

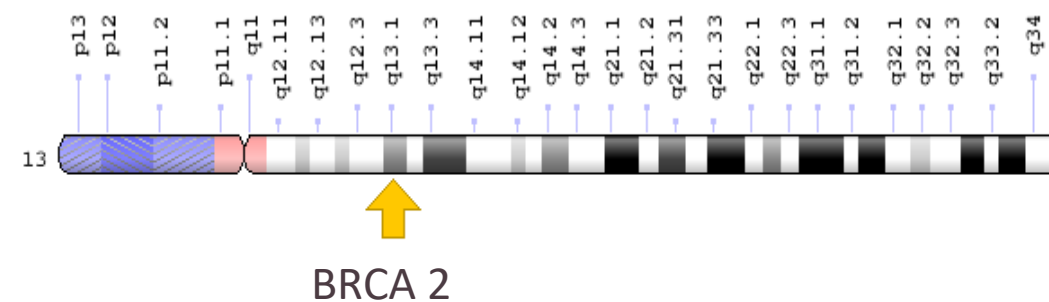
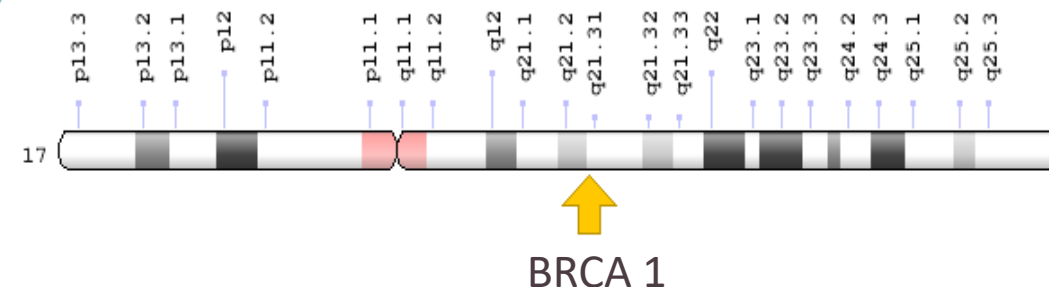
# Roles of BRCA1/2 Mutations in Breast Cancer Outcomes

Yixuan (Sherry) Wu

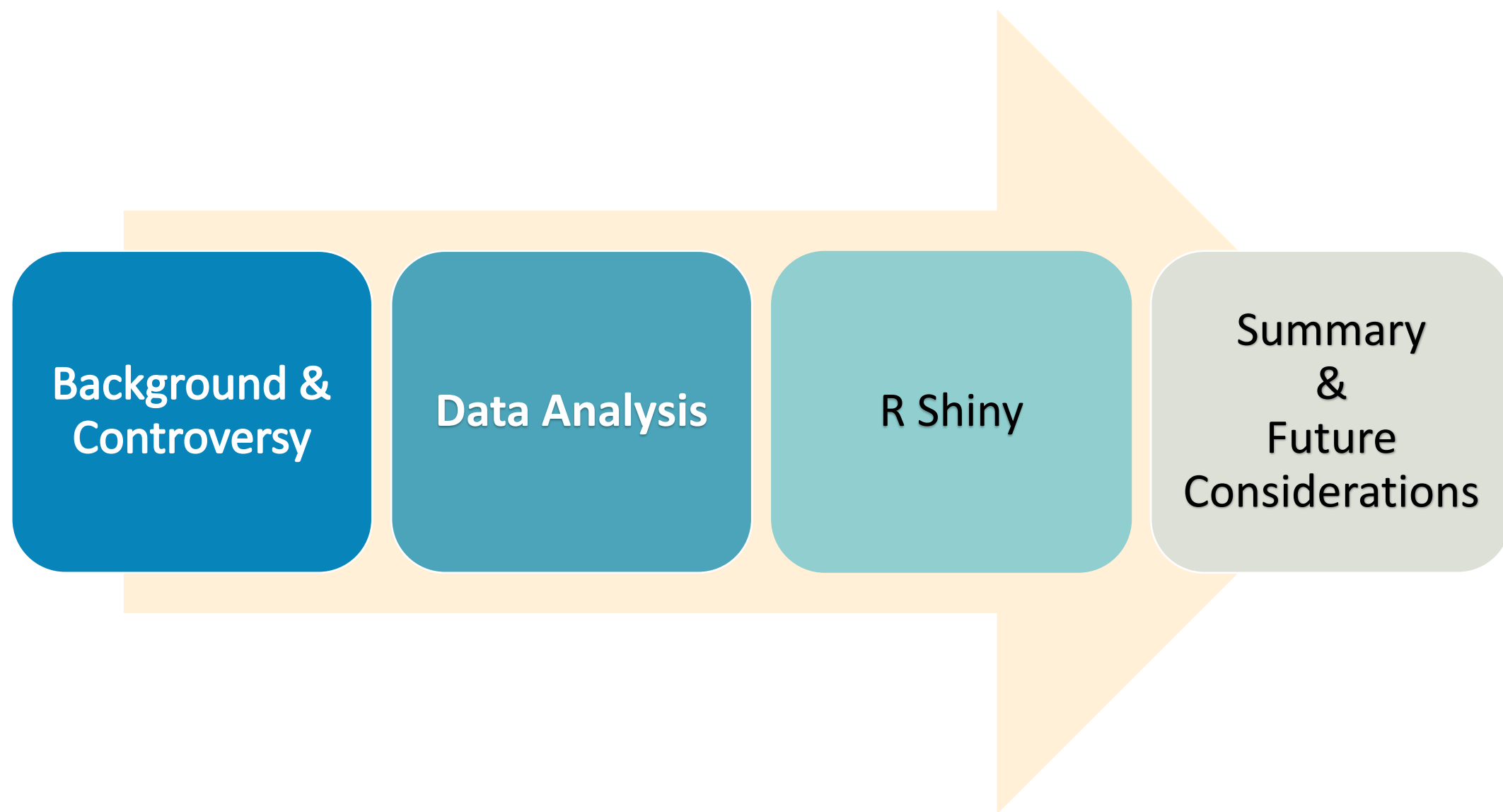
Georgetown University

Mentor: Dr. Jaya Satagopan

Memorial Sloan Kettering Cancer Center



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Cancer Center



Background

Analysis

R Shiny

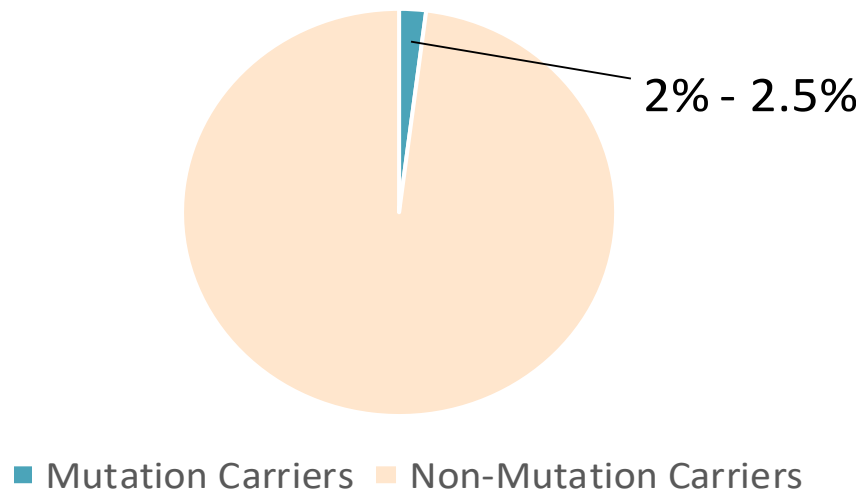
Summary



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# 3 specific types of BRCA1/2 mutations are prevalent in Ashkenazi Jewish individuals

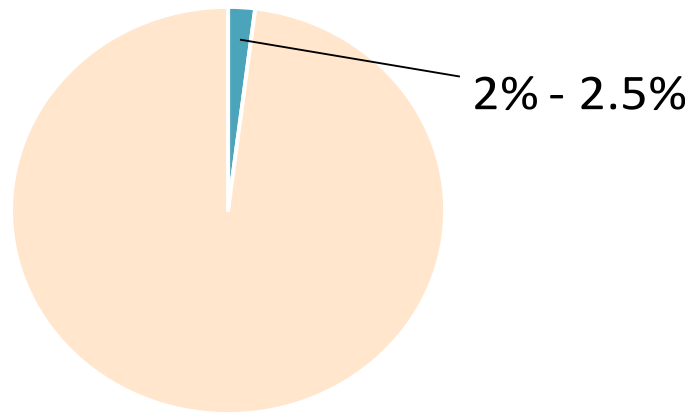
Ashkenazi Jewish Population



3 specific types of BRCA1/2 mutations are prevalent in Ashkenazi Jewish individuals

Mutation carriers are at a higher risk of developing breast cancer.

