Healthy Arizona
WORKSITES
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HEALTHY ARIZONA WORKSITES PROGRAM (HAWP) PRESENTS:

BREAST CANCER - ASK THE EXPERT- ANSWERS TO YOUR QUESTIONS

Presented by:

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The University of Arizona Cancer Center at Dignity Health
St. Joseph's Hospital and Medical Center

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WEBINAR HOUSEKEEPING

WELCOME

All lines have been muted.

Please type any questions into the chat or Questions panel and we will do our best to answer them all at the end.

All handouts and a copy of the presentation slides are available in the Handouts panel.

Please complete the survey that will be emailed out after the presentation

A recording will be added to the library of HAWP webinars on our website within 48 hours.

Special thanks to our supporting partner Dignity Health for their generous support in making this webinar possible.

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A NOTE FOR EMPLOYERS

HOW TO HELP YOUR COWORKERS WITH BREAST CANCER

- *Cultivate a compassionate worksite.*
- *Staff may need additional breaks to recuperate from fatigue.*
- *If staff or their family are undergoing treatment, they may need adjustments to their schedule to accommodate (i.e. starting work later or finishing their day earlier).*
- *If undergoing surgery, staff or their family will need time off.*
- *Check with your HR department to give options for psychological support.*
- *Many people wish to remain private regarding their illness and some are very open, so there could be a great deal of variability in how you support each employee.*
- *Human kindness, compassion, and understanding supersede the needs of the business.*

Breast Cancer -Ask the Expert – Answers to Your Questions

Albert Guy Wendt, M.D.
The University of Arizona Cancer Center at Dignity Health St. Joseph's Hospital and Medical Center
October 17, 2019

THE UNIVERSITY OF ARIZONA Cancer Center

Dignity Health.
St. Joseph's Hospital and Medical Center

Outline

- General Information
  - Breast Cancer Incidence
  - Mortality
- How is Breast Cancer Found?
- Risk Factors
- Treatment
- Future and What You Can Do

BREAST CANCER

General Information

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Breast Cancer Incidence -- Female

- 2019 estimated 268,600 cases of breast cancer
- 2018 63,960 cases of DCIS (confined to milk duct but not invasive)
- Breast cancer deaths 40,920 in 2018 (15.3% of new cases) and 42,260 estimated in 2019
- Increases as population increases and ages
  - 40 million women born between 1946 and 1964 will be in the highest risk age group by 2030 (average risk 2-4% over 10 years)
  - Total number of cases of invasive and in situ cancers expected to have increased from 283,000 in 2011 to 441,000 in 2030

Source: American Cancer Society

Breast Cancer Incidence -- Male

- 2700 male breast cancers in 2018, all stages
- Higher percentage of men die of their breast cancer, present a little older and more advanced stages

Cancer Incidence And Death - **How Are We Doing In Arizona?**

CA CANCER J CLIN 2015;65:5–29

TABLE 3. Estimated Deaths for Selected Cancers by State, 2015*

STATE	ALL SITES	BRAIN & OTHER NERVOUS SYSTEM	FEMALE BREAST	COLON & RECTUM	LEUKEMIA	LIVER & INTRAHEPATIC BILE DUCT	LUNG & BRONCHUS	NON-HODGKIN LYMPHOMA	OVARY	PANCREAS	PROSTATE
Alabama	10,560	290	680	930	420	360	3,280	330	270	660	580
Alaska	1,040	†	70	90	†	50	290	†	†	70	50
Arizona	11,540	330	770	990	510	530	2,800	410	310	830	600
Arkansas	6,760	160	410	620	260	270	2,180	210	140	410	290
California	58,180	1,690	4,320	5,180	2,550	3,250	12,370	2,070	1,530	4,240	3,180
Colorado	7,590	260	540	650	330	350	1,710	250	240	530	430
Connecticut	6,840	190	460	440	300	270	1,730	220	170	540	360
Delaware	2,010	50	120	150	80	90	600	60	†	140	100

TABLE 2. Estimated New Cases for Selected Cancers by State, 2015*

STATE	ALL CASES	FEMALE BREAST	UTERINE CERVIX	COLON & RECTUM	UTERINE CORPUS	LEUKEMIA	LUNG & BRONCHUS	MELANOMA OF THE SKIN	NON-HODGKIN LYMPHOMA	PROSTATE	URINARY BLADDER
Alabama	26,150	3,680	230	2,150	660	730	4,150	1,380	1,020	3,590	1,000
Alaska	3,700	470	†	290	100	110	420	100	140	490	180
Arizona	32,440	4,750	200	2,440	940	950	3,740	1,400	1,300	4,090	1,580
Arkansas	15,830	2,090	150	1,420	420	480	2,620	360	670	2,050	630
California	172,090	25,270	1,490	14,510	5,800	5,970	18,430	8,560	7,870	21,060	7,150
Colorado	24,540	3,640	170	1,800	740	870	2,560	1,400	1,090	3,600	1,080
Connecticut	21,970	3,190	130	1,580	810	660	2,870	780	920	3,170	1,140

Breast Cancer Incidence - Future

- 40 million women born between 1946 and 1964 will be in the highest risk age group by 2030 (average risk 2-4% over 10 years)
- Total number of invasive and in situ expected to increase from 283,000 in 2011 to 441,000 in 2030
- Estimated 4,400 men with breast cancer in 2030

Breast Cancer – How Are We Doing?

