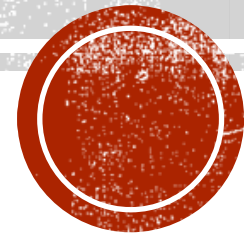


# RISK OF DEATH OF INDIVIDUALS WITH DIFFERENT COMORBIDITY PROFILES DURING THE COVID-19 PANDEMIC.

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# INTRODUCTION



Underlying chronic health conditions



COVID-19 pandemic



Higher hospitalization and mortality



# BACKGROUND

- Prevalent comorbidities associated with increased risk : hypertension, diabetes, obesity, cardiovascular diseases, respiratory ailments, cancer, and acute kidney.
- Different comorbidities can have different effects (e.g. higher or lower likelihood of invasive interventions).
- Age and age-comorbidity interactions: having a comorbidity at early age is a much stronger discriminatory factor for poor health than having is at an older age.



# IN DENMARK

- Comorbidities played a detrimental role in worsening COVID-19 outcomes.
- Some results:
  - higher risk of hospitalization and ICU admission for older male patients with hypertension, diabetes, and chronic pulmonary disease.
  - higher risk of death for those with chronic pulmonary disease, active cancer, and multiple comorbidities (higher Charlson Comorbidity Index) across age groups and genders.
  - Cardiovascular comorbidities had a modest effect compared to other conditions.
  - Age and gender: younger blood donors (under age 51) had a lower infection fatality rate than older ones; among older blood donors, higher infection fatality rate for men compared to women.
- Most studies focused on the first wave, on fatality rates, and on hospitalized individuals only.



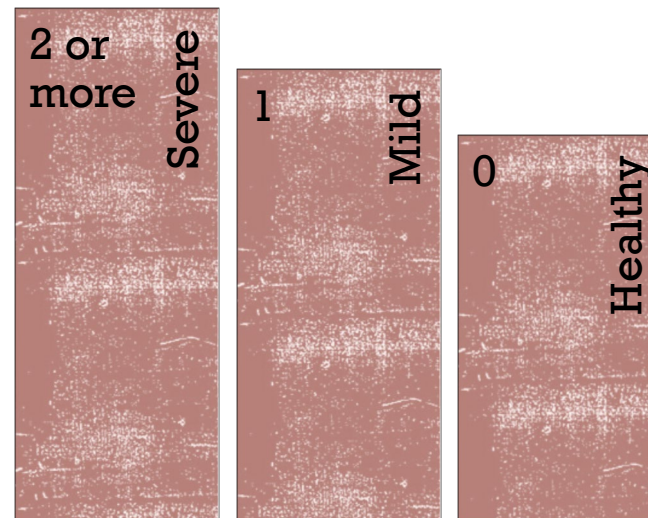
# OUR ANALYSIS

- However, the pandemic may have had differing effect on the risk of death, directly or indirectly, of comorbid individuals even if not hospitalized.
- **Goal: Investigate whether the mortality risk for individuals with and without comorbidities changed during the pandemic.**



# DATA AND METHODS

- Danish registry data (nationwide, high quality, comprehensive)
- Excess death estimation: compare 2017-2019 with 2020-2021 (both waves).
- We consider the entire population (not just hospitalized individuals), aged 45+.
- Comorbidity: diagnosed chronic condition before the pandemic (2015-2019 ):  
Autoimmune diseases, Cancer, Cardiopathies, Chronic Kidney Disease, Chronic Obstructive Pulmonary Diseases, Dementia (and Alzheimer), Diabetes (type I and II), Digestive Diseases, High Blood Lipids, HIV, Hypertension, Neurologic Diseases, Organ Transplant, and Vasculopathies.



# DATA AND METHODS

- Relative risk of death of healthy and comorbid individuals, before and during the pandemic.

- Mortality follow up



- **Covariates**

- Comorbidity level (healthy, mild, severe)
- Gender
- Education (low, middle, high)

