer guidelines set forth for typical women, with no specification

toward women with Down syndrome. With over 50 years of combined experience caring for patients with Down syndrome, Drs. Chicoine and Martin recommend a different and unique protocol that drew upon a recently created simulation model of incidence and prevalence.

The simulation model was created by doctors from 4 states and 2 countries (Colorado, Illinois, Massachusetts, Illinois, Netherlands, and Turkey) who took part in a collaborative study of the harms and benefits of breast cancer screenings for women with Down syndrome, which was published in the *Journal of General Internal Medicine* in August of 2019. Their goal? For women with Down syndrome and their families to have as much information as possible to weigh the risks and benefits themselves before making decisions on breast cancer screenings.

TRISOMY 21 - A PROTECTION FROM BREAST CANCER

“We are often asking, ‘What about the triplication of chromosome 21 causes people with Down syndrome to be protected from most solid tumor cancers?’” Dr. Chicoine explains. “There is a lot of research to be done on this still, but researchers have hypothesized it has to do with their different immune system functionalities or perhaps a difference in genes that suppress tumors.”

People with Down syndrome have dysregulated and sometimes overactive immune systems, which could be the reason they are more susceptible to certain diseases such as Alzheimer’s disease or autoimmune disorders, while being protected from others, such as

such as solid tumor cancers, including breast cancer.

“This begs the question: should people with Down syndrome take the risks associated with testing for things they are unlikely to get, like breast cancer?” adds Dr. Martin, “Or should perhaps they keep their focus on conditions they are likely to get, such as Alzheimer’s disease.”

Dr. Martin says he has never had a patient with Down syndrome with breast cancer and Dr. Chicoine reports that over a 16-year period of observation at the Adult Down Syndrome Center, only 2 women were detected with cancer among 993 mammography reports. Additionally, neither of these patients had invasive breast cancer or fully complied with treatment recommendations. Ultimately, both passed away to complications related to Alzheimer's disease at ages 55 and 63. Since that observation report thirteen years ago, Dr. Chicoine shared that there have been no additional cases of breast cancer in his patient population.

A common breast cancer screening tool is a mammogram, a procedure which uses an X-ray machine to examines a patient’s breast by compressing the tissue in between two plates. This test can detect abnormal areas in the breast such as tumors and cysts, but it cannot prove if the abnormal area is cancerous. That needs to be done through a biopsy, where tissue is removed from the area and analyzed by pathologists. Women with Down syndrome have a greater health risk than the typical population when going under anesthesia, which is usually needed for follow-up procedures such as a biopsy. This can add to the risk of the follow up testing required for an abnormal mammogram.

Amongst 684 patients included in Dr. Chicoine’s study of women with Down syndrome, 51 of them could not cooperate with mammography. “For some women with Down syndrome, we have determined that subsequent mammograms have to be avoided because the experience was too frightening and overwhelming for the patients, making the procedure dangerous for both the patients and the radiology technicians,” says Dr. Chicoine.

“The first thing we are taught in medical school is to ‘do no harm,’” says Dr. Martin. “But we have seen women with Down syndrome who are so traumatized and frightened by the procedure, followed by sometimes false-positives that require further unpleasant and unproductive screening visits.”

People with Down Syndrome Protected from Most – But Not All – Solid Tumor Cancers

People with Down syndrome have a different disease profile than the typical population. They are highly predisposed to certain conditions, such as Alzheimer’s disease and autoimmune disorders, while being protected from others, such as heart disease and most solid tumor cancers. There is much to be researched about this phenomenon, with current research pointing to this being a product of the overactive immune system in people with Down syndrome.

While those with Down syndrome are very unlikely to develop most solid tumor cancers, including breast cancer, there are some exceptions. For example, men with Down syndrome have a higher risk for testicular cancer. The testes are protected from the immune system by a barrier wall of cells, attacking any invading immune cells to protect developing sperm. Because the testes are separated from this dysfunctional immune system in the body of a person with trisomy 21, it is believed they are able to develop a solid tumor cancer whereas in most other areas of the body they are not.



(L-R): Megan, Dr. Barry Martin, Ray, Dr. Brian Chicoine, Connor, Kat, Bryn Gelaro, Beth



Dr. Barry Martin and Elyssa

A STUDY WITHOUT HUMANS?

Drs. Chicoine and Martin decided to conduct a study using a digital simulation modelling called Cancer Intervention and Surveillance Modelling Network (CISNET). “There were simply no studies like this being done, and we needed to start somewhere,” says Dr. Chicoine. “We ensured the computer model took into account a diversity of age, geographic origin, and ethnicity.”

“However, the lack of studies and relatively small sample size to work with did leave us with limitations and discrepancies in the study,” Dr. Chicoine adds. To address these limitations, they conducted an extensive statistical modeling sensitivity analysis on the breast cancer risks for women with Down syndrome.