- 40 years ago about 1/3 of women diagnosed with breast cancer died of it– now it is about half that or close to 1/6.
- Is that good enough—absolutely not!

What have we done to improve the outcome?

- Earlier detection
- Clearly there is better treatment

What are the things we can do to continue to make progress?

BREAST CANCER

How is it detected?

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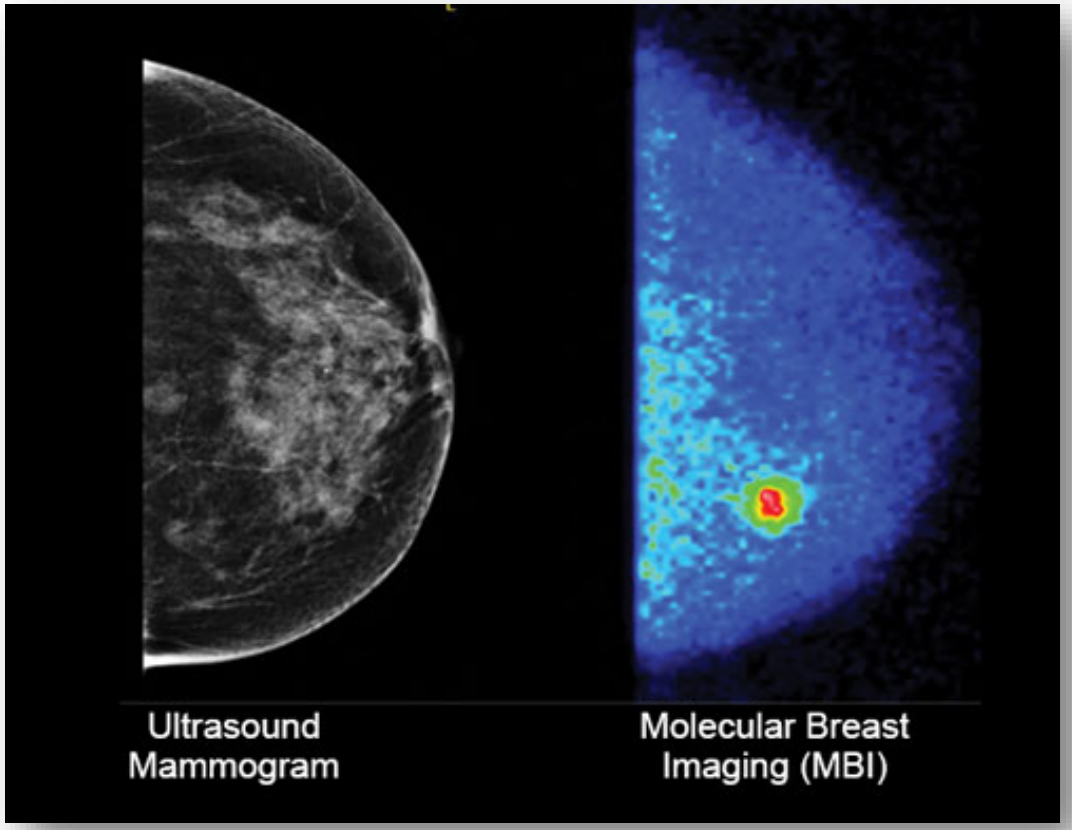
Breast Cancer Discovery

- Patient presents with symptoms
  - Most common symptom is a lump is felt
  - Could be nipple discharge or retraction
  - Other change in the breast: redness, edema, warm to touch, asymmetry in appearance
- Discovered by physician on exam
- Screen detected
  - Majority of breast cancers are found by screening (mammogram, MRI or ultrasound)

Screening

WHY WOULD SCREENING MAKE A DIFFERENCE?

DOES EARLY DETECTION MAKE A DIFFERENCE?



TUMOR SIZE
5-year Relative Breast Cancer Survival

TUMOR SIZE	Five-year relative breast cancer survival
Smaller than 1 cm	93%
1-1.9 cm	91%
2-2.9 cm	85%
3-3.9 cm	71%
4-4.9 cm	68%
Larger than 5 cm	63%

SEER, 21,465 women localized breast cancer between 1995 and 1999

Recent data in tumors 1 to 10 mm, TNBC, 98% survival with local therapy only

Is Earlier Detection Important?

- Finding a cancer in earlier stages improves the chance of cure
- May lessen the amount of treatment required (less surgery, less radiation and perhaps less systemic therapy)

Screening Controversy

- Multiple groups have offered screening guidelines and they do not all agree—
- It depends on the focus
- **USPSTF recommends for <u>average risk women</u> to start mammograms at age 50, continue every other year until 74 and stop**– their focus is on preventing "unnecessary" biopsies, psychologic stress of mammograms and biopsies and "over diagnosis" (over diagnosis is finding a cancer that won't become clinically meaningful in the patient's lifetime)

Screening Controversy --Continued

- My focus would be to save lives and morbidity
- “Under diagnosis” I would define as death from breast cancer due to failure to diagnose in a timely manner due to lack of screening
- I would argue that 1 under diagnosis is far more important than the stress of screening, biopsy or even over diagnosis

Screening—so what do the trials show?

