Sleep Apnea and Bone Marrow Transplant Recovery

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1.
Context and Hypotheses

Context

- Sleep apnea (SA) - est 26% prevalence in 30-70 y/o
  - Negatively impacts the immune system
- Bone Marrow Transplant - common cancer treatment
- Mouse model suggests mimicking SA increases cancer susceptibility / progression

Questions

- Do the earlier results (from mice model) generalize to humans?
- Does SA or its risk factors worsen recovery?
- What metrics should we use to quantify immune system recovery?
- How do we work with censored and incomplete data?

Hypotheses

- SA + risk factors are related to:
  - longer hospital stay
  - slower immune recovery
  - decreased survival post-surgery
- Risk factors = obesity, diabetes, hypertension, age

2.
Data & Methods

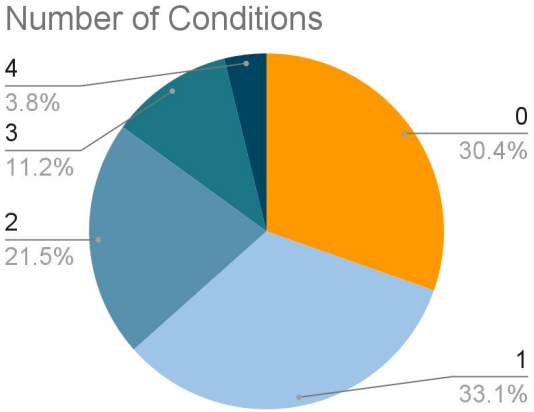
Electronic medical record (EMR)

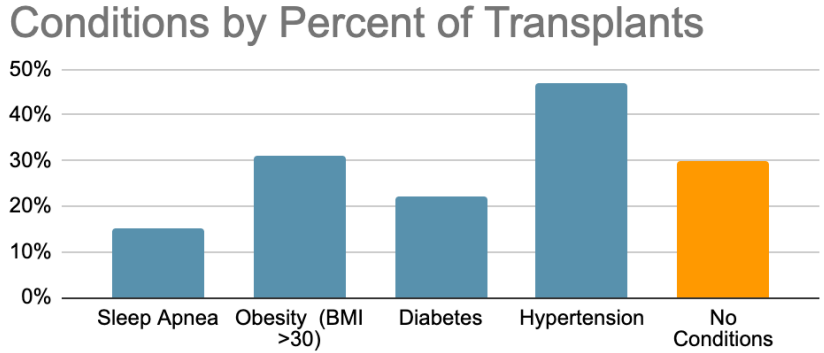
- Source: BMT records at UIowa Hospital (2015-2021)
- 599 transplants on 510 unique patients
- Key feature of EMR data:
  - Not collected for research purposes
  - Diabetes, Sleep Apnea, Hypertension: ICD-10 codes
  - Obesity: Patient vitals

Cohort Demographics

Characteristic	N (%)
Deaths	**153 (30%)**
Hospital Deaths	**19 (3%)**
Gender (Male)	**365 (61%)**

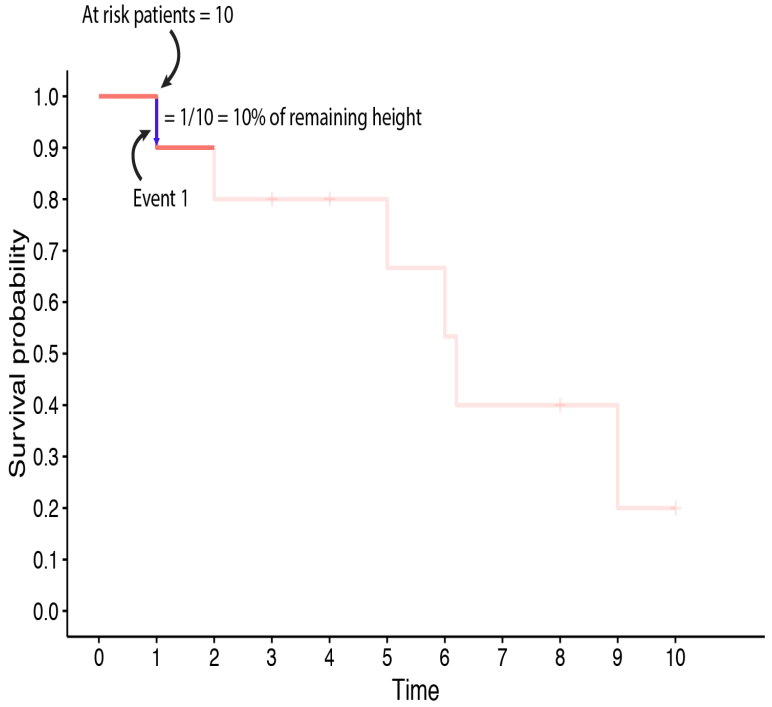
Characteristic	Mean (Range)
Age	**57 (18-79)**
BMI	**29 (16-50)**





Time to Event Analysis

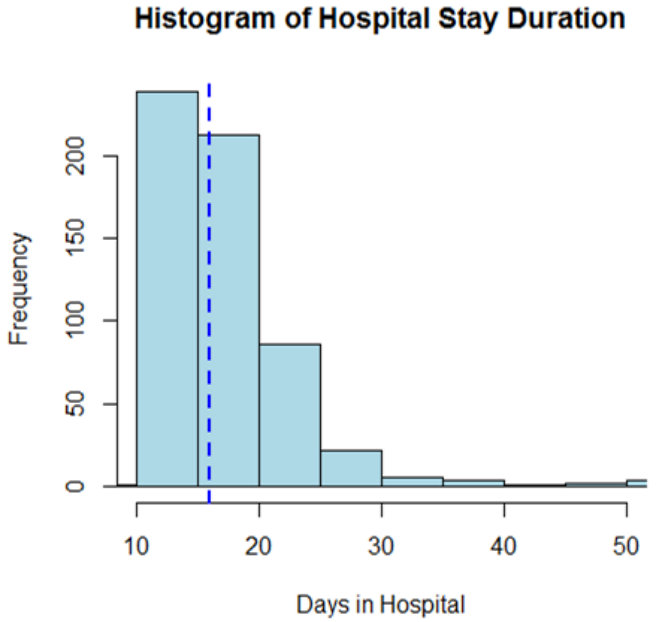
- Time to death (survival)
  - Handle partial information
  - Can estimate median time
- Time to hospital discharge
- Censoring = died in the hospital
  - T-test would be misleading (Dying is the fastest way out of a hospital)



