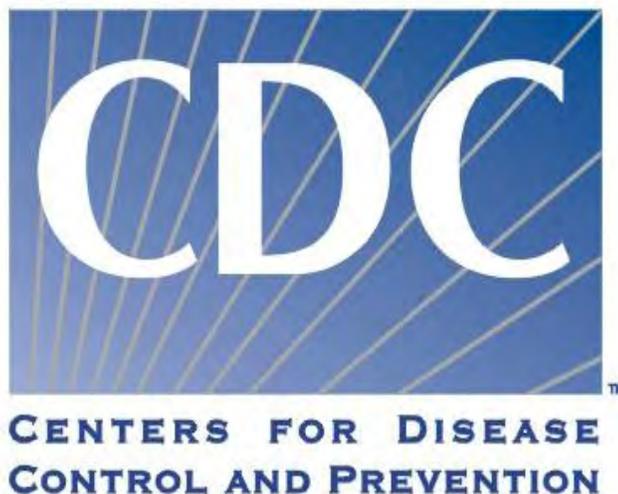


CENTERS FOR DISEASE CONTROL AND PREVENTION

Advisory Committee on Breast Cancer in Young Women



**January 31, 2011 - February 1, 2011
Atlanta, GA**

Emory Conference Center Hotel
1615 Clifton Road
Atlanta, GA 30329

Detailed Meeting Minutes

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The Centers for Disease Control and Prevention (CDC) Advisory Committee on Breast Cancer in Young Women convened January 31, 2011 through February 1, 2011, at the Emory Conference Center Hotel, 1615 Clifton Road, Atlanta, GA.

Day 1

Welcome and Introductions

Dr. Temeika Fairley

Designated Federal Officer (DFO),
Advisory Committee on Breast Cancer in Young Women (ACBCYW),
Division of Cancer Prevention and Control (DCPC), CDC

Dr. Fairley called the meeting to order by conducting a roll call of the Advisory Committee including voting members, ex-officio members, and liaison representatives. Voting members were asked to review the agenda for any conflicts of interest that would require them to exempt themselves from the meeting. No conflicts of interest were identified.

Dr. Ursula Bauer

Director
National Center for Chronic Disease Prevention and Health Promotion (NCCPHP), CDC

Dr. Bauer welcomed the participants to the meeting and gave special thanks to Congresswoman Debbie Wasserman Schultz for her leadership in raising awareness about the issue of breast cancer in young women.

Dr. Bauer provided an overview of the Committee's charge to advise the Secretary of the Department of Health and Human Services (HHS) and the Director of the CDC regarding the formative research, development, implementation, and evaluation of evidence-based activities designed to prevent breast cancer, particularly among those at heightened risk. It is also charged with promoting the early detection of breast cancer and support of young women who develop the disease.

To reach this goal, more information is needed to better understand the causes of increased

risk, ascertain women's perceptions of cancer that influence their health care decisions, and create recommendations for advising women. There is also a need to find better ways to disseminate information and educate young women on breast cancer.

It was Dr. Bauer's desire that this meeting be engaging and informative, and she looks forward to the forthcoming recommendations.

Opening Remarks

Congresswoman Debbie Wasserman Schultz

U.S. House of Representatives
Florida, District 20,

Congresswoman Wasserman Shultz is a breast cancer survivor and author of the Education and Awareness Requires Learning Young Act (EARLY Act). The goal of this legislation is to transform the approaches to fighting breast cancer in young women.

Congresswoman Wasserman Schultz joined the meeting by telephone. She expressed her appreciation to all members of the Advisory Committee and those who were engaged in the process of developing and passing the EARLY Act. She also shared her personal experiences with breast cancer and emphasized the importance of education women around this issue.

She explained that cancer can affect all, but disproportionately affects some groups; therefore, helping women to understand risk factors is vital. One in eight women can get breast cancer, and unfortunately, more than 25,000 women under the age of 35 have been diagnosed with breast cancer. Young women's breast cancers can be more aggressive and are often diagnosed at a later stage due to a lack of education regarding their risk and falsely low risk perception.

CDC along with the advisory committee will help make the EARLY Act a success. Congresswoman Wasserman Schultz encouraged members to tap into the creativity of their individual organizations to empower women and save lives.

She thanked all for being present and invited the members to contact her or Danny Gilbert in her office if they have any further questions or require her assistance.

Dr. Marcus Plescia

Director
Division of Cancer Prevention and Control (DCPC), CDC

Dr. Plescia offered his thanks to all for serving on the Advisory Committee, for their participation in this Committee, and commitment to this health issue. He also thanked Congresswoman Wasserman Schultz for all her diligent work on the EARLY Act and for sharing her reflections.

Dr. Plescia provided the Committee with an overview of CDC, the National Center for Chronic Disease Prevention and Health Promotion, and the Division of Cancer Prevention and Control (DCPC). He highlighted 3 of the DCPC's funded programs that might be relevant to the Committee's work: National Breast and Cervical Cancer Early Detection Program (NBCCEDP),

National Program of Cancer Registries (NPCR), and the National Comprehensive Cancer Control Program (NCCCP). He also provided the Committee with an overview of the division's Epidemiology and Applied Research Branch including types of relevant subject matter expertise and areas of research focus. Dr. Plescia expressed his desire for the members to acquaint themselves more with the programs offered as they move forward. He welcomed suggestions on how CDC can assist the committee in any way.

Dr. Ann H. Partridge

Associate Professor of Medicine
Dana Farber Cancer Institute
Chair for the Advisory Committee

Dr. Partridge expressed her appreciation for being invited to serve as Chair of the Advisory Committee. Her career has focused on improving treatment and care for young breast cancer survivors. The EARLY Act will help screen and educate women, and will promote gathering information about their family histories. She also emphasized that there should be a focus on educating women regarding the importance of following instructions once diagnoses has been made.

Dr. Partridge then introduced the Advisory Committee members, ex-officio members, and liaison representatives. Dr. Lisa Newman joined the meeting by telephone. Each member was allowed approximately 2 minutes to introduce themselves and their agency. The binders provided at the meeting included biographies on each member.

Epidemiology of Breast Cancer in Young Women

Jacqueline Miller, M.D.

Medical Director, National Breast and Cervical Cancer Early Detection Program
Division of Cancer Prevention and Control (DCPC), CDC.

Dr. Miller's presentation focused on the epidemiology of breast cancer in women under 40 years of age.

Breast cancer is the most commonly diagnosed cancer among women and is the second leading cause of cancer death among women. Nearly 5% of the invasive cancers occur in women under the age of 40. Breast cancer in young women is often associated with either a family history or a genetic mutation. Other known risk factors include:

- Increasing age
- Alcohol use
- Obesity
- Late menopause
- Early menarche
- Not breast feeding
- Late pregnancy
- Benign breast disease
- Hormone replacement therapy
- Family history of breast cancer
- Inherited genetic mutations

In addition to these risk factors, new studies have linked breast cancer to tobacco, especially relating to smoking at an early age and second-hand smoke exposure. The data is preliminary, but it does appear to indicate an increased risk for breast cancer in young women.

Although younger women have a lower risk of developing breast cancer than older women, learning about it at an earlier age may make a difference in lifetime risks. In 2007, 202,964 women were diagnosed with breast cancer, and about 5% or 9663 of those women were under the age of 40. In this same year, approximately 51,000 women were diagnosed with in-situ breast disease, and among those, about 1,000 were under the age of 40. In addition, in 2007, 40,598 women died of cancer; 1,080 of these women were under the age of 40.

CDC examined breast cancer incidence for women under 40 using *United States Cancer Statistics* data for 2003-2007. Incidence is lowest in the youngest women, ages 15-19, which represented 84 cancers, followed by the 20-24 group representing about 700 cancers. For the 25 to 29 age group, about 4,000 cancers were diagnosed. For the women 30 to 34, there were about 13,000 cancers. There were 30,000 women diagnosed between the ages of 35-39. Similar patterns exist in the mortality data. When separated by race, black and white women in this age group have the highest incidence and death rates of breast cancer and the numbers are significantly smaller for other races. Given these differences in incidence and death by age and race, consideration should be given to developing culturally and age appropriate messages and interventions for these women.

Five-year survival rates for young women are considerably lower than in older women. More specifically, women 20 to 34 and women 35 to 39 have a much lower five-year survival rate than all other women, including women over the age of 85.

In summary, there are several issues to consider when developing programs, research proposals, or interventions for this population:

Diagnostic dilemmas: Diagnostic workup is often more difficult in this population because there are no perfect tools for young women. Breast density and fibrocystic changes in young women's breasts contribute to this problem. MRI is currently being used for screening/diagnosis in this population; however the high number of false positives detected by this method is problematic. Because the risk of disease is low and disease is rare in young women, thought should be given to the development of tools and resources to assist healthcare providers in the identification and diagnosis of breast cancer in young women.

Surveillance/Data availability: Given the rarity of the disease in this age group and other limitations in cancer registry data collection procedures, there we are unable to identify or access high risk subpopulations, detailed genetic data, and complete tumor marker data. Small sample sizes/numbers of women also prevent more detailed epidemiological analyses.

So where do we go from here? While the numbers may be very small, the impact on young women diagnosed with breast cancer is huge. Support for those diagnosed with breast cancer is critical. It has been identified that knowledge of family history is key for this population. Health care providers and young women should also be aware of mechanisms for primary prevention and early detection of the disease.

Dr. Miller responded to questions from the Advisory Committee.