- **Outcome in 2017-2019**

- Censored
- Death

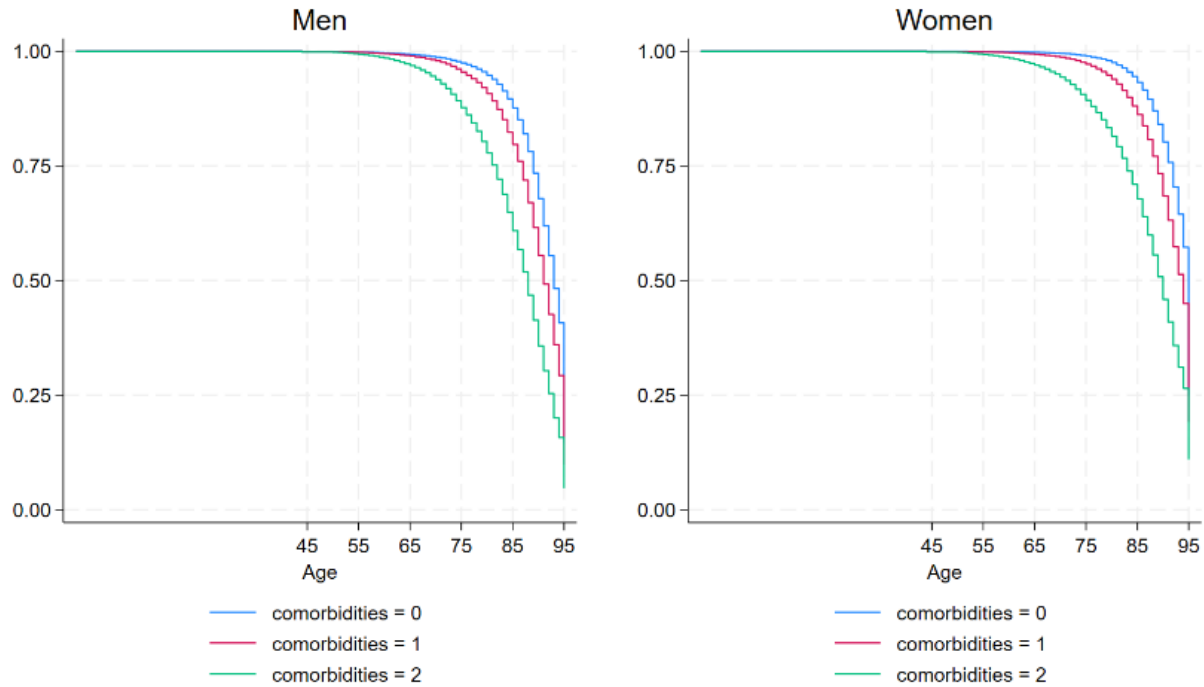
- **Outcome in 2020-2021**

- Censored
- Death (Covid-19-related, not covid related)



# RESULTS — KAPLAN MEIER SURVIVAL

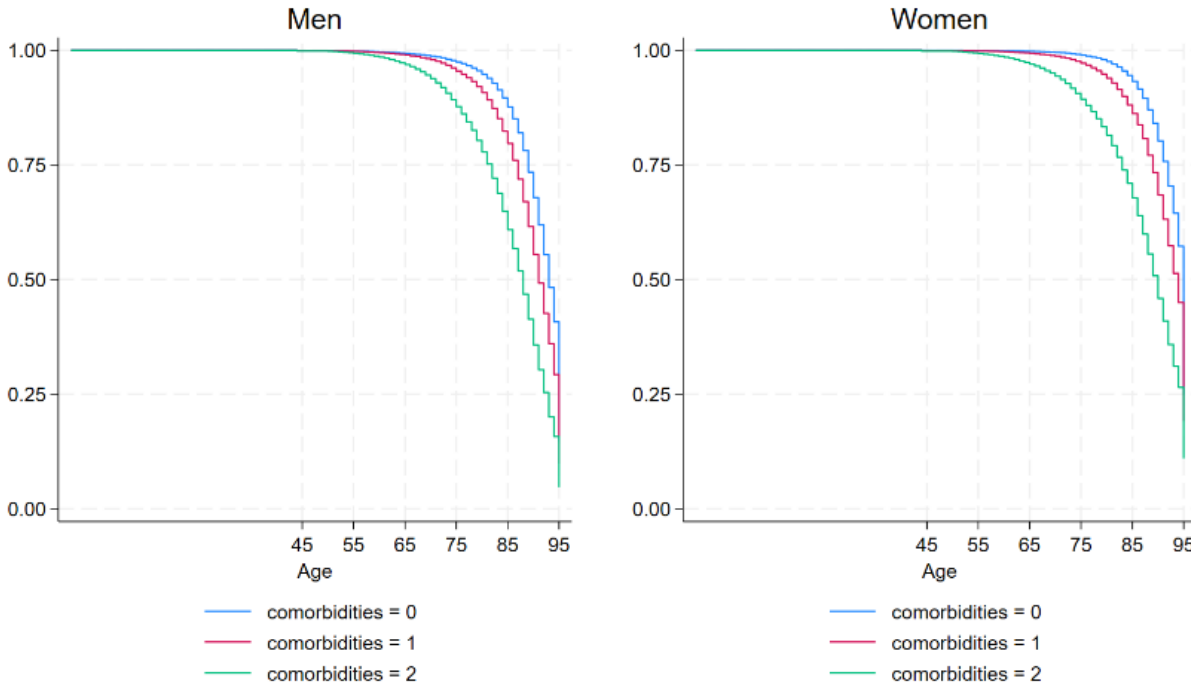
All deaths - comorbidity level survival in 2017-2019



