

# Integrated Survival Estimates from Cancer Treatment Delay during the COVID-19 Pandemic



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# Acknowledgments

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# Cancer and COVID-19

Cancer patients are at increased risk of COVID-19 mortality

Going to the hospital increases the risk of contracting COVID-19 (more potentially infectious contacts)

Delaying cancer treatment means the cancer can spread and increase mortality rates

# Cancer treatments and COVID-19

Immunosuppressed people are at increased risk of COVID-19 mortality

Chemotherapy makes people immunosuppressed

Surgery requires ventilation and also increases the risk of contracting COVID-19

# Big question: How to treat cancer patients during the COVID-19 pandemic?

[The Coronavirus Outbreak](#) > [LIVE](#) [Latest Updates](#) [Maps and Tracker](#) [New Symptom List](#) [Markets](#) [Life at Home](#) [Newsletter](#)

## DOCTORS

### Weighing Risks for My Patients at a Time of Covid-19

When should the fear of catching a virus, and one that usually causes a mild infection, outweigh the need to address urgent medical issues?



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By Barron H. Lerner, M.D.

April 30, 2020 Updated 5:50 a.m. ET



## The dilemmas facing cancer doctors and patients in the coronavirus pandemic

"Oncologists are in a very particular predicament right now," says Dr. Siddhartha Mukherjee.

By Caroline Hopkins | Mar 20, 2020, 7:30am EDT

## Coronavirus is forcing breast cancer patients to make tough decisions

[Los Angeles Times](#) [Joel Rubin](#), LA Times • April 12, 2020



A nurse places a patient's chemotherapy medication on an intravenous stand. The coronavirus crisis has complicated treatment options for women with breast cancer. (Matt Rourke / Associated Press)

When a routine mammogram led to a breast cancer diagnosis for Yoko Williams

What to Read Next

[BostonGene and Washington University in St. Louis are racing to find a COVID-19 vaccine](#)

Currently: Making blanket decisions across geographical, age, comorbidities, etc

- Tier systems based on cancer site and stage may:
  - Ignore comorbidities
  - Ignore geographical differences in the state of the pandemic
  - Ignore age
  - Ignore treatment plans

# OncCOVID

- Web app to guide clinicians and help make personalized treatment decisions for patients
- 47 customizable inputs
- Outputs infection risk, mortality risk, survival curves, and RMST
- <http://onccovid.med.umich.edu/>



## OncCOVID Models

OncCOVID

OncCOVID(+)

Methods

Acknowledgements

Patient Characteristics

Cancer Characteristics

Community COVID-19 Data

Treatment Information

Immediate Treatment

Delayed Treatment

Advanced Settings

Change default values

Change estimated values

The OncCOVID model estimates an individual's integrated risk of mortality (survival) from immediate (routine care) versus delayed cancer treatment. Cancer treatment variably impact cancer-specific survival, while delayed treatment reduce immediate exposure to the healthcare system and therapies which variably impacts COVID-19-specific survival. This model is intended to estimate outcomes in individuals not yet infected by COVID-19. This model should not be used to estimate survival outcomes in individuals infected or recovered, or actively infected with COVID-19.

Patient age

60

Check here if the patient has immunodeficiency.

How many of the following comorbidities does your patient have: asthma, cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes, hypertension, and obesity.

# 4 Big Pieces

Cancer mortality under immediate treatment

Cancer mortality under delayed treatment

COVID-19 infection risk

COVID-19 mortality risk

# Cancer mortality under immediate treatment

- Used SEER data and a cox proportional hazards model to estimate overall survival
- Used Fine-Grey regression to model cancer specific survival
- Estimate survival based on age, cancer type, and cancer stage

# Cancer mortality under delayed treatment



Collaborators at Penn State used NCDB to estimate the effect of delaying treatment by cancer disease site and stage



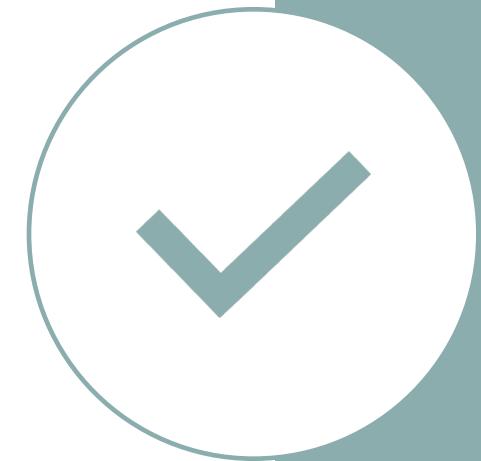
Conducted literature review to find the impact of delay of treatment by stage and disease site



Results from both the lit review and the NCDB analysis are available in the app.