- J. Simha: I had a question about the slide about percentage of women who develop breast cancer at 10 year intervals by age. I did not understand this slide.
- J. Miller: When you're at age of 30, what is your risk of developing cancer in the next 10 years? That's .43%. At the age of 30 developing breast cancer over the next 20 year span is 1.86%. At the age of 30 you're percent of women who will develop breast cancer over the next 30 years would be 4.13%. So that means that by age 30, 4.13% of those women will have developed breast cancer within the next 30 years. We are taking a snapshot of women at one age at time. What percentage of 30 year old women will develop breast cancer in 10 years, 20 years, and 30 years?
- M. Watson: I have two questions. On your slide related to age-specific, five-year relative survival rates. Was that for invasive cancers only?
- J. Miller: Invasive only.
- M. Watson: My second question is on your breast cancer death counts slide in 2007, there were no deaths for in-situ. What happens to the undetected in situ disease?
- J. Miller: They may become an invasive cancer and metastasize.
- M. Watson: So, we don't really know how many of these people who had invasive cancer initially could have had in situ right?
- J. Miller: Right. This is something that we've been interested in. How many people who were initially diagnosed with DCIS developed invasive disease? However, this is not captured so easily.
- J. Mullen: Thanks for the wonderful data. It's good to put together like this. Given the relatively lower five-year survival, it would also be useful to look at the years of potential life loss within this age group as well. I think that would be a strong advocacy point to know that data point as well.
- J. Miller: Good point. Health economists in our division are looking that this issue.

Biology of Breast Cancer in Young Women

Lisa A. Newman, MD, MPH, FACS

Director and Professor of Surgery
University of Michigan Breast Cancer Center
University of Michigan Health Systems

Dr. Newman's presentation focused on the biology of breast cancer in younger women.

Pre-menopausal women are affected disproportionately by breast cancer and have a higher risk of mortality compared to older women. Five and ten year survival rates for young women are also significantly lower than in older women. The loss of younger women also has a significant impact on families, since these women are often working to support others and raising children.

There are several approaches to defining breast cancer biology: stage at diagnosis, tumor subtype, and survival and recurrence. Stage at diagnosis includes tumor size, nodal status, metastatic burden, and/or LRD (local, regional, or distant). There have been some exciting developments in tumor subtypes. It is known that different subtypes have different growth rates and respond to different treatments. While there have been exciting developments in this area, there's much potential for future research, which may ameliorate disparities in treatment outcomes. Lastly are outcomes such as survival and local/regional recurrence.

When looking at breast cancer outcomes, lower survival rates in younger breast cancer patients is partially explained by more advanced stage distribution and delays in diagnosis. Numerous studies have demonstrated higher local/chest wall recurrence rates for young breast cancer patients. Higher local recurrence rates following breast conserving surgery are partially explained by the increased frequency of the extensive intraductal component, making margin control more difficult; this provides further evidence that young women have breast cancer associated with an inherently more aggressive nature.

Some recent studies about genetic content have been extremely exciting and lead to better targeted therapies. Luminal (A or B) subtypes tend to be positive for estrogen receptors. Unfavorably basal-like subtypes are lack estrogen receptors and are thus resistant to most targeted therapies.

Basal-like subtypes are the most tightly clustered subgroups in gene expression arrays. Their morphology is high grade, mainly ductal or medullary, high mitotic count, scant stroma, central necrosis, pushing border, lymphocytic infiltrate, and apoptotic figures. Dr. Newman noted that triple negative is not a synonym for basal-like phenotype. The two do not directly overlap.

In the case of triple negative breast cancer (TNBC), the risk of metastatic spread exists. The risk is lower for early stage breast cancer and can be decreased with adjuvant systemic therapy. Systemic therapy options are determined by estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2)/new. There are fewer systemic therapy options for TNBC. The inherently aggressive biologic behavior makes endocrine therapy and Trastuzumab ineffective. It has been very clearly demonstrated that younger women are more likely to be diagnosed with TNBC.

Research regarding racial-ethnic identities usually focuses on White American, African American, Hispanic American, and Asian American. There is limited information about incidence in Native Americans. Hopefully this Committee will be able to address this and achieve a better understanding of that population's risk. There's a need to answer the question: Do we know how to appropriately define racial/ethnic identity? There are heritable contributions from geographically-defined racial/ethnic ancestry to the biology of breast cancer influenced by centuries of genetic admixture in the U.S. Our current system for reporting racial-ethnic identity does not account for this admixture.

Although there are variations between different ethnicities, there is some consistent data. Mortality rates tend to be higher for African American women at all age categories but the incident rate is lower, except for in very young women. The differences are not extensive for women younger than 25 years of age, but the implications on mortality do cause concern. In addition, African American women are more likely to be diagnosed with estrogen receptor negative breast cancer. This population has a two-fold higher incident rate and is less likely to respond to estrogen receptor therapies. Statistics from the National Cancer Database show that regardless of age, stage of diagnoses, and income level, African American women have higher frequencies of estrogen receptor negative breast cancers than white women. These findings have been confirmed by independent population-based assessments. Data from the Lisa Carey, using data from the Carolina Breast Study Group, revealed that African American women are at higher risk for TNBC. Other investigators have gone on to confirm these results.

Findings from a TNBC study using California Cancer Registry data revealed that younger African American women have substantially higher incidence rates of the triple negative breast cancer compared to age matched women of other racial and ethnic backgrounds. The rates were also higher than rates of TNBC among older-aged white women. The recently updated United States Preventive Services Task Force's (USPSTF) mammography recommendations included a recommendation against screening women 40-49 years of age. This recommendation may worsen breast cancer outcome disparities between African American women and white American women as African American women are more likely to be diagnosed at younger ages. Adherence to those guidelines will likely result in delayed diagnosis of disease in African American women.

Several investigators have attempted to identify risk factors for developing biologically aggressive breast cancer in young women. Bob Millikan has shown that certain potentially modifiable risk factors can account for the development of basal-like-like breast cancers associated with increased parity, increased age at first live birth (FLB), decreased breast feeding, and abdominal adiposity. He estimates that two-thirds of basal-like-like cancers in premenopausal African American women could be prevented by modifiable risk factors. A subsequent study using data from the San Francisco Area Breast Cancer Study found an inverse relationship between BMI and abdominal adiposity and the risk of ER-positive breast cancer. However, no association with the ER-negative disease was detected.

Is African ancestry associated with a heritable marker for high risk breast cancer subtypes? There is a unique opportunity to gain insights regarding the etiology of breast cancer disparities and the pathogenesis of TNBC. Dr. Newman's group at the University of Michigan and Dr. Olufunmilayo Olopade's group at the University of Chicago and other investigators have published research comparing the breast cancer burden of African American, Sub-Saharan African, and white American women. Their findings reveal consistent step-wise patterns between the three groups when looking at the proportion of TNBC, proportion of high grade tumors, and proportion of patients with ER negative tumors. It has been speculated that these findings are related to extent of African ancestry.

Another way to look at the question of African ancestry and high risk breast cancers is through studies of mammary stem cells. There is some work using ALDH1 as marker of normal and malignant human mammary stem cells and a predictor of poor clinical outcomes. Some of Dr.

Newman's group's preliminary studies have demonstrated a higher intensity and expression of the stem cell marker, which again suggests that ancestry may be an indicator of risk.

In summary, we can certainly say that breast cancer risk increases with age but young women account disproportionately for breast cancer mortality. African American women have an increased risk for breast cancer in the pre-menopausal age range compared to White American women. They have an increased risk for the ER negative, triple negative breast cancer that is most notable in this pre-menopausal age range. There are exciting research opportunities in our future.

- identifying therapeutic targets for treatment of TNBC;
- studying heritable and modifiable risk factors for early-onset and biologically-aggressive breast cancer patterns;
- improving screening for appropriately-selected young women;
- improving data collection on breast cancer risk in pre-menopausal women of other racial and ethnic backgrounds; and
- redefining the definitions for racial and ethnic identity so that they are more scientifically relevant.

Dr. Newman then responded to some from the Advisory Committee.

- N. Lythcott: "At the area where you indicated no stage, where do you place the zero staged women? Were they unstaged or staged?"
- L. Newman: "No, these are for invasive cancers. Unstaged are not included in these data."
- R. Shoretz: "Do you have any incidence data for the Ashkenazi Jewish heritage?"
- L. Newman: "I do not have any, but it is a trigger that we need to look at for genetic consideration. Tomorrow's lecture is supposed to present more about this population."
- R. Shoretz: "It is my hypothesis that some of this data may be lacking."
- A. Partridge: "There is some good data out there for the Jewish community."
- R. Nicholas: "What is happening in [the] private sector for drugs that impact triple negatives? What research is being done currently and how do we push that forward?"
- L. Newman: "I think that's an extremely powerful question, but I can say that that question spills over into how we will be conducting our research in the future. There

will be a shift in where our patients are treated, and so we have to figure out ways to recruit patients from these various facilities more aggressively. Many more people will be treated in community practices, so our partnerships will have to be more aggressive in the future.”

- O. Brawley: “In order to have a drug you have to have a target. There are PARP [poly ADP-ribose polymerase] inhibitors, but there is a shortage of targets in order to develop the drug. You’re pointing in an area that we need more research in the lab.”
- A. Partridge: “There is a lot of research being done in (PARP) inhibitors.”
- T. Fairley: “And we will have a little more discussion this afternoon that will address

Breast Cancer Genetics in Young Women

Cecelia Bellcross, PhD, MS, CGC
 Department of Human Genetics
 Emory University School of Medicine

Dr. Bellcross’s presentation focused on breast cancer genetics and counseling.