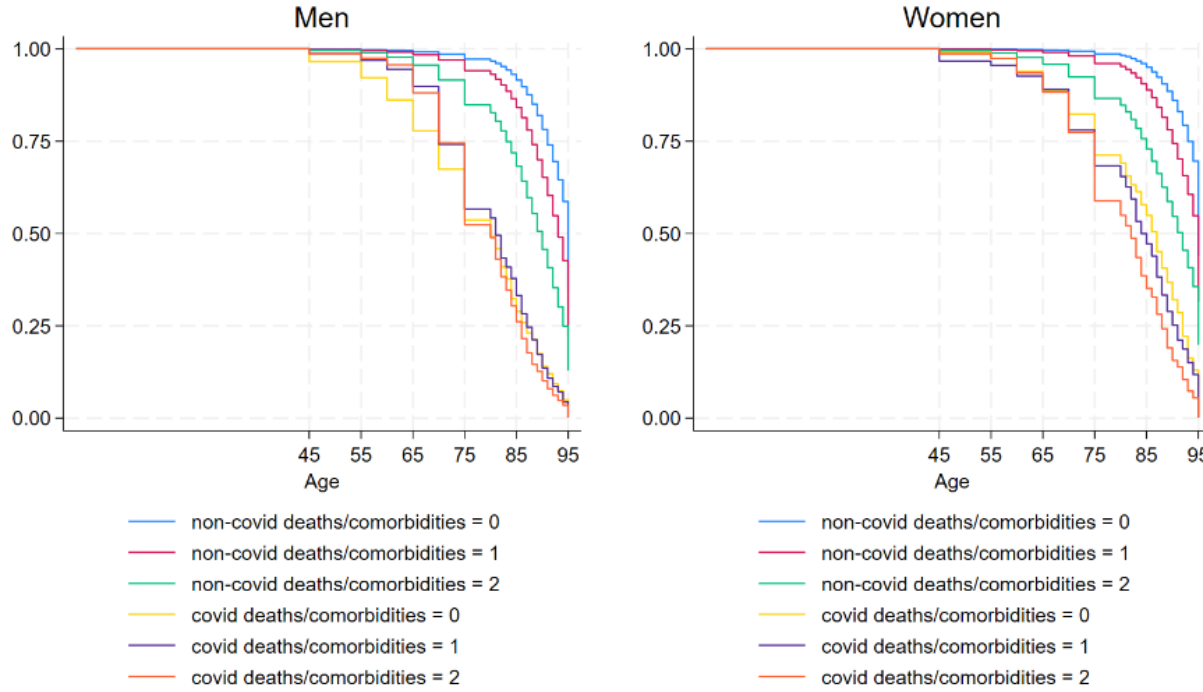


# RESULTS – KAPLAN MEIER SURVIVAL

All deaths - comorbidity level survival in 2017-2019

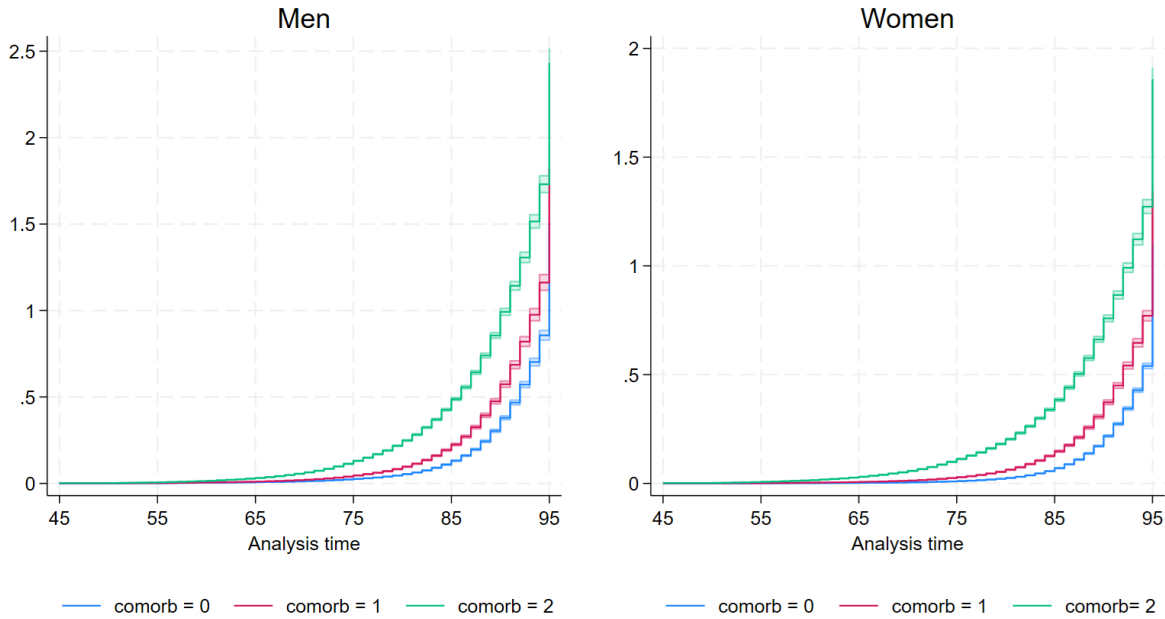


Covid-19 deaths and all other deaths - comorbidity level survival in 2020-2021

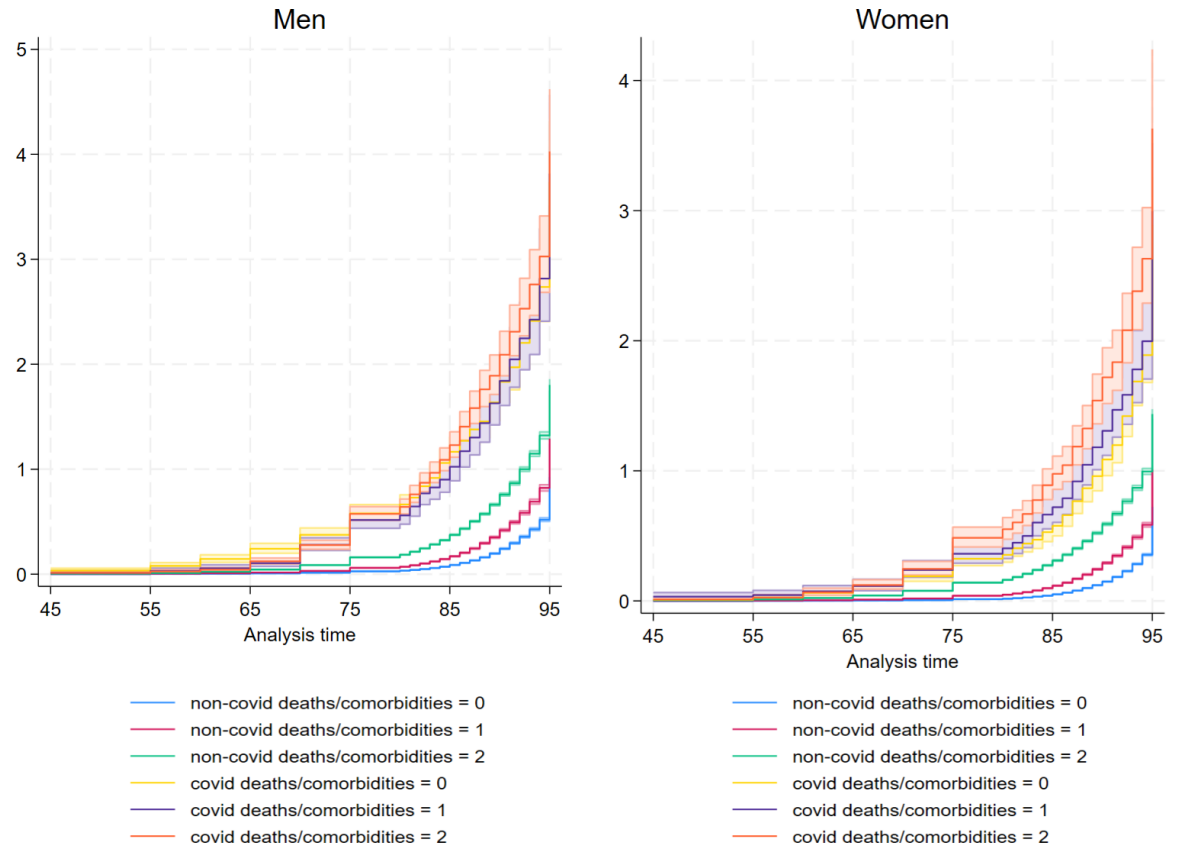


# RESULTS – N-A CUMULATIVE HAZARD

All deaths – cumulative hazard by comorbidity in 2017-2019

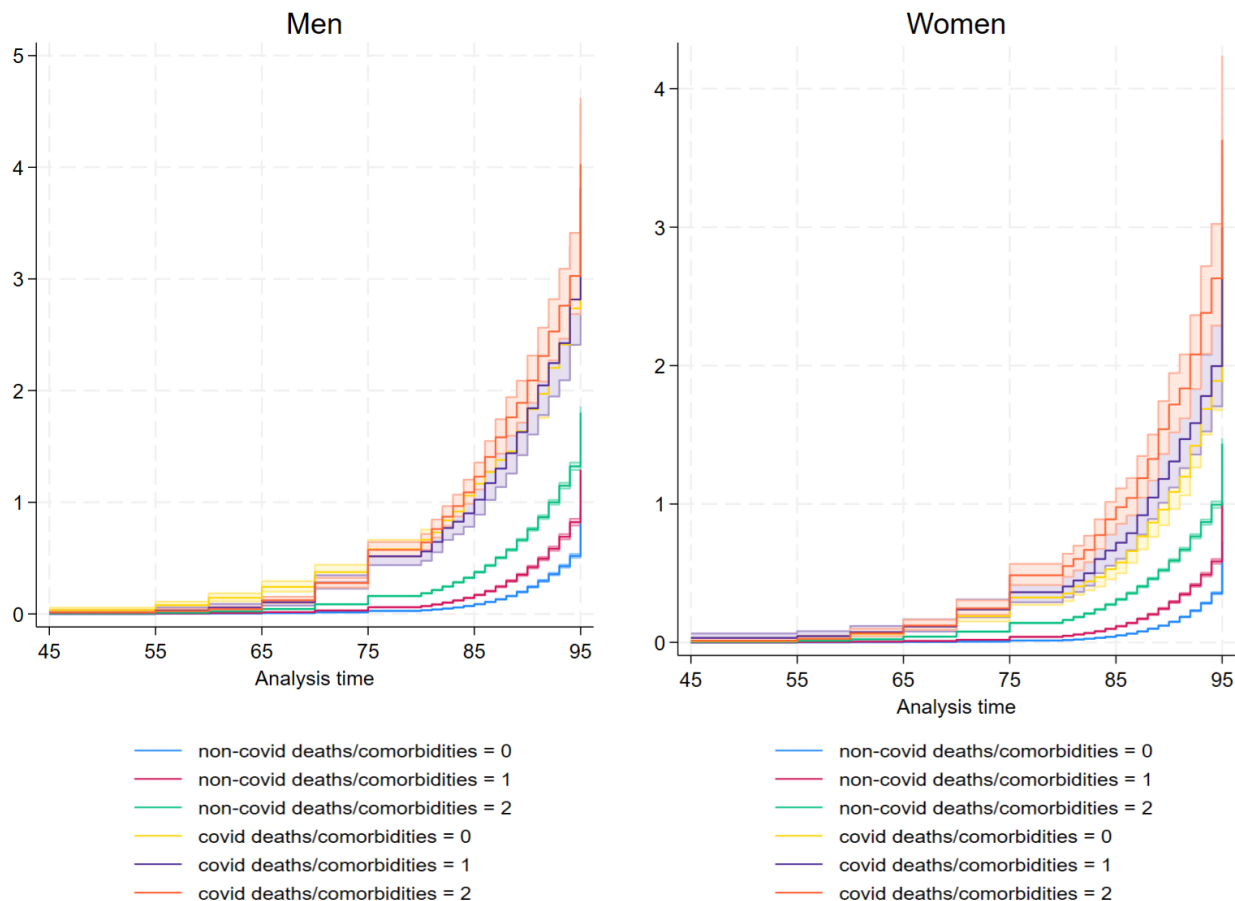


Covid-19 deaths and all other deaths – cumulative hazard by comorbidity in 2020-2021



# RESULTS – N-A CUMULATIVE HAZARD

Covid-19 deaths and all other deaths – cumulative hazard by comorbidity in 2020-2021



- Cumulative hazards of death higher for men than for women (for all combinations of comorbidities and type of deaths)
- Until age 70 (65 for women)
  - Men with no comorbidity have higher risk of covid death than men with comorbidity.
  - No comorbidity level difference in risk of death for women.
- After age 70
  - Risk of covid-deaths accelerates more than the risk from all other causes.
  - Risk of covid-deaths accelerates more for men than for women.
  - For men the comorbidity level doesn't change the risk covid-death.
  - For women the comorbidity level matters: 2+ comorbidities have significantly higher risk of death compared to the other comorbidity levels.