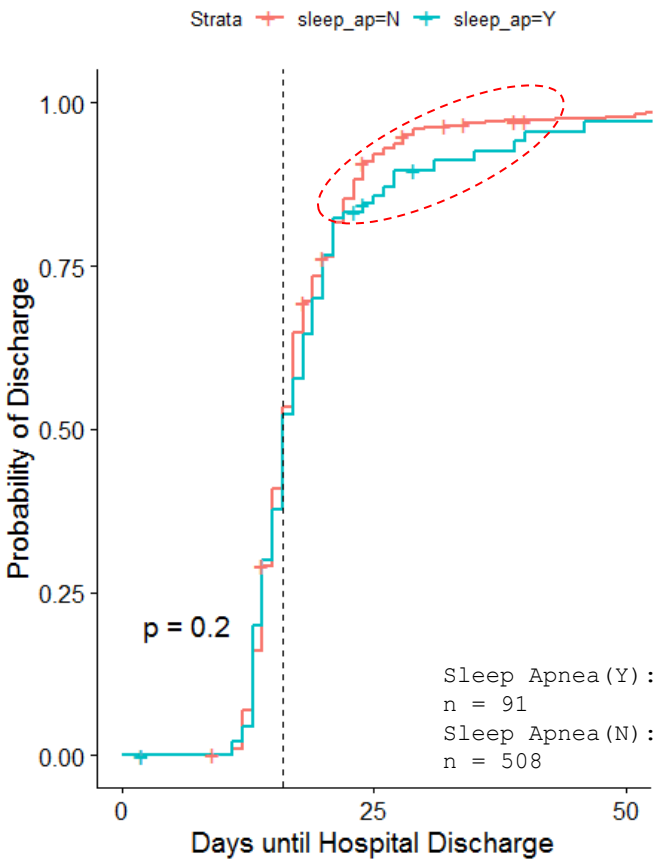
3.
Results

Distribution of Hospital Stay Duration

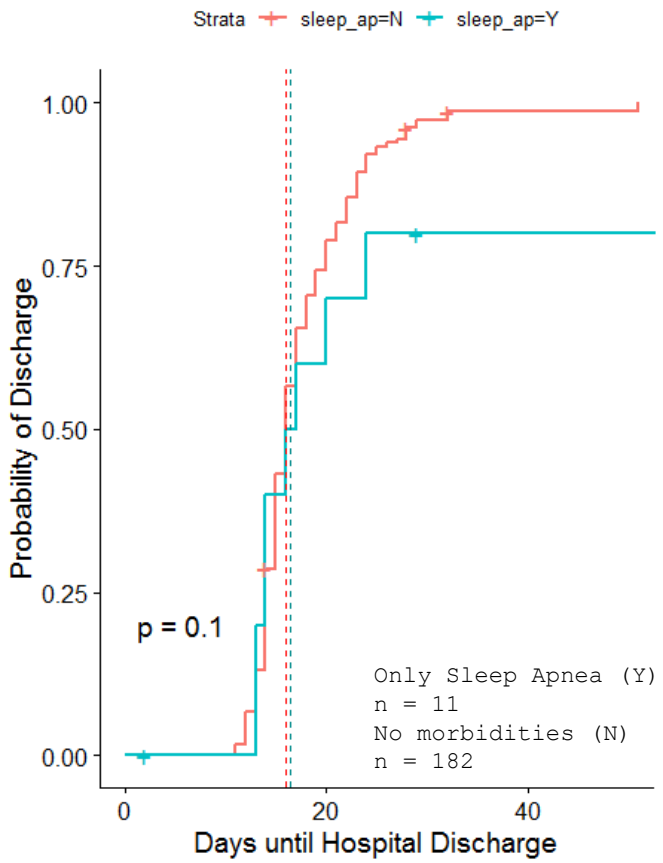
- “Long” hospital stay appears to be rare outcome
  - Range: 10 - 91 days
  - Overall median ≈ 16 days
  - Hospital stay ≥ 20 days: 158 (26%)
  - Hospital stay ≥ 25 days: 56 (9%)
  - Hospital stay ≥ 30 days: 26 (4%)



