# N3C Short Course
## *Session 5*

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UNMC COLLEGE OF MEDICINE

# Overview

- Data Preparation Requirements
  - Site Quality Checks
  - Inclusion/Exclusion Criteria
- Study variables
- Data Analysis
- Homework Overview

# Analytic Plan

**This is what we'll be looking at in class today**

**COVID and No Hx of Malnutrition** vs **COVID and Hx of Malnutrition**

**COVID and Hospital-Acquired Malnutrition**

**Covariates**

- Age
- Sex
- Race/Ethnicity
- Charlson Comorbidity Index
- Smoking Status
- Region

**Outcomes**

- Death or Transfer to Hospice (primary)
- Invasive Mechanical Ventilation
- Oxygen Support
- Acute Respiratory Distress Syndrome (ARDS)
- ECMO
- Hospital-acquired pressure injuries

**Inclusion Criteria**

- Age >18
- Positive COVID diagnosis or lab test (PCR, Ag)

**Exclusion Criteria**

- Missing age, gender
- Data partners with low death reporting and no hospitalizations

# Analytic Plan

**This is what you'll be doing for homework!**

**COVID and No Hx of Malnutrition** vs **COVID and Hospital-Acquired Malnutrition**

**Covariates**

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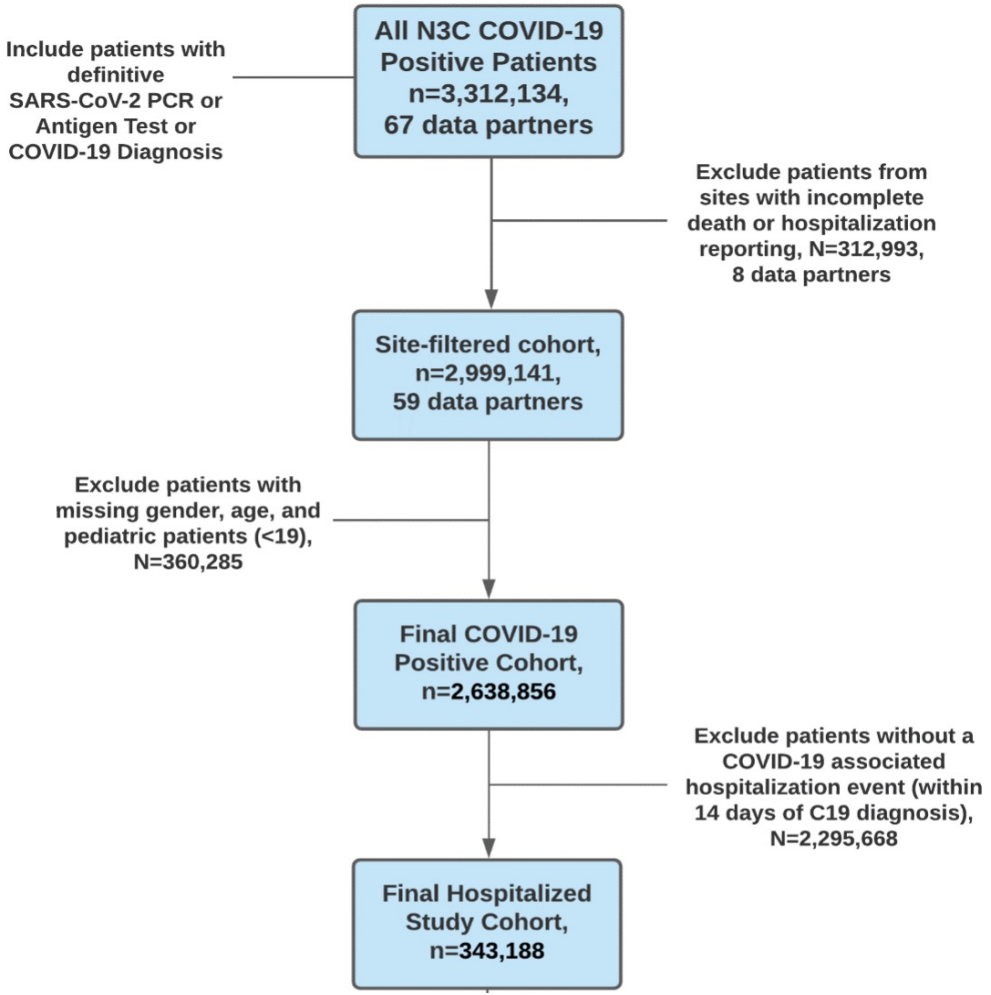
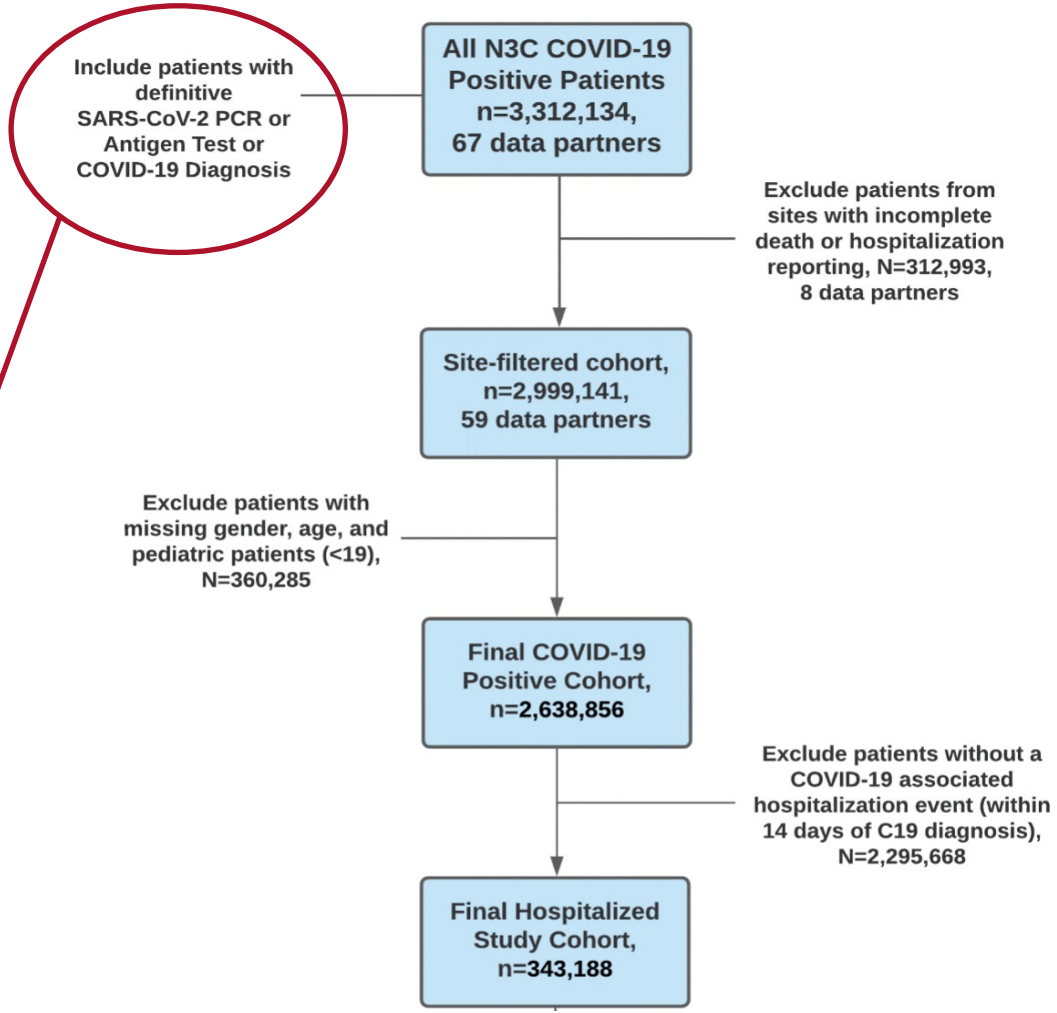
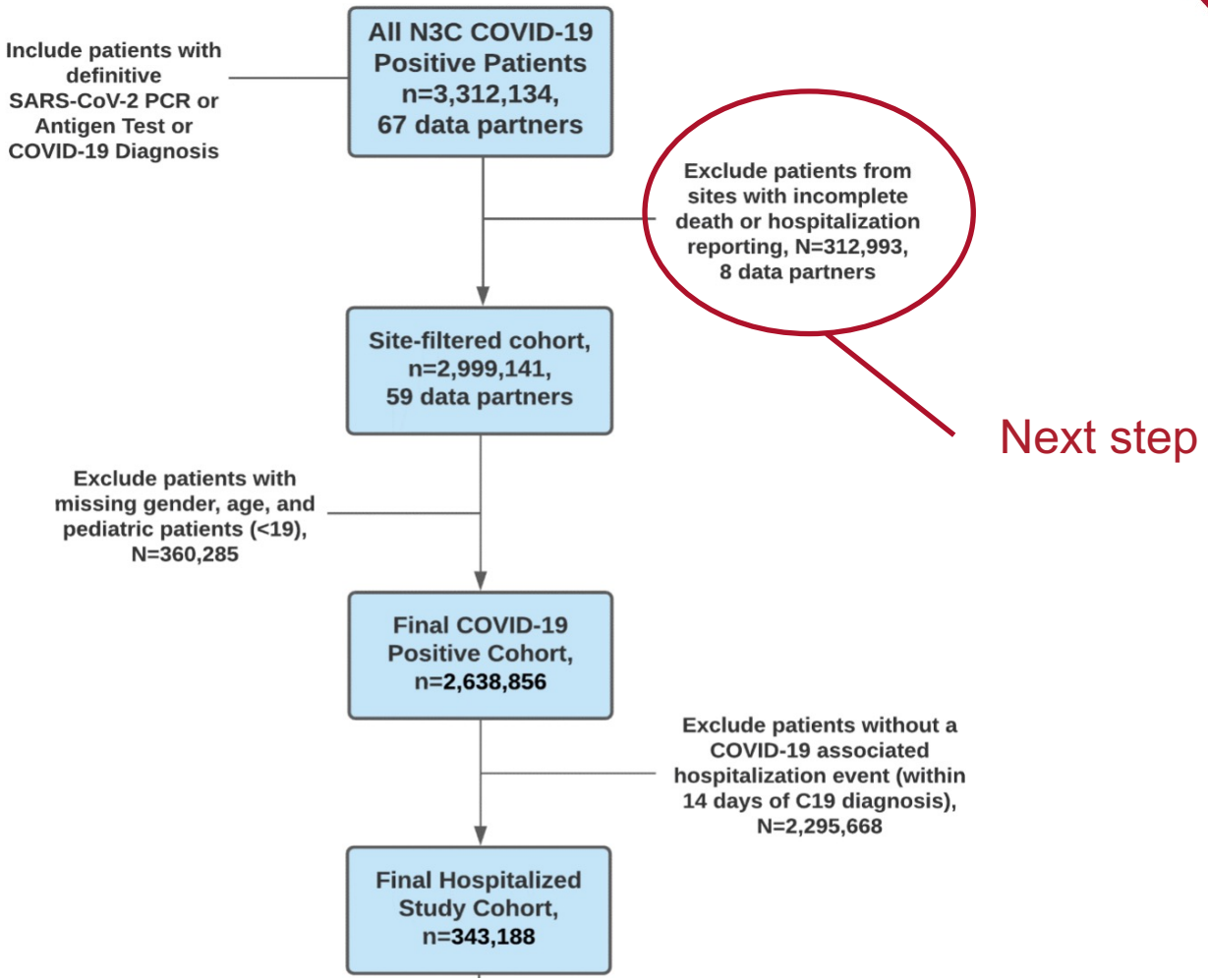
# Data Preparation Requirements