# RESULTS — COX REGRESSION

- Cox regressions for pre-pandemic period and pandemic period.
- Progressively including additional variables and interaction terms.
- Selection of the best model based on the AIC criterion.
- Dependent variable: risk of death over age.
- Independent variables:
  - sex (male vs female)
  - comorbidity level (having 1 or 2+ comorbidities vs zero comorbidities)
  - education level (medium and high education level vs low education level).
  - type of death (covid-related vs non covid-related) – for the pandemic period regression



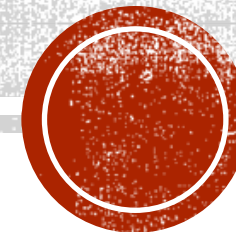
Model 5

LR chi2(13) = 45172.23  
 Prob > chi2 = 0.0000

|                         | _t | Haz. ratio | Std. err. | z      | P> z  | [95% conf. interval] |          |
|-------------------------|----|------------|-----------|--------|-------|----------------------|----------|
| 2.sex                   |    | .5388335   | .0070183  | -47.47 | 0.000 | .5252521             | .5527661 |
| comorbidities           |    |            |           |        |       |                      |          |
| 1                       |    | 1.443342   | .0242323  | 21.86  | 0.000 | 1.396621             | 1.491627 |
| 2                       |    | 2.789886   | .0374487  | 76.44  | 0.000 | 2.717445             | 2.864258 |
| education               |    |            |           |        |       |                      |          |
| 1                       |    | .8266617   | .0120441  | -13.07 | 0.000 | .8033896             | .850608  |
| 2                       |    | .575269    | .0109784  | -28.97 | 0.000 | .5541492             | .5971936 |
| sex#comorbidities       |    |            |           |        |       |                      |          |
| 2 1                     |    | 1.163256   | .0212414  | 8.28   | 0.000 | 1.12236              | 1.205643 |
| 2 2                     |    | 1.358681   | .0198617  | 20.97  | 0.000 | 1.320305             | 1.398172 |
| sex#education           |    |            |           |        |       |                      |          |
| 2 1                     |    | 1.03407    | .0146163  | 2.37   | 0.018 | 1.005816             | 1.063118 |
| 2 2                     |    | 1.25686    | .0232276  | 12.37  | 0.000 | 1.212149             | 1.30322  |
| education#comorbidities |    |            |           |        |       |                      |          |
| 1 1                     |    | 1.149657   | .0231729  | 6.92   | 0.000 | 1.105125             | 1.195985 |
| 1 2                     |    | 1.358861   | .0218903  | 19.04  | 0.000 | 1.316627             | 1.40245  |
| 2 1                     |    | 1.254315   | .0331133  | 8.58   | 0.000 | 1.191065             | 1.320924 |
| 2 2                     |    | 1.597226   | .0336688  | 22.21  | 0.000 | 1.532581             | 1.664598 |