# Cancer mortality under delayed treatment - NCDB

- Multivariate cox proportional hazard model for overall survival
- Adjusted for confounders (age, race, insurance status, facility information, etc).
- Ended up with a HR for a per day increase by disease site and stage.
- Some estimates were less than 1 so we default to 1 and state that we don't have a good estimate.



# COVID-19 infection risk

- Susceptible-Infected-Recovered (SIR) Model
- Modeled the health care system separately from the general population due to the increased incidence of COVID-19 among healthcare workers
- Assume patients have increased risk when visiting hospital for treatment due to increase in number of potentially infectious contacts
- Also assume increased infection risk due to surgery based on prior study.



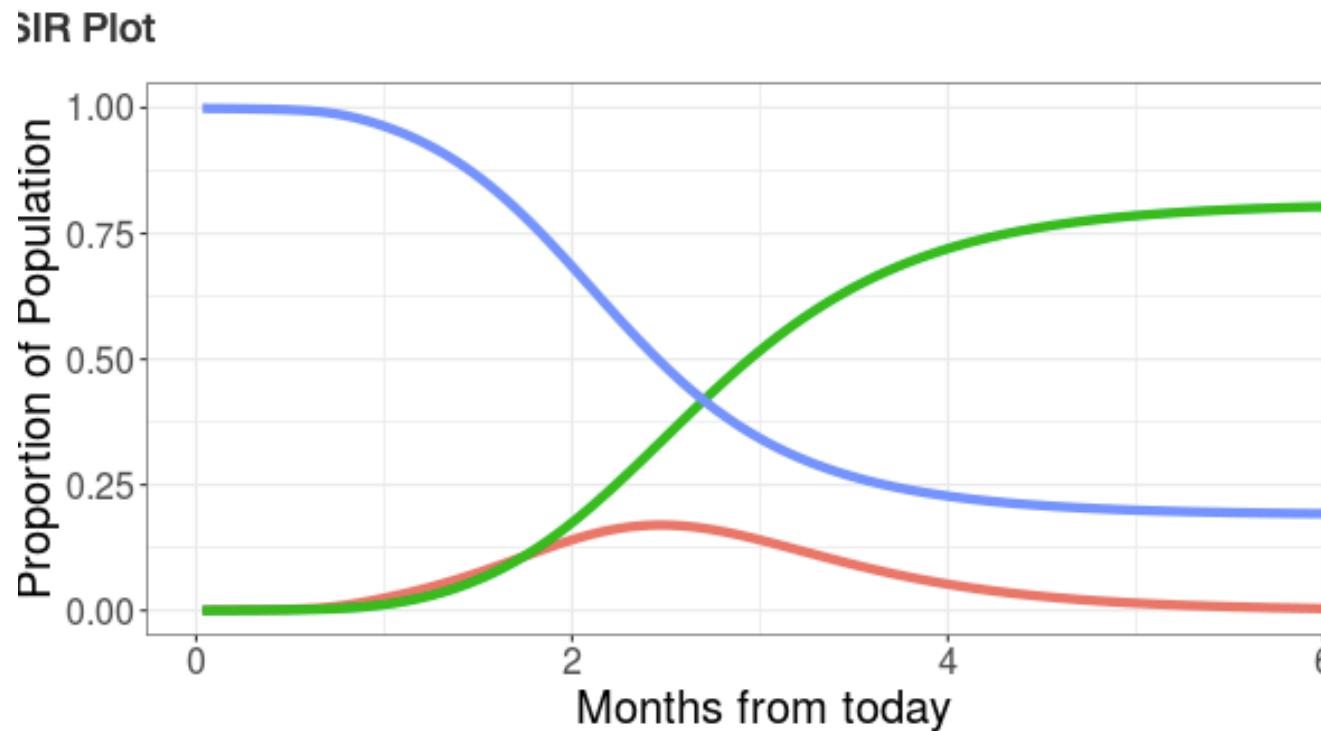
# Reproduction rate

- $R_0$  - the number of new infections caused by one person in an entirely susceptible population
- $R_t$  - the current number of new infections caused by one person
- $R_t$  changes based on social distancing measures and the number of immune people in the population
- China saw the reproduction rate drop from 3.86 to 0.32

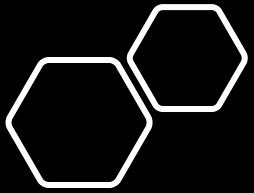
# SIR Models

- Let  $N$  be the population size,  $I_t$  be the number currently infected at time  $t$ , and  $M_t$  be the number recovered/removed. Then the number of people susceptible,  $S_t$  is  $S_t = N - I_t - M_t$ .
- We denote the average number of people infected from one person on day  $t$  is  $R_t$ .
- Let  $D$  denote the average duration of infectiousness and
- Define  $\gamma = 1/D$ .
- Define  $\beta = R_t/D$  as the number of infectious contacts made during 1 day, also called the transmission rate.