Ashkenazi Jewish Population



■ Mutation Carriers ■ Non-Mutation Carriers

GPOP without  
BRCA1/2 Mutation  → 7%

Background

Analysis

R Shiny

Summary

Hartge et al. A.I.J.G. 1999  
cdc.Gov  
Satagopan et al., 2001

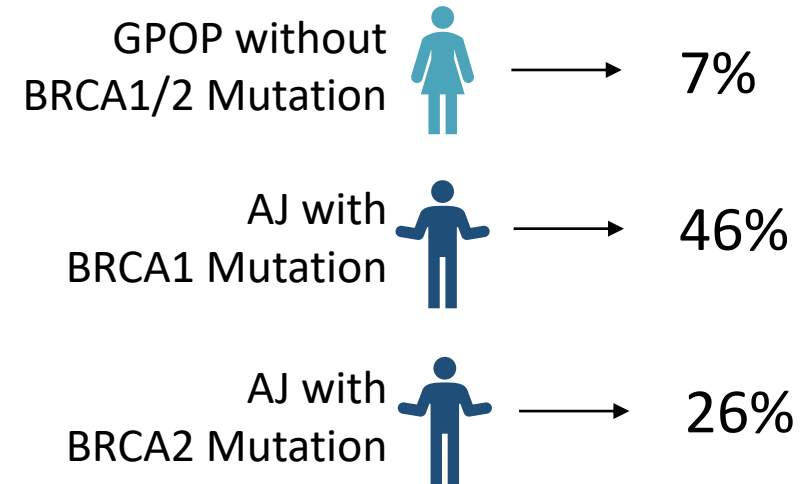
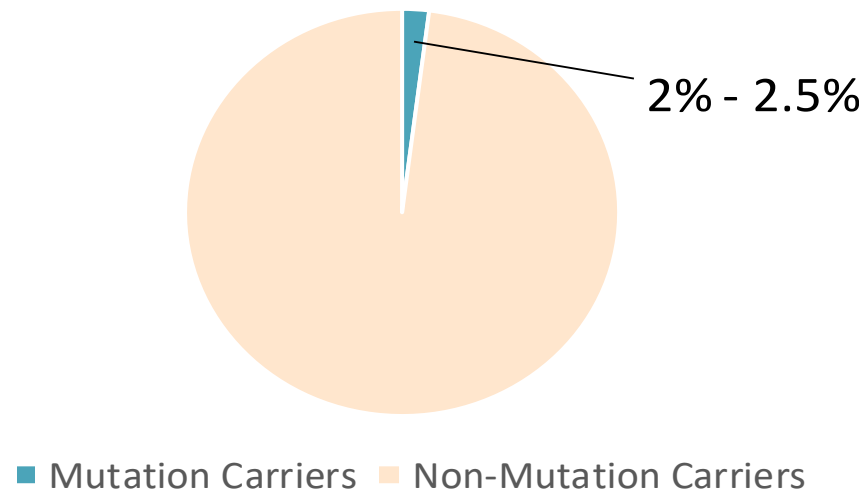


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## 3 specific types of BRCA1/2 mutations are prevalent in Ashkenazi Jewish individuals

Mutation carriers are at a higher risk of developing breast cancer.

Ashkenazi Jewish Population



What about  
Ashkenazi Jewish  
who already had  
breast cancer?



**What is the prognosis of  
breast cancer patients  
who had breast  
conservation therapy?**



**Do mutation  
carriers do worse  
than non-mutation  
carriers or not?**

# Mutation Carriers have Worse Prognosis than non-carriers

OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

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# Mutation Carriers have **Similar** Prognosis than non-carriers



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ScienceDirect

journal homepage: [www.ejconline.com](http://www.ejconline.com)



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Bernard Asselain · Dominique Stoppa-Lyonnet · Alain Fourquet

Possible Reasons: Groupings, Follow up time, Adjuvant treatment

Background

Analysis

R Shiny

Summary



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# **Breast Conservation Therapy for Invasive Breast Cancer in Ashkenazi Women With BRCA Gene Founder Mutations**

*Mark Robson, Deborah Levin, Mark  
Federici, Jaya Satagopan, Faina  
Bogolminy, Alexandra Heerdt,  
Patrick Borgen, Beryl McCormick,  
Clifford Hudis, Larry Norton, Jeff  
Boyd, Kenneth Offit*

Journal of the National Cancer Institute, Vol. 91, No. 24, December 15, 1999

Background

Analysis

R Shiny

Summary



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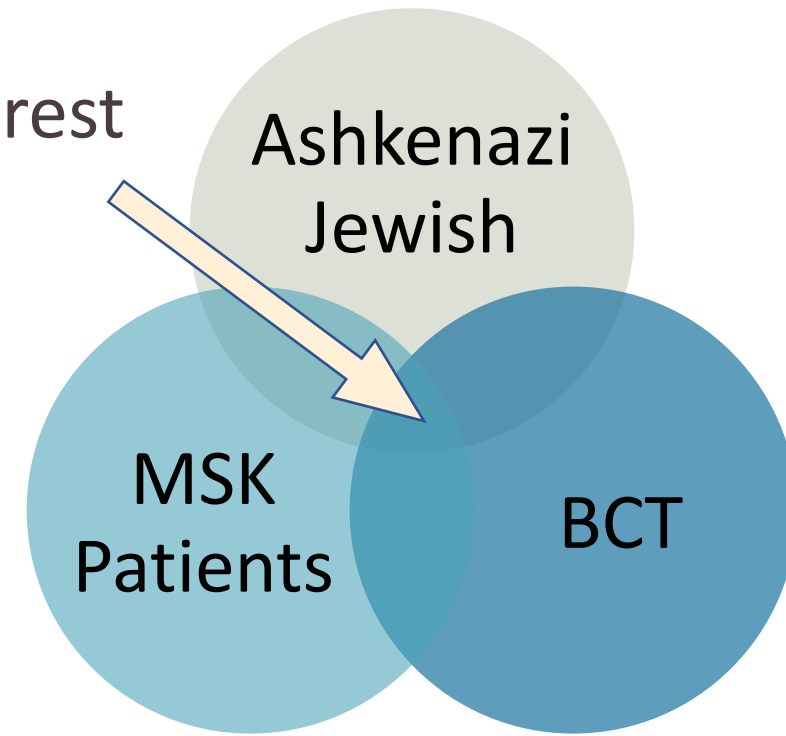
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Journal of the National Cancer Institute, Vol. 91, No. 24, December 15, 1999

■ Factors to Examine:  
Mutation Status, Age, Tumor Stage, and Node

■ Population of Interest  
(**305** patients)



■ Outcome: Breast cancer- specific survival

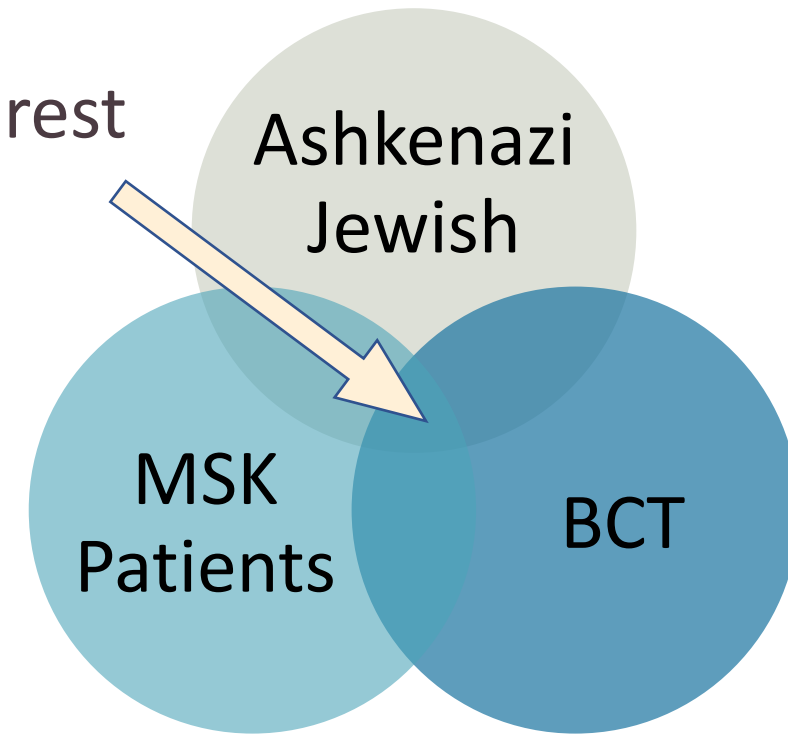
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■ Outcome: Breast cancer- specific survival