All cancers start with some level of genetic predisposition. Other factors, such as environmental exposures, add to this predisposition until cancer develops. When considering genetic components of breast cancer there are three loose categories: sporadic (70-75 percent), familial (15-20 percent), and hereditary (5-10 percent). Sporadic cancers require a lot of time and numerous factors to develop. Familial cancers require less time and less environmental factors, but hereditary cancers require little time and few factors at all before cancer develops.

In sporadic cancer, the majority of cases are not usually inherited and have onset later in life. There is low or no increased risk to family members beyond general population risk. These individuals should be screened like the general population.

Familial cancers have some degree of heritability and can skip generations. The size of the family and number of women in the family should be examined. There can be two or more affected 1st and 2nd generation relatives. These cancers usually have a later onset, present unilaterally or in one breast, and have unclear inheritance patterns.

Hereditary cancers have multiple affected individuals in multiple generations. There tends to be early age of onset, multiple primary tumors, and dominant inheritance. It’s equally inherited for males and females. Many members of the cancer community don’t know that cancer can come from the mother and father equally; so physicians should not only ask about mother and sisters but both sides of the family and first and second degree relatives at a minimum. There are specific cancer syndromes in hereditary cancer, so physicians should also ask about ovarian cancer as well, because they may also indicate a risk for breast cancer. Hereditary breast-

ovarian cancer syndrome (due to BRCA1 and 2 mutations) is the most common cancer syndrome. However other syndromes exist and should be inquired about by physicians.

Genes that are not inherited in a strongly dominant fashion are called moderate penetrance. These may be more frequent in younger onset cases, but data are inconclusive. They account for 2-4 percent of familial breast cancers. The benefit of genetic testing for these is debatable. In low penetrance alleles the predictive value is nonexistent. There is an unclear relationship between these and early-onset breast cancer, but it is unlikely to be the major factor. There is at this point in time no clinical validity or utility in assessing these alleles in terms of helping identify somebody at increased risk for breast cancer.

Factors that indicate an increased likelihood of having breast cancer susceptibility gene include: 1. early onset breast cancer in women younger than age 50; 2. at least one bilateral breast cancer at age 50 or below. 3. male breast cancers; 3. Ashkenazi Jewish heritage; 4. breast and ovarian cancer in the same woman; 5. pathology including TNBC especially at young age; and 6. multiple breast cancers (bilateral or ipsilateral breast cancer), if one occurs before age 50.

There are no large population based studies, but from existing studies, it is evident that the Jewish population is more likely to carry the BRCA mutations than other women. If there has been a woman with breast cancer in a generation in a Jewish family, the risks increase dramatically. Providers need to understand this.

For women with unknown family history, (i.e., adopted female), or for non-Jewish women, it is unlikely for 25 year-old women to carry a ER/PR negative disease to carry the mutation, but for those with Jewish heritage that number changes substantially. In these cases, there is much uncertainty.

Today with family sizes being smaller, there is also the challenge of limited family structure. This makes it harder to determine risk compared to baby-boomers whose families were larger and therefore yielded a bigger picture. Smaller families can cause false predictions and, therefore, it is important to ask about second generation relatives and sometimes third to see who did and who didn't get cancer. It is sometimes hard for clinicians to understand that if one person tests positive for the mutation that siblings need to be elevated in their risk also and not be handled similarly to general population.

There are several management options available for BRCA1 and 2 mutation carriers. Early clinical surveillance, including breast and ovarian/fallopian tube cancer screenings, begins at age 20-25 and is done annually or semi-annually. Surveillance for breast cancer may include mammograms, MRIs, and CBE. Ovarian cancer surveillance is limited to CA125 and trans-vaginal ultrasounds; however the efficacy of these tests is uncertain.

Other management options for BRCA 1 and 2 mutation carriers include prophylactic mastectomy and/or oophorectomy. It is believed that prophylactic mastectomy or preventive removal of the breast results in a 90 percent or higher reduction in breast cancer risk. Prophylactic preventive removal of the tubes and/or ovaries can bring about 80-95 percent reduction in ovarian/fallopian tube cancer risk and a 50 percent or higher reduction in breast cancer risk. If a woman has, in her history, someone who has had fallopian cancer, she should be placed in a higher risk category.

Finally, cancer genetic counseling is not genetic testing. It is a process of information gathering, risk assessment, and education. The goal of cancer genetic counseling is to provide the individual, family, and their health care provider with accurate cancer risk information to facilitate personal management decisions. Cancer genetic counseling should include preparation, education, and discussion.

Dr. Bellcross responded to questions from the Advisory Committee.

O. Brawley: “With the EARLY Act, there are some that will conduct genetic counseling it over the phone for a fee. That concerns me. There are also companies that go to areas where the affluent population reside or recreate and give one-day talks or advertise to scare women into these genetic counseling sessions, again for a fee. Can you talk about that?”

C. Bellcross: “Our field is a small field and specialized. Good telephone genetics counseling can be done by a well-trained, board certified genetic counselor. There are different kinds of telephone counseling. Getting access to a quality counselor is the primary issue.”

A. Partridge: “Where do you draw the line? Being that resources are limited and the fact that we have false positives, who do you recommend gets tested?”

C. Bellcross: “It is primarily a question of who gets referred for genetics counseling and risk assessment that is most important. There are screening tools out there to help determine who is appropriate for referral including simple tools like www.brcagenscreen.org and other pedigree assessment tools. There are more complicated models, but we need simple tools that refer patients for genetic testing.”

D. Warne: “Working in a rural and impoverished region, what other tools are available when resources are limited?”

C. Bellcross: “There are some emerging decision support-modeling and referral tools that can help. There are not enough counselors or trained physicians to do counseling let alone testing. But I think referral tools are important. One thing clinicians can do is go to the FORCE (Facing our Risk of Cancer Empowered) Web site. It’s written on a level for clinicians and is a good place to start. Sometimes phone counseling is an option. There is an effort with the medical school to increase this area including discussions of making this part of the board exams.”

Dr. Fairley will make Dr. Bellcross’ contact information available to participants, since a lot of questions arose in this session.

Otis W. Brawley, MD

Chief Medical Officer for the American Cancer Society
American Cancer Society

Dr. Brawley's presentation focused on public health aspects breast cancer screening as related to this population.

The United States is the most expensive country for health care in the world, but only ranks 29th in life expectancy. The United States spends more money on health care than any other country, but the people do not appear to receive the services for which they have paid. When the high murder and infant mortality rates are factored in, the United States only moves up to the 16th position. There are disparities within our healthcare system. Some patients consume too much or are given unnecessary care. Others consume too little and are not given the care that's necessary. The goal should be to decrease waste and improve overall health at the same time.

Overall, whites have higher cancer incidence than all minority groups. However mortality rates for blacks are often higher than in whites. This pattern was first noticed in 1982-83. Prior to this, mortality rates were similar in these populations.

As a rule, national cancer statistics are collected and presented for the following race categories: White, Black, Asian/Pacific Islander, Native American, and Hispanic. These categories are pre-defined by the U.S. Office of Management and Budget. Unfortunately there is no category for the Jewish race in the population-based cancer surveillance system at this time.

Of the 207,090 people diagnosed with breast cancer in 2010, the median age was 61, and median age of death was 68. The risk factors for breast cancer include gender, age, and family history. Approximately 10,100 women diagnosed with breast cancer annually are under the age of 40. One in five women diagnosed under the age 40 has a family history of breast cancer. It should be remembered that risk due to family history is not the same as genetic risk. Ten percent of Jewish women diagnosed with breast cancer have BRCA mutations, but 90% do not.

Other modifiable risk factors for breast cancer include weight or obesity, estrogen and progestin use, physical activity, and alcohol consumption. Medical findings that predict higher risk include certain genetic mutations, high breast tissue density, high bone mineral density, biopsy confirmed hyperplasia, and high dose radiation to the chest. Reproductive factors that increase risk are long menstrual history, recent use of oral contraceptives, never having children, and having the first child after age 30.

Studies show that 5 to 10 percent of breast cancers are hereditary, resulting from gene defects inherited from a parent. Not all genetic mutations in genes cause breast cancer. Certain mutations increase risk at variable levels. Many who are screened have genetic mutations of undetermined significance and some mutations are of no significance.

Genetic testing has serious personal, emotional, and psychological implications for persons that receive screening and possibly their families. Screening should be done by well-trained genetic

counselors. Few physicians are trained and qualified to be genetic counselors. This is critically important as several entities have used genetic testing to manipulate individuals into testing for a fee, but have not provided appropriate counseling services.

Let's turn our attention to screening. The best evidence of the effectiveness of a screening test is decreased mortality rates. However this premise has not always been agreed to. For some, merely detecting cancer, detecting cancers early, and increasing 5-year survival is evidence of effectiveness for a screening test. There are some lessons that can be learned from the 1960s Lung Cancer Screening project in which chest x-ray screening was shown to detect cancer at earlier stages and increases survival. Chest x-ray screening for lung cancer was promoted nationally based on these initial findings.

A prospective randomized lung cancer trial was later conducted by in the Mayo Clinic to address the efficacy of chest x-ray as a screening mechanism. The study revealed death rates of 3.4 per 1,000 per year among those screened annually for 10 or more years and 2.9 per 1,000 per year in the control group. Unfortunately, the completion of these randomized trials was delayed until well into the 1970s, because so many people were certain that chest x-ray screening was superior. In summary, when dealing with complicated and often conflicting concepts involving screening, treatment, and other health interventions, it is important to understand what is known, what is unknown, and what is believed. We must also realize that clinicians have a tendency to confuse what they believe with what they know.