# SIR Model



- New infections on day  $t + 1$  is estimated to be  $\beta \frac{S_t I_t}{N}$
- Number susceptible on day  $t + 1$  is given by  $S_{t+1} = S_t - \beta \frac{S_t I_t}{N}$
- Number recovered/removed on day  $t + 1$  is  $M_{t+1} = M_t + \gamma I_t$
- The predicted total number infected on day  $t + 1$  is  $I_{t+1} = I_t + \beta \frac{S_t I_t}{N} - \gamma I_t$ .



# Multi-setting SIR

- Altered to allow  $\beta$  to vary between the general public and the health care setting.
- Modeled health care and general population separately assuming a percentage of the general population come in for treatment each day and that a percentage of those are there for surgery.

# Multi-setting SIR

- Let  $S_{g,t}$  and  $S_{h,t}$  be the number susceptible on day  $t$  for the general population and the healthcare population, respectively.
- Let  $I_{g,t}$  and  $I_{h,t}$  be the number infected on day  $t$  for the general population and the healthcare population, respectively.
- Let the number of new infections be  $F$  with subscripts as above and  $F_{s,t}$  be new infections from surgery.
- Let  $P_t$  be an indicator variable for if the patient is going in for treatment on day  $t$  and let  $U_t$  be an indicator for if the patient is receiving surgery
- Then the cumulative probability of infection to time  $T$  is:

$$\sum_{t=1}^T \frac{F_{g,t} + P_t F_{h,t} + U_t F_{s,t}}{N}$$

# COVID-19 Mortality Risk

We know comorbidities increase the mortality rate of COVID-19, but we also know that age plays an important role.

We also know that age and the number of comorbidities are correlated.

Need to find COVID-19 mortality by age and number of comorbidities.

Data we have:

COVID-19 nested case control data with number of comorbidities

NHANES

Large study with overall mortality rates by age range

# COVID-19 Mortality Risk

- Constrained logistic regression (to ensure monotonic relationship between age and mortality and also # comorbidities and mortality) to obtain estimates of mortality by age and number of comorbidities.
  - Adjusted for the case control design.
- Obtained estimates of proportion of population with a given number of comorbidities by age decade from NHANES
- Used NHANES data as weights for the data analysis results and normalized to the large study mortality rates

## Comorbidity results

Age	# Comorbidities			
	0	1	2	3+
40-50	0.32%	0.40%	0.49%	1.15%
51-60	0.96%	1.18%	1.45%	3.39%
61-70	2.46%	3.01%	3.69%	8.51%
71-80	5.61%	6.86%	8.42%	19.43%
81+	11.60%	14.16%	17.34%	39.30%

- Also account for the healthcare system being overwhelmed and chemotherapy

# Geographic Information

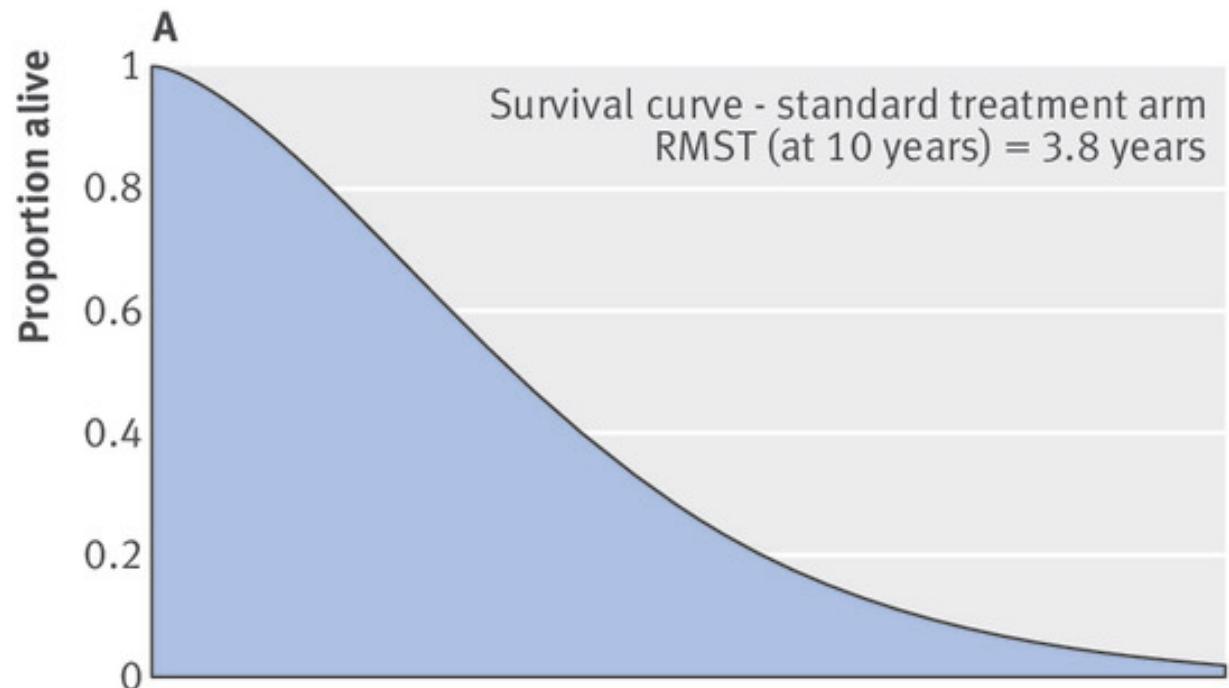
Able to use Johns Hopkins data (publicly available on GitHub) for daily COVID-19 data by county, province, or country