■ **Goal: Mutation Carriers have a better or worse Prognosis?**

Background

**Analysis**

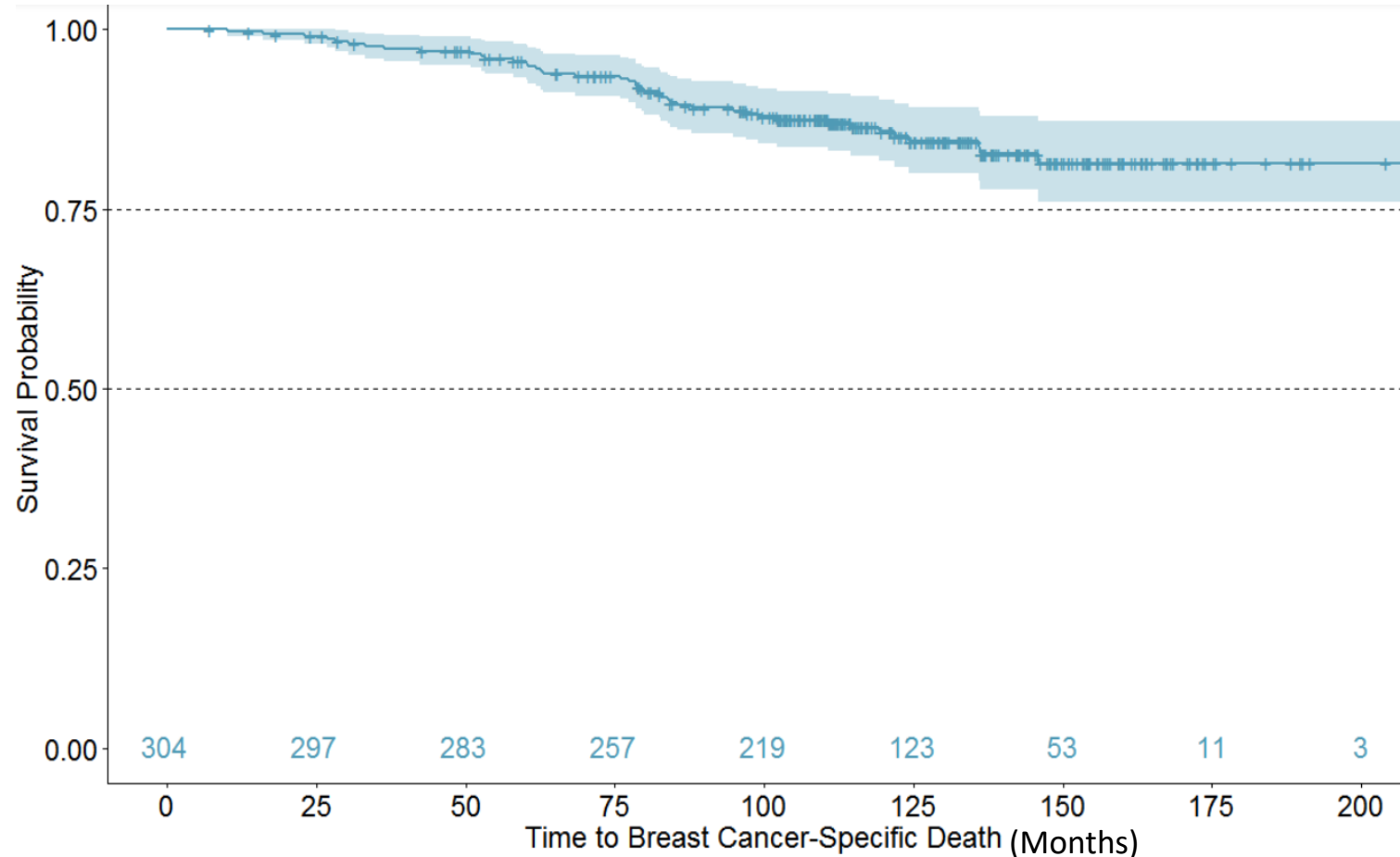
R Shiny

Summary



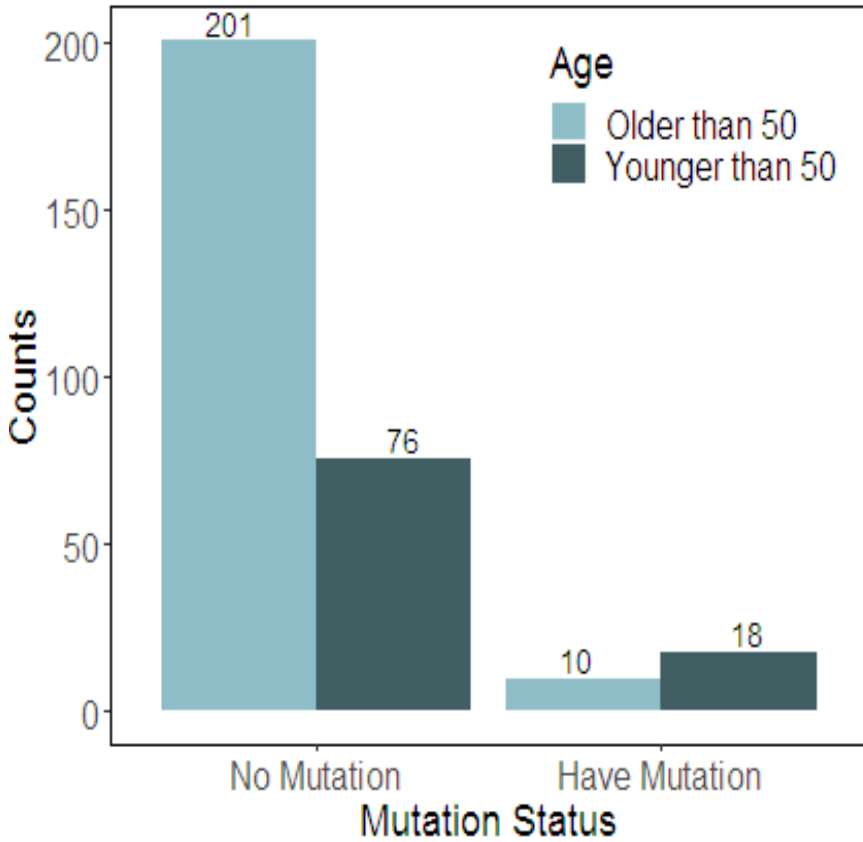
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# Overview of Data



- Median Survival Time:  
Never Reached
- Median Follow Up Time:  
121 months = 10 years.
- Mutation Carriers:  
28 out of 305  
= 9% of total sample
- Event:  
43 out of 305  
= 14% of total sample  
≠ total death