Include patients with definitive SARS-CoV-2 PCR or Antigen Test or COVID-19 Diagnosis
All N3C COVID-19 Positive Patients n=3,312,134, 67 data partners
Exclude patients from sites with incomplete death or hospitalization reporting, N=312,993, 8 data partners
Site-filtered cohort, n=2,999,141, 59 data partners
Exclude patients with missing gender, age, and pediatric patients (<19), N=360,285
Final COVID-19 Positive Cohort, n=2,638,856
Exclude patients without a COVID-19 associated hospitalization event (within 14 days of C19 diagnosis), N=2,295,668
Final Hospitalized Study Cohort, n=343,188

This part is largely taken care of by the LL COVID+ template!

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Final COVID-19 Positive Cohort, n=2,638,856
Exclude patients without a COVID-19 associated hospitalization event (within 14 days of C19 diagnosis), N=2,295,668
Final Hospitalized Study Cohort, n=343,188

Next step

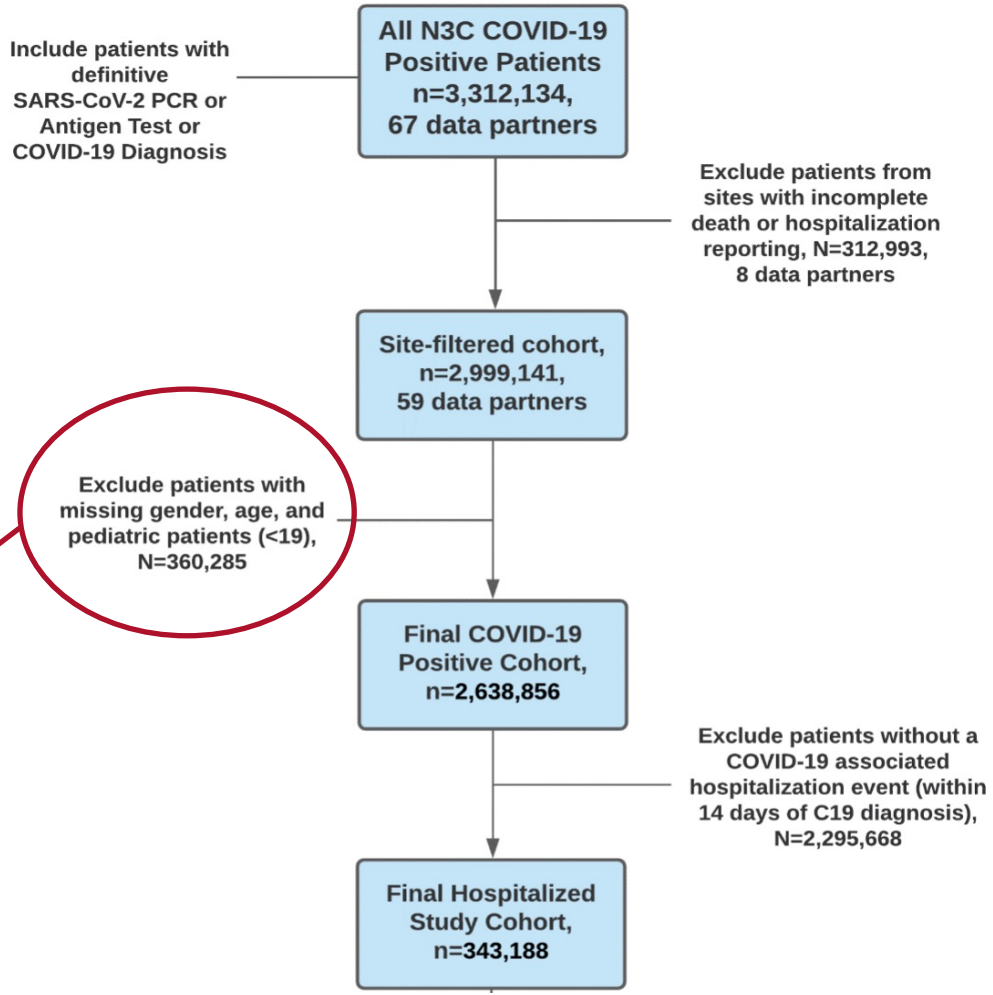
# Site Data Quality Considerations

- We decided to filter sites that had: A) ‘incomplete’ death reporting and B) no hospitalization data