US Census estimates by county for 2019 for population estimates for US Counties

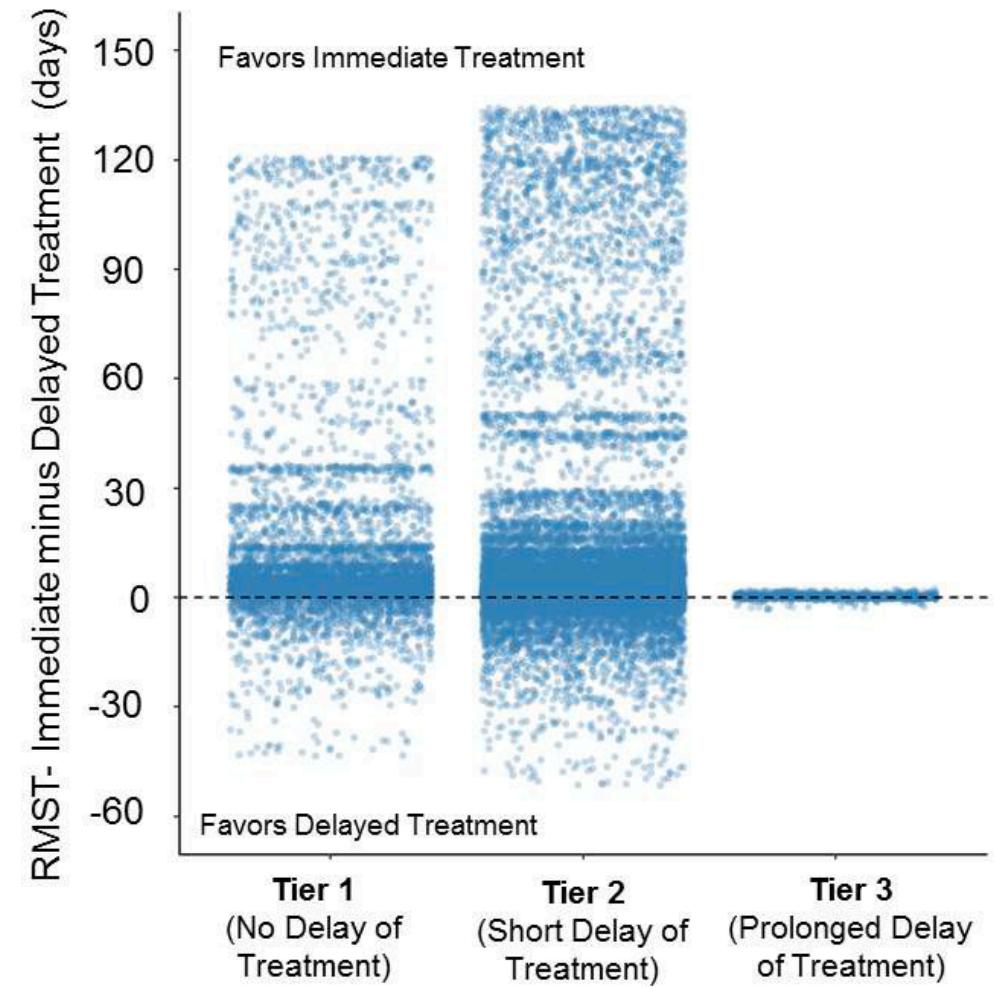
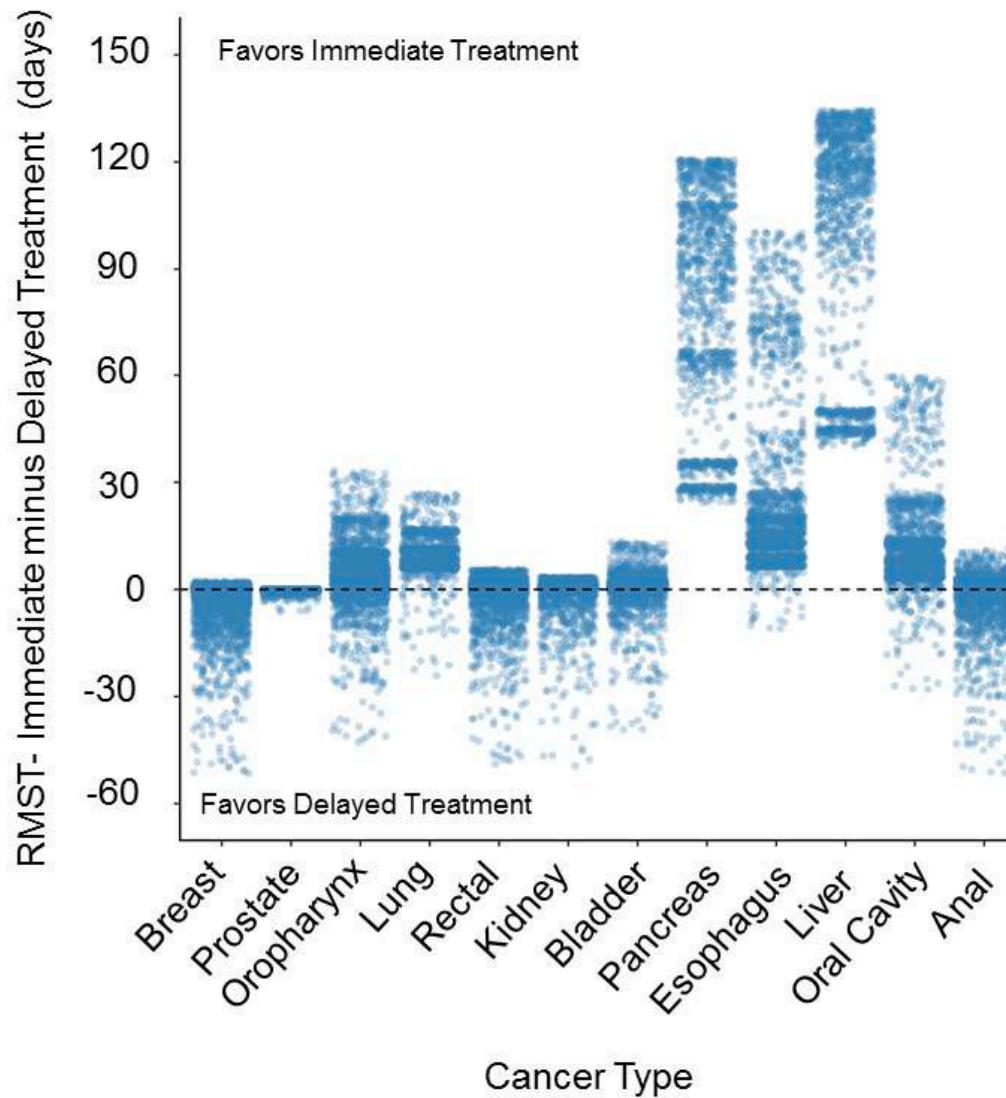
Used World Bank population estimates for non-US countries, states, or provinces.