Some of you may be familiar with the term "length bias". Length bias is the principal that not all cancers grow at the same rate. There are slow-, medium- (or interval), and fast-growing cancers. Cancers diagnosed between scheduled screenings are fast-growing and very aggressive. Medium-growing cancers that are often diagnosed at scheduled screenings. Those diagnosed at initial screenings are slow-growing and the least aggressive of all cancers. Of these three types, only the medium-growing cancers will benefit from screening. Patients are often "over-diagnosed" as some cancers will not need to be cured because they are slow-growing and unlikely to cause death.

Breast cancer screening is less sensitive and less effective in women aged 40 to 49 compared to women 50 to 59. This is because of rapid tumor growth, increased breast density, and lower risk of breast cancer. Screening is even less effective in women under 40; however, the effectiveness of screening younger women at high risk is unknown.

Length bias is also an issue to consider in breast cancer. In studies of screened populations, younger women have more fast-growing cancers than older women thus 5-year survival is low. A fundamental problem with breast cancer screening is that it's less efficient and less effective in people with fast growing tumors. In the entire U.S. population, it is estimated that up to 30 percent of breast cancers are over-diagnosed cancers. They appear malignant but are of no threat to the patient.

There are eight prospective randomized breast cancer trials involving normal risk women over the age of 40 using mammography and clinical breast exam. Most of the research is focused on women over the age of 50. All but one was completed before adjuvant therapy was proven effective and technology was changed. The collective interpretation is "screening saves lives for women age 40 and above". In one large prospective randomized trial of more than 260,000

women, intensive instruction in breast self examination (BSE) did not lead to finding more cancers nor saving more lives. It did, however, increase the number of breast biopsies and the number of benign lesions diagnosed. A second study of more than 60,000 women intensively taught BSE showed similar results.

Caution should be taken in deciding which screening guidelines to follow as the methodology for developing these guidelines is not standard. Some are a consensus of experts based on belief and opinion whereas others include a consensus of experts based on a structured review of the published literature.

The American Cancer Society (ACS) believes that women age 20 to 39 should have a clinical breast examine done every three years by a physician, a physician's assistant, or someone trained to do this appropriately. Women 40 and over should have a mammography done annually. These guidelines differ from the USPSTF recommendation, which recommends against routine screening in women age 40-49 and for biennial screening between ages 50-74. However, both organizations believe that women should be made aware of the limitations of mammography. The ACS de-emphasizes the use of breast self exam (BSE). ACS recommends MRI for women who know that they have more than a 20% lifetime risk of breast cancer starting at 30. According to the American College of Obstetrics and Gynecology, screening for this group should start at age 25.

In closing, Dr. Brawley noted the need to develop better breast cancer screening tests for women and educate women about the limitations of current screening methodologies. Additionally, we need to be thoughtful about the messages that we disseminate to women, given the risk of overwhelming them or blurring important messages with less important messages. Messages that address the importance of modifiable risk factors such as obesity and smoking should also be considered. Finally, consideration should also be given to the population of uninsured women who often have higher mortality rates.

Dr. Brawley responded to questions from the Advisory Committee:

- M. Watson: "Regarding ductal carcinoma in-situ (DCIS) for most young women, it feels like cancer, and your life mirrors those women with cancer. Can you elaborate on this disease?"
- O. Brawley: "A pathologist in 1950 was using the light microscopes and made a series of drawings and drew what he thought was cancer. From that, the cancer definition was created. And these definitions have stayed the same in spite of advancements in medicine. I now know epidemiologically that frank cancers are not genomically programmed to ever really progress, and this is a huge problem with prostate cancer. When you look at DCIS, which is not frank cancer, I'm okay of thinking of it as pre-cancer and if left alone has a chance to become cancer. But I also acknowledge that we sometimes see scare tactics in medicine. There's a group of people who are working to change the name and take carcinoma out of it."
- A. Partridge: "Whether or not the name gets changed, we should change the way we view

DCIS. But we do need to inform women of their risk. A majority of our younger women won't be DCIS, but we still need education."

- O. Brawley: "We need to do a series of genomic tests where we can let them know that they have cancer but it won't cause an issue, versus you have a concern and it needs to be addressed quickly. We have to inform and acknowledged that there are scare tactics sometimes employed. Instead we need to look at where we should move in research."
- M. Watson: "Both my radiologist and surgeon believed that this would advance and suggested double mastectomy and no other consultations took place, so I just want to gain understanding of DCIS."
- O. Brawley: "Some doctors don't understand."
- A. Partridge: "And remember there're different flavors or types of DCIS that determine whether you should be treated aggressively or less aggressively, and we need to do further screening."
- O. Brawley: "I understand your confusion as a patient because I constantly have to explain to doctors the correct definition of DCIS."
- A. Partridge: "There's no doubt that people who have DCIS do feel that they need the same support as cancer patient because we treat it similarly to invasive cancer aside from chemotherapy."
- L. Newman: "And we don't know sometimes how to pick out the bad apples so sometimes we just react on the side of hazard."

Diagnosis and Treatment of Breast Cancer in Young Women

Dr. Ruth O'Regan

Associate Professor of Hematology and Medical Oncology, Winship Cancer Institute
 Chief of Hematology and Medical Oncology at Georgia Cancer Center for Excellence, Grady Memorial Hospital
 Medical Director, Emory Breast Center,
 Louisa and Rand Glenn Family Chair in Breast Cancer Research
 Director, Hematology Oncology Fellowship Program
 Director, Translational Breast Cancer Research Program,
 Vice Chair for Educational Affairs
 Emory University School of Medicine,
 Winship Cancer Institute

Dr. O'Regan's presentation focused on treatment aspects of breast cancer in young women. She also provided a brief overview of the epidemiology, risk factors (including genetics), and

screening methodology and guidelines for breast cancer in young women.

Younger patients appear more likely to get more aggressive breast cancers. There are four (genetic) subtypes of breast cancer: luminal A and B, basal-like (or triple negative breast cancer; TNBC), and HER2+. These subtypes are all very different in terms of their genetic make-up and associated prognosis. The luminal A cancers, which are estrogen receptor +, have favorable outcomes over the first few years including overall survival. However, these cancers can recur 20-25 years after the initial diagnosis.

The luminal B cancers have very high recurrences rates over the first five years with poor survival. These cancers do not generally respond to hormonal therapy, which contributes to worst outcomes. HER2+ cancers are very aggressive cancers, with high recurrence rates over the first five years and poor survival. They are also quite common in younger patients. Advancements in treatment have contributed significantly to the improved prognosis of HER2+ cancer--making it one of the more favorable types of cancer.

Basal-like and triple negative breast cancers (TNBC) have a very high recurrence rate over the first five years, but are unlikely to re-occur after 5 years. Survival for this cancer is very poor. In a Carolina study of the 657 breast cancer patients, rates of TNBC were higher among black women than white women. The highest incidence rate of TNBC was noted in pre-menopausal Black women. A subsequent study of breast cancer found that TNBCs were most common in younger patients, regardless of race. However, rates of TNBC were lower for white women over 40 and 2-fold higher in blacks over 40. A third population-based study, looking at breast cancer in women 35 or younger, studied 967 patients. Of those patients, 105 were aged 35 years or younger. Compared to older patients, younger patients are more likely to present with late stage cancer, large tumors, and lymphovascular invasion, and higher grade cancers. Thus physicians are more likely to recommend chemotherapy for these patients.

Young patients generally present with a palpable mass, likely because they are not being screened. General diagnostic procedures include biopsy and breast imaging via mammogram, ultrasound (both breast), or MRI.

Local therapy regimens may include mastectomy, which can equal partial mastectomy plus radiation. However preliminary evidence suggests that mastectomy may show greater efficacy in young patients. Sentinel biopsy of the lymph nodes is optimal as full dissection can be avoided if negative. There should be a full axillary dissection if the sentinel lymph node is positive. Post-mastectomy radiation is recommended for patients with larger cancers and/or positive lymph nodes.

For systemic therapy, the goal is to eradicate micro-metastatic disease outside of the breast area. Currently there is no effective means of accurately determining which patients have micro-metastatic disease. Therapy options include: hormonal therapy with Tamoxifen, chemotherapy, and/or Trastuzumab. Therapy is administered based on cancer subtype, however research (i.e., Meta-analysis) suggests that younger women benefit more from adjuvant chemotherapy. This is likely due to the high prevalence of TNBC and HER2+ cancers in this population.

Trastuzumab is a humanized anti-HER2 antibody. It is approved for all stages of HER2+

breast cancer. When added to chemotherapy it decreases the risk of relapse by 50 percent and improves survival. Tamoxifen targets ER and is effective in both pre- and post- menopausal women. It decreases recurrence by 50 percent and improves survival in about a third of patients. It is also approved for the prevention of breast cancer in high risk women. While Tamoxifen is considered a safe and effective drug, there are issues for pre-menopausal women with compliance to its 5-year treatment plan. It is given for 5 years because this time span was found to be most effective. It should be noted that patients may need to have some adjustments if they are closer to menopause.