# Characteristics of the Data



Background

Analysis

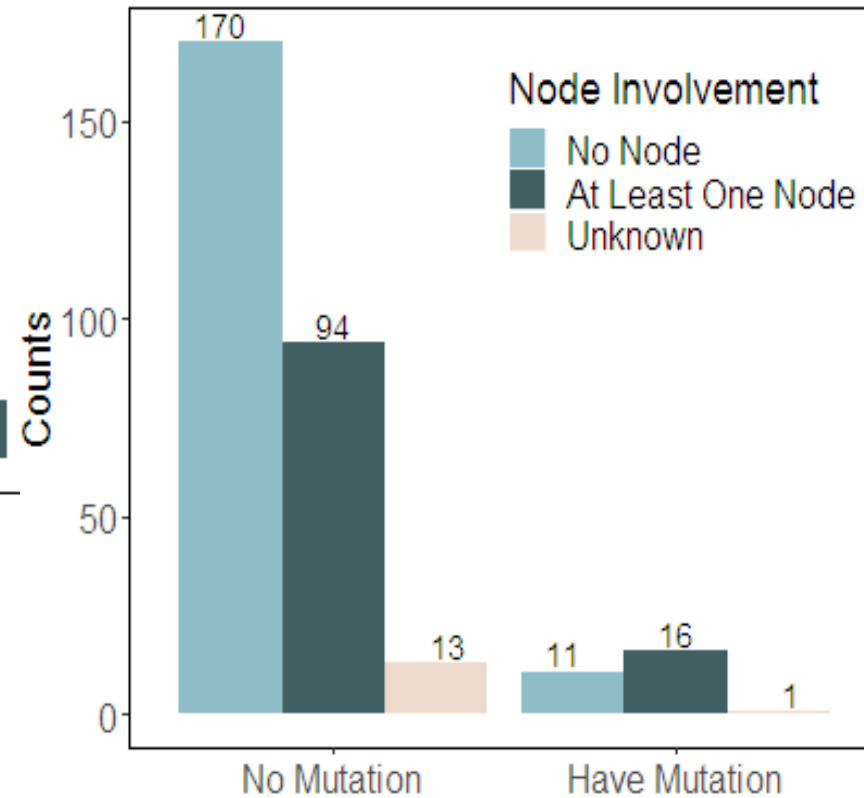
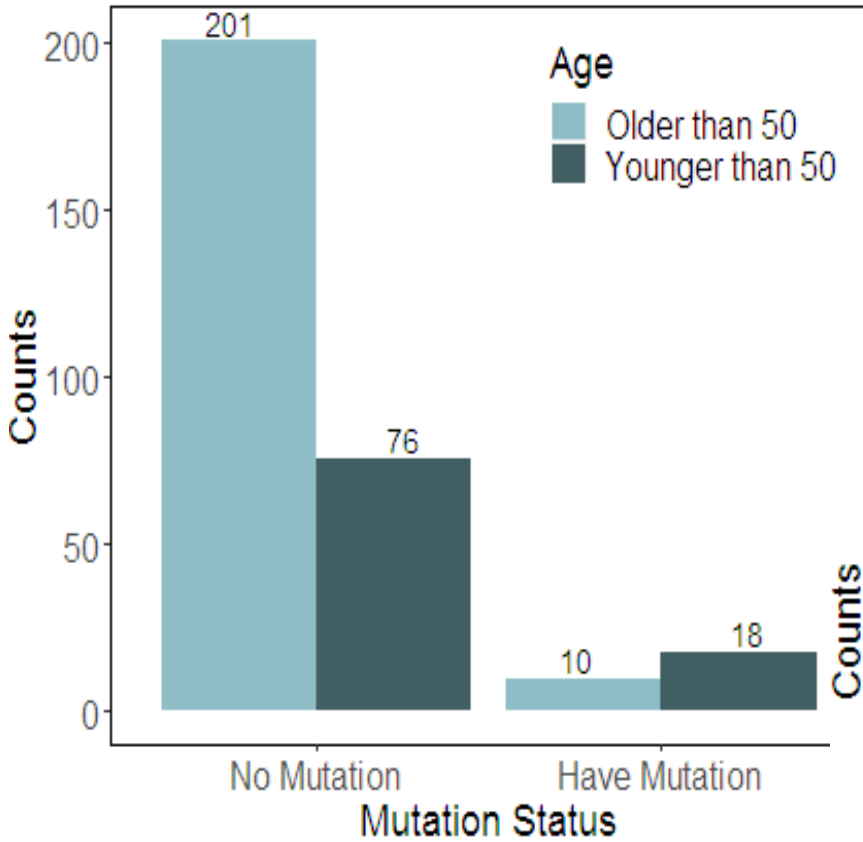
R Shiny

Summary



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# Characteristics of the Data



Background

Analysis

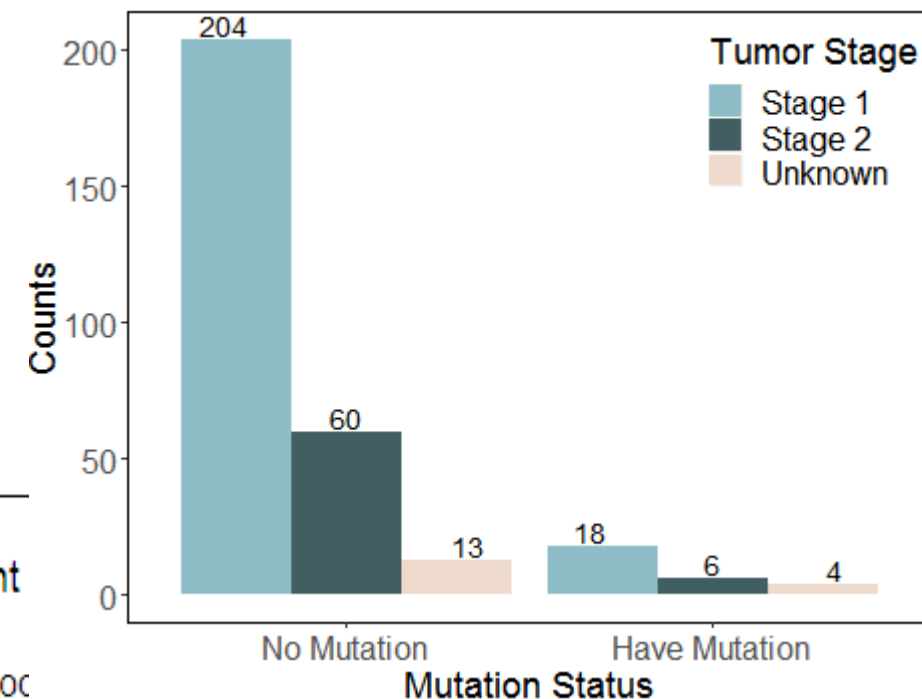
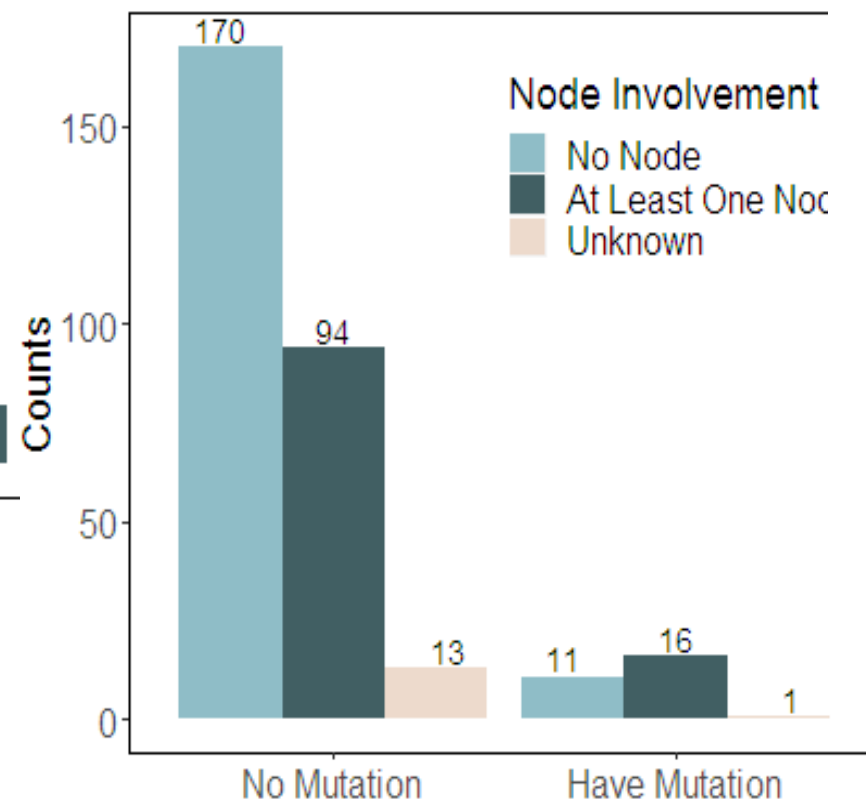
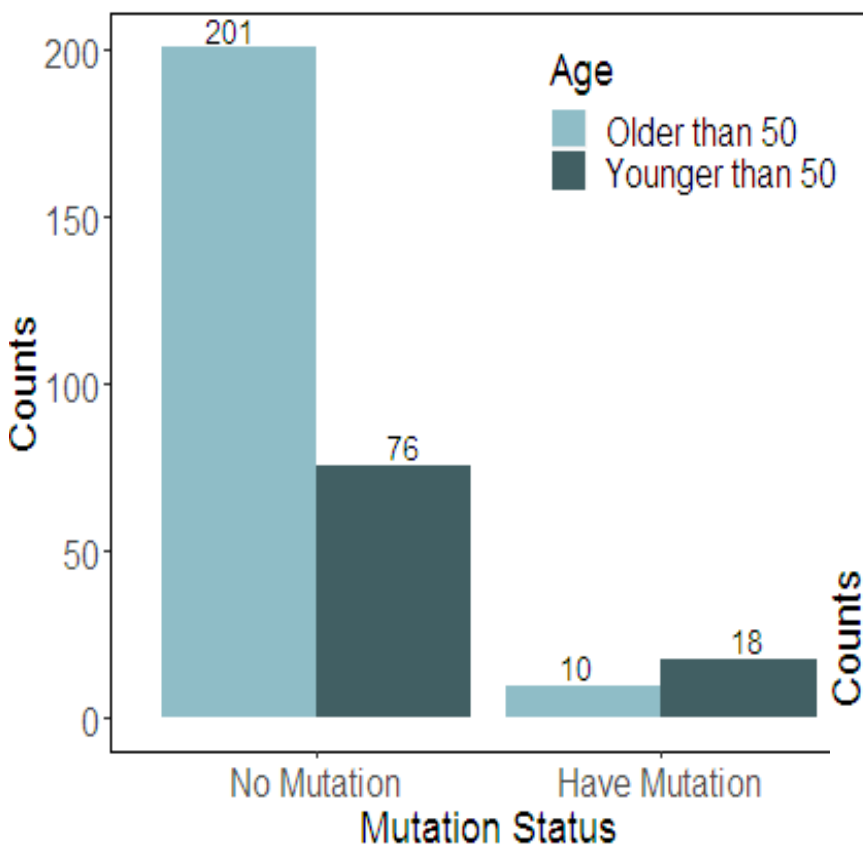
R Shiny