# Restricted Mean Survival Time - RMST

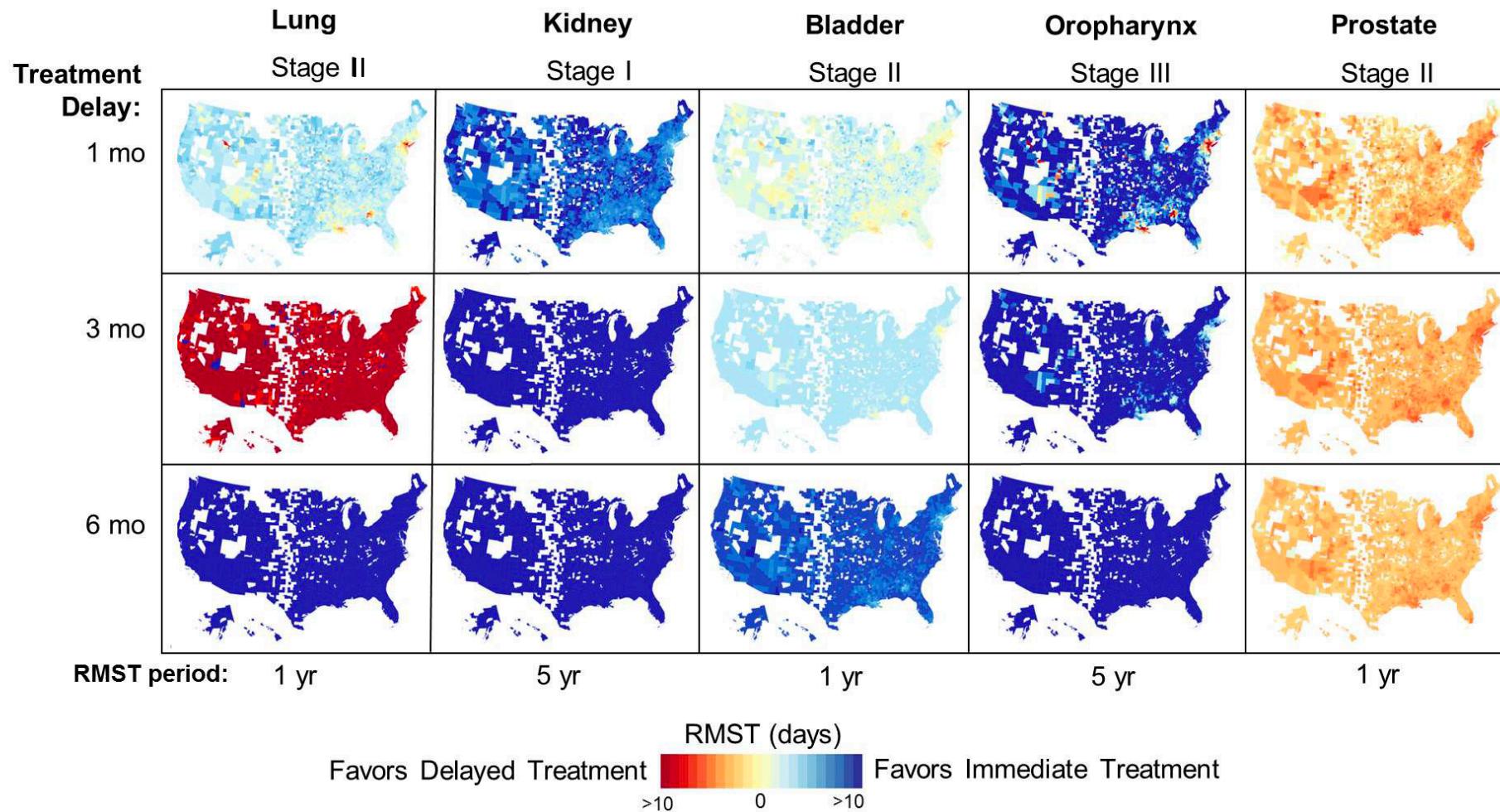
- The expected time a person will live through a fixed time point.
- Area under the survival curve
- Alternative measure to HR that works when the assumption of proportional hazards is not valid.