Screening Trials

- CANADIAN NATIONAL BREAST SCREENING STUDY - 88,835 women, 40-59, 6 yrs. of screening, 25 yr. fu, no difference in breast cancer or overall mortality, with some “over diagnosis”

- OXFORD - 40 years no benefit

- SWEDISH TWO-COUNTRY - 30 year follow up, 7 years of screening, 40-49(q 24 mo), 50-74 (q 33 mo); 77,080 screen, 55,985 in control. 126 deaths prevented

SCREENING RCTs

Study	Number	Follow Up Yrs.	Screened Age	Relative Risk Mortality RR (95%CI)
UK Lancet 2006	161,196	11	39-48	0.83 (0.66-1.04)
Canada NBCSS	50,643	25	40-49	1.09 (0.80-1.49)
HIP (USPSTF)	27,626	18	40-49	0.78 (0.56-1.08)
Gothenburg	26,034	14	39-49	0.70 (0.46-1.06)
Malmo	25,966	13	43-49	0.73 (0.51-1.04)
Stockholm	22,371	14	40-49	1.47 (0.77-2.78)
Ostergotland	20,805	17	40-49	1.05 (0.64-1.73)
Kopparberg	14,651	13	40-49	0.72 (0.38-1.37)
Edinburgh	11,371	14	40-49	0.78 (0.46-1.32)

SCREENING RCTs

- Lancet Vol 16, No. 9, pp1123-1132, September, 2015
- 160,921 patients age 38-40, 10/14/1990 to 9/25/1997
- 106,953 control patients (no mammograms)
- 53,883 screened patients
  - Annual screening beginning at age 38-40 for 10 years, then continued screening
- Mortality hazard ratio, 0.88 (0.74-1.04); that is 12% reduction in mortality from breast cancer in screened women.
- Mortality after the first 10 years of screening was not benefited by subsequent screening.

Breast Cancer Screening
RCT Meta-analyses

STUDY	# STUDIES	FOLLOW UP	AGE SCREENED	RR MORTALIDY (C0NFIDENCE INTERVAL)
KERLIKOWSKE ET AL	13	7-12	40-49	0.92 (0.75-1.13)
U.S. PREVENTATIVE SERVICE TASK FORCE	8		39-49	0.85 (0.75-0.96)
COCHRANE COLLABORATION	8	13	<50	0.84 (0.73-0.96)

Mammograms– so what is a woman to do?

- First, need to decide if you are of average risk and then decide what worries you more?

- The process of imaging and potential for finding something **or** possibly finding a cancer late that could have been found earlier with higher cure rate and with less treatment

- If you are not average risk, that is higher than average, the risk of not screening goes up and the benefit of screening is higher

So Let’s Assess Risk Factors

BREAST CANCER

Risk Factors

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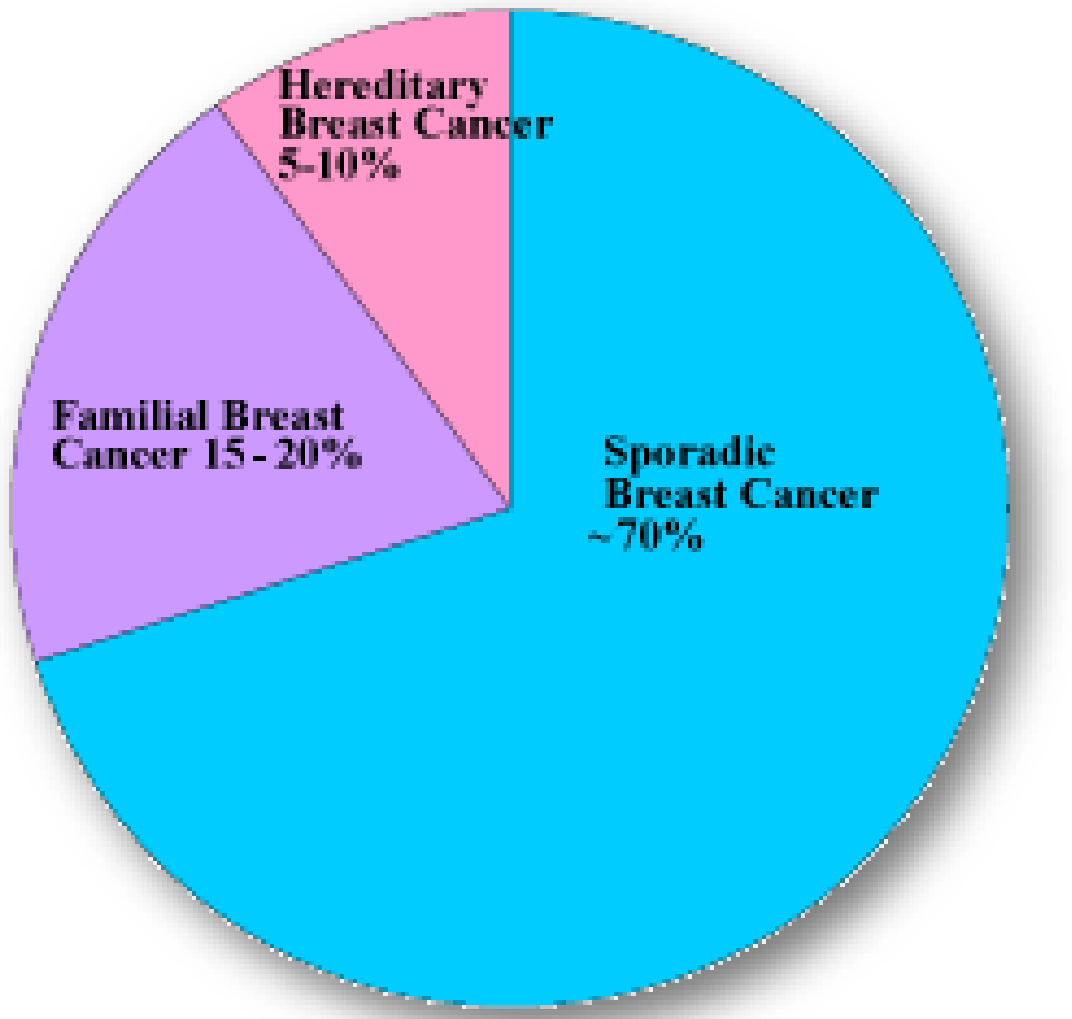
Causes of Breast Cancer