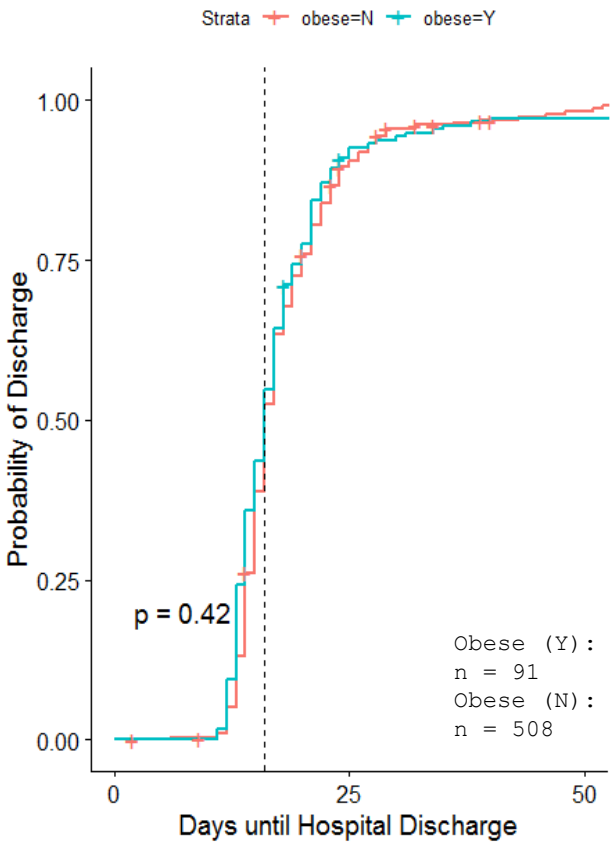
Sleep Apnea



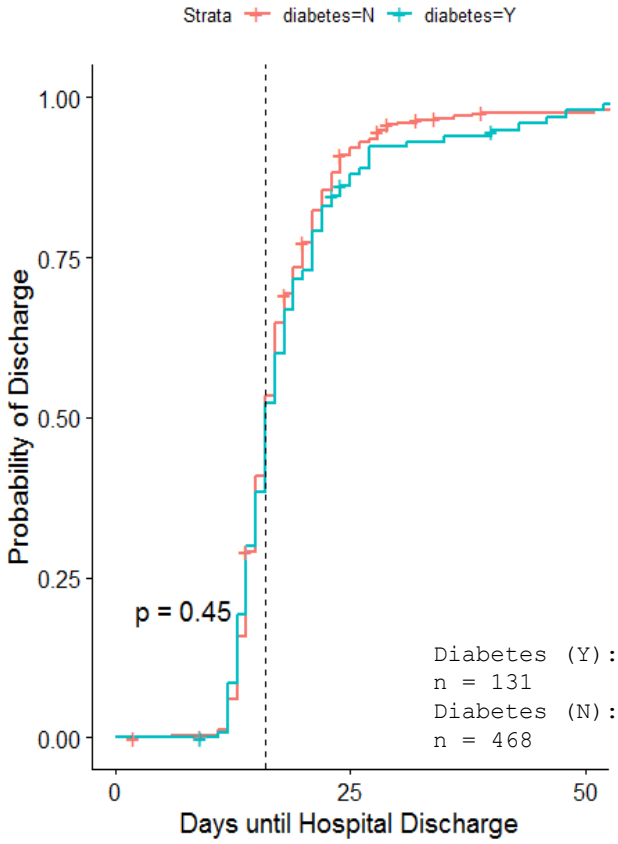
Sleep Apnea vs. No SA Risk Factors



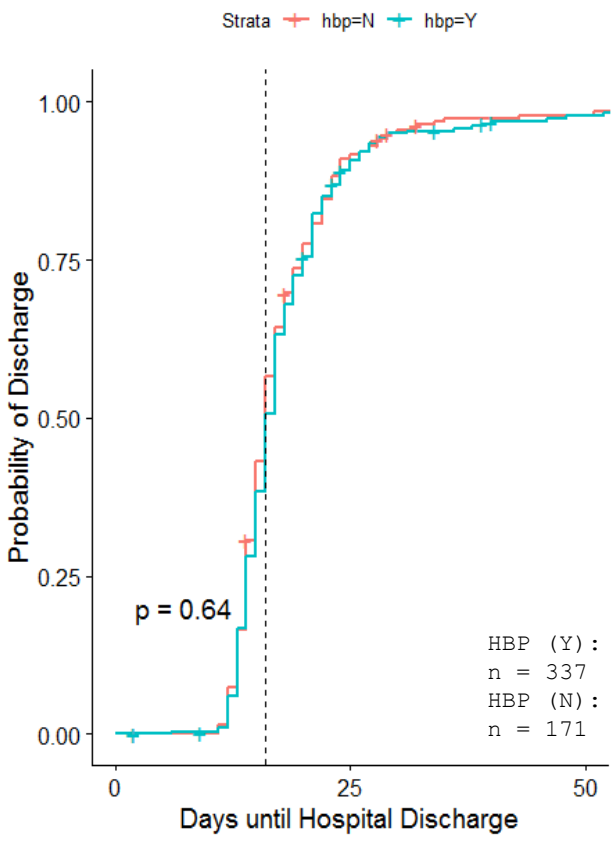
Obesity



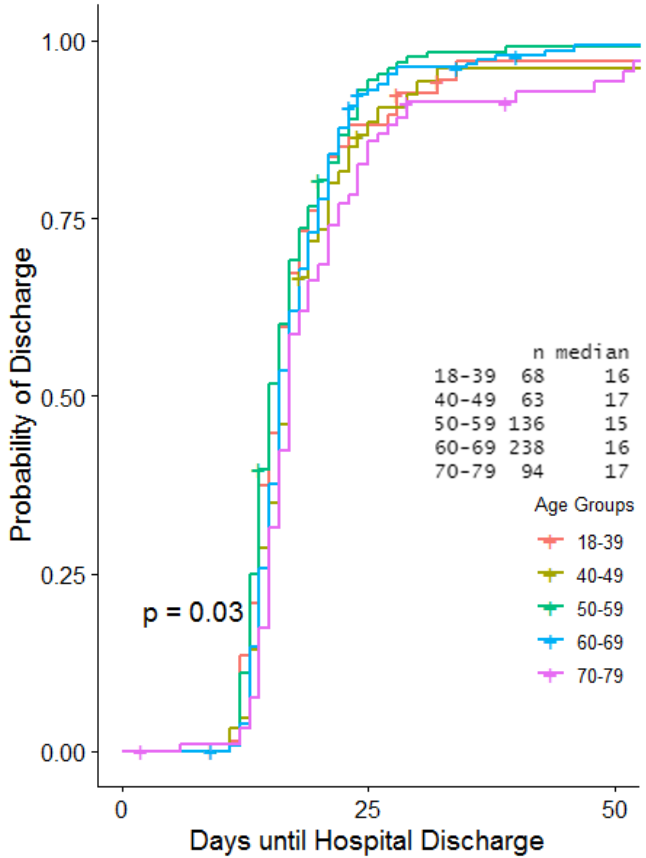
Diabetes



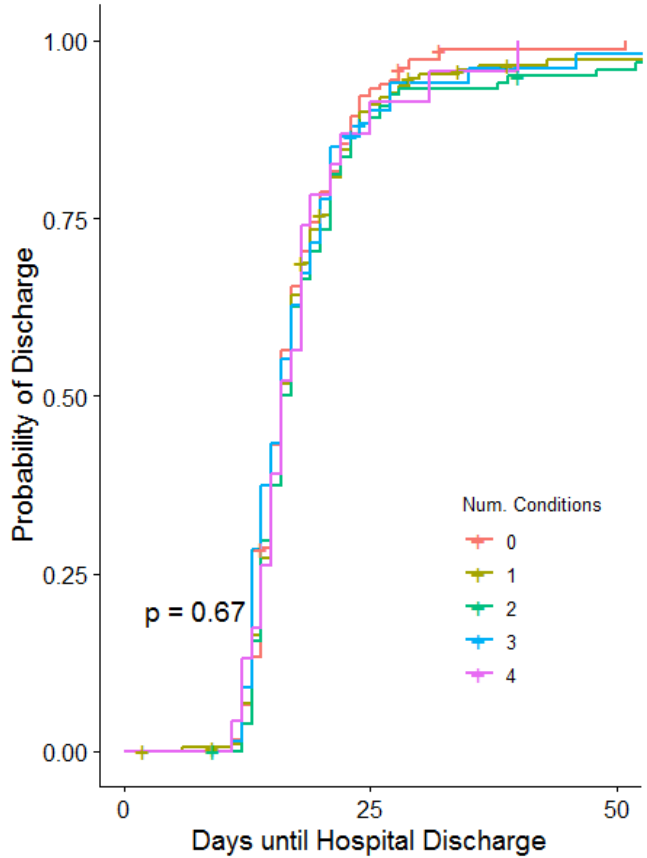
Hypertension



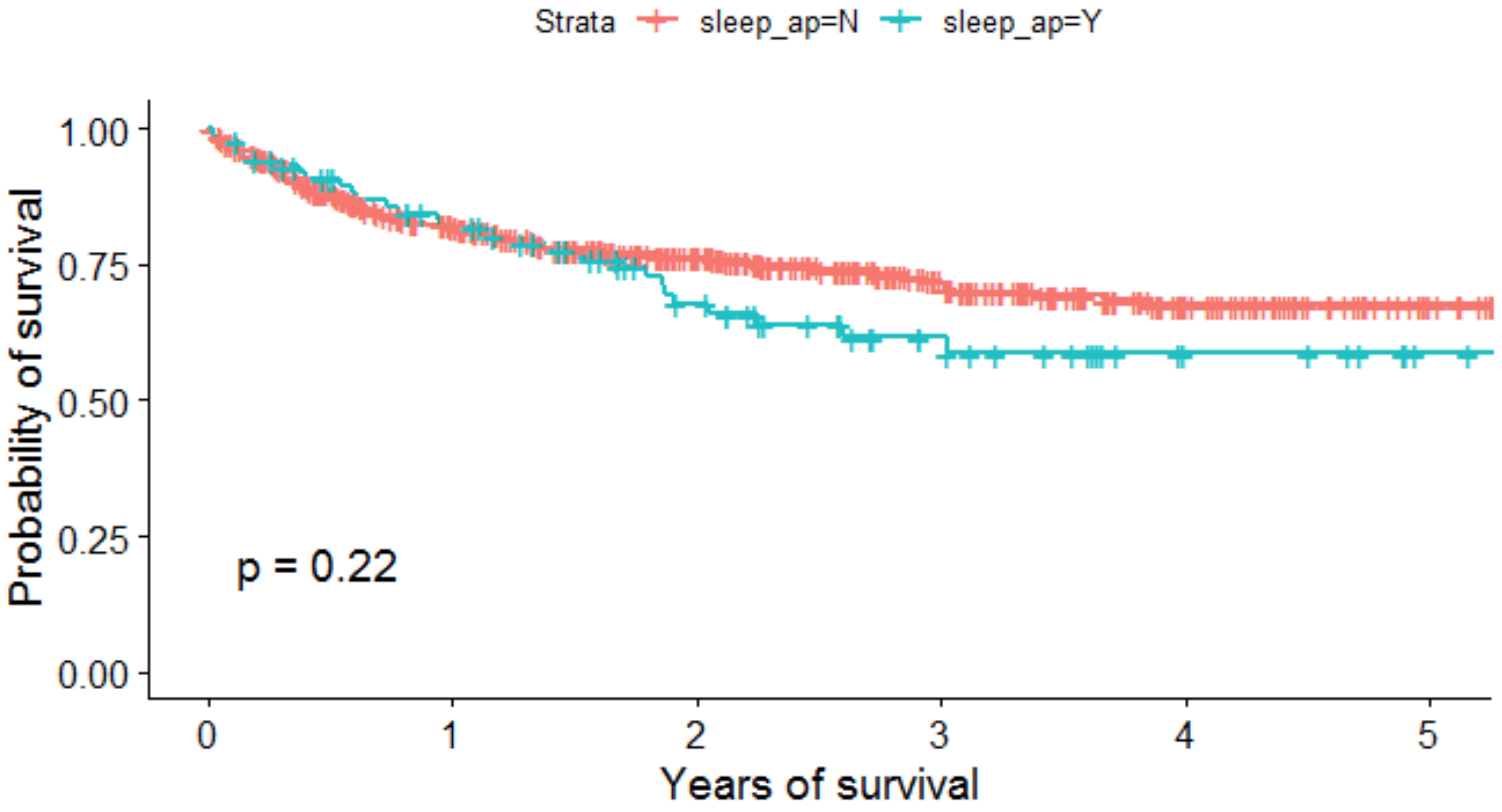
Age

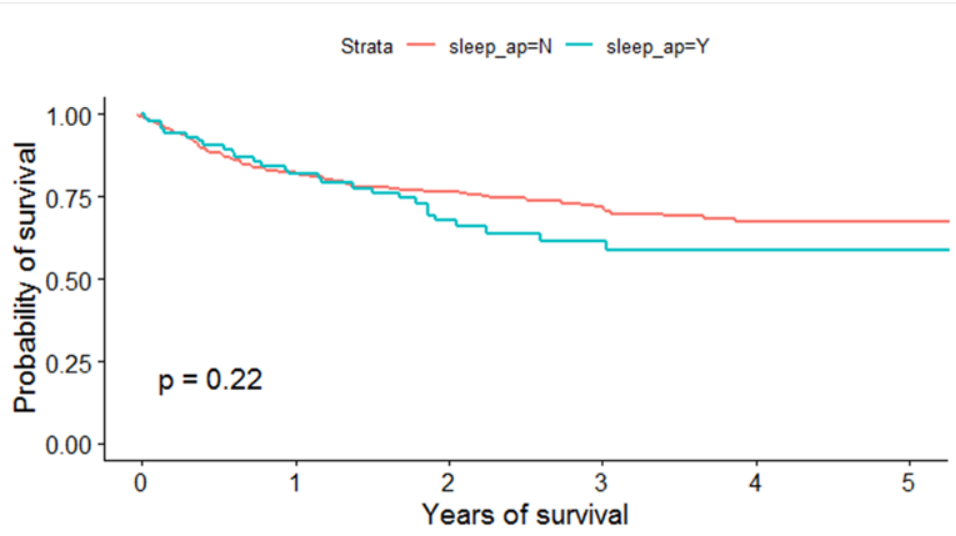


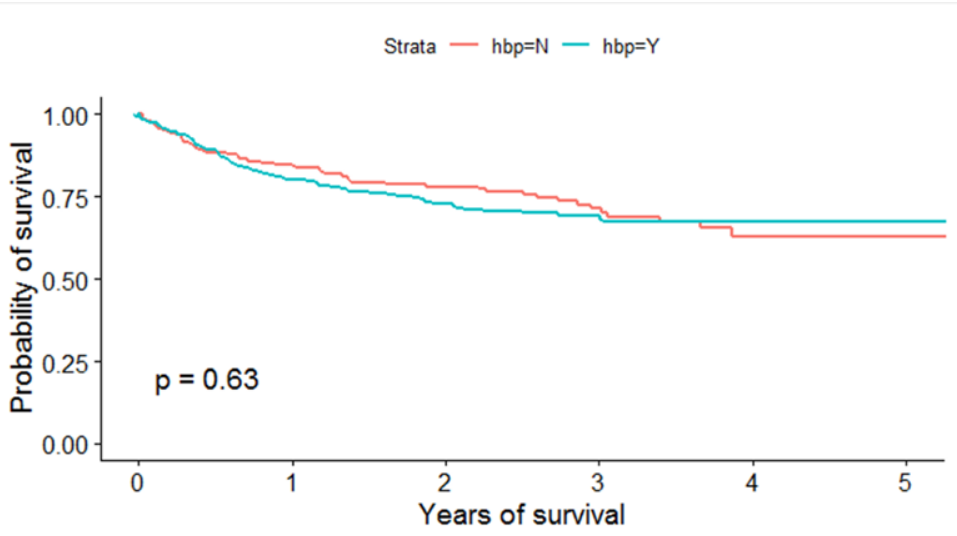
Number of Conditions