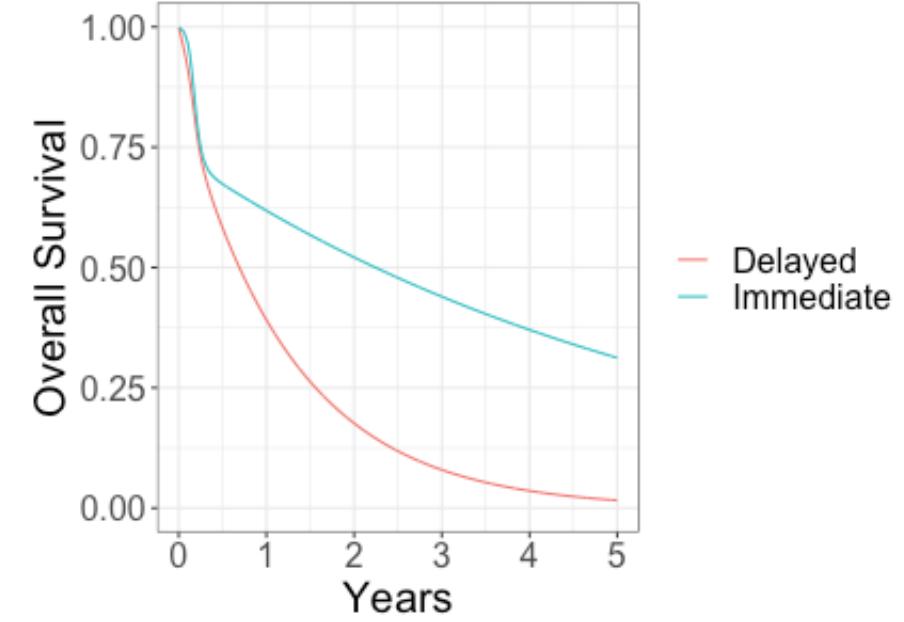
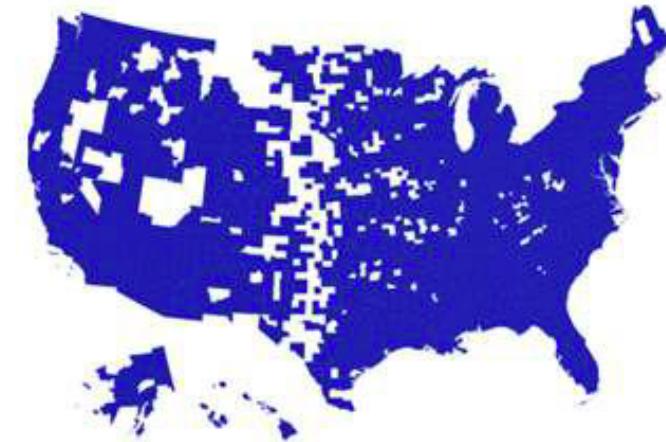
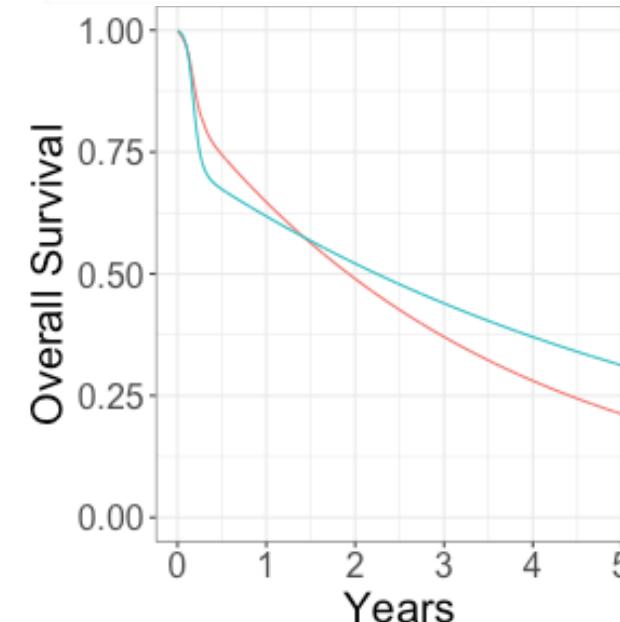