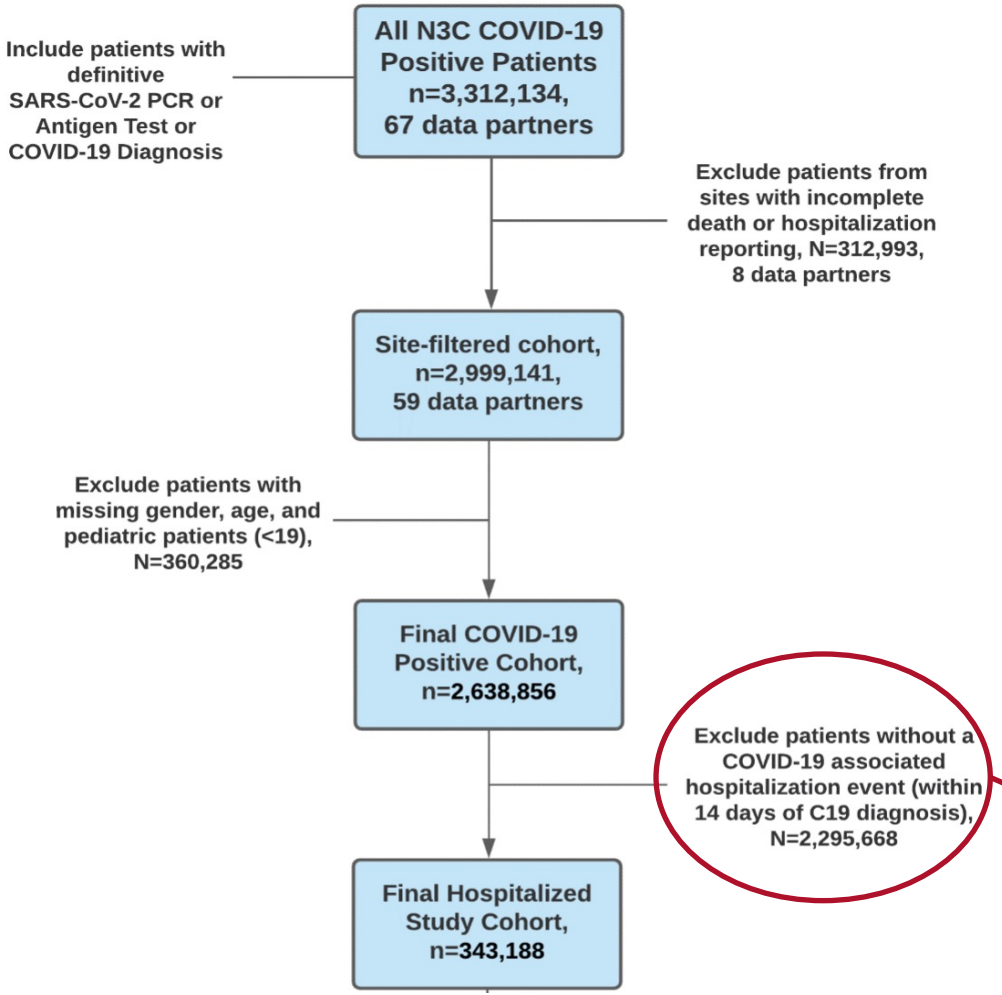
**Exclude patients from sites with incomplete death or hospitalization reporting, N=312,993, 8 data partners**

We set a cutoff of 1 SD below the mean reporting of deaths at the site level. Why this threshold? This seemed as *reasonable* as any other starting point.

# Site Report Cards (link)




This is straightforward and only requires the LL patient-level table




This requires a definition for what we consider a COVID-associated hospitalization.

# Requirements

1. Remove sites with ‘incomplete’ death reporting and sites with no hospitalization events on record.
2. Remove patients with missing sex, age, and pediatric patients (<19 years old).
3. Exclude patients without a hospitalization event documented within 14 days of their COVID-19 diagnosis or positive SARS-CoV-2 PCR or Ag lab test.
4. Bonus! Restrict the patient window to exclude weird positive results (e.g., before the COVID-19 pandemic) and those that are potentially very close to the current date, which may impact the amount of follow-up time available to accurately capture adverse events (this would be easier with the observation_period table, so we have to get creative).