Sleep Apnea


Strata
sleep_ap=N
sleep_ap=Y
Probability of survival
1.00
0.75
0.50
0.25
0.00
p = 0.22
0
1
2
3
4
5
Years of survival


Strata sleep_ap=N sleep_ap=Y
Probability of survival
1.00
0.75
0.50
0.25
0.00
p = 0.22
0
1
2
3
4
5
Years of survival


Strata hbp=N hbp=Y
Probability of survival
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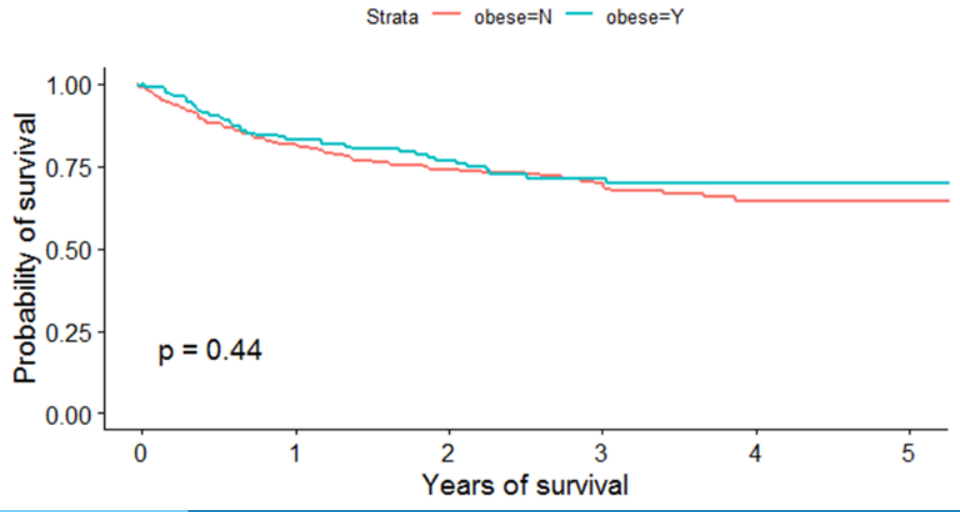
0.75
0.50
0.25
0.00
p = 0.63
0
1
2
3
4
5
Years of survival