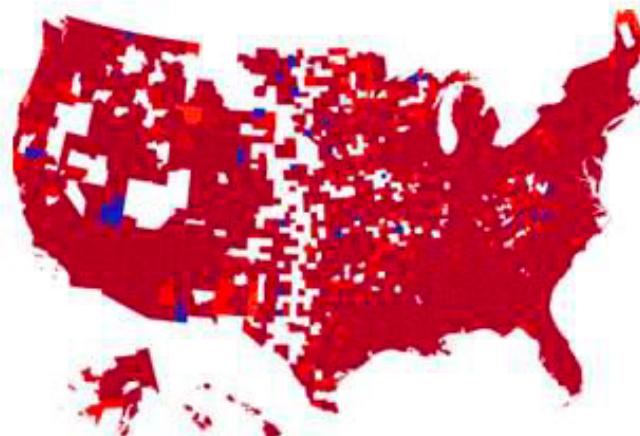
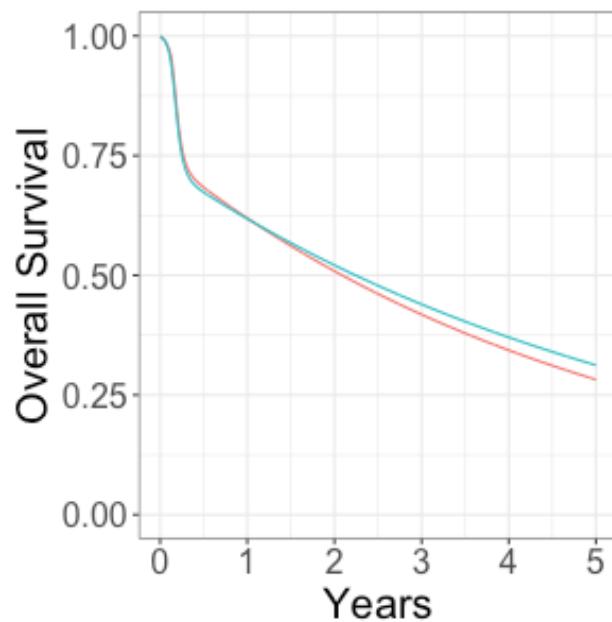
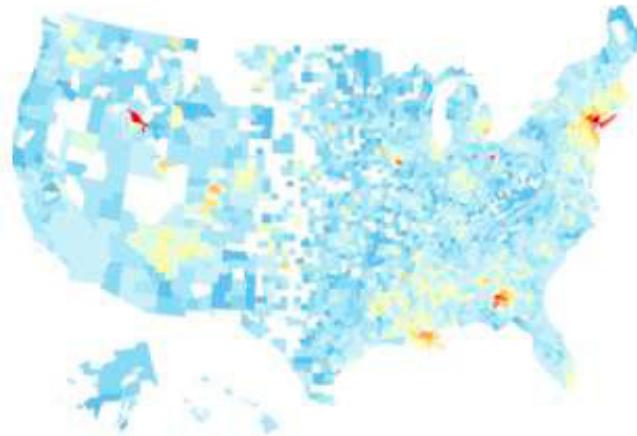
# Heterogeneity in patients