To develop a fair and robust study, the team followed standards set forth by the Breast Cancer Surveillance Consortium (BCSC). The hypothetical cohort consisted of 1,000 women with Down syndrome in the United States women who were born in 1970. The simulation evaluated several strategies with different starting and stopping times between ages 40–74, as well as one-time screening at ages 40, 45, and 50 years.

While this type of study does not assess actual human subjects, it has been reported to be effective in addressing important breast cancer policy issues such as the impact of comorbidities in screening and diagnosis, the cost of transitioning from plain-film to digital mammography, the efficacy of recent advancements in screening strategies and treatments, and more.

THE FINDINGS: POTENTIAL HARMS & BENEFITS

The results of the doctors’ study determined that the benefit of breast cancer screening using mammography for women with Down syndrome is indeed less pronounced than it is for typical women because of the former’s lower breast cancer risk and shorter life expectancy. Additionally, there may be added harms for women with

Down syndrome, including physical and mental trauma.

The model found that if 1,000 women with Down syndrome underwent biennial screening between ages 50-74, 6,317 mammograms would be performed to achieve a benefit of 0.4 averted breast cancer related deaths and 2.9 life years gained compared to women with Down syndrome who did not undergo mammogram screening. The mammograms would find 571 abnormalities that were not cancer (false positives) and in follow-up, 80 biopsies that were benign would be done.

Put another way, when doing biennial screening between ages 50-74, the model found that to save one life, women with Down syndrome would have to undergo 14,000 mammograms compared to only 2000 for women without Down syndrome. Women with Down syndrome would undergo about 175 benign biopsies compared to about 25 for women without Down syndrome. The potential concern for the risk of the larger number of biopsies for women with Down syndrome compared to women without Down syndrome is magnified by the aforementioned greater risk of anesthesia required to do the biopsies for women with Down syndrome.

Based on this study, the potential benefits of screening, including life-years gained, and breast cancer mortality averted, are relatively small. The potential harms for screening, including the number of mammograms, number of false-positives, and number of benign biopsies, is greater for women without Down syndrome. Results similarly showed lower benefit and higher potential harm when the model assessed a variety of screening patterns such as annual mammograms, once-in-a lifetime mammogram, or starting at a younger age.

“Our goal is to help each individual understand the potential risks and benefits of a variety of screening protocols and assist them in making a decision to forego or partake in mammogram screening,” says Dr. Chicoine.

Important Factors to Consider on Breast Cancer Mammography

Brian Chicoine, MD and Barry Martin, MD offer key questions women with Down syndrome should ask before deciding whether or not to get a breast cancer screening.

1. Do I understand the mammogram procedure? How comfortable am I with that?
2. Have prior tests indicated I have high breast density or denser breasts?
3. Would I consider a biopsy?
4. Does my family have a history of breast cancer?
5. How would I react to a false-positive test result?
6. How is my health overall?
7. Have I had any surgeries in the past? Were there any complications?
8. What is my calculated risk of developing breast cancer?
9. What does my doctor recommend?
10. If breast cancer was found, do I think my best quality of life would come from Treatments such as surgery or chemotherapy?



WHAT NOW?

“We advise everyone to consider the risks along with their own unique situation and family history,” says Dr. Martin. “For instance, women with Down syndrome who have a family history of breast cancer or a high breast density may be at higher risk for breast cancer and therefore would want to consider these factors in making their decision.”

“While this study gives us important factors to consider on breast cancer screenings for women with Down syndrome, it is clear there is still much work to be done to properly evaluate the potential impact of mammography screenings for women with Down syndrome,” says Dr. Chicoine.

As the life expectancy for women with Down syndrome continues to increase, this study will need to be expanded upon and revisited, especially since the model parameters are based on earlier birth rates of women born in 1970.

“This also highlights the increased need for best practices training of medical providers to support women with Down syndrome as well as all women with intellectual and developmental disabilities that undergo mammography,” adds Dr. Chicoine.

Both doctors are eager to continue studying adults with Down syndrome and provide medical insights that improve health outcomes. As two of the key authors associated with the recently published *GLOBAL Medical Care Guidelines for Adults with Down Syndrome*[®], they are committed to ensuring that new topics, including how to treat cancer in people with Down syndrome, are addressed in the near future. ●

To read the full “Benefits and Harms of Mammography Screenings for Women with Down Syndrome: A Collaborative Modeling Study,” visit <https://link.springer.com/article/10.1007/s11606-019-05182-5>

To learn more about the *GLOBAL Medical Care Guidelines for Adults with Down Syndrome*[®], visit www.globaldownsyndrome.org/medical-care-guidelines/