Strata obese=N obese=Y
Probability of survival
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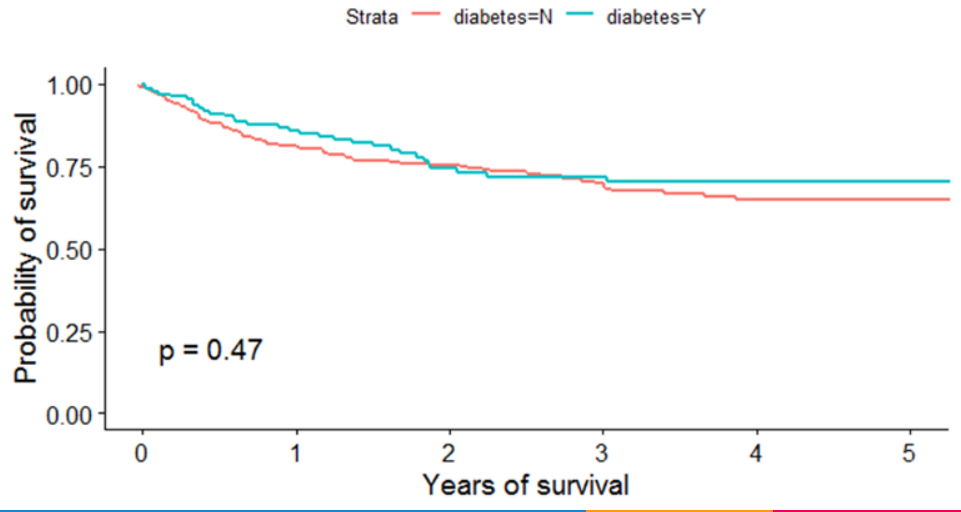
0.75
0.50
0.25
0.00
p = 0.44
0
1
2
3
4
5
Years of survival


Strata diabetes=N diabetes=Y
Probability of survival
1.00
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0.50
0.25
0.00
p = 0.47
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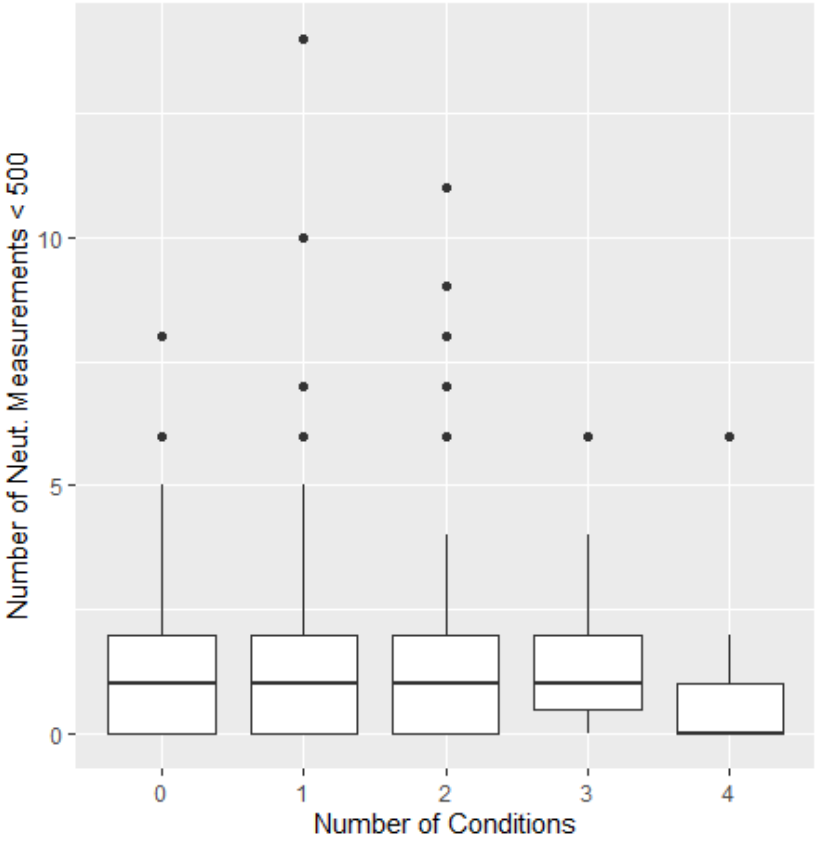
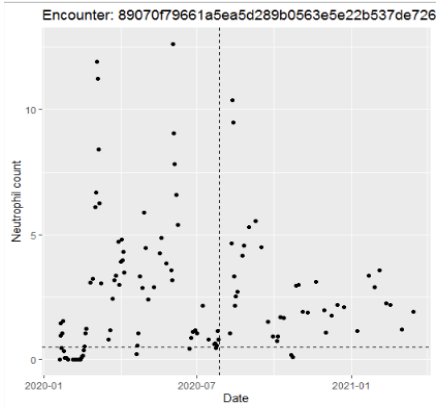
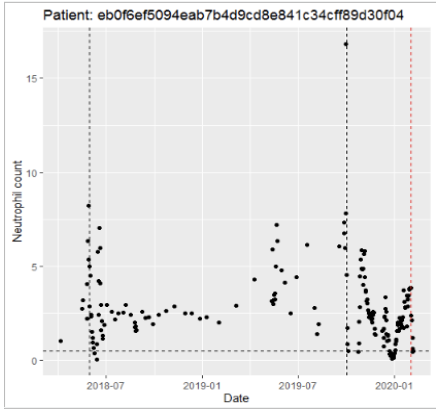
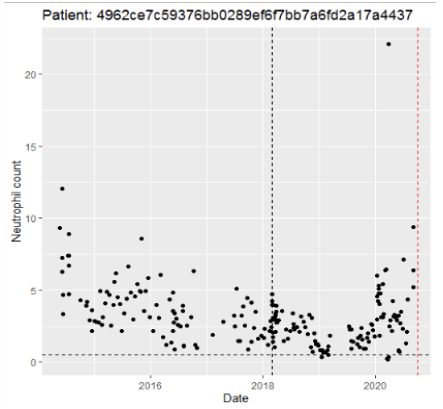
1
2
3
4
5
Years of survival

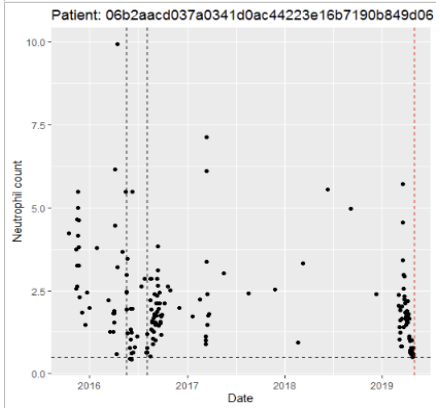
Neutrophil Counts







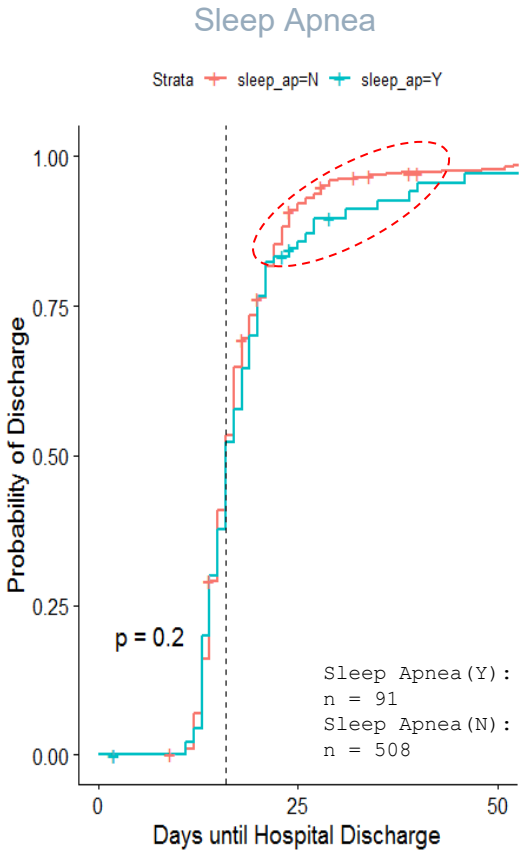




4. Conclusions

Conclusions

- No significant evidence of relationship between morbidities, hospital stay length, or low neut counts
- Suggestive association with sleep apnea
  - Sleep Apnea underdiagnosed
  - Lack power to detect rare outcomes
- Hospital stay- imperfect proxy for recovery
  - Hospitals aim to minimize inpatient stay
- Difficult to interpret number of low neutrophil count measurements