# COX REGRESSION MODEL OF RISK OF DEATH

## PRE-PANDEMIC PERIOD (2017- 2019)



Model 5

LR chi2(13) = 45172.23  
Prob > chi2 = 0.0000

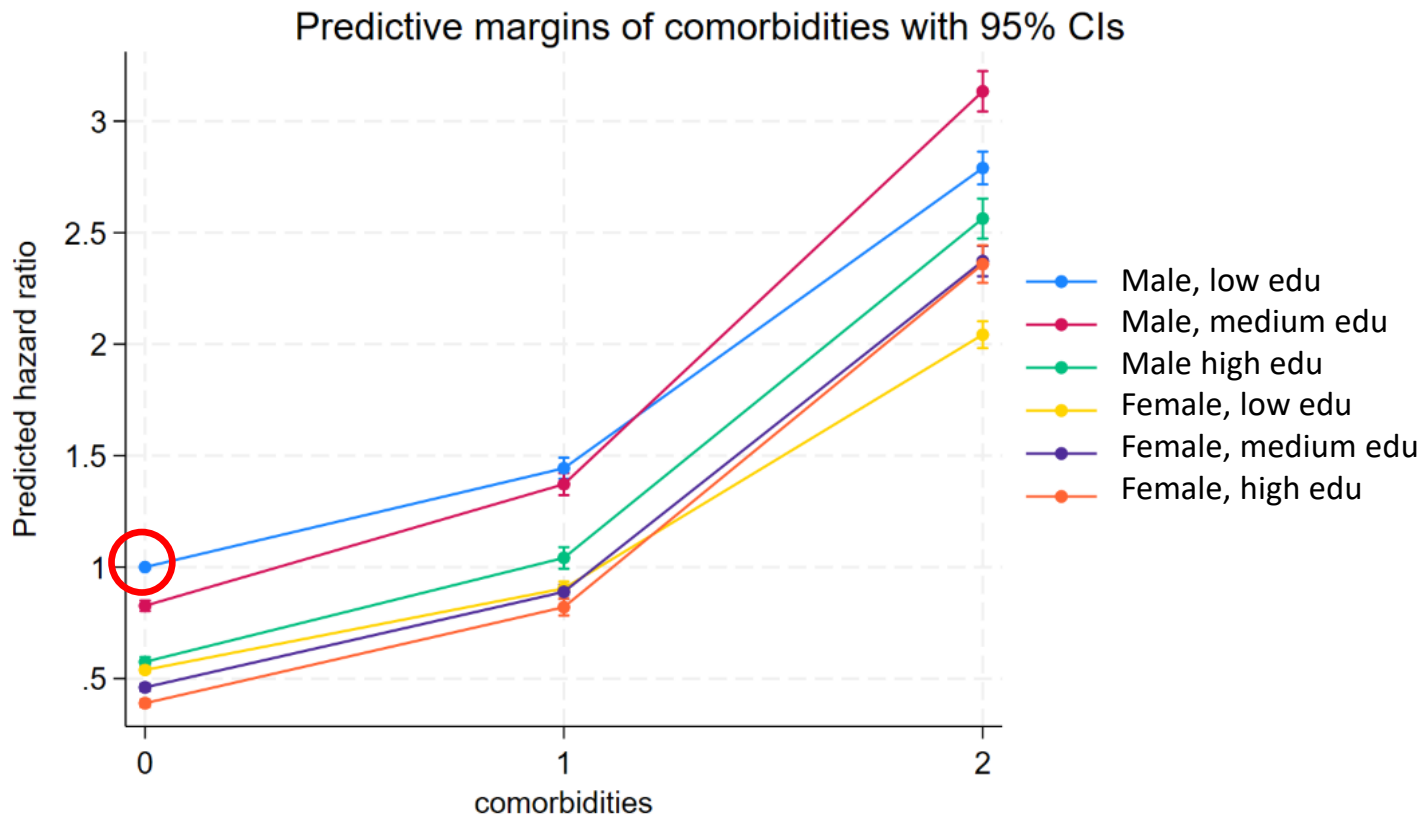
Nothing surprising

|                         | _t | Haz. ratio | Std. err. | z      | P> z  | [95% conf. interval] |          |
|-------------------------|----|------------|-----------|--------|-------|----------------------|----------|
| 2.sex                   |    | .5388335   | .0070183  | -47.47 | 0.000 | .5252521             | .5527661 |
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| sex#education           |    |            |           |        |       |                      |          |
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| 2 2                     |    | 1.25686    | .0232276  | 12.37  | 0.000 | 1.212149             | 1.30322  |
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# COX REGRESSION MODEL OF RISK OF DEATH

PRE-PANDEMIC  
PERIOD (2017-  
2019)





# COX REGRESSION MODEL OF RISK OF DEATH

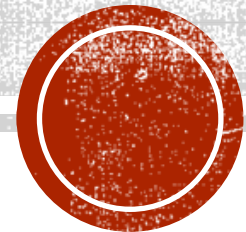
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**PRE-PANDEMIC  
 PERIOD (2017-  
 2019)**



- Three models:
- all the deaths pooled together (plus type of death covariate)
- non-covid-related deaths only
- covid-related deaths only

## **COX REGRESSION MODEL OF RISK OF DEATH**

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**PANDEMIC  
PERIOD (2020-  
2021)**

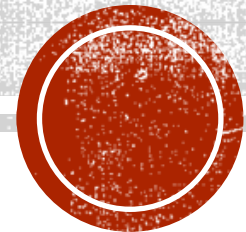


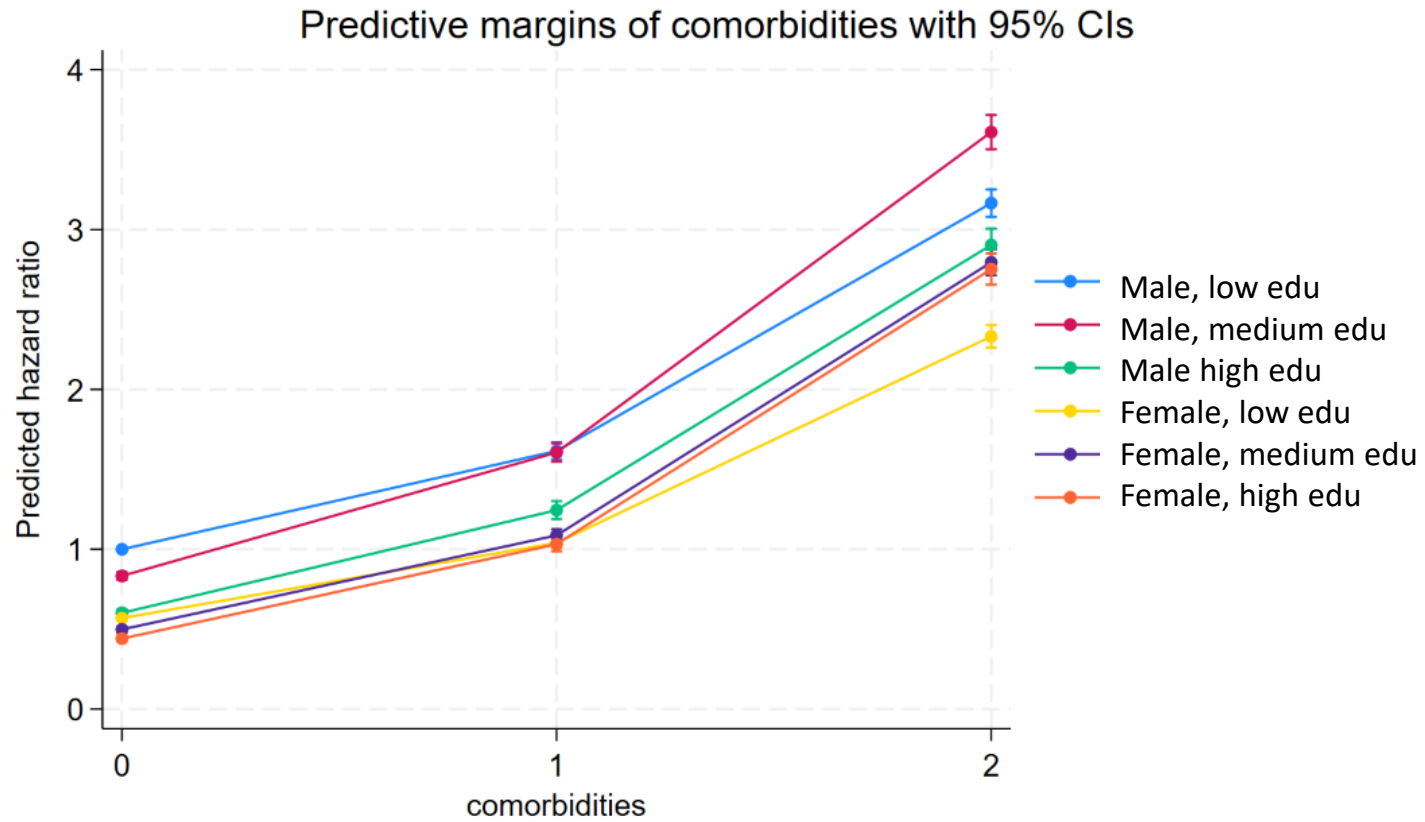


- Three models:
- all the deaths pooled together (plus type of death covariate)
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## **COX REGRESSION MODEL OF RISK OF DEATH**