Risk Factors -- FEMALE
Genetic

- BRCA1/2 REPRESENT ABOUT 7.5% OF IDENTIFIED MUTATIONS
- EXPANDING NUMBER SINCE SUPREME COURT DECISION IN JUNE, 2013
- MORE TESTING COMPANIES AND NUMBER OF GENES HAS INCREASED OVER TIME
- NOW ABOUT 11 GENES IDENTIFIED THAT CODE FOR INCREASED RISK OF BREAST AND OVARIAN CANCER
- MANY TIMES WOMEN WILL BE TESTED FOR 16 TO 35 GENE PANELS

RISK Factors – MALE
Genetic

- 18% OF MEN WITH BREAST CANCER HAVE A GENETIC MUTATION
- BRCA2 BUT NOT BRCA1 VERY OFTEN
- PALB2 AND OTHERS
- MEN WITH BRCA2 MUTATION HAVE A 6% LIFETIME RISK OF BREAST CANCER
- ALL MEN WITH BREAST CANCER SHOULD HAVE GENETIC TESTING—IF THERE IS A MUTATION PRESENT EACH OF THEIR CHILDREN HAVE A 50% CHANCE OF INHERITING THAT MUTATION

GENETIC PREDISPOSITION TO MALE BREAST CANCER

What is previously known?

512 male patients with breast cancer tested for 16 breast cancer genes

- **18.1%** of those without prior *BRCA1/2* testing had pathogenic or likely pathogenic variant
  - *BRCA1/2* 11.0%
  - Non-*BRCA1/2* 5.9%
  - Multiple genes 1.1%

Pritzlaff et al BCRT 2017

Genetic Testing– Why Is It Important

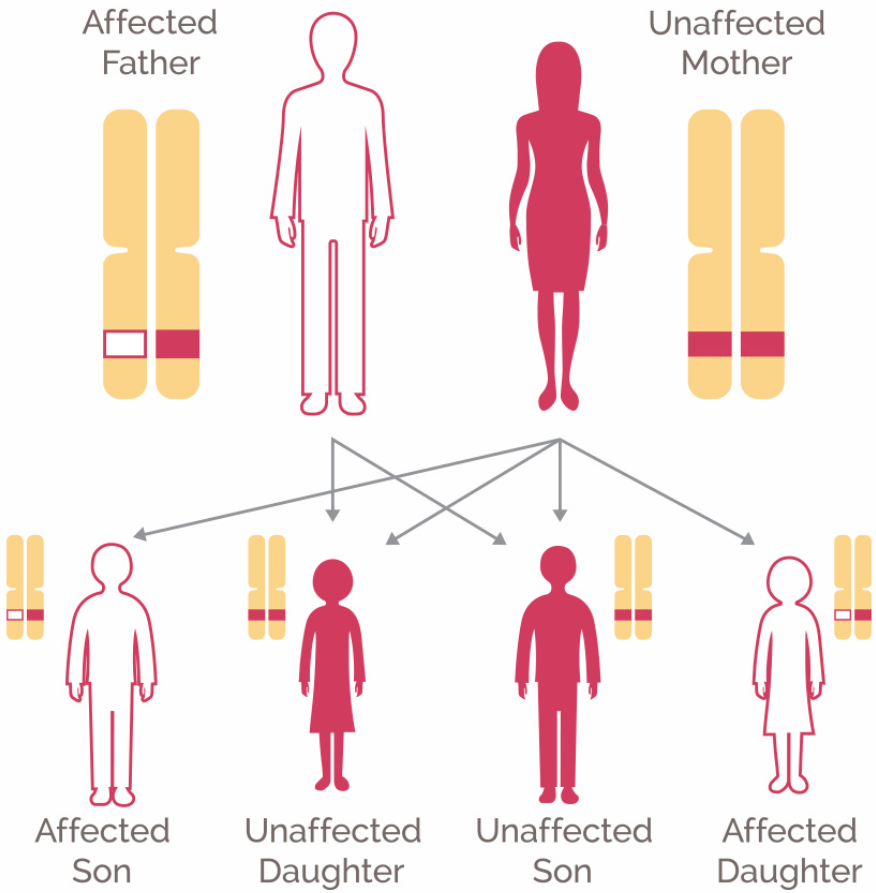
- It could explain why a person has cancer
- It could make a person aware of other cancers for which they are at high risk
- It could alter treatment choices in early treatment as well as in later treatment
- It could be informative to other family members so that they can be appropriately screened