# Inclusion and Exclusion Criteria (link)

# Study Variables

# Analytic Plan – What else?

## Primary Exposure: Malnutrition

**COVID and No Hx of Malnutrition**

**COVID and Hx of Malnutrition**

**COVID and Hospital-Acquired Malnutrition**

**Covariates**

- Age
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**Inclusion Criteria**

- Age > 18
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**Exclusion Criteria**

- Missing age, gender
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DONE

# Analytic Plan – What else?

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DONE

# Study Variables (link)

# Analytic Plan – Anything else??

## Primary Exposure: Malnutrition

**COVID and No Hx of Malnutrition**

**COVID and Hx of Malnutrition**

**COVID and Hospital-Acquired Malnutrition**

**Covariates** DONE

- Age
- Gender
- Race/Ethnicity
- Charlson Comorbidity Index
- Smoking status
- Region

**Outcomes** DONE

- Death or Transfer to Hospice (primary)
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- Acute Respiratory Distress Syndrome (ARDS)
- ECMO
- Hospital-acquired pressure injuries

**Inclusion Criteria** DONE

- Age > 18
- Positive COVID diagnosis or lab test (PCR, Ag)

**Exclusion Criteria**

- Missing age, gender
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# Analytic Plan – Anything else??

## Primary Exposure: Malnutrition

**COVID and No Hx of Malnutrition**

**COVID and Hx of Malnutrition**

**COVID and Hospital-Acquired Malnutrition**

**Covariates**

- Age
- Gender
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- Smoking status
- Region

DONE

**Outcomes**

- Death or Transfer to Hospice (primary)
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DONE

**Inclusion Criteria**

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**Exclusion Criteria**

- Missing age, gender
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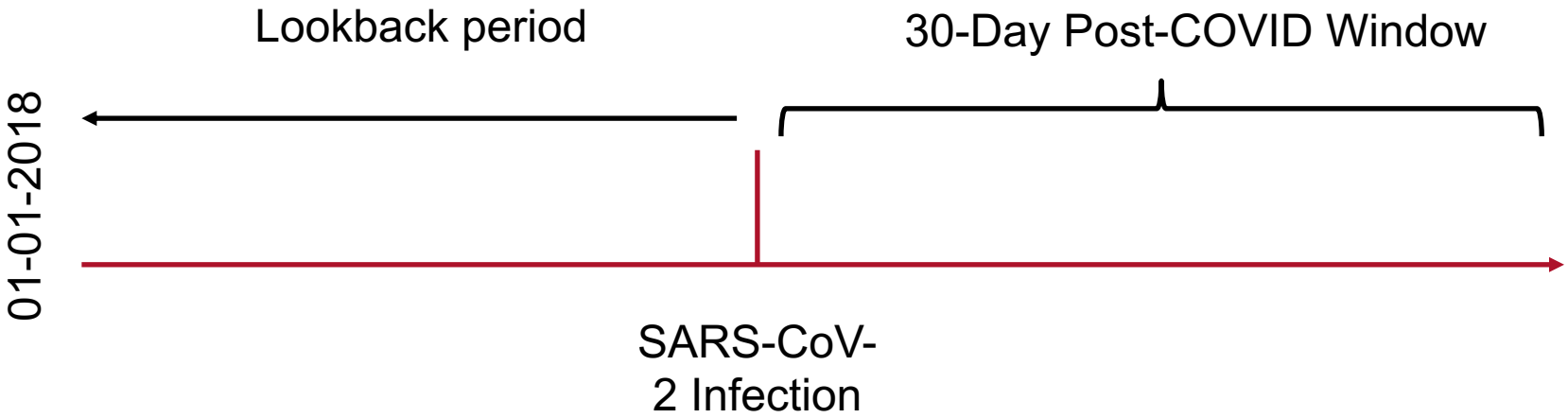
DONE

# Primary Exposure

- We have yet to define our primary exposure, which is malnutrition status before COVID-19 and during the COVID-19 hospitalization event.

