

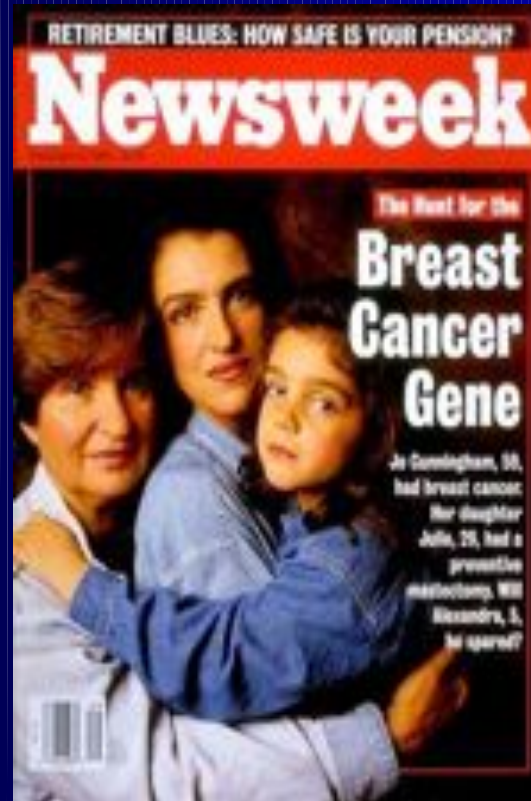
# Validation of the Pedigree Assessment Tool (PAT) in Families with BRCA1 and BRCA2 Mutations

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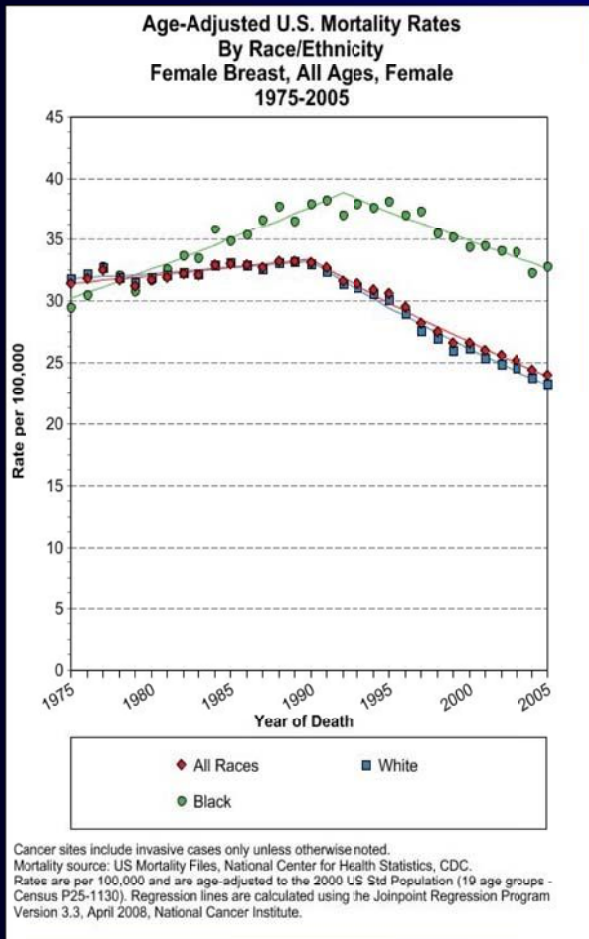
■ Ann Surg Oncology Sept 18<sup>th</sup>, 2009, epub

# Public



# Awareness

# Impacting further on mortality...



# New Standards of Care for Women at Increased Breast Cancer Risk

- **Chemoprevention: SERM's**  
*5 year risk >1.67%*  
*USPSTF (2002)*  
Annals of Internal Medicine, July 2002
- **Genetic counseling/predictive testing BRCA genes**  
*USPSTF (2005)*  
Annals of Internal Medicine, September 2005
- **Intensified Surveillance (screening breast MRI)**  
*BRCA mutation or lifetime risk >20-25%*  
*American Cancer Society (2007)*  
CA Cancer Journal for Clinicians, March/April 2007