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**PANDEMIC  
PERIOD (2020-  
2021)**

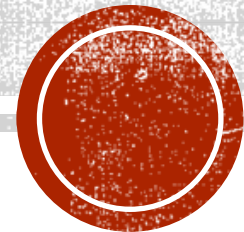


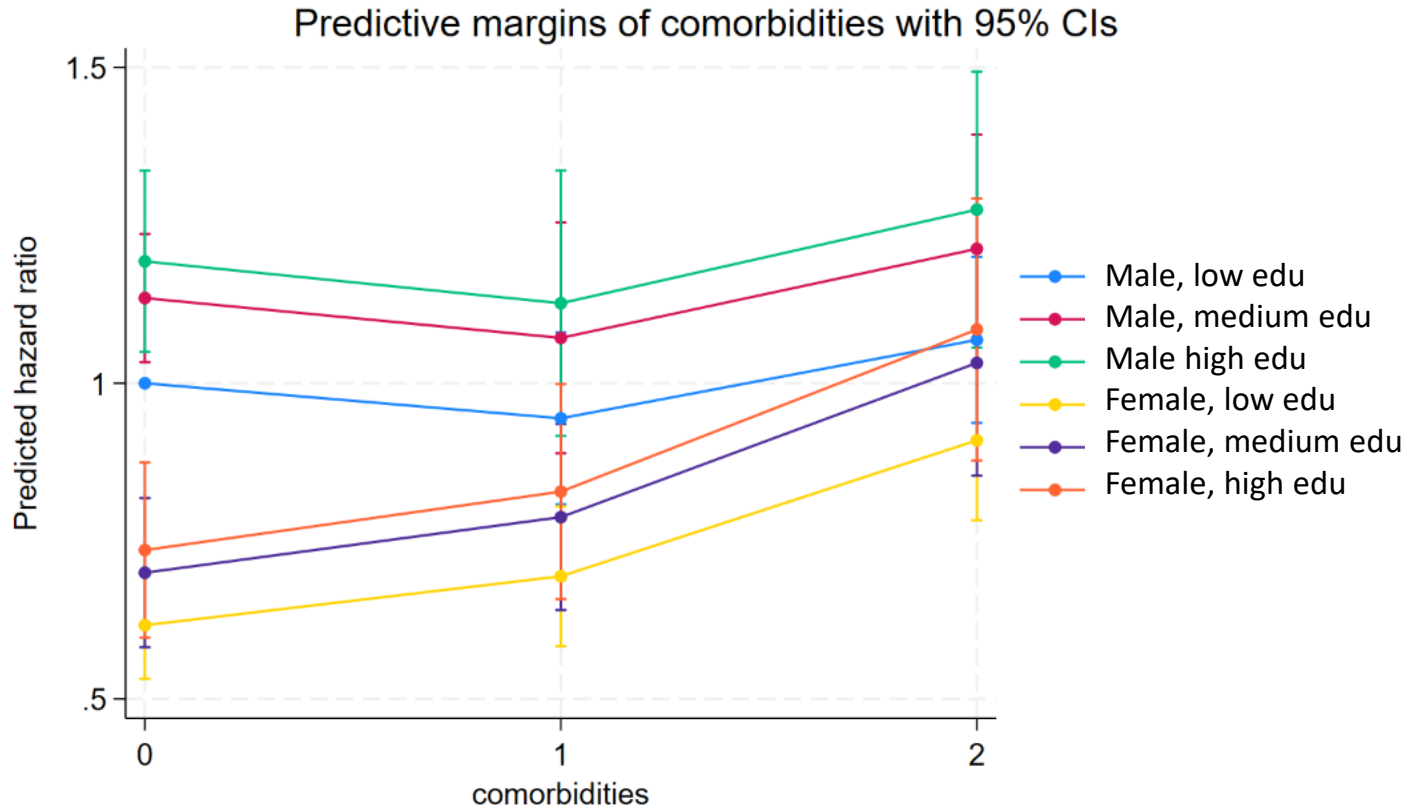


# COX REGRESSION MODEL OF RISK OF DEATH

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**PANDEMIC  
PERIOD (2020-  
2021)**  
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**NON COVID-  
DEATHS**

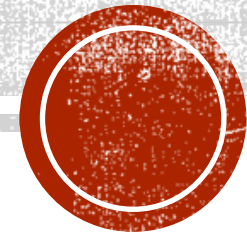




# COX REGRESSION MODEL OF RISK OF DEATH

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**PANDEMIC  
 PERIOD (2020-  
 2021)**

-----  
**COVID-DEATHS**



# CONCLUSIONS



**THANK YOU**



**Pre-pandemic years (2017-2019), all deaths**

|                   | Men                                    |                 | Women                                  |                 |
|-------------------|--|-----------------|--|-----------------|
| Comorbidity level | Observed                               | Expected        | Observed                               | Expected        |
| 0                 | 15405                                  | 27441.79        | 19557                                  | 33220.23        |
| 1                 | 10361                                  | 11643.22        | 10671                                  | 10431.99        |
| 2+                | 27846                                  | 14526.99        | 22460                                  | 9035.78         |
| <b>total</b>      | <b>53612</b>                           | <b>53612.00</b> | <b>52688</b>                           | <b>52688.00</b> |
|                   | chi2(2) = 18763.23<br>Pr>chi2 = 0.0000 |                 | chi2(2) = 27660.49<br>Pr>chi2 = 0.0000 |                 |