# Primary Exposure

- We created mutually exclusive categories based on our malnutrition concept set



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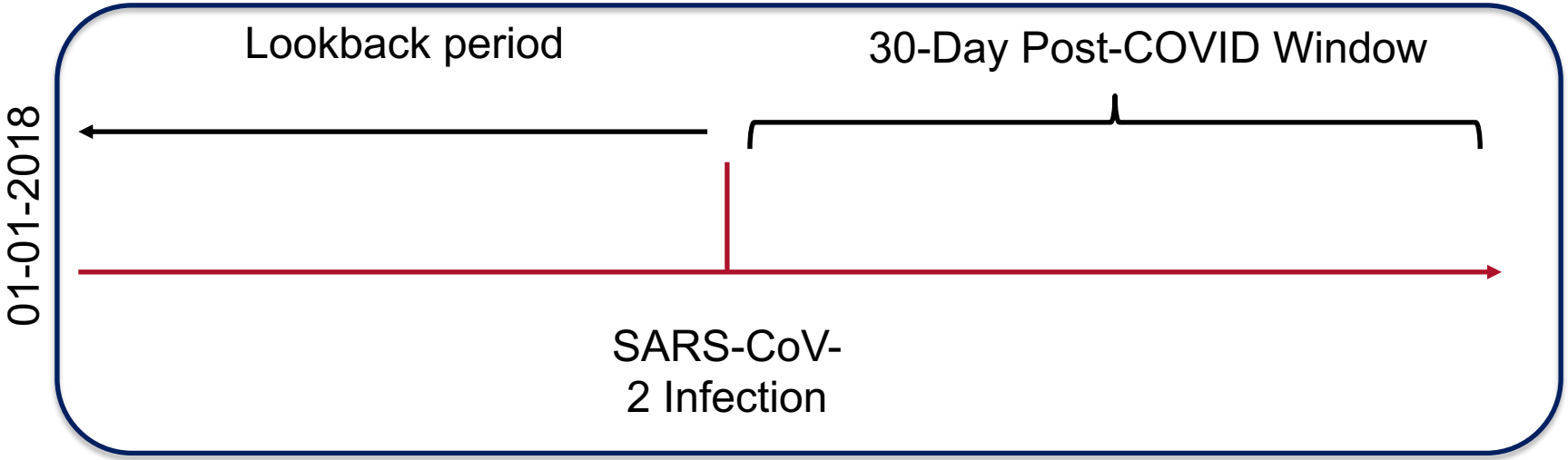
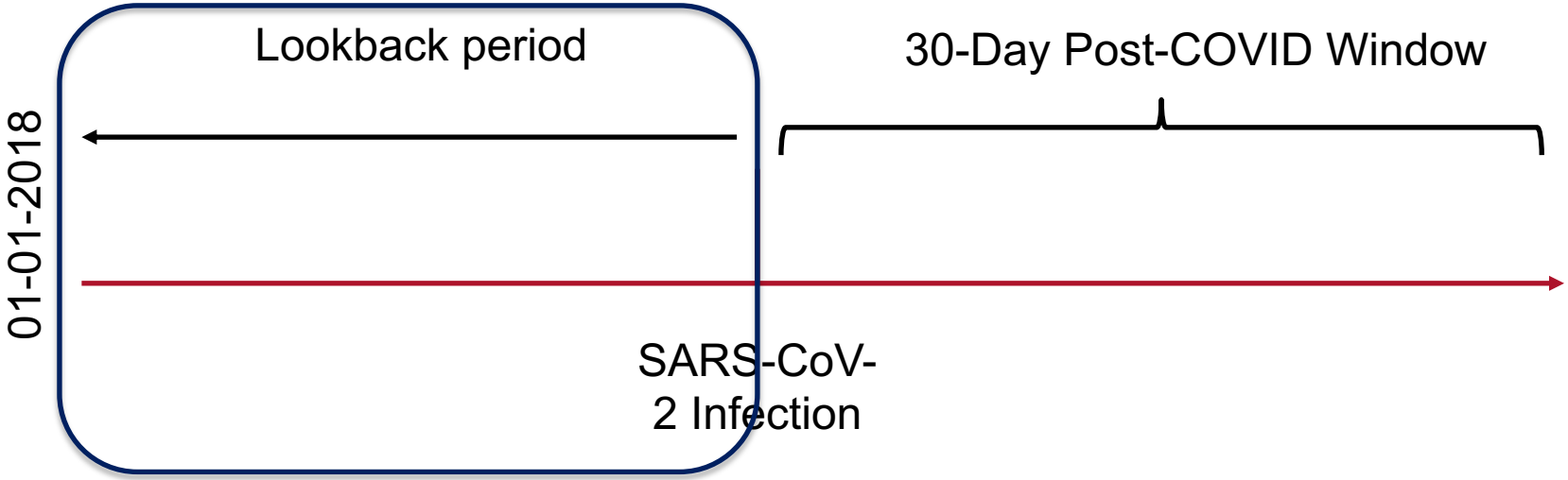



**Group 1: No Malnutrition**

# Primary Exposure

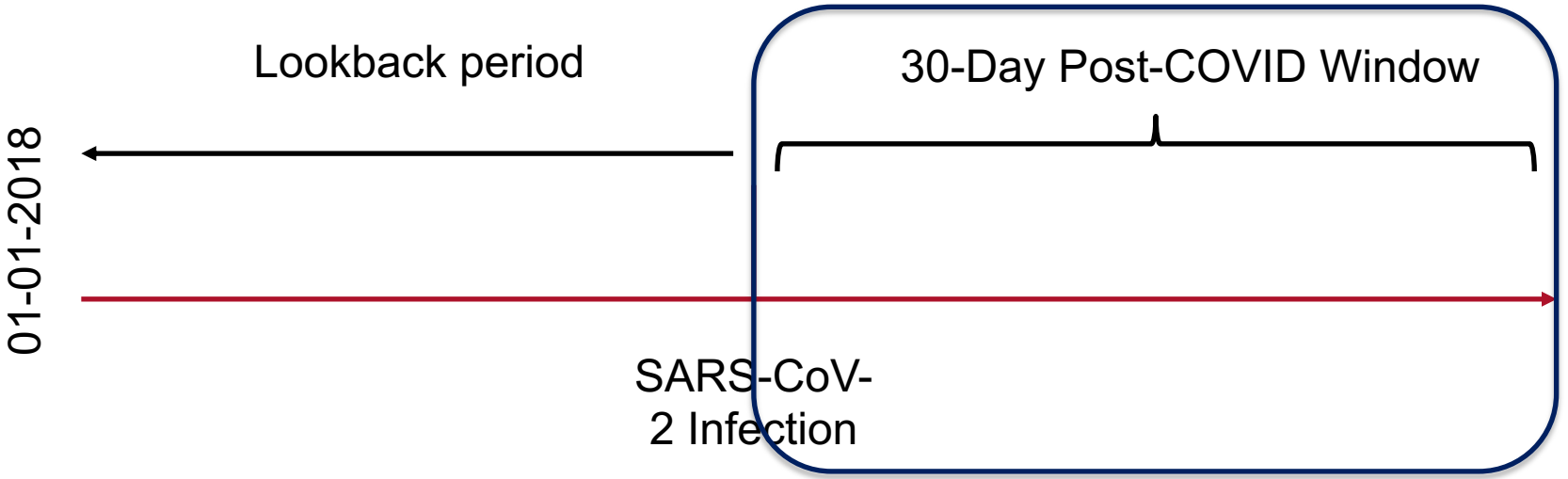
- We created mutually exclusive categories based on our malnutrition concept set




**Group 2: Hx of Malnutrition**

# Primary Exposure

- We created mutually exclusive categories based on our malnutrition concept set




**Group 3: Hospital-Acquired Malnutrition**

# Study Variables (link)

# Data Analysis

# Data Analysis – What now?

## Primary Exposure: Malnutrition

DONE!