# Risk Analysis Using Gail Model



Age: 39

Age at menarche: 12

Previous breast biopsies: 2

Atypical hyperplasia: No

Age at birth of 1st child: none

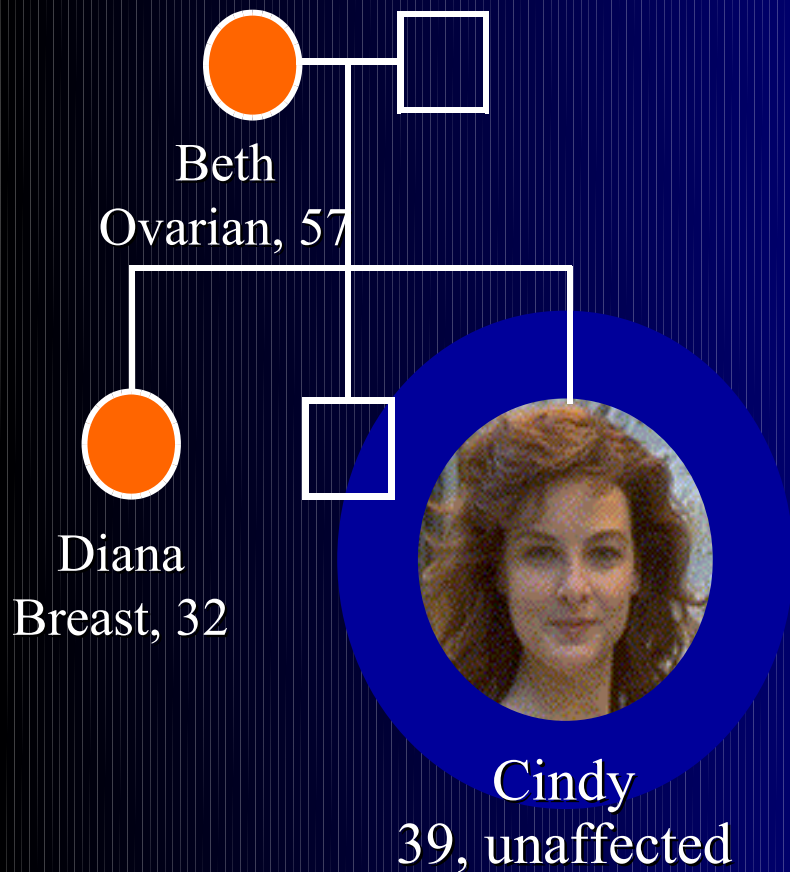
Sister with breast cancer: 1

Gail Model

5 year risk: 2.6%

Lifetime risk: 29.3%

# Estimating Breast Cancer Risk



Age: 39  
 Age at menarche: 12  
 Previous breast biopsies: 0  
 Atypical hyperplasia: No  
 Age at birth of 1st child: none  
 Mother/sisters with breast cancer: 1

Gail  
model

BRCA1  
carrier

5 yr: 1%  
 Life: 18.9%

80%

# Pedigree Assessment Tool (PAT)

- Screening tool for risk assessment
- Identify families at increased risk for hereditary breast cancer (HBC)
- Weighted point scoring system
  - ▣ Breast and ovarian cases
  - ▣ 3 generations
  - ▣ Both lineages
- Score of **≥8** prompts genetic referral

Patient's Name First :  Middle Initial :  Last :  (Optional)

Patient's Date Of Birth \* : 01 / 01 / 1970 Age : 39

Patient's Sex \* : Female Patient's Ethnic Background \* : Caucasian Ashkenazi (Eastern European) Jewish Ancestry \* : Unknown

### Non-familial Risk Factors

Patient's age at First Menstrual Period \* : Unknown

Patient's age at Birth of First Child \* : Unknown

No. of Breast Biopsies Patient has had \* : None

Atypical Hyperplasia \* : No

Lobular Carcinoma in situ \* : No

### Family Cancer History

Sex *	Relation *	Maternal/ Paternal *	Breast Cancer History			Ovarian Cancer √ *
			Breast Cancer √ *	Number of breasts involved with cancer	Age at Diagnosis	
Female	Sister	Both	<input checked="" type="checkbox"/>	One	Under 50	<input type="checkbox"/>
Female	Mother	Maternal	<input type="checkbox"/>			<input checked="" type="checkbox"/>

### Risk Results

#### Risk of Developing Invasive Breast Cancer

Gail Model

	<u>Your Risk</u>	<u>Woman with Avg Risk Factors</u>
Over Next 5 Years:	2.2 %	0.5 %
Over Your Lifetime:	37 %	12.4 %

#### Risk of Hereditary Breast Cancer Syndrome

Saint Anthony Pedigree Assessment Tool (PAT)

**High**

Maternal Score = 9, Paternal Score = 4

The Gail model predicts that risk for developing invasive breast cancer in this individual is increased compared to the average risk in the U.S. general population, and family cancer history indicates high risk for a hereditary breast cancer syndrome. Information on genetic susceptibility to breast cancer can be found at [The National Cancer Institute](#).

Consider further evaluation by a healthcare professional(s) with experience in genetic counseling for cancer susceptibility and cancer risk counseling for formal risk assessment and discussion of options for cancer risk-reduction and early detection. Information on breast cancer prevention can be found at [The National Cancer Institute](#).