Implications for Clinical Assumptions

- Neut Count < 500 cells/mm^3 is a somewhat extreme outcome
  - Pre/post transfusion neut counts coded together
- Similar median hospital stay regardless of condition or number of comorbidities
  - Potentially make transplant criteria more inclusive

Future research:

- Investigate commonalities in cases of hospital stay > 20 days
- Explore different outcome metrics

National Heart, Lung, and Blood Institute

Thank you to

ISIB

The NIH- grant # HL-147231

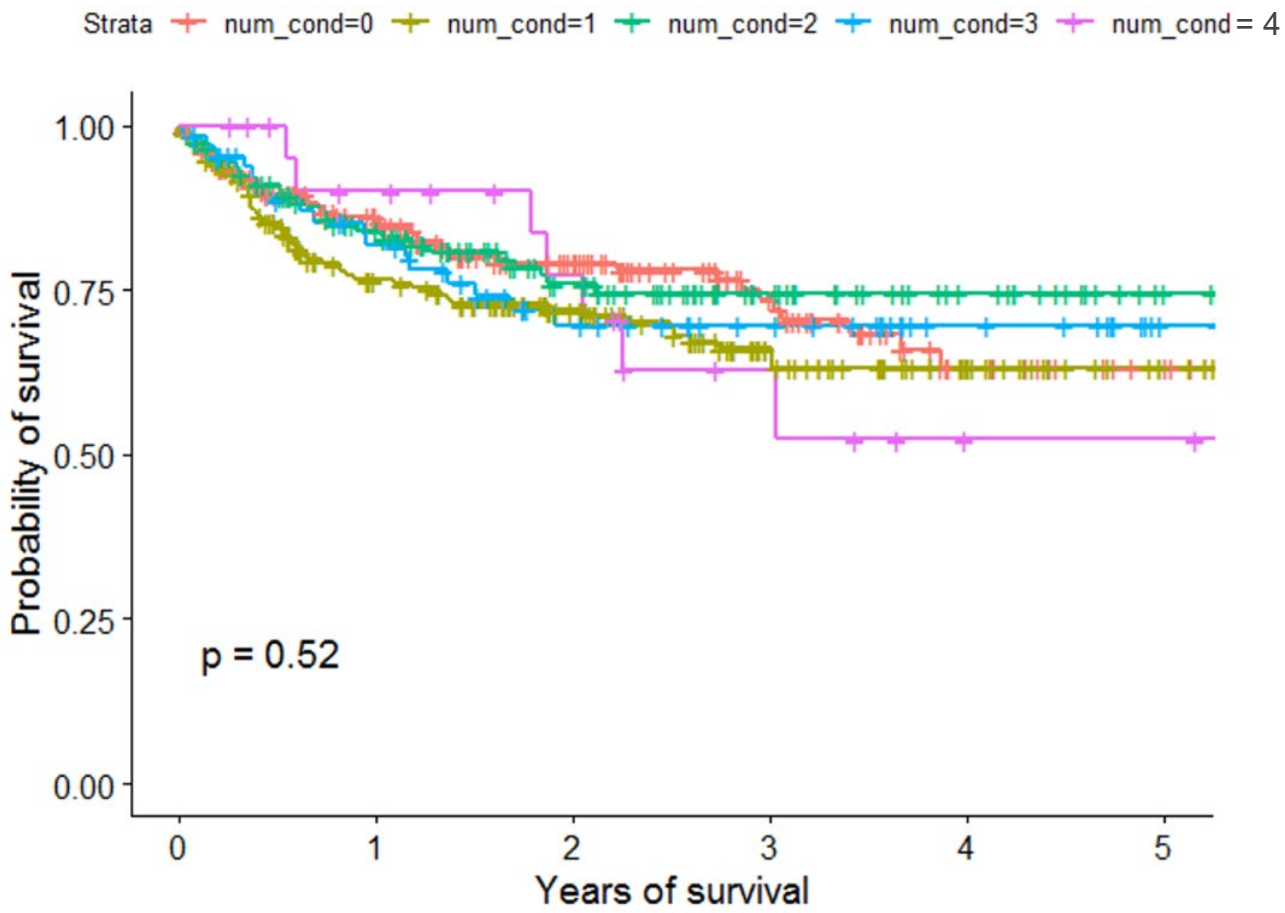
Melissa Bates PhD

And our fearless leader

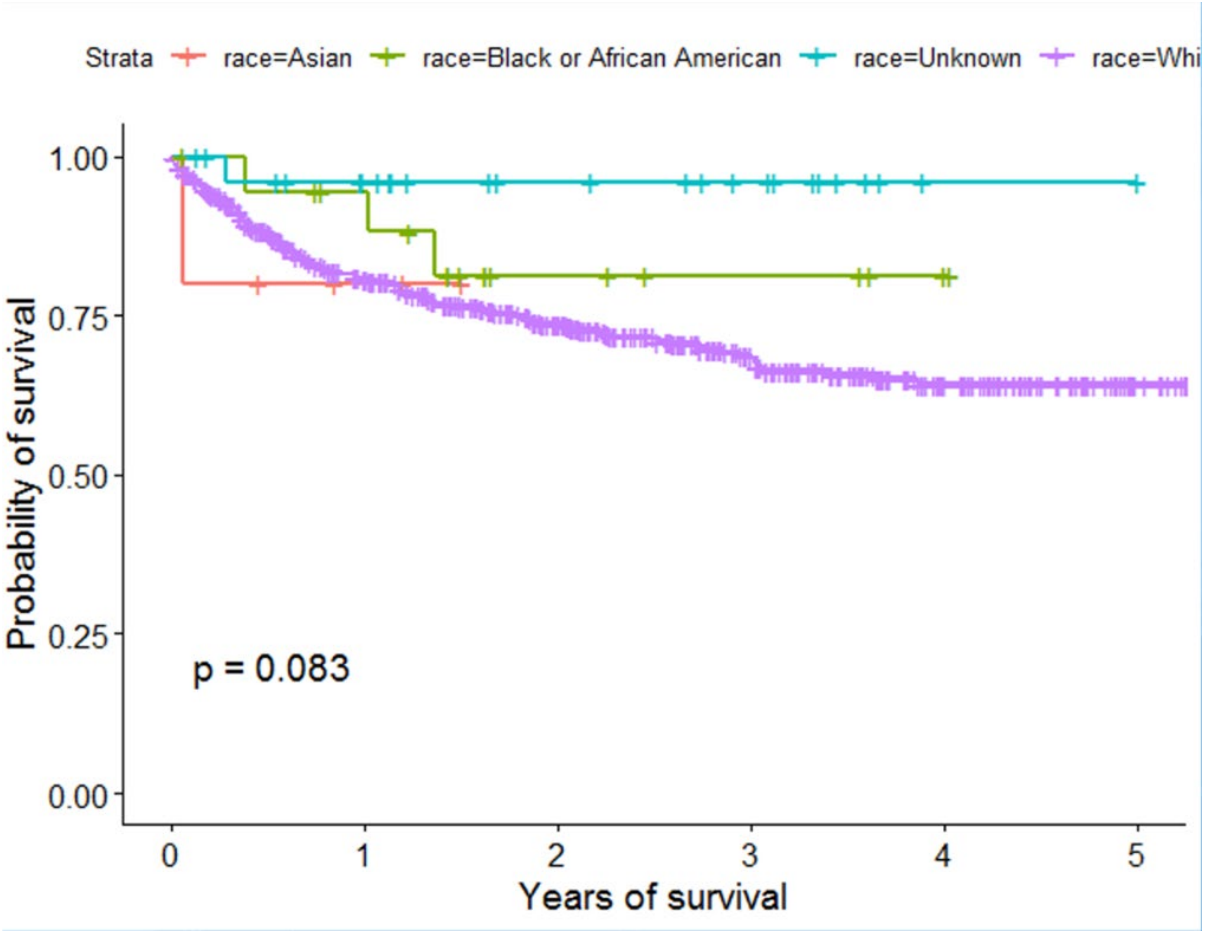
Patrick Breheny PhD

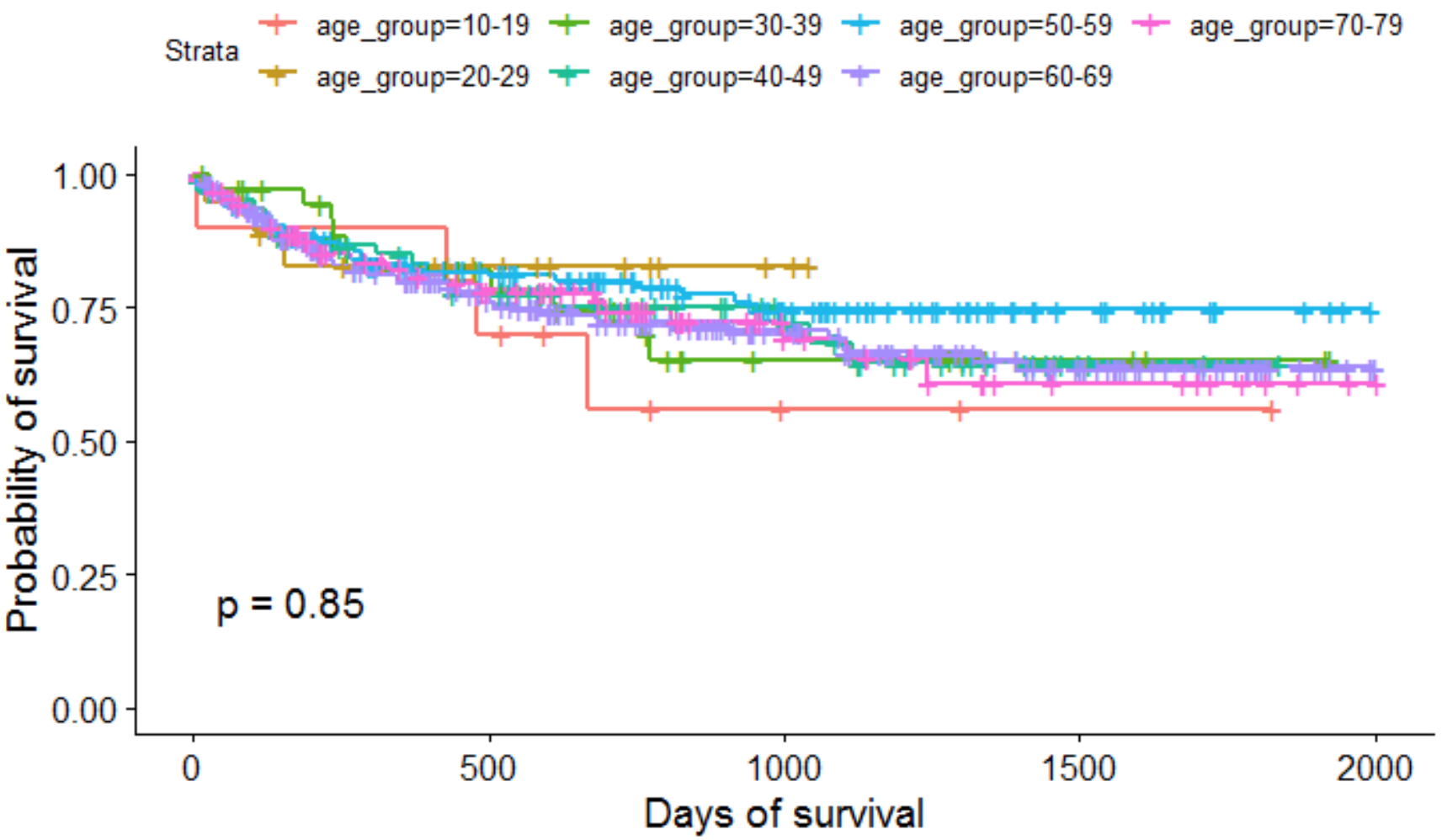
...Questions?