Side effects related to various types of cancer treatment can be acute or permanent. The acute side effects are nausea and vomiting, decreased blood clots, ovarian cysts, menopause/amenorrhea, and hair loss. Potentially permanent effects include early menopause resulting in infertility and cardiac toxicity. There are significant fertility issues with treating younger women diagnosed with breast cancer. Patients and physicians should consider a reproductive endocrinology consultation prior to starting chemotherapy. However, consideration should be given to the effects of the use of high dose hormonal therapies in retrieving oocytes.

Follow-up for patients with a history of breast cancer should follow recommended guidelines and minimally include a regular history, physical examination, and mammography. Monthly self breast examination is also encouraged. Follow-up should be structured based on breast cancer subtypes. Triple negative and HER2+ cancers should be followed closely for the first 3 to 5 years but less often after 5 years. ER+ cancers should regularly for an indefinite time period.

Exercise has been shown to be beneficial in reducing and preventing recurrences and improving survival. Pre-diagnosis, exercise has also been associated with improved outcomes for breast cancer. Randomized trials found that people who decreased fat intake, BMI, and weight were less likely to have recurrence, especially if the cancer was ER-. These women were also less likely to die from breast cancer.

Multiple retrospective studies have evaluated the effect of pregnancy in patients following a diagnosis of breast cancer. None have demonstrated an increased risk of recurrence. The general recommendation is to wait at least 2 years. Those taking Tamoxifen should not attempt pregnancy until completing recommended 5-year treatment.

Dr. O'Regan responded to questions from the Advisory Committee:

M. Watson: On your slide regarding breast cancer risk factors, it says late age at birth of first child. What age is that?

R. O'Regan: So that would be an age of 35 is what was used in that model. So if you look at women who either have no children or have their first child over the age of 35, they're at a higher risk of developing breast cancer than women who have their first child around the age of 20. It's a relatively weak risk factor, but it is part of that model essentially, so 35 is the cutoff.

R. Nicholas: "You talked about chemotherapy and hormonal therapy. What about radiation therapy?"

- R. O'Regan: "That's an evolving field as well. Radiation is used more when lymph nodes are affected. There's not much data on radiation in younger patients. Most of it is in the older patients, but we aren't seeing a lot of concern there."
- M. Karmo: "There're some issues about soy being good and bad. What's your opinion?"
- R. O'Regan: "The data is all over the place. I don't tell my patients to omit it. It's a complex situation, but the jury is still out about the soy."

Federal Activities Related to Breast Cancer in Young Women: Research, Program and Innovation

Temeika L. Fairley, PhD

Designated Federal Officer (DFO),
Advisory Committee on Breast Cancer in Young Women (ACBCYW),
Division of Cancer Prevention and Control (DCPC), CDC

Dr. Fairley's presentation focused on the CDC's current activities related to breast cancer in young women.

In response to legislation of the EARLY Act, CDC formed a workgroup to identify key areas of applied research initiatives, communication approaches, communication messages, and programmatic support. Dr. Fairley outlined the portfolio of CDC's work related to the EARLY Act. Projects were grouped into the three aforementioned categories.

Applied research:

1. Comprehensive review of the scientific literature, a media audit, and an environmental scan related to breast cancer in young women. This review will be followed by an expert panel and publication of the panel's findings.
2. Genomics research activities related to BRCA 1 and 2 testing and service delivery, family history of breast cancer, and insurance coverage for genetic testing and follow up in the United States.
3. Surveys added to the National Institute of Environmental Health Science's (NIEHS) Sister's Study and Two Sister's Study. Information gleaned will allow CDC to assess risk perceptions, provider communication, and information-seeking behavior among young siblings of young breast cancer survivors as well as describe the current issues among current young breast cancer survivors.

4. Walking Together: Making a Path towards Healing, a study aimed at identifying and describing the barriers to care for American Indian and Alaskan Native women seeking care for breast cancer or related issues.
5. Studies assessing the magnitude of infertility among breast cancer survivors in the U.S.

Program Support:

1. An evaluation project, *Developing psycho-social and reproductive health support for young breast cancer survivors*, aimed at providing programmatic support for up to three national organizations that address the needs and provide intervention programs for young survivors. The objectives are to assess the organizations' capacity to effectively develop, implement, and disseminate interventions, assess if current interventions and tools yield intended outcomes, and if newly developed interventions are effective and can be applied. CDC ultimately wants to increase evidence-based interventions around this area. Its next steps are to establish centers of excellence or program models, expand partnerships with organizations doing this work, establish promising practices, and contribute to the knowledge base.

Communications activities:

1. Body Talk, a smart-phone application created to enhance conversations between women and their providers about lifestyle, family history, and where women with breast cancer can go for support.
2. A clinic and web accessible decision support tool to improve communication between women and their providers during the primary care visit and specifically to educate on things such as family history, direct patients for further support, and promote healthy lifestyle.

The next steps include strategic planning sessions to assess research and program gaps. The Advisory Committee on Cancer in Young Women (ACBCYW) meeting will engage experts, who will continue to advise the Committee as it moves forward.

Dr. Fairley responded to questions from the Advisory Committee.

- J. Steiner: "A question came up about the CDC screening and treatment program and about it being unknown on a national level. It's governed state-by-state. Is there a way of allowing that program to serve women who present with suspicious symptoms?"
- J. Miller: "We do serve those women."
- J. Steiner: "In every state?"
- J. Miller: "It is a national rule, but states can opt out. Most states do cover for those who are high risk."

- M. Plescia: "Some people opt out due to limited funding."
- A. Partridge: "What about the 80 percent? Are they not reached out to?"
- M. Plescia: "There are other mechanisms that will provide free services, so there's a broad safety net."
- D. Warne: "For health insurance plan projects will Medicaid plans be assessed as well?"
- T. Fairley: "The way that it is listed is public and private, so we will likely reach into some of the public options."
- D. Warne: "Hopefully IHS [Indian Health Service] is included in that."
- R. Nicholas: "Regarding networking and collaboration efforts around social media, what are some groups that you're working with?"
- G. Cole: "We are doing a number of strategies including Facebook. As far as working directly with those social media providers, we have not."
- R. Nicholas: "We can help you with that component."
- J. Mullen: "Among the activities, is there a thought to considering performance measures?"
- T. Fairley: "Yes, we are addressing the performance measurement issue in a broader community."
- N. Lythcott: "When you think about providers, you should also think about the education of providers."

Mrs. Frances Ashe-Goins

Acting Director for the Office on Women's Health (OWH)
U.S. Department of Health and Human Services

Mrs. Ashe-Goins presentation included an overview of the Office on Women's Health's (OWH) programs and activities.

OWH was established in 1991 to address women's health issues in the U.S. It is the focal point for women's health in HHS, and has recently expanded its charge to include girls. OWH's vision is that all women and girls are healthier and have a better sense of well-being. Its mission is to provide leadership to promote health equity for women and girls through sex/gender-specific approaches. The goals of the Agency are to develop and impact national health policy as it relates to women and girls; develop, adapt, implement, evaluate, and replicate model programs on women's and girl's health; to educate, influence, and collaborate with health and human services organizations, health care professionals, and the public; and to increase OWH's

organizational efficiency and performance. OWH has 10 regional offices with Regional Women's Health Coordinators assigned to each office.

The Agency offers model programs and education outreach. It promotes the development and implementation of model initiatives that address the health needs of diverse populations of women and girls. It has several program areas and model programs. Some of the programs include ending violence against women on college/university campuses, AIDS-related services for survivors of domestic violence, intergenerational approaches to HIV/AIDS prevention education, and HIV/AIDS prevention services for female youth at greater risk for juvenile delinquency.

There are many education and outreach programs that are conducted through Web sites and the Resource Center. Also available are national databases, publications, and exhibits. It has a Quick Health Data Online that goes down to State and county levels. Women report about how helpful and easy to understand the Agency's exhibits and publications are.

OWH also has campaigns such as Lupus Awareness, BodyWorks, Best Bones Forever, and Heart Truth. It has spent \$2.3 million to create the Lupus Awareness Campaign and received \$45 million dollars of donated media. The Agency works with organizations that deal with lupus and in turn work with providers. BodyWorks is a toolkit designed to help parents make small changes over time to improve the health of their families. It is a community approach and works very well. The Heart Truth campaign is a collaborative project that improves professional and community education.

Public Comment

This session was open to the public to pose questions to the panelists and members.

- C. Bugle: "Thank you for being here. When will the public hear what the priorities are within the Bill, like health care provider education and how transparent will the budget be for this process?"
- M. Plescia: "Part of the purpose of the Committee is bringing folks together for a state-of-the-science gathering on the issues and to hear the data. But ultimately the role of the Federal Advisory Committee will be to deal with some of the issues that you've raised. Regarding education to health care providers, we will have some time to talk about those things with the Committee. For the first year of funding, we received the money early and you heard Dr. Fairley talk about some of the activities that have been put forth thus far. It is our desire to be very transparent throughout this process. Our intent is to address each component of the legislation, providing updates and study findings from our work to the Committee."

**Wrap-Up/Announcements**

Day 1 adjourned by Dr. Fairley and Dr. Partridge.

Day 2
8:00a.m.-1:30pm

Meeting adjourned early due to inclement weather

Survivorship Issues among Young Breast Cancer Survivors

Dr. Fairley called roll for Committee members, ex-officio members, and liaison representatives and called the meeting to order after determining that there was a quorum.

Dr. Ann Partridge welcomed everyone to Day 2 and gave a brief recap of Day 1. Day 2's presentations were conducted around the topic of young breast cancers survivors.

