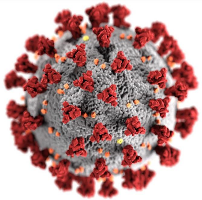

Mixture Cure Rate Models for the Analysis of Survival Times in the COVID-19 Scenario

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Summary

Introduction

- The pandemic of the new coronavirus has become an enormous health challenge worldwide
- The COVID-19 infection can be asymptomatic, but a significant proportion of the cases require hospitalization, including intensive care unit admission
- A few factors have been linked to the risk of more severe disease and death, such as age and sex

Survival modeling : helps us understand the correlation between human and environmental factors (age, sex) and the survival probabilities of each person

Methods

- Choice: motivated by the imbalance present in the data (deaths versus censored observations)
- Let T be the time to some specific event (death, for example), treated as a non-negative random variable
- In survival analysis, we commonly the survival function $S(t) = P(T > t)$, that is nothing more than $S(t) = 1 - F(t)$, where $F(t)$ is the cumulative distribution function of T

Mixture Cure Rate Models

- Two sub-populations: one with a standard failure rate (**cured fraction**) and one with the same rate **added** with a subject-specific parametric failure rate
- The mixture survival function has the form

$$S_{pop}(t|\mathbf{x}, \mathbf{z}, \mathbf{n}) = (1 - \pi(\mathbf{z}))S(t|\mathbf{x}, \mathbf{n} = 1) + \pi(\mathbf{z}),$$

where $\pi(\mathbf{z})$ is the cured proportion, $S(t|\mathbf{x}, \mathbf{n} = 1)$ is the survival function of susceptible (uncured) individuals, and $\mathbf{x}$ and $\mathbf{z}$ are the covariates associated with π and S, respectively.

GAMLSS Models

- GAMLSS: generalized additive models for location, scale, and shape [2]
- Semi-parametric *Weibullcr* [1] distribution, for which the survival function will be

$$S_{pop}(t|\mu,\sigma,\nu) = \nu + (1-\nu)\exp\left\{-\left[\frac{t\Gamma(1/\sigma+1)}{\mu}\right]^{\sigma}\right\}.$$

- The parameters $\theta = (\mu,\sigma,\nu) =$ (location, scale, shape) are estimated through a regression model that allows for complex regression structures

Data

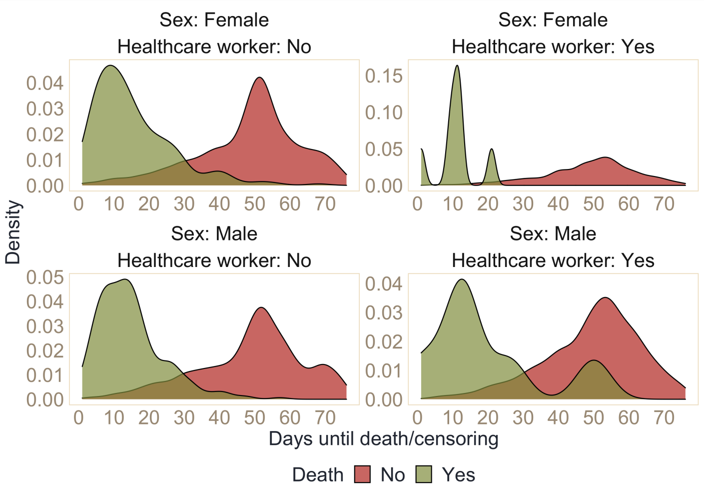
- ➔ Time until death or the end of the study (censoring)

Explanatory variables:

- ➔ Age
- ➔ Sex
- ➔ ICU status (yes or no)
- ➔ Healthcare worker status (yes or no)

Note: the results presented here are from 'faked data', because the true Irish cases data is confidential

Data



Sex: Female
Healthcare worker: No
Sex: Female
Healthcare worker: Yes
Sex: Male
Healthcare worker: No
Sex: Male
Healthcare worker: Yes
Density
0.00
0.01
0.02
0.03
0.04
0.05
0.10
0.15
0 10 20 30 40 50 60 70
Days until death/censoring
Death No Yes