- **Genetic assessment is a dynamic process as family and personal history changes and as technology changes—may need to be reassessed in the future**

Breast Cancer Risk Factors—Family History

- Having a family history of breast cancer increases the risk of breast cancer even if we have not identified a genetic predisposition.
  - This could be due to a variety of environmental factors, cultural factors and even unidentified genes

Genetic Testing for Breast Cancer



Breast Cancer Risk Factors -- FEMALE
Estrogenic

- Early onset of menses at < 12 years of age
- Late parity, that is first full term live birth after age 30 or not at all
- LATE MENOPAUSE IN MID TO LATE 50s
- Hormone replacement therapy (increased risk of stroke, heart disease, dementia and 24% increased risk of breast cancer (women's health initiative, 2002)
- Prior biopsy showing "atypia"
- Dense breast tissue on mammogram is an independent risk for breast cancer (AZ is one of 38 states that require notification of dense breast tissue on letter)

MALE ---Breast Cancer Risk Factors

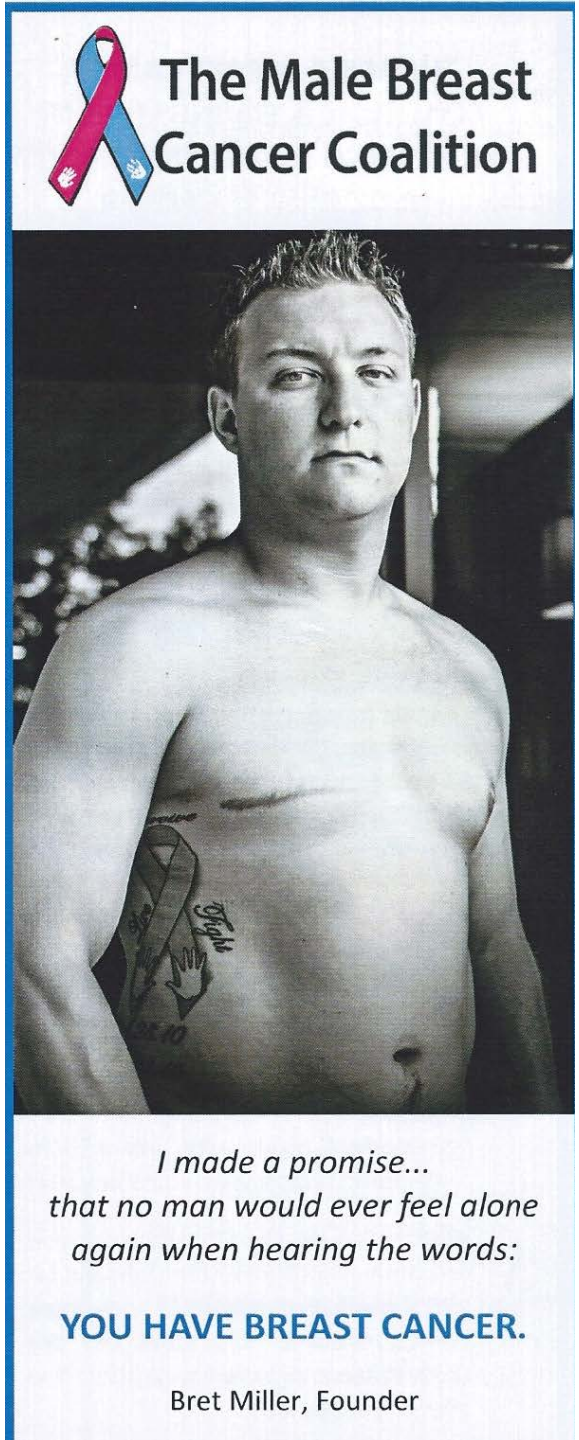
- At higher risk if never married
- Prior breast pathology
- Gynecomastia
- History of testicular pathology
- Family history of breast cancer (30% have positive family history, BRCA2 positive men have 6% lifetime risk of breast cancer {100 times higher than men with out mutation})
- Cirrhosis
- Klinefelter Syndrome (XXY)-- >1 in 500 and <1 in 1000 {delayed puberty, hypogonadism, gynecomastia, sterility, decreased libido – normal life expectancy}