Brandon Hayes-Lattin, MD

Medical Oncologist

Oregon Health and Science University

Dr. Hayes-Lattin's presentation provided the Committee with an overview of survivorship issues of adolescent and young adult cancer survivors.

There are about 70,000 cases of cancer diagnosed per year among 15-29-year-olds. It is the leading cause of death for those individuals. In contrast to younger and older cancer patients, survival rates for young adults have not increased since 1975. Some of the issues seen are delayed diagnosis, rare tumors, misunderstood biology, and lack of clinical trials, poor prognosis, and lack of local specialists. Some individuals in this population live alone or are having to return home to live with parents because of their disease. They have issues with insurance, have no steady finances, no experiences with cancer, and have never considered fertility.

Dr. Hayes-Lattin then spoke about isolation. In the instance of breast cancer between the ages of 20 to 40, the incident rate is low. Therefore, the women diagnosed with this disease don't see many women in their cohort like themselves, possibly leading to feelings of isolation and loneliness.

Another issue is trust. Dr. Hayes-Lattin talked about a blog on the PLANET Cancer website titled "What was it before it was cancer." Patients are able to blog about the different diagnosis they were given before it was discovered that they had cancer. Some common diagnosis were depression, panic attacks, stress, mono, TB, SARS, gall bladder, appendix, kidney stones, cat scratch fever, excessive drinking, and bad narcotics. All of these misdiagnoses led to a mistrust of the medical system.

There are other cultural narratives which speak to cancer survivorship, particularly in young adulthood. There is a struggle to find meaning or the idea that you should be struggling to find meaning. This puts an extra burden on cancer patients and can lead to survivor guilt.

Another issue patients must contend with is the practical consequences of treatment. Treatments can cause late effect and chronic medical conditions, including gonadal dysfunction,

secondary malignancy and relapse risk. There can also be the long-term burden of the illness. Survivors tend to experience a loss of productivity and rate their health as fair or poor. There are high rates of difficulties obtaining life and health insurance, employment, and loans and mortgages.

In 2006, the National Cancer Institute created the Progress Review Group to address topics such as biology, prevention, cancer control, epidemiology, risk, insurance, clinical care models, psychosocial effects, and long-term care in adolescent and young adult survivors of cancer. One of the recommendations was to establish distinguishing characteristics of cancers in young adults and create education, training, and communication tools for this age group. There were also recommendations to create new tools to study young adult problems, develop excellence in care delivery, form standards of care, and promote advocacy.

Regarding standards of care, the National Cancer Institute and The Lance Armstrong Foundation formed the LiveStrong Young Adult Alliance, which is a coalition of about 150 organizations. They hosted an annual national meeting, participated in the creation of an international charter of rights for young people with cancer, and published position statements regarding cancer in young adults.

The Knight Institute of Oregon Health and Science University helps coordinate a large range of services, such as pharmacy, pain management, pathology, radiation medication, psychiatry, child life and adolescent health, and a host of other services. It employs external partners and makes assessment plans based on 10 dimensions, which include symptom management, emotional and psychological health, function, and physical and social well-being.

Dr. Ann H. Partridge

Associate Professor of Medicine
Dana Farber Cancer Institute
Chair for the Advisory Committee

Dr. Partridge's presentation complimented the information presented by Dr. Hayes-Lattin and included more specific information about survivorship issues of young breast cancer survivors.

Breast cancer for young women is different, and there are many issues and concerns exclusive to women who are young at diagnosis. If this disease is different biologically for young women, then there's a necessity to figure out how in the coming decade. Young women's issues are unique. They are at increased risk for recurrences and often request and receive more aggressive therapy. It is important to note, however, that not all breast cancers in this population warrant aggressive treatment. Thus, efforts should be made to identify the women who need aggressive therapies.

Both the disease and treatment can have profound effects on menopausal symptoms, fertility and family planning, genetic risk, psycho-social distress, role functioning at home or work, beauty and attractiveness, and sexual functioning. Issues are further compounded by isolation, lack of information about risk, lack of provider awareness and resources to address younger women issues with patients, and a lack of peer group support. Though it hasn't been measured, young patients may also suffer from a lack of resiliency.

Young breast cancer survivors have overall high levels of physical function. However, social and emotional functioning and vitality are lowest in the youngest women. The youngest women also had more symptoms of depression and other negative psychosocial outcomes.

In a Nurses' Health Study, over 122,000 nurses between the ages of 29 to 71 responded to pre- and post-functional status evaluations. In this study, they found that women with breast cancer who were younger than 40 experienced significant functional declines compared to young women without breast cancer. Young women with breast cancer had the larger relative declines in health-related quality of life (HRQOL) compared to older women with breast cancer. There were also declines for the younger women in physical roles, bodily pain, social functioning, and mental health. Much of the decline in HRQOL for older women was attributed to aging. Younger women also reported worse sexual functioning compared to older women.

A Web-based survey on fertility issues was conducted on 657 women with a median age of 33 at the time of diagnosis. Of those, 57 percent of women recalled substantial concerns at diagnosis about fertility after treatment, and 29 percent reported that fertility concerns influenced treatment decisions. A follow-up study validated these findings. There is some good additional information about what women are doing to preserve their fertility. It was also reassuring to hear that doctors were discussing fertility.

Other issues faced are chemotherapy-induced amenorrhea, menopause, and infertility. This is due to the effects of chemotherapy on rapidly dividing cells that surround eggs in the ovaries. When these estrogen-producing cells are destroyed, eggs are also destroyed. If no eggs remain at all, there will be no menstrual period and the lack of estrogen often causes menopausal symptoms. Chemotherapy-related amenorrhea may be temporary. In women under 30, these risks are low but increase with age.

Questions still arise regarding the safety of pregnancy after breast cancer. The concern is that the stimulation of breast cancer growth from the high estrogen state of pregnancy and increased disease recurrence and decreased survival. There are methods of analysis of available studies such as case-control studies and retrospective cohort studies. Evidence suggests that pregnancy after breast cancer is safe. When counseling these patients, clinicians should suspend their own biases and look to the data to help them make the best decisions.

Young women with breast cancer face a variety of unique treatment and psychosocial problems at diagnosis and follow-up. Increasing attention to their unique issues may improve care and outcomes for this vulnerable population. Available evidence suggests that women are not well-informed historically about these issues and risks. Providers may not be addressing them, leading to gaps in care.

Over 6 years ago Dana-Farber Cancer Institute started *the Program for Young Women with Cancer* using a three-pronged approach: clinical care, education, and research. They developed a comprehensive care plan to make sure that all three areas were covered for every patient. There are several program goals:

- to support and care for young women with breast cancer;
- to educate patients and health care providers about the unique issues for young women with breast cancer;

- to provide a model of comprehensive care that can be adapted to settings within and outside of Dana-Farber/Brigham and Women’s Hospital Cancer Center; and
- to provide a unique setting for research to understand more fully and improve the experience and outcomes of young women.

Dana-Farber also conducted outreach for this program through newsletters and patient oriented social/educational gatherings. Dana-Farber recently secured an *Improving Cancer Care* grant from the American Society of Clinical Oncology and the Susan G. Komen Foundation. Dana-Farber used this grant to further develop their program into a web-based intervention for patients and oncologist called *Young & Strong*, which is currently being piloted at 4 locations throughout the country. Upon completion of pilot testing, *Young & Strong* will be evaluated via a randomized control trial.

Interventions like these have the potential to provide cost-effective, easy-to-disseminate strategies to improve quality of care for young women beyond large cancer centers. The key to potential success is that the intervention is implemented by oncology providers. Future directions include the virtual survivorship program, which will include links to advocacy organizations.

Dr. Hayes-Lattin and Dr. Partridge then answered questions from the Advisory Committee.

F. Ashe-Goins: “The tools that are developed, are they interactive?”

A. Partridge: “We developed an intervention to get some information to the patient at the point of care. What I see is patients don’t tune in, not that the tools are not available. We developed a new patient binder through YSC [Young Survival Coalition].”

J. Simha: “We do have samples of things coming out, and our challenge is getting to patients at the right time. There are smaller packages that can be stored at the hospital since they have limited space, and patients can then request the bigger binders. The website is an instant tool, and it would be great if hospitals had laptops for women to be able to access these websites right away.”

F. Ashe-Goins: “What about journaling?”

A. Partridge: “We have heard that it has helped for some.”

J. Simha: “Blogging also helps patients, friends, and others stay involved. It has been great for a lot of survivors.”

B. Lattin: “Electronic tools are wonderful. We received funding from CDC to build an electronic dissemination platform. Patients can enter 10 dimensions and are matched with resources.”

R. Nicholas: “Regarding fertility, when I was diagnosed, I was talked to about fertility. It was a pivotal moment, and it let me know that I was going to live and gave

me hope. Fertility options are incredibly expensive, and we need to address that.”

A. Partridge: “There are people fighting for insurance to cover this type of potential infertility. Massachusetts has been able to lobby for it, and one of the big insurers has made some changes. We, as a Committee, can do some good at putting that out there and making insurance and the public know that this should be supported.”

M. Nitta: “Are there resources for women who are diagnosed while pregnant?”

A. Partridge: “There is information. Elyse Cardonick focused on women diagnosed during pregnancy, and it’s not uncommon. It’s about 1 in 1,000 who are diagnosed with breast cancer will be pregnant. We formed a working group to address that. We have about six people under treatment who are pregnant.”

G. Grana: “Alicia is providing resources for the women and will also follow those children to assess the impact on them. There’s also a study going on in Europe as well.”