Summary



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# Characteristics of the Data



Background

Analysis

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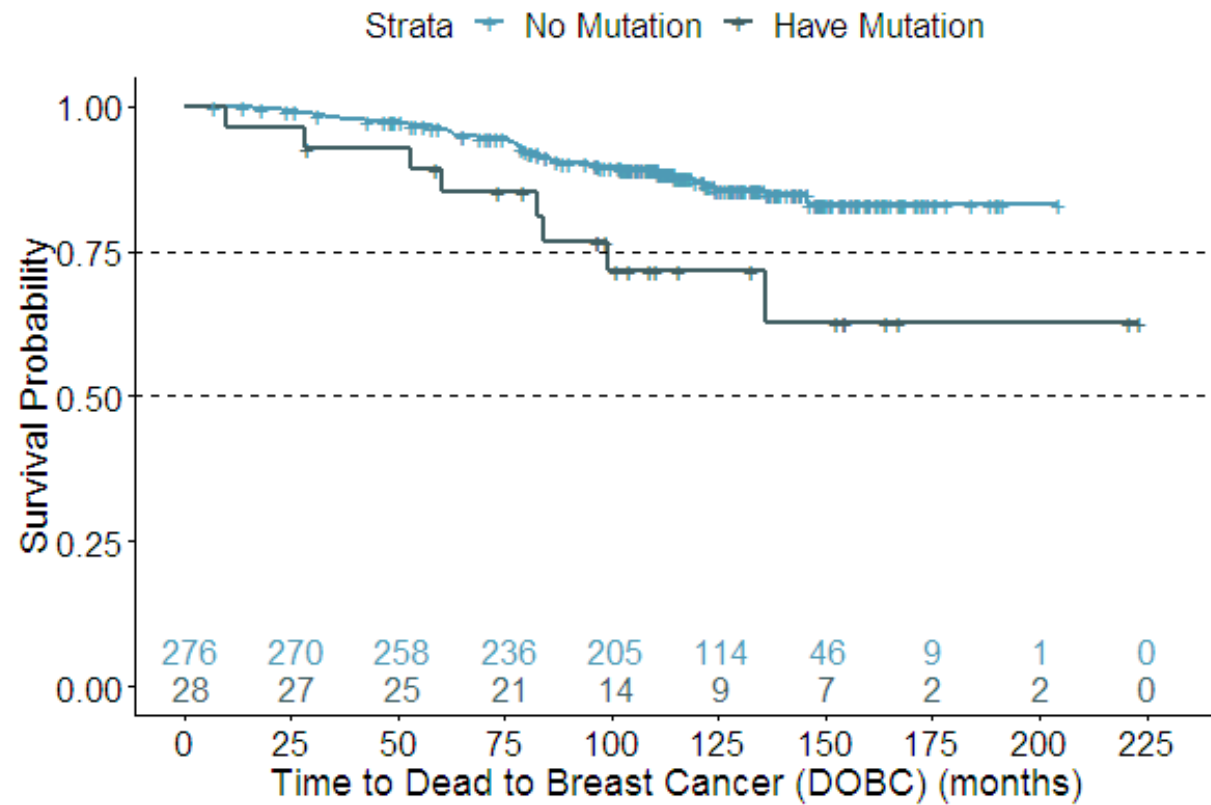
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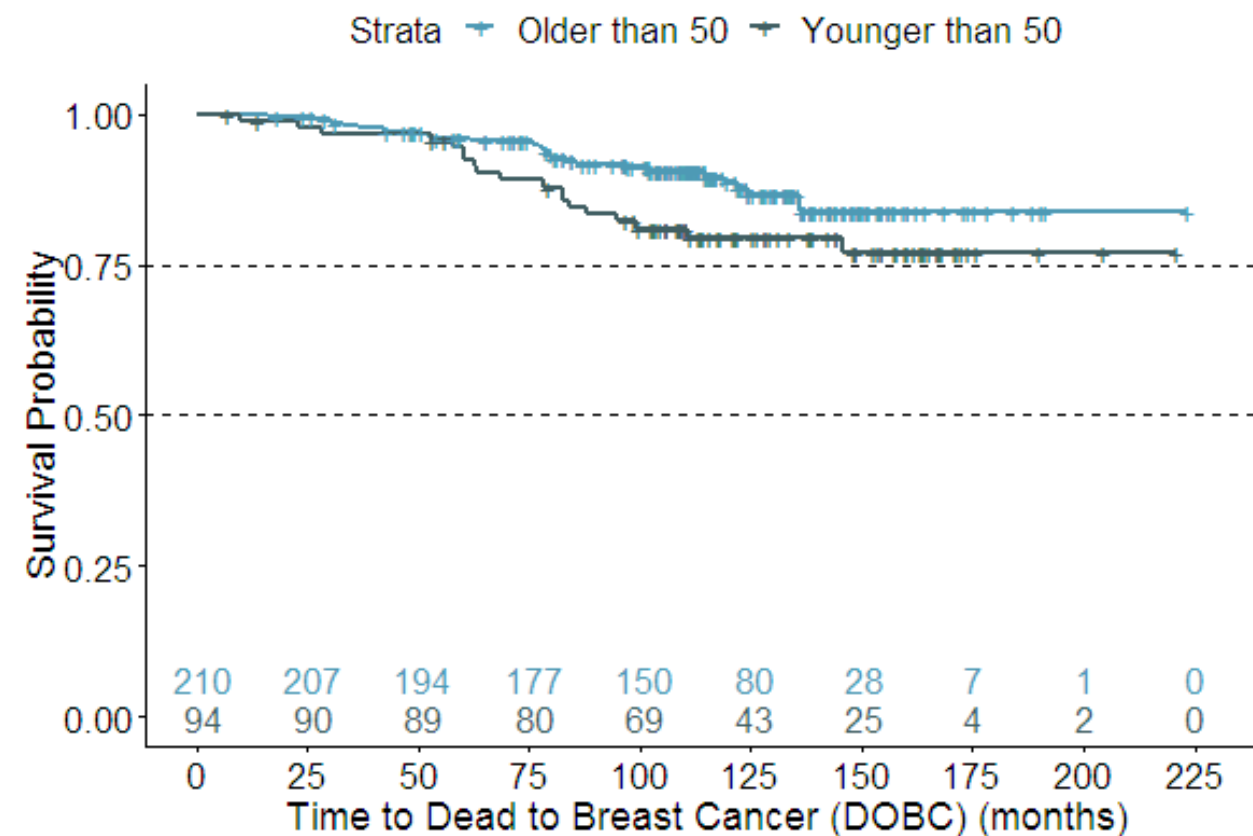