MALE ---Breast Cancer Risk Factors (Continued)

- High estrogen levels such as in transsexuals (male to female)
- Numbers too small to reliably assess for the usual risk factors in women such as obesity, sedentary life style, alcohol consumption, dietary fat consumption
- Exogenous hormone therapy for prostate cancer HAS NOT BEEN ASSOCIATED WITH BREAST CANCER RISK
- No association with reproductive history, education or exposure to drugs (with legalization of marijuana we will have to wait and see)

MALE ---Breast Cancer Risk Factors (Continued)

- Surprising number of male first responders on 9/11/2001 in New York have had breast cancer

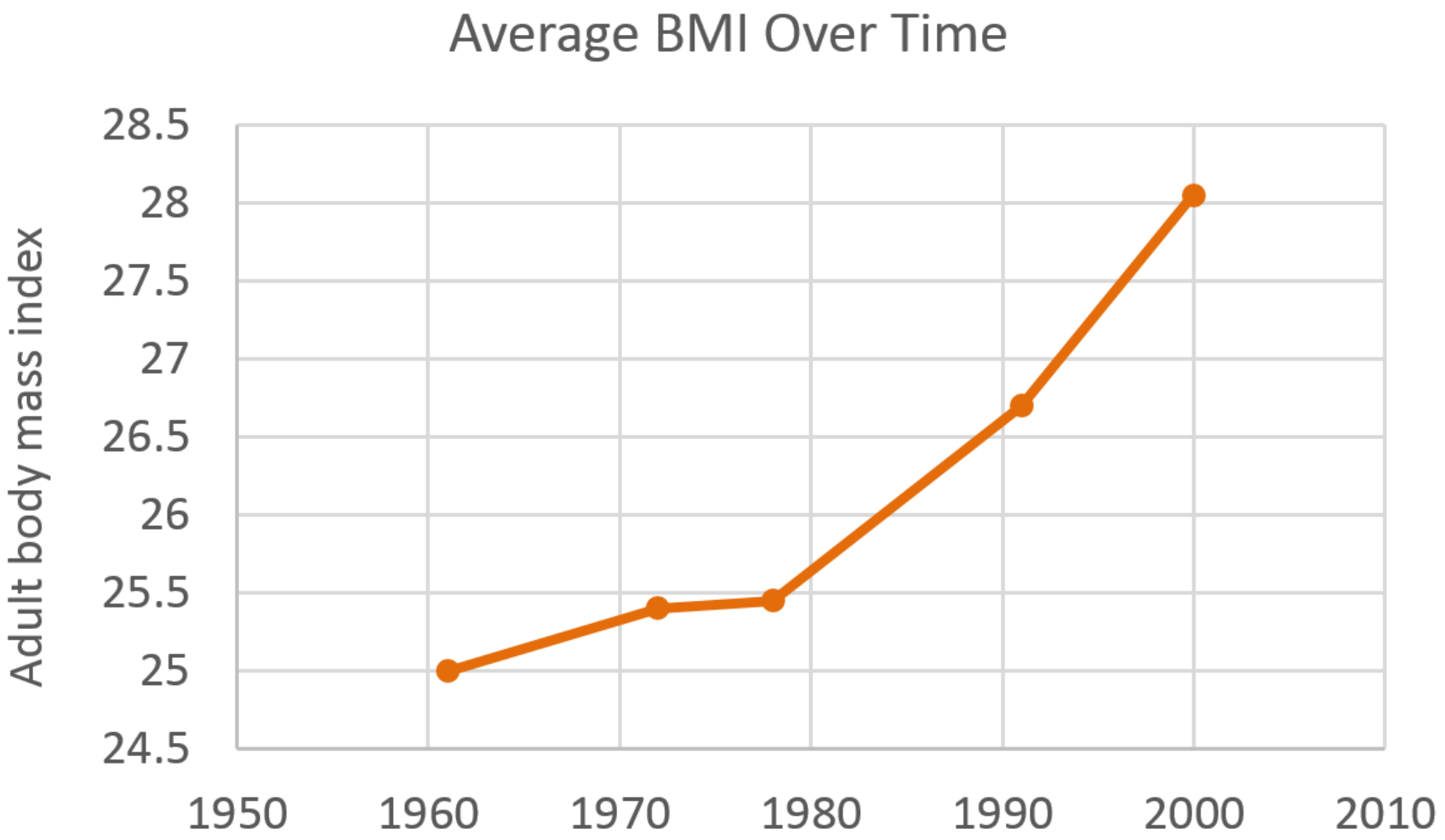


3RD WEEK IN OCTOBER IS MALE BREAST CANCER WEEK

Breast Cancer Risk Factors
Lifestyle--Opportunities

- Sedentary lifestyle (exercise 3 hours or more per week protective against breast cancer)
- Diet rich in fats (Japanese women 3% calories from fat)
- Alcohol consumption (8-12% increased risk for every drink per day average)
- Elevated body mass index (> 25)
- Tobacco (less for breast cancer than for other cancers)