Results

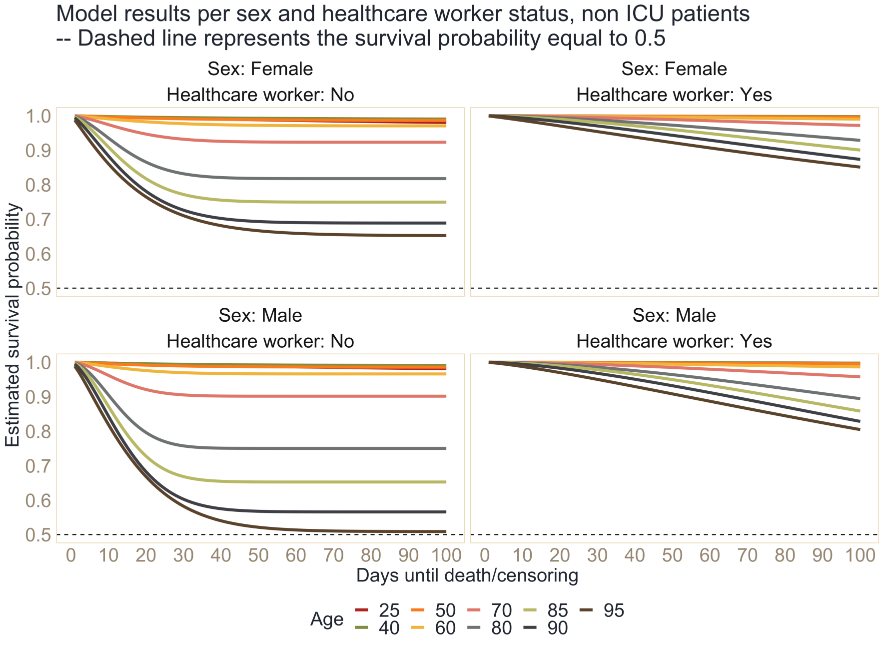
- Best model: selected by minimising the AIC
- Final model: does not use the same covariates in all parameters, and includes polynomial and interaction terms

$$\log(\mu_i) = \beta_{01} + \beta_{11}\text{age} + \beta_{21}\text{age}^2 + \beta_{31}\text{sex} + \beta_{41}\text{HW} + \beta_{51}\text{ICU} + \beta_{61}(\text{age} \times \text{sex}),$$

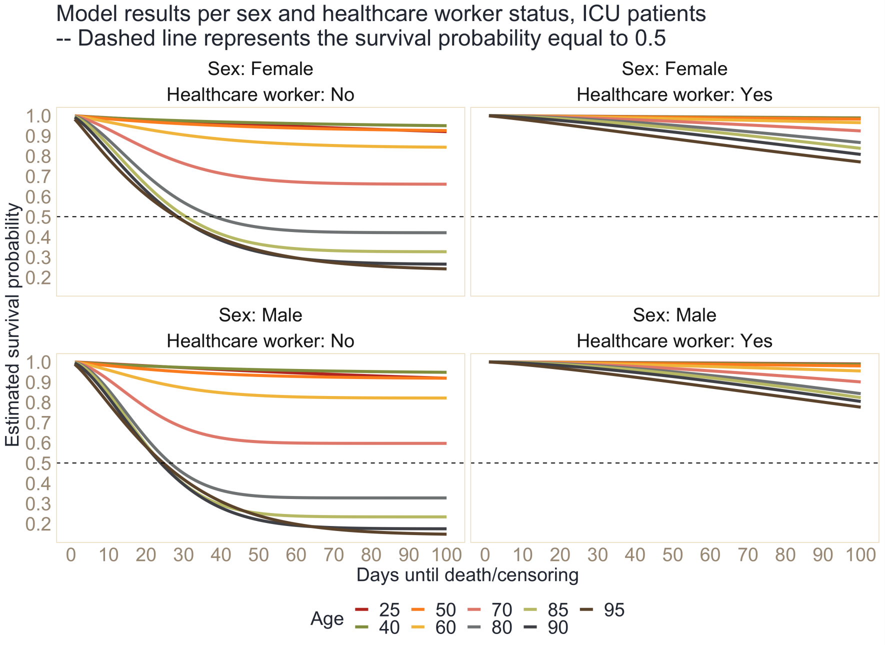
$$\log(\sigma_i) = \beta_{02} + \beta_{12}\text{sex} + \beta_{22}\text{age} + \beta_{32}\text{age}^2 + \beta_{42}\text{age}^3,$$

$$\text{logit}(\nu_i) = \beta_{03} + \beta_{13}\text{age} + \beta_{23}\text{age}^2 + \beta_{33}\text{age}^3 + \beta_{43}\text{ICU} + \beta_{53}\text{sex} + \beta_{63}(\text{age} \times \text{sex}),$$