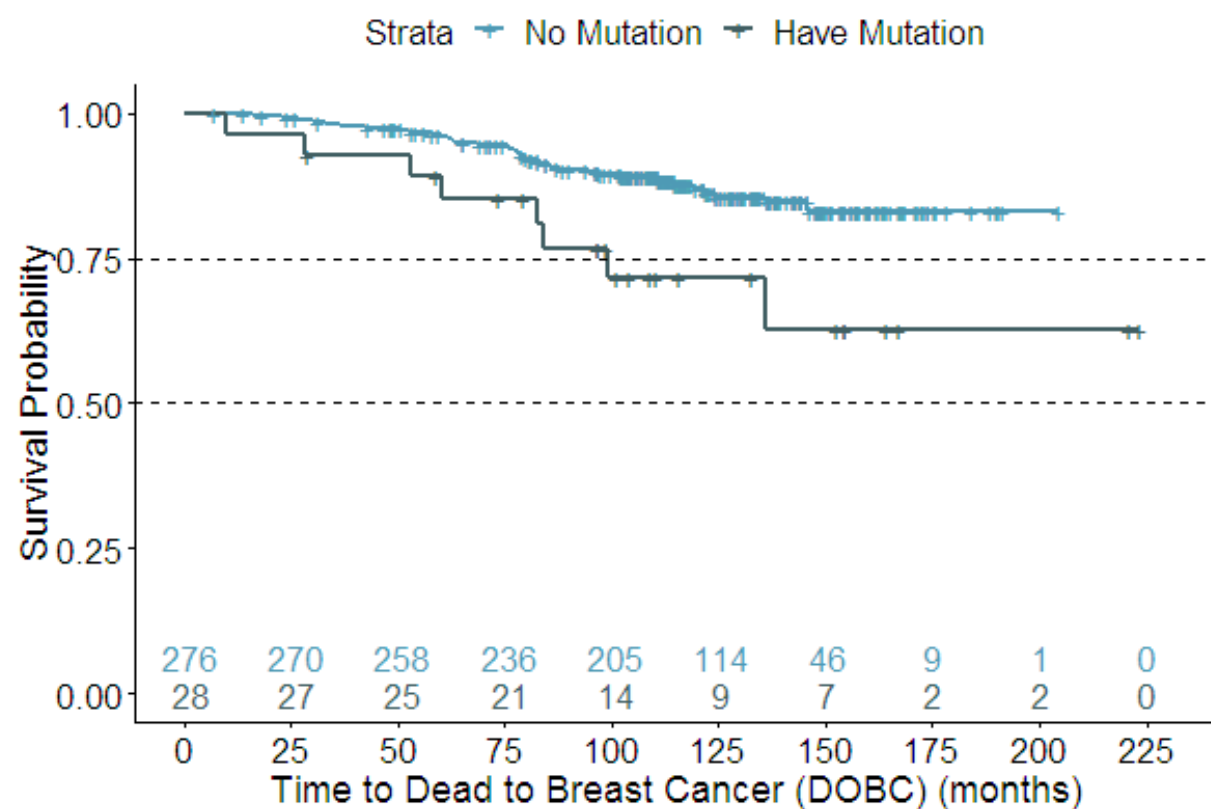
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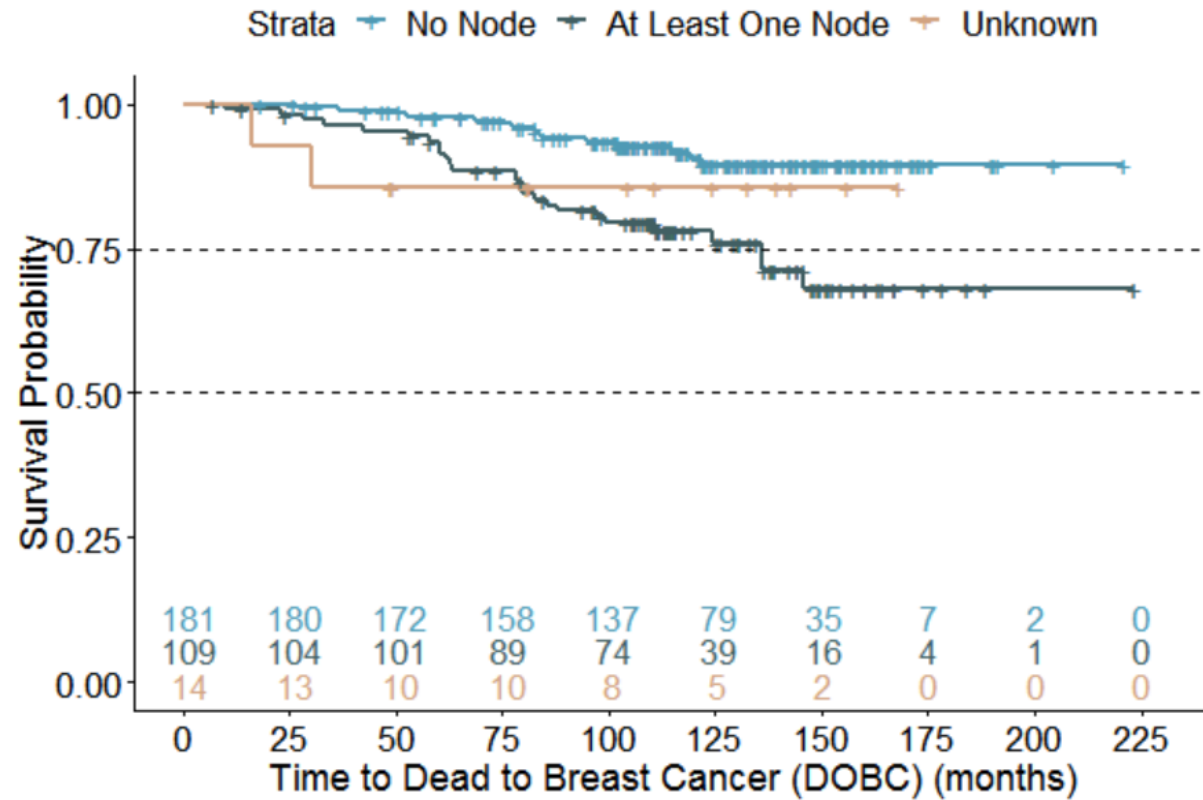
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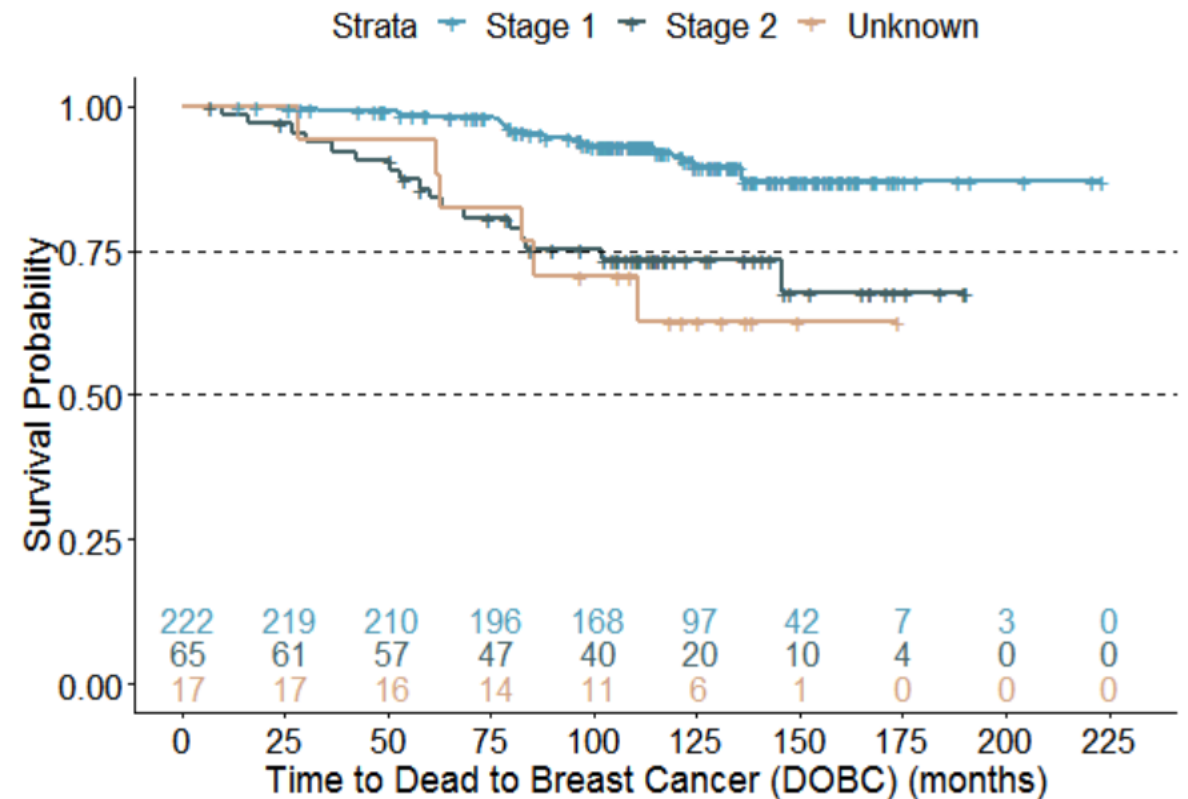
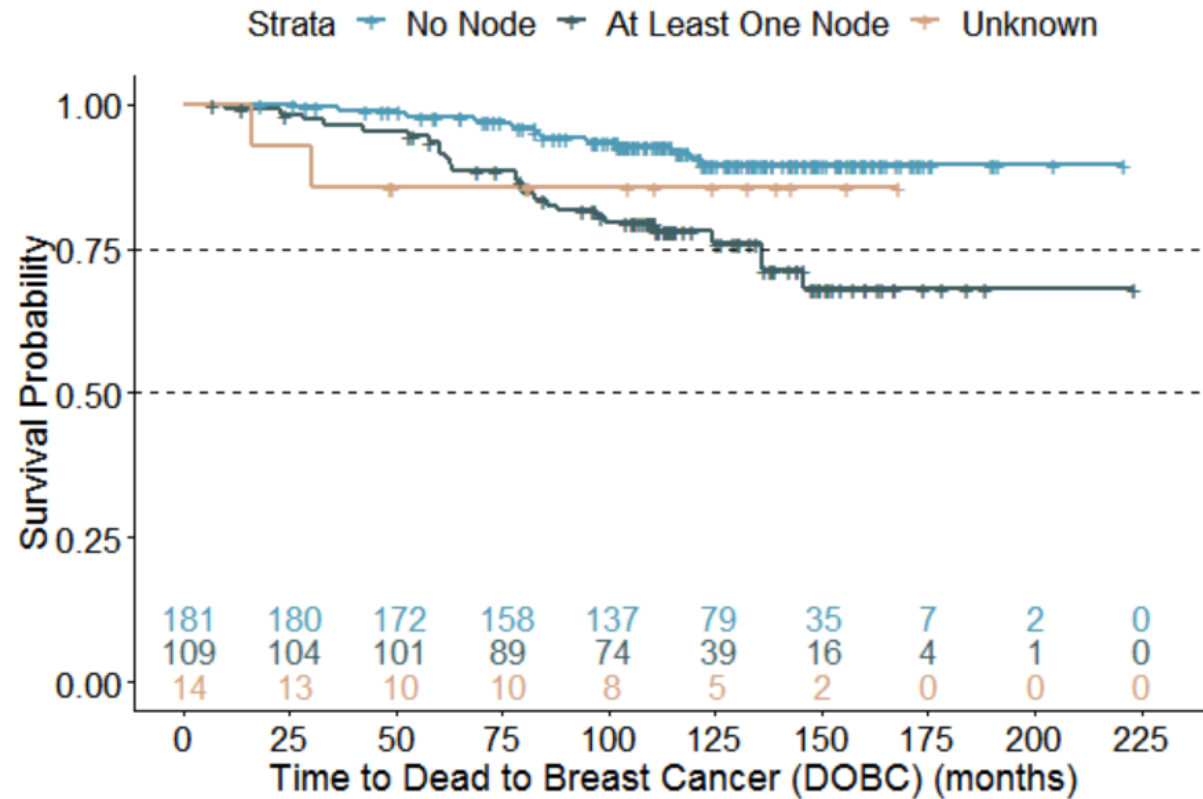
# Characteristics of the Data