**COVID and No Hx of Malnutrition**

**COVID and Hx of Malnutrition**

**COVID and Hospital-Acquired Malnutrition**

### Covariates

DONE

- Age
- Gender
- Race/Ethnicity
- Charlson Comorbidity Index
- Smoking status
- Region

### Outcomes

DONE

- Death or Transfer to Hospice (primary)
- Invasive Mechanical Ventilation
- Oxygen Support
- Acute Respiratory Distress Syndrome (ARDS)
- ECMO
- Hospital-acquired pressure injuries

### Inclusion Criteria

DONE

- Age > 18
- Positive COVID diagnosis or lab test (PCR, Ag)

### Exclusion Criteria

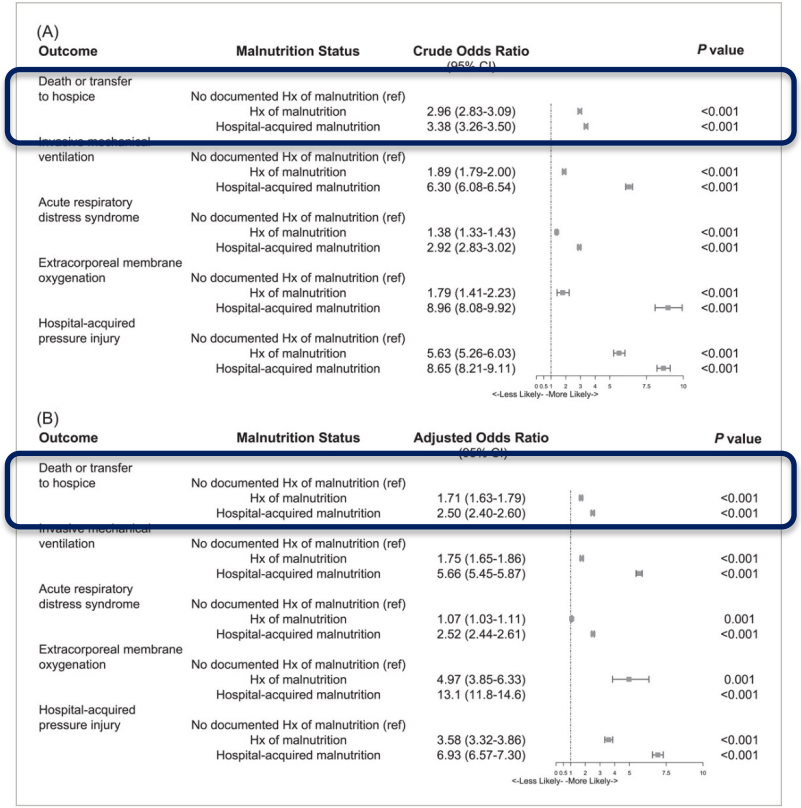
- Missing age, gender
- Data partners with new death reporting and no hospitalizations

# Descriptive Statistics

**Table 1.** Baseline characteristics of patients who were hospitalized and positive for COVID-19, by malnutrition status

| Characteristic | No Hx of malnutrition, *n* = 316,271 [a] | Hx of malnutrition, *n* = 11,206 [a] | HAC malnutrition, *n* = 15,711 [a] | *P* value [b] |
|---|---|---|---|---|
| Age, years | 59 (43–71) | 66 (53–76) | 67 (56, 77) | <0.001 |
| Age group | | | | <0.001 |
| <29 years | 28,389 (9.0%) | 550 (4.9%) | 417 (2.7%) | |
| 30–49 years | 77,091 (24%) | 1692 (15%) | 2065 (13%) | |
| 50–64 years | 89,476 (28%) | 3043 (27%) | 4405 (28%) | |
| >65 years | 121,315 (38%) | 5921 (53%) | 8824 (56%) | |
| Sex | | | | <0.001 |
| Female | 157,830 (50%) | 5493 (49%) | 6396 (41%) | |
| Male | 158,441 (50%) | 5713 (51%) | 9315 (59%) | |

# Logistic Regression



(A)

| Outcome | Malnutrition Status | Crude Odds Ratio (95% CI) | *P* value |
|---|---|---|---|
| Death or transfer to hospice | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 2.96 (2.83-3.09) | <0.001 |
| | Hospital-acquired malnutrition | 3.38 (3.26-3.50) | <0.001 |
| Invasive mechanical ventilation | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.89 (1.79-2.00) | <0.001 |
| | Hospital-acquired malnutrition | 6.30 (6.08-6.54) | <0.001 |
| Acute respiratory distress syndrome | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.38 (1.33-1.43) | <0.001 |
| | Hospital-acquired malnutrition | 2.92 (2.83-3.02) | <0.001 |
| Extracorporeal membrane oxygenation | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.79 (1.41-2.23) | <0.001 |
| | Hospital-acquired malnutrition | 8.96 (8.08-9.92) | <0.001 |
| Hospital-acquired pressure injury | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 5.63 (5.26-6.03) | <0.001 |
| | Hospital-acquired malnutrition | 8.65 (8.21-9.11) | <0.001 |