**Pandemic years (2020-2021), covid-related deaths**

|                   | Men                                |                | Women                               |                |
|-------------------|------------------------------------|----------------|-------------------------------------|----------------|
| Comorbidity level | Observed                           | Expected       | Observed                            | Expected       |
| 0                 | 464                                | 467.88         | 424                                 | 488.37         |
| 1                 | 325                                | 349.24         | 246                                 | 254.70         |
| 2+                | 632                                | 603.88         | 384                                 | 310.93         |
| <b>total</b>      | <b>1421</b>                        | <b>1421.00</b> | <b>1054</b>                         | <b>1054.00</b> |
|                   | chi2(2) = 3.71<br>Pr>chi2 = 0.1568 |                | chi2(2) = 32.26<br>Pr>chi2 = 0.0000 |                |

**Pandemic years (2020-2021), non-covid-related deaths**

|                   | Men                                    |                 | Women                                  |                 |
|-------------------|--|-----------------|--|-----------------|
| Comorbidity level | Observed                               | Expected        | Observed                               | Expected        |
| 0                 | 14108                                  | 28052.11        | 17855                                  | 32893.11        |
| 1                 | 10855                                  | 11502.59        | 11249                                  | 10440.92        |
| 2+                | 28748                                  | 14156.59        | 23266                                  | 9035.97         |
| <b>total</b>      | <b>53711</b>                           | <b>53711.00</b> | <b>52370</b>                           | <b>52370.00</b> |
|                   | chi2(2) = 23383.97<br>Pr>chi2 = 0.0000 |                 | chi2(2) = 31249.07<br>Pr>chi2 = 0.0000 |                 |

**Table 1. Log-rank test for equality of survivor functions.**



Log Model 5 other deaths

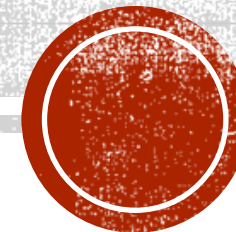
LR chi2(13) = 49649.14  
 Prob > chi2 = 0.0000

|                         | _t    | Haz. ratio | Std. err. | z      | P> z  | [95% conf. interval] |          |
|-------------------------|-------|------------|-----------|--------|-------|----------------------|----------|
|                         | 2.sex | .5693748   | .0076869  | -41.72 | 0.000 | .5545063             | .584642  |
| comorbidities           |       |            |           |        |       |                      |          |
|                         | 1     | 1.615054   | .0274926  | 28.16  | 0.000 | 1.562058             | 1.669847 |
|                         | 2     | 3.165599   | .0437165  | 83.44  | 0.000 | 3.081065             | 3.252452 |
| education               |       |            |           |        |       |                      |          |
|                         | 1     | .833029    | .0124679  | -12.21 | 0.000 | .8089474             | .8578275 |
|                         | 2     | .6020769   | .011591   | -26.35 | 0.000 | .5797822             | .625229  |
| sex#comorbidities       |       |            |           |        |       |                      |          |
|                         | 2 1   | 1.131343   | .0205267  | 6.80   | 0.000 | 1.091818             | 1.172298 |
|                         | 2 2   | 1.293577   | .0191376  | 17.40  | 0.000 | 1.256607             | 1.331635 |
| sex#education           |       |            |           |        |       |                      |          |
|                         | 2 1   | 1.051244   | .0147594  | 3.56   | 0.000 | 1.022711             | 1.080574 |
|                         | 2 2   | 1.287279   | .0232854  | 13.96  | 0.000 | 1.242441             | 1.333737 |
| education#comorbidities |       |            |           |        |       |                      |          |
|                         | 1 1   | 1.193462   | .0238948  | 8.83   | 0.000 | 1.147536             | 1.241226 |
|                         | 1 2   | 1.368882   | .0223186  | 19.26  | 0.000 | 1.32583              | 1.413332 |
|                         | 2 1   | 1.280207   | .0328003  | 9.64   | 0.000 | 1.217507             | 1.346136 |
|                         | 2 2   | 1.523347   | .0319629  | 20.06  | 0.000 | 1.461972             | 1.587299 |

# COX REGRESSION MODEL OF RISK OF DEATH

## ----- PANDEMIC PERIOD (2020- 2021)

## ----- NON COVID- DEATHS



Model 3 covid

LR chi2(7) = 116.82  
 Prob > chi2 = 0.0000

|                   | _t  | Haz. ratio | Std. err. | z     | P> z  | [95% conf. interval] |          |
|-------------------|-----|------------|-----------|-------|-------|----------------------|----------|
| 2.sex             |     | .6167813   | .0432374  | -6.89 | 0.000 | .5376016             | .7076228 |
| comorbidities     |     |            |           |       |       |                      |          |
|                   | 1   | .9444076   | .0694848  | -0.78 | 0.437 | .8175838             | 1.090904 |
|                   | 2   | 1.068673   | .0670194  | 1.06  | 0.290 | .9450696             | 1.208443 |
| education         |     |            |           |       |       |                      |          |
|                   | 1   | 1.13485    | .0518448  | 2.77  | 0.006 | 1.037653             | 1.241152 |
|                   | 2   | 1.192981   | .073224   | 2.87  | 0.004 | 1.057761             | 1.345487 |
| sex#comorbidities |     |            |           |       |       |                      |          |
|                   | 2 1 | 1.192005   | .1322589  | 1.58  | 0.113 | .9590318             | 1.481573 |
|                   | 2 2 | 1.379866   | .1327102  | 3.35  | 0.001 | 1.142803             | 1.666104 |

# COX REGRESSION MODEL OF RISK OF DEATH

## ----- PANDEMIC PERIOD (2020- 2021) -----

## COVID-DEATHS