# Characteristics of the Data



# Characteristics of the Data



# Missing Data

Examples:

- Node Involvement & Tumor Stage
- Estrogen Receptor (ER) & Progesterone Receptor (PR)

Amy's Project on Missing Data

# Cox Proportional Hazard Model

$$h(t|x) = h_o(t)e^{x\beta}$$

Variable Name	Hazard Ratio (HR = $\exp(\beta)$ )	SE( $\beta$ )	P-Value
Mutation Status	1.77 (Mutation/No Mutation)	0.49	0.24
Age	1.28 (Under 50/Over 50)	0.37	0.50
Tumor Stage	2.45 (Stage 2/Stage 1)	0.35	0.01*
Node Involvement	2.01 (>0 Node/ 0 Node)	1.96	0.05

N = 273, 17 missing Tumor Stage, 14 missing Node

Global Test of Proportional Hazard Assumption:  $p = 0.28$

→ Assumption not violated

# Conclusion of Controversy: Tumor Stage is what Matters!

Mutation Carriers have **Worse** Prognosis than non-carriers

Mutation Carriers have **Similar** Prognosis than non-carriers

ORIGINAL ARTICLE – BREAST ONCOLOGY

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Variable Name	P-Value
Mutation Status	0.24
Age	0.50
Tumor Stage	0.01*
Node Involvement	0.05

Background

Analysis

R Shiny

Summary



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# R Shiny App for Survival Probability



Background

Analysis

**R Shiny**

Summary



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# Survival Probability:

$$S(t) = P(\text{surviving} > t) \\ = [e^{-H_o(t)}]^{e^{x\beta}}$$

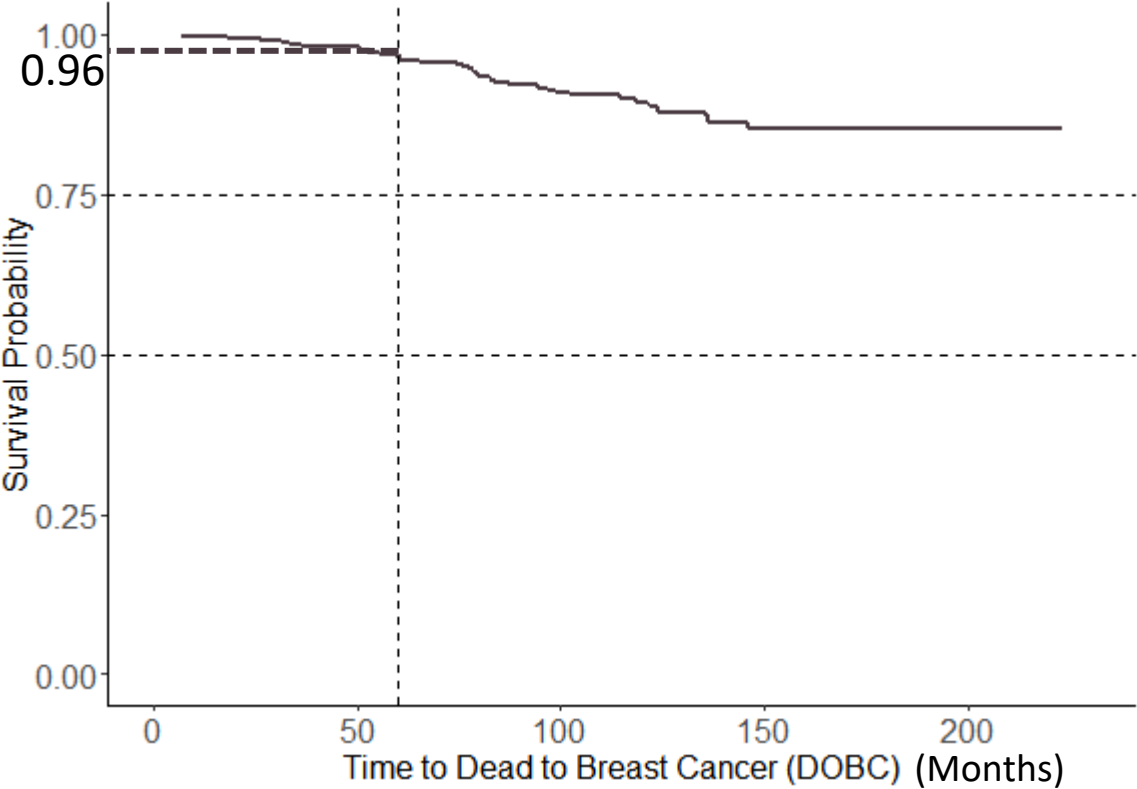
## R Shiny App for Survival Probability



Estimated Baseline Cumulative Hazard:  
basehaz() function

**Outcome:** 5-year Breast Cancer  
Specific Survival

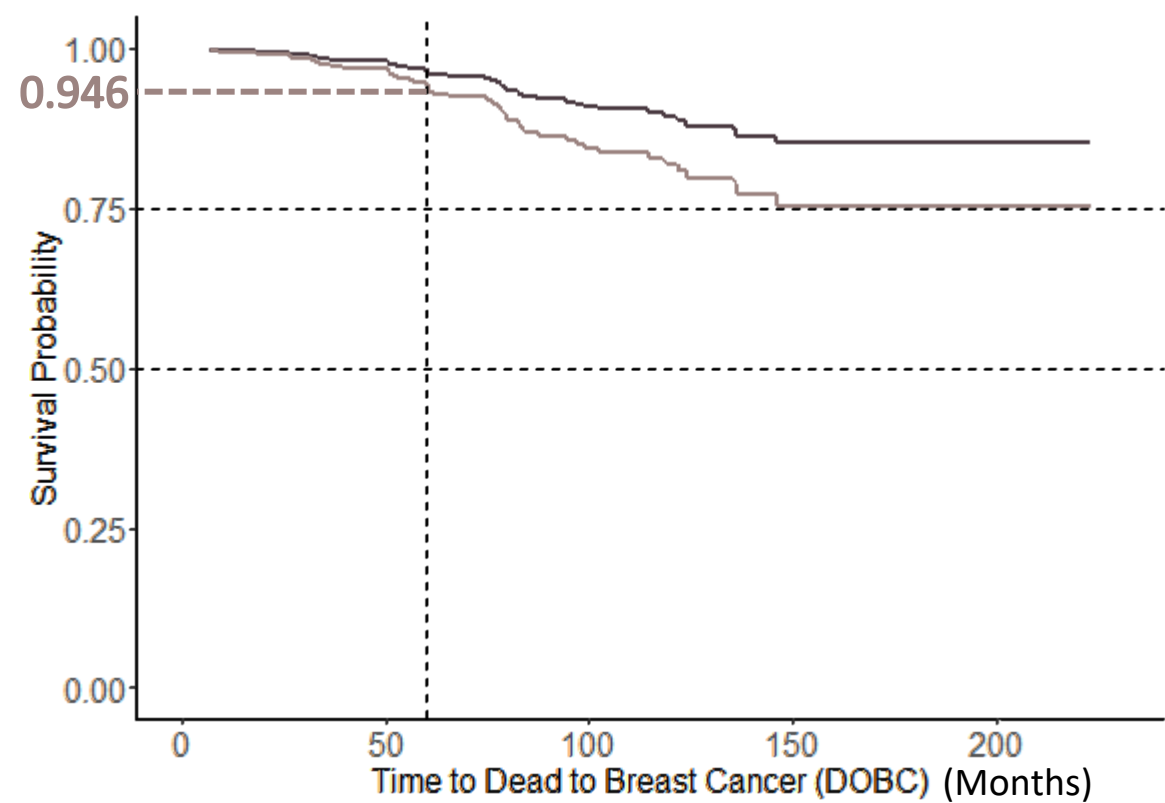
**Factors:** Mutation Status, Age, Tumor  
Stage, and Nodal Involvement