(B)

| Outcome | Malnutrition Status | Adjusted Odds Ratio (95% CI) | *P* value |
|---|---|---|---|
| Death or transfer to hospice | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.71 (1.63-1.79) | <0.001 |
| | Hospital-acquired malnutrition | 2.50 (2.40-2.60) | <0.001 |
| Invasive mechanical ventilation | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.75 (1.65-1.86) | <0.001 |
| | Hospital-acquired malnutrition | 5.66 (5.45-5.87) | <0.001 |
| Acute respiratory distress syndrome | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 1.07 (1.03-1.11) | 0.001 |
| | Hospital-acquired malnutrition | 2.52 (2.44-2.61) | <0.001 |
| Extracorporeal membrane oxygenation | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 4.97 (3.85-6.33) | 0.001 |
| | Hospital-acquired malnutrition | 13.1 (11.8-14.6) | <0.001 |
| Hospital-acquired pressure injury | No documented Hx of malnutrition (ref) | | |
| | Hx of malnutrition | 3.58 (3.32-3.86) | <0.001 |
| | Hospital-acquired malnutrition | 6.93 (6.57-7.30) | <0.001 |

# Data Analysis (link)

# Homework

# Malnutrition Concept Set

| Concept ID | Concept Name |
|---|---|
| 4123542 | Wasting disease |
| 443082 | Starvation |
| 437832 | Malnutrition of mild degree (Gomez: 75 percent to less than 90 percent of standard weight) |
| 4101278 | Moderate protein energy malnutrition |
| 436078 | Malnutrition of moderate degree (Gomez: 60 percent to less than 75 percent of standard weight) |
| 433163 | Deficiency of macronutrients |
| 4028220 | Malnutrition following gastrointestinal surgery |
| 4098458 | Moderate protein-calorie malnutrition (weight for age 60-74 percent of standard) |
| 4156515 | Malnutrition (calorie) |
| 4276360 | Undernutrition |
| 435227 | Nutritional deficiency disorder |
| 4096196 | Mild protein-calorie malnutrition (weight for age 75-89 percent of standard) |
| 4233565 | Severe protein-calorie malnutrition (Gomez: less than 60 percent of standard weight) |
| 432593 | Kwashiorkor |
| 4029268 | Marasmic kwashiorkor |
| 4337279 | Semi-starvation |

# Malnutrition Concept Set

| Severity | Concept ID | Condition Concept Name |
|---|---|---|
| **Mild Malnutrition** | 437832 | Malnutrition of mild degree (Gomez: 75 percent to less than 90 percent of standard weight) |
| | 4096196 | Mild protein-calorie malnutrition (weight for age 75-89 percent of standard) |
| **Moderate Malnutrition** | 436078 | Malnutrition of moderate degree (Gomez: 60 percent to less than 75 percent of standard weight) |
| | 4101278 | Moderate protein energy malnutrition |
| | 4098458 | Moderate protein-calorie malnutrition (weight for age 60-74 percent of standard) |
| **Severe Malnutrition** | 4233565 | Severe protein-calorie malnutrition (Gomez: less than 60 percent of standard weight) |
| | 4123542 | Wasting disease |
| | 432593 | Kwashiorkor |
| | 4029268 | Marasmic kwashiorkor |
| **General Malnutrition** | 4156515 | Malnutrition (calorie) |
| | 4276360 | Undernutrition |
| | 435227 | Nutritional deficiency disorder |
| | 433163 | Deficiency of macronutrients |
| | 4028220 | Malnutrition following gastrointestinal surgery |
| **Starvation and Related Conditions** | 443082 | Starvation |
| | 4337279 | Semi-starvation |

# Homework Assignment

- We want to see if malnutrition severity is associated with worse outcomes among those with a history of malnutrition.
- Using the newly created malnutrition severity type variable, we want to re-run our analyses.

- You will each be assigned either:
  A. The multilevel severity measure to compare them collective versus no hx of malnutrition (level 1)
  B. One of these severity types to compare individually to those with no hx of malnutrition (level 2)
  C. Stratified among only those with malnutrition to compare relative differences among those with malnutrition (level 3)

# Homework Assignment

- Requirements:
  - If your last name is between A and H, you are group A (level 1)
  - If your last name is between I and O, you are group B (level 2)
  - If your last name is between P and Z, you are group C (level 3)
- Based on your group assignment:
  - Create a Table 1 for your cohort (e.g., descriptive statistics) with an overall column and comparison groups. Include *p* values using the gtsummary package. Be sure to include additional code to censor small counts.
  - Using the approach we covered in class, run crude and adjusted logistic regression for 30-day all-cause mortality using the exposure group you were assigned above. If you include event rates, include an additional step to censor small cell counts.

# Module 5 Homework (link)

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