See "[About the Risk Screening Tool](#)" on the home page for information regarding limitations of both the Gail model and the PAT. For additional information about the Gail model go to "[About the Gail Model](#)."

# Pedigree Assessment Tool

- Cindy 39 yo  
Caucasian female  
unaffected
- Family history:
  - Mother with ovarian cancer
  - Sister age 32 with breast cancer

Diagnosis	Points Assigned
Breast Cancer ≥ 50 yo	3
Breast Cancer < 50 yo	4
Ovarian cancer any age	5
Male breast cancer any age	8
Bilateral breast cancer	x2 points to 1 <sup>st</sup> cancer
Ashkenazi Jewish heritage	+4 points to final score

Maternal	Paternal
4	4
5	0
<hr/>	<hr/>
9	4

# Model Selection: Differences

- Myriad II
  - ▣ Assesses only 2 generations
  - ▣ Evaluates only a single lineage
- Penn II
  - ▣ Requires additional family history
    - Pancreatic & prostate cancers
    - Mother and daughter breast cancers
  - ▣ Not for families with ovarian cancer only

# Hypothesis:

- The PAT is:
  - ▣ Better at identifying families with deleterious mutations
  - ▣ Logistically simple to perform

# Study question:

How does the PAT compared to two BRCA mutation probability models (**Myriad II & Penn II**) in identifying families with BRCA mutations?

All 3 models:

- ▣ Available online access
- ▣ Calculations based on affected members only

# Methods

- **Retrospective chart review**

- ▣ 520 families
- ▣ 2001 to 2008



- **Two institutions**

- ▣ Emory University Department of Genetics  
Atlanta, GA
- ▣ OSF Saint Anthony Center for Cancer Care  
Rockford, IL