	Mutation Status	Age	Tumor Stage	Node Involvement	5-yr Survival
Example 1	No	>50	Stage 1	0	0.96

**Outcome:** 5-year Breast Cancer  
Specific Survival

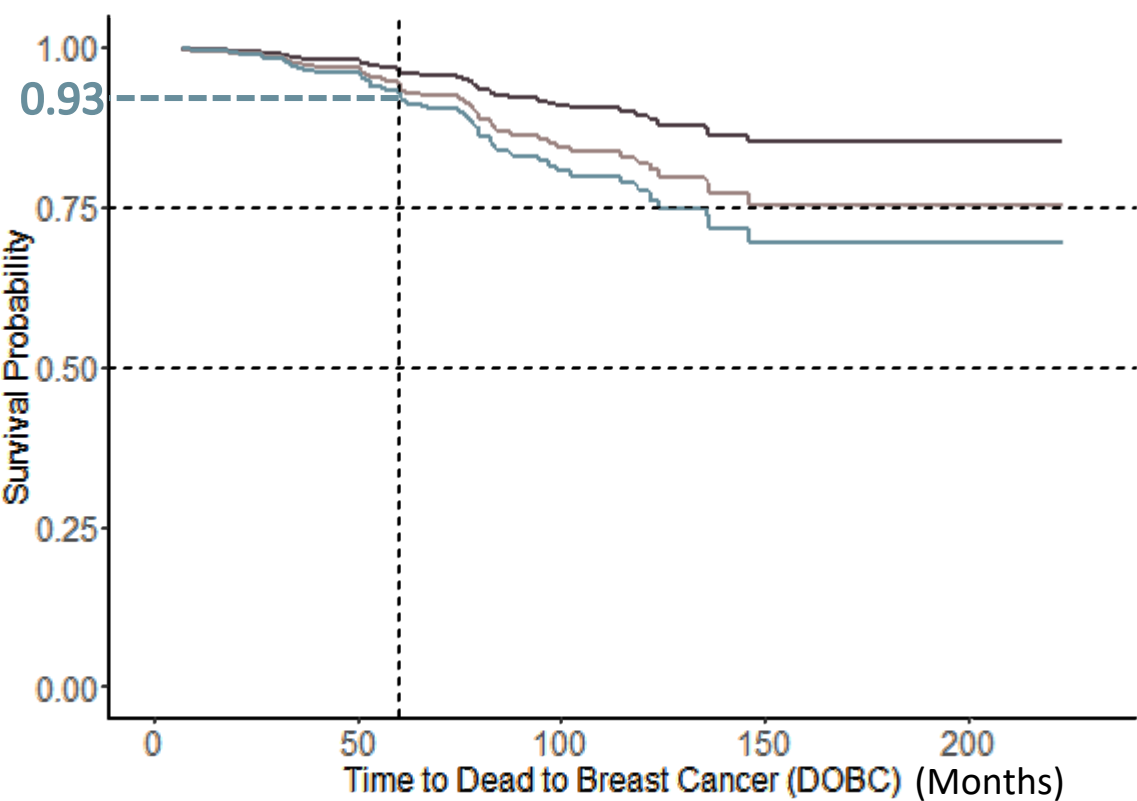
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	Mutation Status	Age	Tumor Stage	Node Involvement	5-yr Survival
Example 1	No	>50	Stage 1	0	0.96
Example 2	Yes	>50	Stage 1	0	0.946

**Outcome:** 5-year Breast Cancer  
Specific Survival

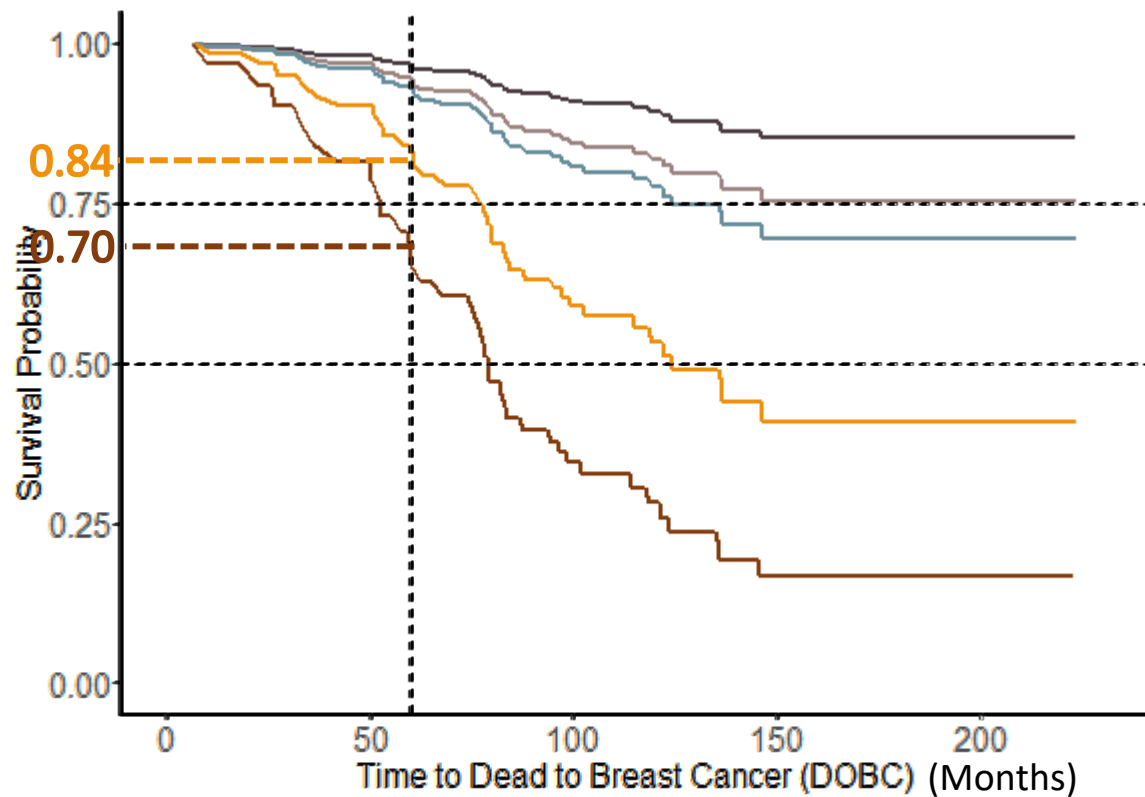
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	Mutation Status	Age	Tumor Stage	Node Involvement	5-yr Survival
Example 1	No	>50	Stage 1	0	0.96
Example 2	Yes	>50	Stage 1	0	0.946
Example 3	Yes	<50	Stage 1	0	0.93

## Outcome: 5-year Breast Cancer Specific Survival

**Factors:** Mutation Status, Age, Tumor  
Stage, and Nodal Involvement



	Mutation Status	Age	Tumor Stage	Node Involvement	5-yr Survival
Example 1	No	>50	Stage 1	0	0.96
Example 2	Yes	>50	Stage 1	0	0.946
Example 3	Yes	<50	Stage 1	0	0.93
Example 4	Yes	<50	Stage 2	0	0.84
Example 5	Yes	<50	Stage 2	>0	0.70

## Conclusion:

- Regarding controversy – mutation is not the key, but stage plays an important role in breast cancer specific survival in Ashkenazi Jewish patients

## Future Consideration:

- Fit the model again with missing data filled in – Amy's Work! Yeah!
- Examine new data set and for validating the model
- Refine the R shiny app, which can be potentially useful for patients/physicians

## Special Thanks to:

Dr. Satagopan

Dr. Seshan & Dr.

Richard, Shireen, Kay See, Elena  
QSURE FELLOWS!!!!