Supplemental Number of Conditions



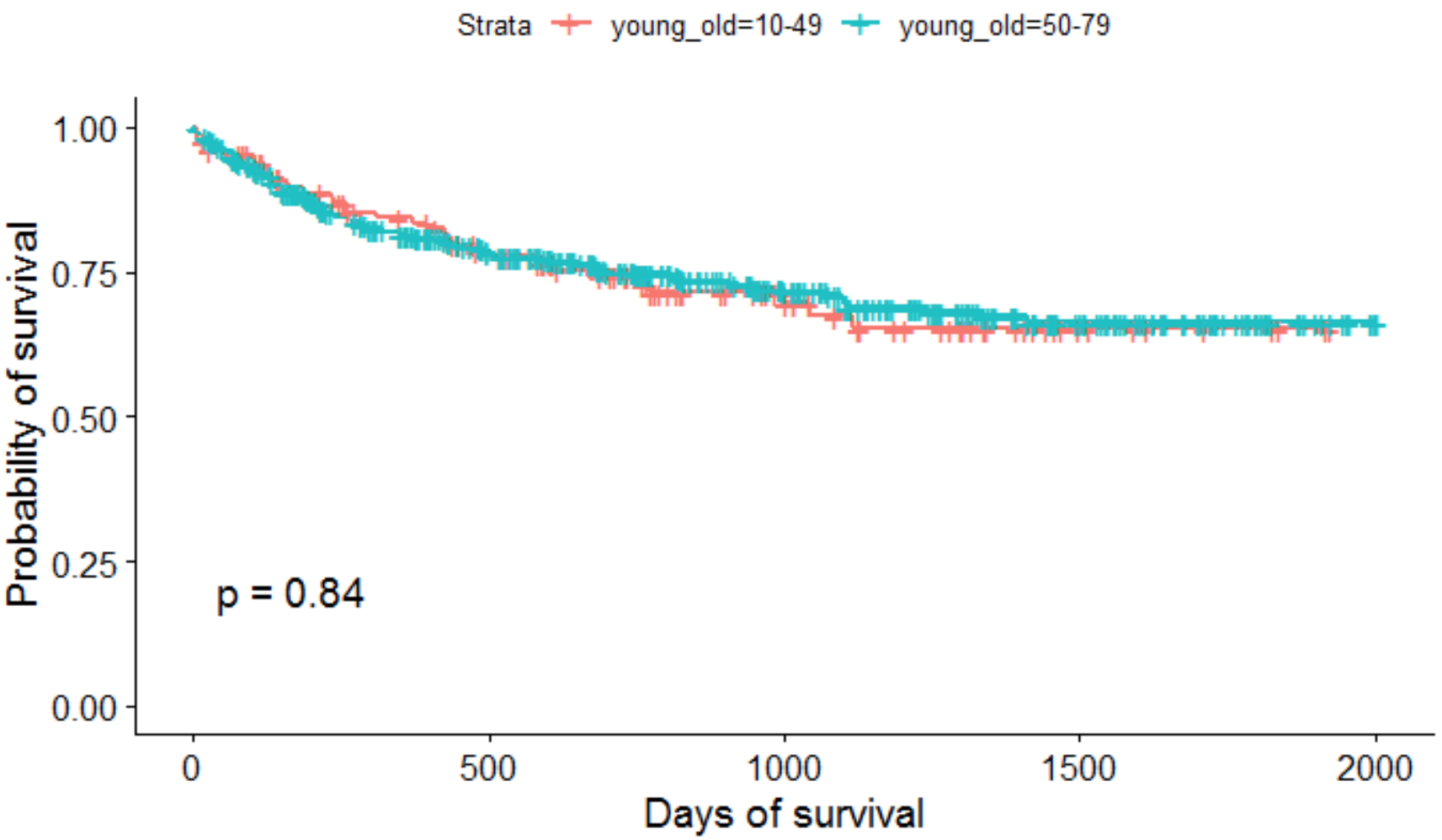
Supplemental Race




Strata
age_group=10-19
age_group=20-29
age_group=30-39
age_group=40-49
age_group=50-59
age_group=60-69
age_group=70-79
Probability of survival
1.00
0.75
0.50
0.25
0.00
p = 0.85
0
500
1000
1500
2000
Days of survival

Supplemental Outcomes + Clinical Assumptions

- Hospital stays: well-documented in EMR
  - Proxy for time to immune system recovery
- Low neutrophil count concentration (< 500 cells/mm^3) is a reliable indicator of poor immune system recovery.
  - <500 is severe and should not be discharged
- Comorbidities believed to inhibit immune system recovery post-transplant


Strata
young_old=10-49
young_old=50-79
1.00
0.75
0.50
0.25
0.00
Probability of survival
p = 0.84
0
500
1000
1500
2000
Days of survival

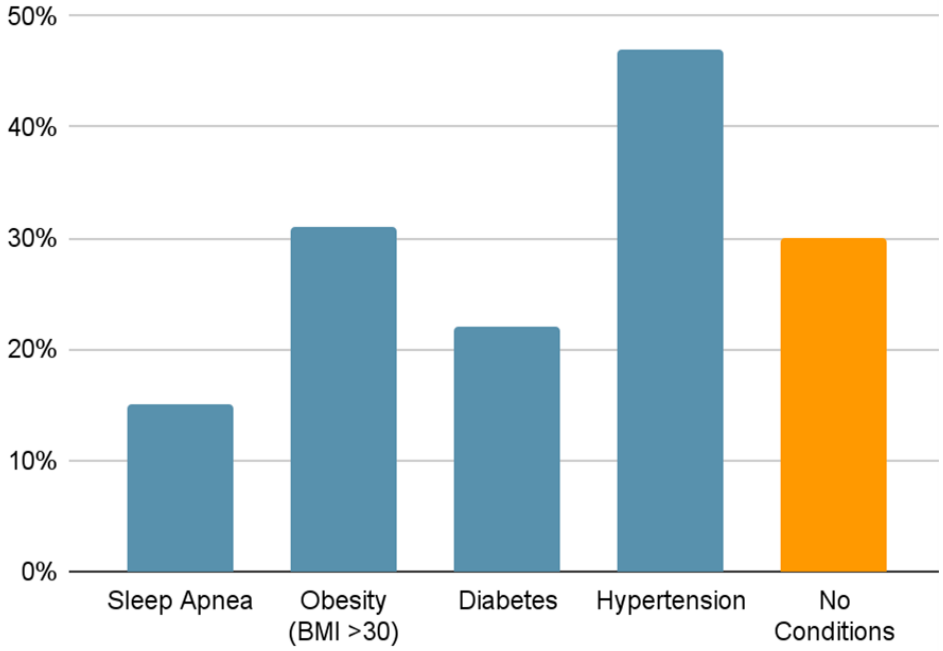
Summary

Condition	% of transplants
Sleep Apnea	15%
Obesity (BMI >30)	31%
Diabetes	22%
Hypertension	47%
No Conditions	30%
Total	n = 599

Number of Conditions	% of transplants
0	182
1	198
2	129
3	67
4	23
Total	n = 599

Summary: Risk Factors

Conditions by Percent of Transplants



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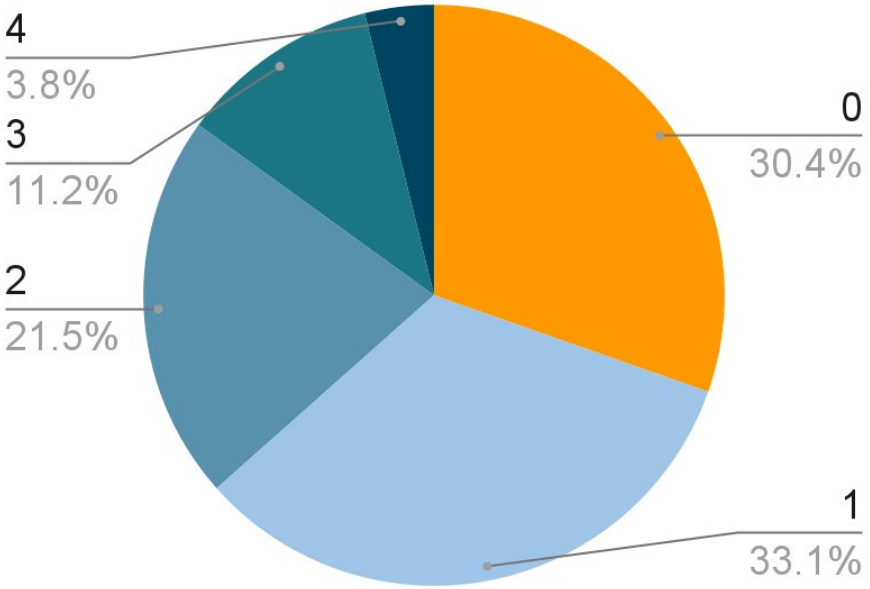
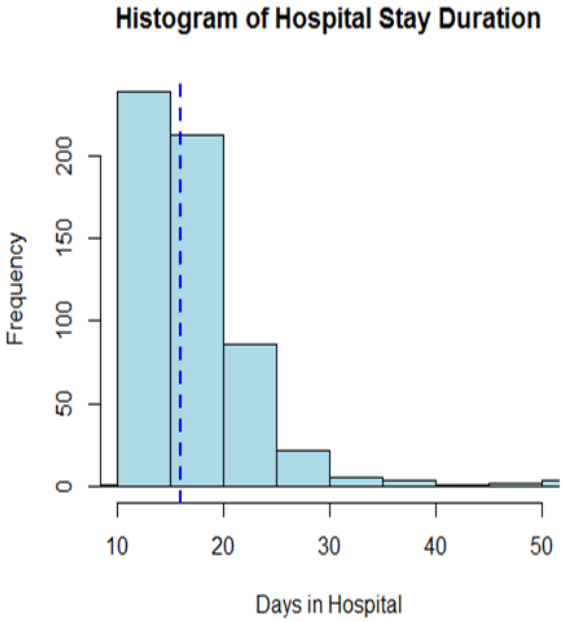


Cohort + Distribution of Hospital Stay

Characteristic	N (%)
Participants	**510**
Transplants	**599**
Deaths	**153**
Hospital Deaths	**19 (3%)**
Gender (Male)	**365 (61%)**

Characteristic	Mean (Range)
Age	**57 (18-79)**
BMI	**29 (16-50)**
Year of transplant	**2015-2021**

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