US Trend In BMI



Breast Cancer Risk Factors
External

- Therapeutic radiation
  - Mantle radiation for Hodgkin's disease
  - Thymic radiation of infant

- Environmental radiation exposure
  - Us “downwinders” / uranium workers
  - Chernobyl
  - Japan Tsunami
  - Japan WWII (Nagasaki Hiroshima)
  - Diagnostic radiation ????
  - Therapeutic (Hodgkin's disease =<30, pediatric)
  - Airline workers flying at high altitudes

Breast Cancer Risk Factors–Other

- HAVING HAD BREAST CANCER THERE IS AN INCREASED RISK OF A SECOND OR THIRD BREAST CANCER—
  - With a first degree relative with breast cancer about 8% risk per 10 year block of time
  - Without a first degree relative with breast cancer about 4% risk per 10 year block of time
  - Lobular breast cancer – higher risk for second breast cancer

Breast Cancer Risk Factors – 2 Most Common Risk Factors

- FEMALE GENDER
  - Men get breast cancer about 1% as often

- ADVANCING AGE
  - Half are 60 or older
  - Two thirds are 50 or older
  - Three quarter are 40 or older
  - Half of men with breast cancer are 68 (64?) or older at diagnosis

BREAST CANCER

Treatment

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Breast Cancer Treatment—Early Breast Cancer Curative Intent

- Surgery
  - Lumpectomy vs mastectomy
- Radiation
  - Whole breast (hypo fractionation—i.e. less total treatments)
  - Partial breast (variety of types, balloon catheters, multiple catheters, external cyber knife)
- Medications
  - Endocrine (hormone blockers) {with or with out drugs that enhance the effectiveness}
  - Chemotherapy
  - Her 2 NEU targeted treatments
  - Immunotherapy

Breast Cancer Treatment—Surgery
Purpose of Surgery is Local Control

- Mastectomy was the standard and is still used for many breast cancers
- When feasible, lumpectomy followed by radiation is the standard; at least as good as mastectomy
- New approaches may eventually minimize surgery as we have more effective systemic therapies

Breast Cancer Treatment-Radiation
Purpose is to Help with Local Control

- Radiation to the breast is not a substitute for surgery; it is an adjunct to surgery. This might change - trials avoiding surgery
- Whole breast radiation with daily fractions (m-f) from 18 treatments to 6 weeks or so
- Partial breast radiation, usually 5 treatment days {variety of devices to insert in to lumpectomy cavity and some external beam non catheter type approaches}

Breast Cancer Treatment--Medications

- Endocrine or hormone blocking drugs are appropriate consideration in majority of breast cancers (hormone receptor positive breast cancer)
- Chemotherapy is a consideration in more aggressive and more advanced breast cancers
- Her 2 NEU targeted treatment (appropriate even in small tumors, in combination with chemotherapy and in some patients hormone blockers as well)

Breast Cancer Treatment--Sequence

- Surgery followed by radiation followed by endocrine or hormone blocking drugs (adjuvant) for early favorable breast cancers
- Initial chemotherapy (neoadjuvant) followed by surgery followed by radiation and when appropriate endocrine therapy in cancers that are more aggressive and more advanced at detection {improves chance at preserving breast, helps define prognosis and may lead to change in treatments)

Breast Cancer—Metastatic Treatment is Palliative

- Medications
  - Endocrine therapy first choice when estrogen receptor positive
  - Since 2015 usually paired with cdk 4/6 partner
  - Several lines of hormone directed treatment
- Radiation
  - Directed at areas of concern to relieve pain, prevent bone fracture or spinal cord compression, control bleeding
  - Occasionally will treat sites of oligo metastatic disease to render disease free
- Surgery
  - Treat complications of the cancer, such as bone fracture or prevent bone fracture, bowel obstruction, or local control of breast
  - Occasionally will use to treat oligo metastatic disease to render disease free

Breast Cancer– How Are We Doing?

- 40 years ago about 1/3 of women diagnosed with breast cancer died of it– now it is about half that or close to 1/6.
- Is that good enough—absolutely not!

What have we done to improve the outcome?

- Earlier detection
- Clearly there is better treatment

BREAST CANCER

How has treatment changed?