R. Shortez: “We have some resources as well. The Europe presentation was shared in San Antonio, and I can share that information with you.”

A. Partridge: “There are websites. Mother Risk and Pregnant with Cancer can provide more information, but there’s limited data.”

J. Simha: “At YSC, we have a large group of women who were diagnosed while pregnant on our message board.”

Supporting Young Breast Cancer Survivors

Joy Simha

Co-Founders of the YSC
Young Survival Coalition

The Young Survival Coalition (YSC) was founded in 1998 by Joy Simha, Roberta Levy-Schwartz, and Lanita Moss, all young survivors of breast cancer. They chartered the first chapter of YSC with 13 women. YSC is an international organization dedicated to the critical issues unique to young women diagnosed with breast cancer. The mission of the YSC is to improve the quantity and quality of life for young women affected by breast cancer. YSC is headquartered in New York City and has 26 affiliates and 23,000 members across the U.S.

By 2012 YSC hopes to reach 60 percent of the young women diagnosed with breast cancer during the first year after diagnosis and at least 30 percent of all women who have been diagnosed under the age of 40, regardless of their current age.

Young survivors of breast cancer face unique challenges:

- Approaching peak of earning potential
- Treatment impact on fertility
- Early onset of menopause
- Dating and relationships
- Body image and self esteem
- Diagnosis during childbearing years
- Parenting small children
- Limited access to targeted education and support

YSC has identified additional challenges such as being treated by healthcare teams less familiar with young women with breast cancer, insurance, reconstruction, genetics and hereditary breast cancer, and long-term survivorship issues.

YSC has developed numerous tools and resources aimed at improving the life, health, and care of young women diagnosed with breast cancer. YSC's newly designed website (www.youngsurvival.org) is the portal through which many of these resources can be accessed. YSC is using their website to build and inform a global virtual community of young women with breast cancer. This will enable women to have a network of peers and other web-accessible to better help, inform, and educate. YSC also provides educational videos, video file teleconferences, fact sheets, and brochures upon request. Activities, such as the adopt-a-hospital campaign, allow volunteers to ensure that hospitals in their areas have access to these materials for young women. YSC also has a treatment navigator and toolkit to help women organize their care to make sure they're getting effective treatment. YSC affiliates host local meetings that provide young women with access to the educational materials and breast cancer expertise needed to make good decisions.

In closing, Ms. Simha also recognized the life and work of Ms. Randi Rosenberg, one of YSC's founding members, the 3rd President of YSC, and the lead developer of their current research agenda. After being diagnosed at 32, she succumbed to cancer at the age of 44.

Ms. Maimah S. Karmo

Founder and CEO of the Tigerlily Foundation
Tigerlily Foundation

Maimah S. Karmo was diagnosed with breast cancer after finding a lump during self-examination at the age of 32. She visited several physicians before finally being diagnosed with breast cancer. The Tigerlily Foundation was borne out of her experiences with the medical system and passion to help young women facing breast cancer. She believes that there are several questions that need to be answered by the public health community, including:

- Why is there a lack of information about younger women and breast cancer and their need for services and support?
- What do young women need to know?
- Who needs to provide them with this information?
- How do you help women to be open to receiving information and then retain it?

- What do they need most?

The Tigerlily Foundation's mission is to educate, advocate for, empower, and provide hands-on support to young women before, during, and after breast cancer. Tigerlily assessed the needs of young women before, during, and after diagnosis. Before diagnosis, there is a lack of education, a common perception that women of this age are too young to have cancer, common misdiagnoses by physicians, and a lack of focus on this demographic and its cancer issues. During diagnosis and treatment, young women were more likely to have aggressive breast cancers due to aggression rates, challenges with coping, a need for hands-on support, and financial issues. After treatment, there is a need to educate patients about lifestyle adjustments, living with metastatic breast cancer, end-of-life issues, and a need to redefine life and self.

Tigerlily offers programs to address the identified challenges of each stage. In the before stage, Tigerlily offers a program called PETALS, a specialized education and awareness campaign that targets women between the ages of 15 and 40. During the treatment stage, they offer four programs: Chemobuddy, Funds for Families, At Home, and Project Gratitude. Chemobuddy pairs women currently going through treatment with survivors for peer support. Buddy Bag is a care-package program, which gives patients personal bags filled with items such as blankets, aromatherapy items, care planners, and other gifts. The Funds for Families program gives women monetary assistance to pay bills and manage other financial issues. At Home, recently renamed Meals At Home provides healthy meals to families whose loved ones are going through treatment. Lastly, Project Gratitude, unlike the other programs, is not a product-based program, but focuses on psychological effects by promoting gratitude journals to redirect thoughts past cancer. After treatment stage programs include: Fearless Females, a peer program to provide fellowship among survivors; Day of Beauty; and Stage 4, which provides coping tools.

Tigerlily creates "out-of-the-box" events to reach young women, including: mixers at night clubs, bars, and lounges; sporting events, entertainment, fashion, and philanthropic community events; cupcake fundraisers; and partnerships in athletic events with schools. The Foundation's goal is to educate women, empower them, and teach them how to advocate for themselves by speaking up, asking questions, and knowing their bodies.

Tigerlily's activities are also in line with the President's Cancer Panel's report, *Living Beyond Cancer: Finding a New Balance*. Young survivors are often caught between the worlds of pediatric and adult oncology. According to The Lance Armstrong Foundation, this population faces unique long-term effects that will need to be addressed over their lifetimes, such as reentry into schools or the workforce, insurance coverage issues, infertility as a result of treatment, neuro-cognitive effects, and secondary malignancies.

Ms. Rochelle L. Shoretz

Executive Director
Sharsheret

Sharsheret was founded 10 years ago by Rochelle L. Shoretz and a group of women facing breast cancer. Sharsheret supports young Jewish women and families facing breast cancer before, during, and after diagnosis. 1 in 40 Jewish women of Ashkenazi descents carries a

BRCA 1 or 2 genetic mutation, compared to 1 in 345 in the general population. BRCA mutation carriers may have as high as an 80 percent lifetime risk of developing breast cancer and a 44 percent risk of developing ovarian cancer.

Women call upon Sharsheret not only because of the strong genetic risk Jewish women face, but also about questions of spirituality and connection to Judaism. Women call to talk about parenting, a core and important issue for women in this community. These families tend to be large, so infertility can be stigmatizing in this culture. Additional concerns exist around modesty, another a cultural issue, and Jewish rituals. In the orthodox community women cover their hair; therefore concerns arise regarding wearing wigs after chemotherapy.

Sharsheret has launched several national programs in the past 10 years to address the needs of this community. They have responded to more than 23,000 inquires and continue to partner with local Jewish cancer organizations to create a community for young Jewish women and families facing breast and ovarian cancer nationwide. Sharsheret has hosted focus groups to identify core needs of the community and regularly conducts event-specific and online annual surveys.

All of Sharsheret's programs and resources were designed to be convenient, accessible and reflect the target audience in a culturally appropriate way. These programs address a myriad of issues, including, social support, family history/genetics, quality of life, and education and outreach.

The Link program provides culturally sensitive peer support networks. This program connects women newly diagnosed or at high risk of developing breast cancer with others who share similar diagnoses, cultural issues, and life experiences. The matches are based on age, religious affiliations, marital status, family, stage of diagnosis, and surgery treatment. There is sensitivity to confidentiality and core Jewish values. Matches are made with women who have very similar issues, but who live in different states, to protect confidentiality.

The Genetics for Life program addresses hereditary breast and ovarian cancer issues. It provides access to a genetic counselor hotline and a Genetics for Life seminar called *Understanding Our Past, Guarding our Future*. Women are encouraged to know their family history and get tested if a history of breast cancer exists. Sharsheret also disseminates a resource booklet called *Breast Cancer Genetics and the Jewish Woman*.

The Embrace Program supports women with metastatic breast cancer or advanced stage breast cancer. It provides one-on-one counseling sessions with clinical supervisors and bi-monthly culturally sensitive telephone-based support groups.

Family Focus gives support to family members and caregivers of young women facing breast cancer. It provides online and print information and resources. The Ask Sharsheret Hotline provides women with information about diagnosis, treatment, and survivorship.

Busy Box supports women facing breast cancer, who have young children. The box provides age and gender appropriate activities for children and parenting resources.

Best Face Forward addresses the cosmetic side effects of chemotherapy and radiation

treatment. Along with information and resources for young women, it also provides skin care and other beauty products.

Sharsheret on Campus is an educational program, which has hosted annual breast cancer awareness programs at more than 72 colleges and universities nationwide. This program is designed to educate thousands of young men and women about the risks of hereditary breast and ovarian cancer in Jewish families and the risk of breast cancer in young women.

Sharsheret uses social media, performs outreach to young women, and creates partnerships with health and cancer organizations to enhance their efforts as a grassroots organization. For more information, please visit www.sharsheret.org.

Ms. Erica Kuhn

Senior Writer in Medical and Scientific Affairs
Susan G. Komen for the Cure

Susan G. Komen for the Cure's vision is to save lives and end breast cancer forever by empowering people, ensuring quality care for all, and energizing science to find the cure. The organization empowers local communities, promotes innovative research on a national level, advocates for strong public policy across all levels of government, and is working to expand its efforts globally. , Susan G. Komen for the Cure is the world's largest source of nonprofit funding dedicated to ending breast cancer.

The rarity of breast cancer in young women makes it shocking and challenging. Issues facing young women with breast cancer are different from those facing their older counterparts, leading to feelings of isolation and under-representation.