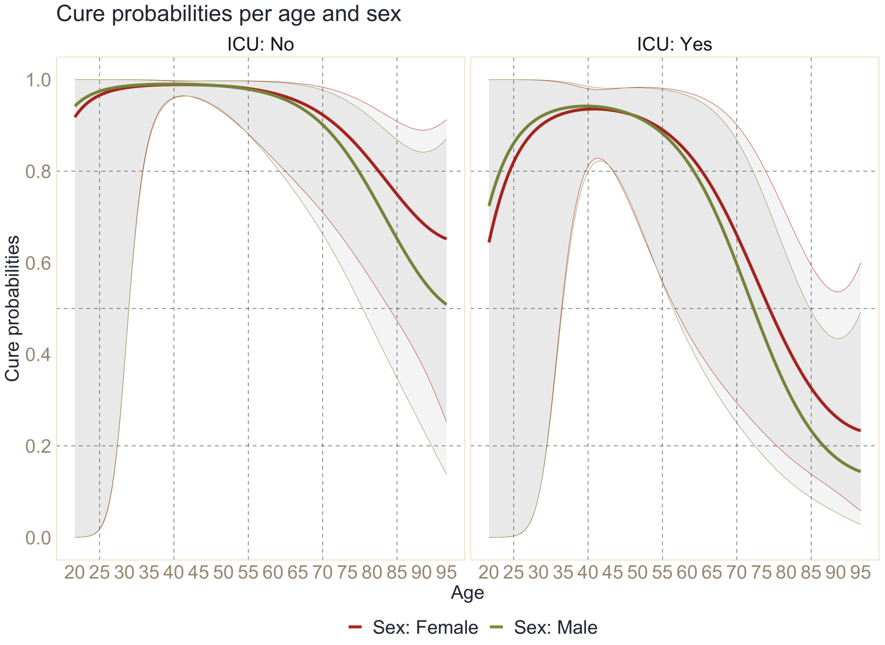
where $\text{logit}(x) = log(x/(1+x))$.



Model results per sex and healthcare worker status, non ICU patients
-- Dashed line represents the survival probability equal to 0.5
Sex: Female
Healthcare worker: No
Sex: Female
Healthcare worker: Yes
Sex: Male
Healthcare worker: No
Sex: Male
Healthcare worker: Yes
Estimated survival probability
1.0
0.9
0.8
0.7
0.6
0.5
0 10 20 30 40 50 60 70 80 90 100
Days until death/censoring
Age
25 50 70 85 95
40 60 80 90



Model results per sex and healthcare worker status, ICU patients
-- Dashed line represents the survival probability equal to 0.5
Sex: Female
Healthcare worker: No
Sex: Female
Healthcare worker: Yes
Sex: Male
Healthcare worker: No
Sex: Male
Healthcare worker: Yes
Estimated survival probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0 10 20 30 40 50 60 70 80 90 100
Days until death/censoring
Age
25
40
50
60
70
80
85
90
95



Cure probabilities per age and sex
ICU: No
ICU: Yes
Cure probabilities
0.0
0.2
0.4
0.6
0.8
1.0
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95
Age
Sex: Female
Sex: Male

Conclusions and Final Remarks

- Age and sex seem to play the most important roles in the decrease of survival chances
- ICU patients, particularly males, have the lowest survival probabilities
- Healthcare workers appear to have a low mortality for COVID-19

- Many factors were not captured here, such as time and spatially variant dynamics and other influential covariates

Acknowledgements

This work was supported by Science Foundation Ireland and their emergency COVID-19 funding portal via grant number 20/COV/0081

Science Foundation Ireland sfi For what's next

`https://www.hamilton.ie/covid19/`

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Thanks!