# Heterogeneity by location



# What is going on with lung?



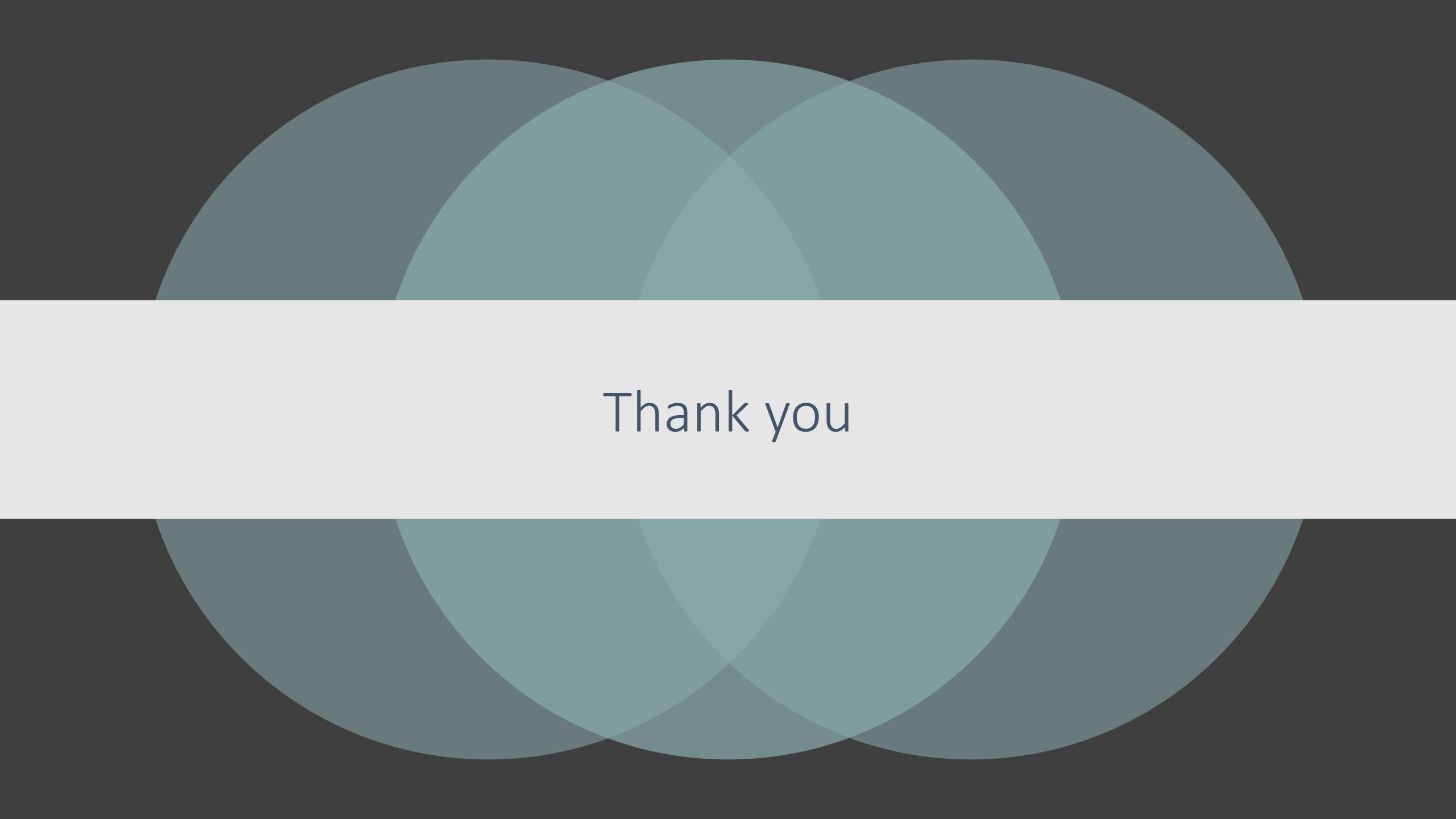
# Next Steps

Update estimates of overall survival by age. Currently, over estimate survival for elderly patients

Update model for delay of treatment HR to better account for age.

Improve SIR model to automatically incorporate historical trends, individual actions, community social distancing measures, and randomness

Attempt to account for uncertainty in estimates and develop method to estimate confidence intervals

The background of the slide features a dark gray gradient. Overlaid on this are four large, semi-transparent teal circles. Two circles are positioned horizontally near the top edge, and two are positioned horizontally near the bottom edge, creating a symmetrical, layered effect.

Thank you

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