New Drugs For Adjuvant And Advanced Disease

1980s
None
Already Using
Doxorubicin
Cyclophosphamide
Mitomycin C
Methotrexate
Fluororacil
Vinblastine
Vincristine
Tamoxifen (1978)
Estradiol
Megestrol
Androgens
Others with no bearing on breast cancer

1990s
Taxol
Taxotere
Carboplatin (CIS Platin now being used)
Xeloda
Anastrozole
Herceptin*
Liposomal Doxorubicin
Epirubicin

21st Century
Letrozole
Exemestane
Fulvestrant
Everolimus
Abraxane
Ixabepalone
Eribulin
Lapatinib*
Tdm-1*
Pertuzumab*
Palbociclib - 2 more dugs in that class
2 Parp Inhibitors - Increasing numbers of her 2 new targeted treatments
Immunotherapy in selected patients with breast cancer

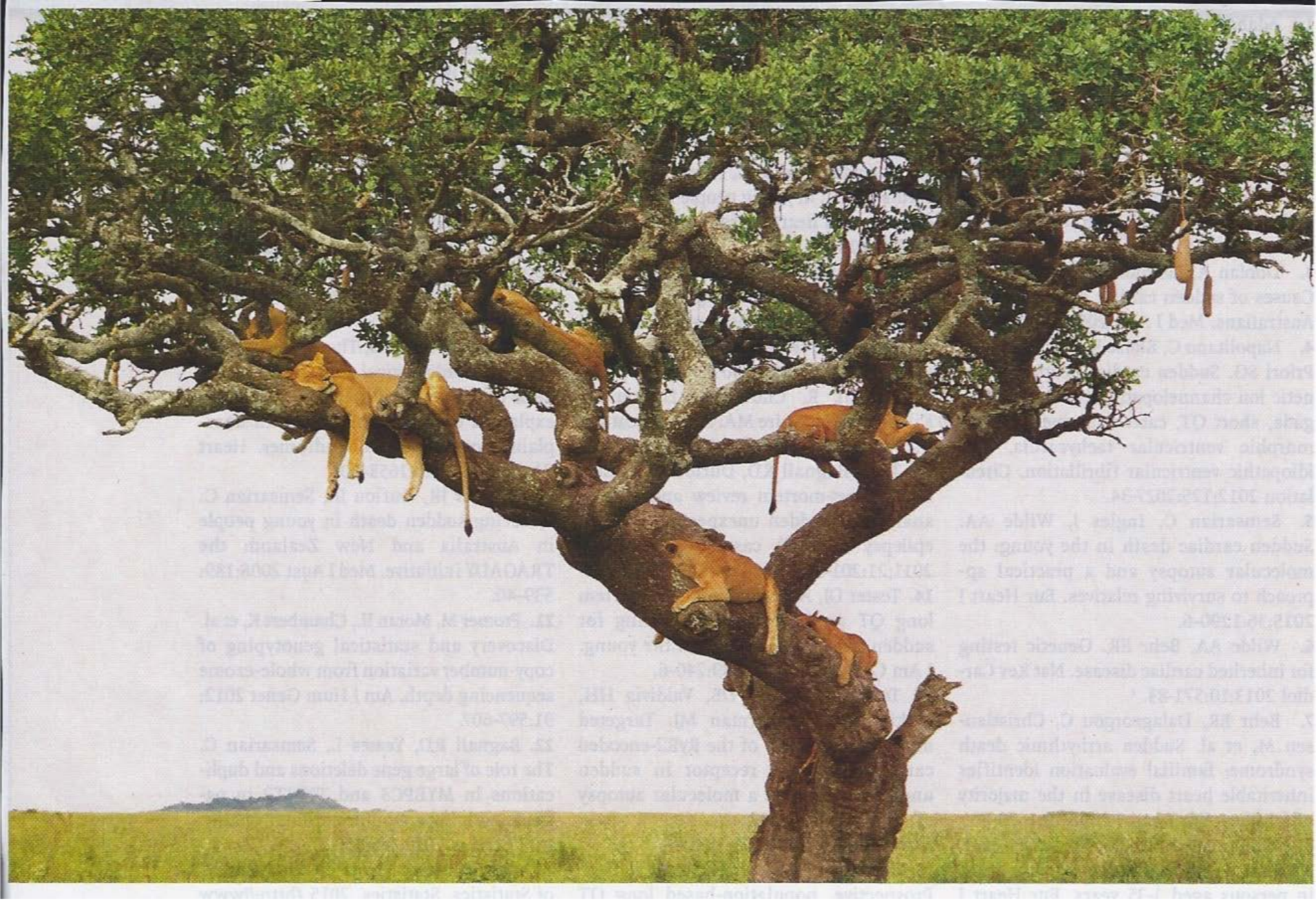

WHAT ABOUT THE FUTURE? JAZZY AND BRAEDEN WOULD LIKE TO KNOW….

Future Directions

- Prevention—drugs but also **lifestyle**
- Better screening (targeting the right population)
- More effective adjuvant therapy
- More effective treatment of metastatic disease
- Cure?

Progress

- All of the progress that we have made over the past 6 decades is because of research and those brave patients who have participated in trials and a dedicated profession (not just doctors, but nurses, medical assistants, pharmacologists, research biologists, genetic counsellors, social workers, patient navigators, statisticians, tumor registrars, administrators, fund raisers, support staff and volunteers)
- Philanthropy



NEJM JUNE 23, 2016, vol. 374 NO. 25; Arthur Grove, M.D.

Thank You

For more information or to request a speaker for any cancer-related topic, **please call: 602.699.3366**

Questions for the presenter?
Email: Albert.Wendt@dignityhealth.org

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Q&A

PLEASE ENTER YOUR QUESTIONS IN THE CHAT.

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