Susan G. Komen conducted a needs assessment, a literature review, and interviews with young women to ascertain the informational needs of young women with breast cancer. The findings from this study were published in the monograph, BREAST HEALTH AND BREAST CANCER INFORMATIONAL NEEDS OF YOUNG WOMEN AND WOMEN OF COLOR 40 AND OLDER MONOGRAPH. Participants indicated a need for information appropriate to their groups and greater access to information. Participants interviewed also suggested a multimedia approach.

Susan G. Komen has developed targeted educational resources based on their findings and began promoting the "All women are at risk" message. The resources provide information on risks, screening, early detection, normal and abnormal lumps, among other issues.

The organization has also developed Komen on the Go, which is a mobile educational tool, where participants use computer kiosks to watch videos and participate in a graffiti wall to share memories. Participants visit malls, local events, colleges, and more to share information. Polling showed that this is an effective tool for educating women of all ages about breast cancer.

SGK has also formed the Young Women's National Advisory Council. This group focuses on breast health and breast cancer issues specific to young women, raises awareness, and promotes engagement in the breast cancer cause among advocates. .

Susan G. Komen leverages their efforts by forming collaborations and partnerships with C4YW, The ASCO Cancer Foundation, FORCE, and Fertile Hope. Komen is focused on bringing cures from the lab to the bedside with its Promise Grants--3-5-year grants that emphasize more quickly reaching specific outcomes for breast cancers with poor prognoses.

Ms. Melissa B. Watson

38-year-old breast cancer survivor
Iowa

Ms. Watson presented her personal story and experiences with breast cancer. She is a married mother of two sons. At the time of her diagnosis, Ms. Watson and her husband were both employed full-time with benefits. She shared a family medical history including the death of her maternal grandmother at the age of 60 due to breast cancer. Ms. Watson also shared personal information about her childhood that she felt made her strong enough to cope with her diagnosis. She also made reference to the close network of friends who supported her during her treatment and recovery.

Ms. Watson's symptoms included pain and fullness in the right breast with a brown discharge. The diagnosing physician, who had a past family experience with breast cancer, referred her to a breast surgeon the same day. Diagnostic testing included a mammogram and ultrasound, which were normal. Due to single duct discharge, she also received a ductogram and biopsy was performed. All of these activities took place between the timeframe of August 7, 2009 to September 4, 2009.

Ms. Watson's pathology report concluded that she had extensive intermediate high grade ductal carcinoma in-situ (DCIS). She was at stage 0 and the status was pre-invasive. There was also a diagnosis of comedo necrosis, no clear margins, and ER+/PR+. It was recommended that she have a mastectomy due to lack of margins and was referred for genetic testing. She also was scheduled to see a plastic surgeon for reconstructive surgery after the mastectomy. The final pathology report said that her cure was probable and recommended that she have radiation. Her medical oncologist decided not to use Tamoxifen or chemotherapy.

Due to unforeseen complications, she chose to terminate reconstruction. Because of the radiation, her skin would be unable to heal properly to support implants.

Ms. Watson also shared her emotional experiences related to diagnosis and treatment with the Committee. These included feelings of fear, loneliness, gratitude, and love. Loneliness was the biggest issue because there were not many women in her age group with breast cancer. She relied upon the medical community, her therapist, and her friends for support.

Ms. Watson discussed the importance of having a strong support system and the roles people played in helping her navigate treatment while maintaining a stable home life for her children. She took an active role in recruiting a support system for herself and her family, and to keep household logistics running smoothly, she wrote a plan, accepted help from others, and learned to let some things go.

Ms. Watson also raised the issues of employment for women facing this disease. While she

was fortunate to have sick and paid leave, most women do not.

Ms. Watson described the difficulty that she experienced in understanding the medical terminology. She tried to educate herself and overcome language barriers in terminology; however, time limitations prevented her from understanding much of the clinical information. Often times, nurses and other caregivers would explain information she obtained. Ms. Watson attempted to educate her physicians on better ways to communicate with patients.

The cost for her surgery was \$166,000, and she was fortunate to have health insurance that was comprehensive, but again, this is not the case for all women.

Once feeling somewhat back to her normal self, Ms. Watson was able to work on her weight, which had increased due to lack of physical activity during treatment and physical therapy. She is still working on acceptance of her cosmetic appearance. She reiterated how fortunate she was to have the financial and social support during treatment and stated that the absence of any these resources would have been devastating to her and family. She believes that Committee should work to ensure that all women receive the level of care she did.

Advisory Committee members engaged in discussions of the presentations and asked additional questions of each of the presenters in this session.

R. Nicholas: "I notice that there are some people missing at this table. Radiation experts have not been addressed and plastic surgery experts. A lot of young women have to navigate these conversations and we should find a way to help them with that."

M. Watson: "I noticed that as well. We need to know the effects of radiation."

F. Ashe-Goins: "Is there an attempt for smaller organizations to come together in a summit format to share lessons learned, and having larger organizations together to help small organizations continue to do their work with resources, advice etc?"

A. Partridge: "There is some collaboration. Lance Armstrong, Susan G. Komen and YSC have one, but there's no one advocacy group forum. Maybe we should think about that."

M. Karmo: "We launched a program to get people together in one room to discuss needs and discuss what's important. We will have the 3rd one in May and it's called Breast Healthy on the Hill."

M. Moore: "We have done it in an ad-hoc kind of way."

W. Susswein: "And private community foundations need to get together."

R. Shoretz: "We also have overlapping missions in some of what we do, and need to find better ways to work together since we're small groups."

M. Rice: "HRSA has a website to help people find centers. We need a website so individuals can find resources in their local area."

A. Partridge: "That's a good idea. We don't have that already, and we do have funding coming."

Public Comment - Open

The floor was then open to the public to make comments or ask questions.

Audience: "At YSC, you can put in zip code and find resources in your area. If something is not listed, you can make suggestions. We don't want to reinvent the wheel, so we offer this resource."

Audience: "For those who spoke, how did you know you had cancer and how did you get it diagnosed?"

R. Shoretz: "I found mine because I was changing into a bathing suit and noticed a change in my breast. I felt a lump upon examining it and went in to get it checked."

R. Nicholas: "That was the same for me, but I unfortunately was blown off by my physician because of my age. But because of my education on the issue I went for a second opinion."

M. Watson: "Mine was found on mammogram and I was lucky that it was picked up."

A. Partridge: "There's a misconception that if there's pain, it's not cancer, but that is not the case. When we look at women under 40, women present with symptoms they picked up versus a screening or a mammogram which is different for women over 40. So younger women usually self detect."

T. Fairley: "We had a written comment from Lieutenant Tim Healy (See attachment for full text). This was regarding Susan Lynn Healy, his wife known as Susie. Her cancer appeared when he was preparing his battalion for deployment. Upon biopsy, she was found positive for cancer. He remained stateside to care for his wife. The doctor asked her to acquire more of her family history, which was very disturbing. Of the nine females before Susie in her family, 7 had cancer and her aunt tested positive for BRCA 1 gene. Because of this, the doctor suggested a double mastectomy. Her family information was known by her father, but he failed to pass that information to Susie.

"After what was said to be successful chemotherapy treatment, she was

found to have a cancer mass near her liver and diagnosed with stage 4 cancers. She was put on a very aggressive cancer treatment plan. The Army tried to help Lieutenant Healy stationing him where Susie could acquire care. In her 2-year battle, she had more frequent trips to the hospital. The cancer spread to Susie's brain and her health continued to deteriorate. Susie passed away February 18, 2009, leaving behind two kids and Lieutenant Healy.”

Key Issues: Actionable Items and Next Steps

The Committee together created the following list of topic areas for which they needed additional information. These lists also represent areas of focus for future committee meetings and conference calls.

People and Informational Needs

- Communication tools (i.e., telecommunication specialists, remote rural care) with cultural competency experts, health experts
- Data issues, minority populations, and subgroups (i.e., Native Americans, Hispanic, Asian Pacific Islanders)
- Nurse practitioners., physician assistants, nurse navigators and other care providers
- Nursing/ medical association training
- Marketing and communication
- Services Provision and assessment of patients
- Organizations with captive audiences
- Men and younger women as supporters
- Psychological oncology
- Information on Jewish females and BRCA

Awareness and Prevention

- Chemo prevention?
- Assessment of other successful awareness campaigns (e.g., STD, HIV, Obesity, Text for Baby, etc), public health campaigns, and evaluation data of their effect on the target audience
- Impact of obesity on risk for disease for young women
- Clearinghouse for resources
- Other chronic disease groups disseminating messages around moderate risk factors
- Potential end products communication risk (e.g., bilateral mastectomy → EBI prevention)
- EB campaigns...outcomes and evaluation
- Screening options—trials in screening for high risk

Survivorship

- Health care provider education
- Differences between survivorship support and mental health
- How do we together impact the health care system?

- Patient navigation for adults and young adolescents

Communication

- Web portal for young breast cancer survivors (resource links, etc.)
- Expanded CME campaign for providers
- Engage pediatrics communication along with other providers

Regarding next steps, Dr. Fairley reported that the Committee will be working together for a few years and, will therefore engage in more conversations. CDC will synthesize the outcomes of this meeting and post transcribed notes and the presentations on the Web as soon as possible. CDC will notify the presenters before presentations are posted. CDC will review for appropriateness.

Wrap-Up/Announcement/Adjourn

Dr. Fairley adjourned the meeting.

Note: Meeting adjourned early due to inclement weather, however all agenda items were discussed completely.