# Methods

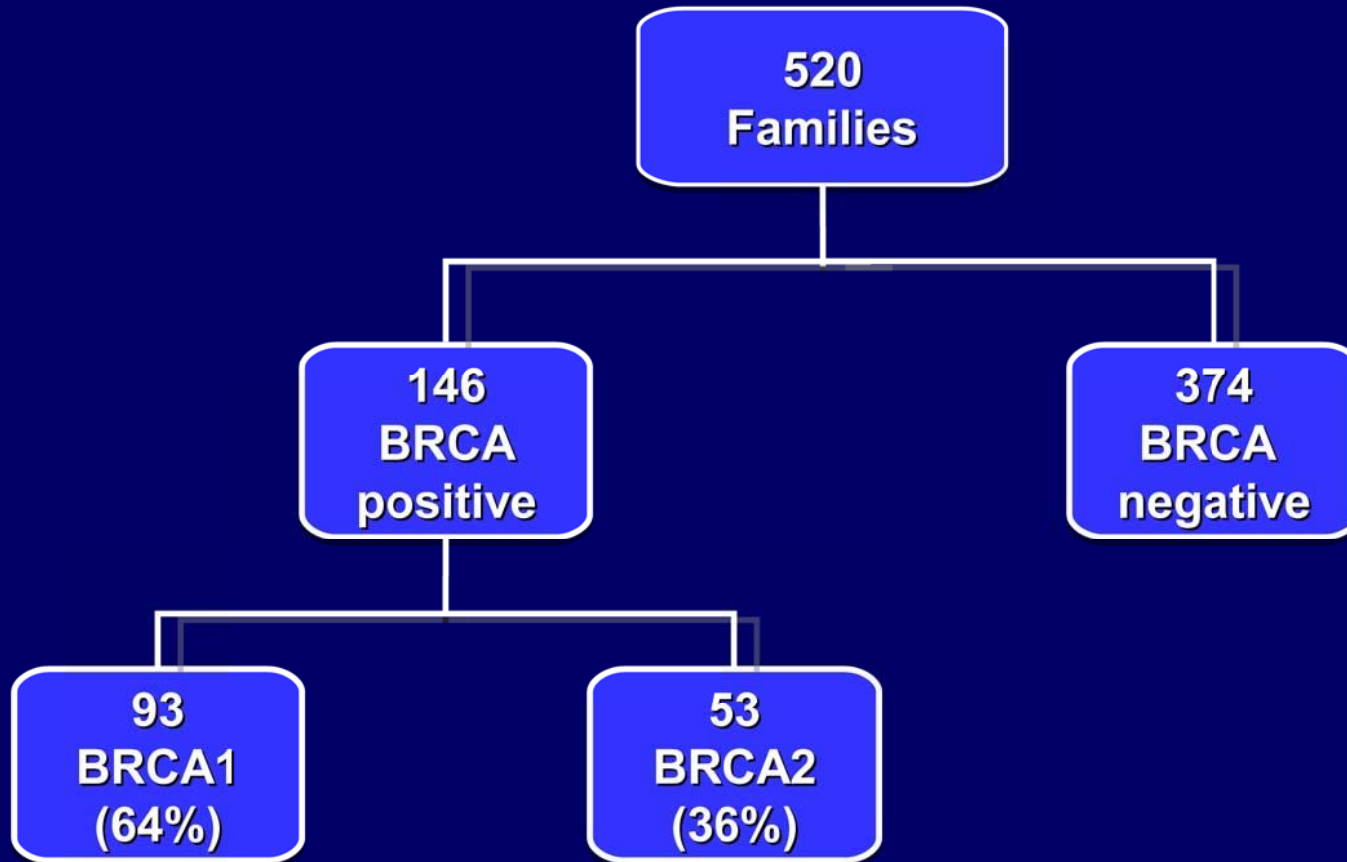
## □ Inclusion criteria

- Genetic counseling
- Complete family history  $\geq 3$  generations
- $\geq 1$  case of breast or ovarian cancer in the family
- Documented BRCA test results (Myriad Genetics Laboratories)

## □ Exclusion criteria

- Multiple subjects from the same family

# BRCA Test Results



# Results: Family Characteristics

	BRCA - (%)	BRCA + (%)
<b>Number of families</b>	<b>374</b>	<b>146</b>
<b>Ethnicity</b>		
Caucasian (non-AJ)	259 (69)	97 (66)
Ashkenazi Jewish (AJ)	48 (13)	23 (16)
African American	48 (13)	20 (14)
Hispanic	10 (3)	2 (1)
Asian	5 (1)	1 (1)
Other	4 (1)	3 (2)
<b>Cancer in Family</b>		
Breast	361 (97)	145 (99)
Ovarian	115 (31)	68 (47)
Male Breast	10 (3)	7 (5)

# Comparison of Prediction Models

	Sensitivity <sup>+</sup>	Specificity <sup>+</sup>	(+) Predictive Value <sup>+</sup> (95% CI)	(-) Predictive Value <sup>+</sup> (95% CI)
<b>PAT</b>	<b>0.959</b> (0.918-0.981)	<b>0.201</b> (0.185-0.209)	<b>0.319</b> (0.305-0.326)	<b>0.926</b> (0.853-0.965)
<b>Myriad II</b>	<b>0.849</b> (0.791-0.896)	<b>0.393</b> (0.370-0.411)	<b>0.353</b> (0.329-0.373)	<b>0.870</b> (0.819-0.910)
<b>Penn II</b>	<b>0.924</b> (0.879-0.956)	<b>0.155</b> (0.137-0.168)	<b>0.305</b> (0.290-0.316)	<b>0.836</b> (0.737-0.904)

<sup>+</sup> Threshold value:

PAT ≥8, Myriad and Penn ≥10% probability of detecting a BRCA mutation

# Conclusion

- Compared to two BRCA mutation probability models (**Myriad II & Penn II**) the PAT is :
  - ▣ Comparable in identifying families with BRCA mutations
  - ▣ Logistically simpler to perform

# Future Directions

## □ Test in Primary Care Clinics

*To refer patients for genetic counseling & evaluation who are at increased risk for deleterious mutations*

USPSTF (2005)



# Acknowledgements...



Paige Teller MD

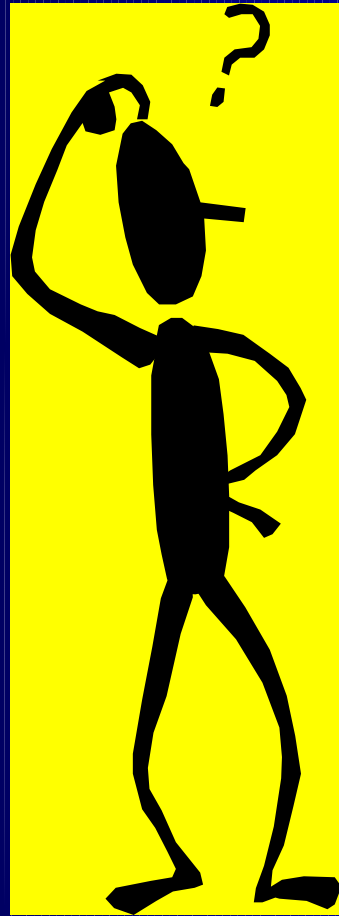


Kent Hoskins MD



Alice Zwaagstra NP

# Questions



[https://myosfhealth.osfhealthcare.org/sites/OSF/BCRA/Web\\_Pages/bcra.aspx](https://myosfhealth.osfhealthcare.org/sites/OSF/BCRA/Web_Pages/bcra.aspx)