Investigating factors that may influence COVID-19 survival

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Abstract

Background:Objective: To Investigate, and identify, the factors that may influence patient survival of coronavirus disease 19.**MethodsMotivation:** You can also have some paragraphs start with bold face.

Introduction

During the past 2years, infections due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have led to a high number of coronavirus 19 disease deaths and in-hospital care. With time, case fatality rates, and in-hospital survival rates, have improved [. . .] as our understanding of coronavirus 19 disease pathogenesis has developed, and hence prevention, mitigation, and treatment measures have improved. Effective disease treatment measures depend on our understanding of the disease's prognosis factors (Riley 2013), the focus of prognostic factors research. Prognostic factor research *aims to identify factors associated with subsequent clinical outcome in people with a particular disease or health condition* (Riley 2013).

This brief investigates the prognostic factor potential of a set of measures associated with a prospective cohort study. The study's hypothesis is that *one or more of the measures has a significant impact on each patient's survival probability.*

Methods

Study design and setting

This investigation's data is an indirect ISARIC (International Severe Acute Respiratory Infection Consortium) 4C (Coronavirus Clinical Characterisation Consortium) study data set. The study is an ongoing prospective cohort study based in more than 200 United Kingdom acute care hospitals. This investigation's data is an England only data set. The reporting . . .

Participants

Inclusion criteria were people of all ages who were admitted to one of 208 acute care hospitals in England, Scotland, and Wales with proven or high likelihood of infection with a pathogen of public health interest, defined as SARS-CoV-2 for this event by Public Health England. Reverse transcriptase polymerase chain reaction was the only mode of testing available during the period of study. The decision to test was at the discretion of the clinician attending the patient, and not defined by protocol. The enrolment criterion "high likelihood of infection" reflects that a preparedness protocol cannot assume that a diagnostic test will be available for an emergent pathogen. Site training emphasises that only patients who tested positive for covid-19 were eligible for enrolment.

National guidance was provided by Public Health England and other UK public health agencies that advised who to test based on clinical case definitions for possible covid-19. We also included patients who had been admitted for a separate condition but had tested positive for covid-19 during their hospital stay. Patients were only enrolled during their index admission. Patients had clinical information from their routine health records uploaded into the case report form. Consent was not required for collection of depersonalised routine

healthcare data for research in England and Wales. A waiver for consent was given by the Public Benefit and Privacy Panel in Scotland.

Data

Although the consortium collects a large variety of demographic, clinical, and outcome data, this investigation's data only included a limited subset of the study's variables. The demographic data variables are sex and age group, the comorbidity variables are asthma (physician diagnosed), mild liver disease, moderate/severe liver disease, renal disease, chronic pulmonary disease (excluding asthma), chronic neurological disorder, malignant neoplasm.

The ISARIC 4C study collects its baseline data via paper case report forms developed by ISARIC, and the WHO (World Health Organization), for outbreak investigations. Additionally, the data brief states that the baseline data records are *uploaded [on] admission, and usually before hospital episodes were complete, to a REDCap database (Research Electronic Data Capture, Vanderbilt University, US, hosted by University of Oxford, UK).*

Outcomes

The ISARIC 4C study outcomes are: discharged alive, remains in hospital, death, transferred, and palliative discharge. Herein, the overarching outcomes of interest are: dead, alive.

Independent Variables

The predictors, factors, under investigation

Factor Analysis

The Cox Hazard, Restricted Mean Survival

Results

Characteristics

The Null Kaplan-Meier Curves

The Cox Model Assumptions

The observations are independent: This assumption requires a set of observations wherein the patients are not related or associated. If there are clusters of relations or associates, the clusters should be, must be, indicated as-such. By virtue of the > study's design, it is quite possible that the observations are not independent - families, friends, and colleagues living in the same area will probably be admitted to the same health centre. Alas, the data set does not have cluster indicators, hence it is impossible to definitively test and state the independence, or otherwise, of the observations.

Independent Censoring: There is neither evidence to suggest nor rule-out outcomes due to systematic drop-outs, induced by study design flaws. What are the prognosis of patients released to palliative care or

In Hospital Mortality

	no	yes	NA
deceased	31724	14049	347
	0.688	0.305	0.008

Comorbidities

	no	yes	NA
asthma	37376	5872	2872
	0.81	0.13	0.06
mild liver disease	42021	666	3433
	0.91	0.01	0.07
renal disease	35158	8056	2906
	0.76	0.17	0.06
pulmonary	35265	8078	2777
	0.76	0.18	0.06
neurological disorder	37227	5806	3087
	0.81	0.13	0.07
liver mod severe	41901	902	3317
	0.91	0.02	0.07
malignant neoplasm	38164	4734	3222
	0.83	0.10	0.07

Demographics

Age Group	**Male**	**Female**	**NA**
80-89	7067	6197	31
	0.153	0.134	0.001
70-79	6388	4445	19
	0.139	0.096	0.000
60-69	4321	2601	9
	0.094	0.056	0.000
50-59	3463	2151	9
	0.075	0.047	0.000
90+	2085	2816	13
	0.045	0.061	0.000
40-49	1846	1110	5
	0.040	0.024	0.000
30-39	784	756	4
	0.017	0.016	0.000

transferred? Is the decision to transfer or release to palliative care influenced or dictated by *lower* survival probability? If the answer to the latter question is yes - it will be in breach of independent censoring.

Proportional Hazards

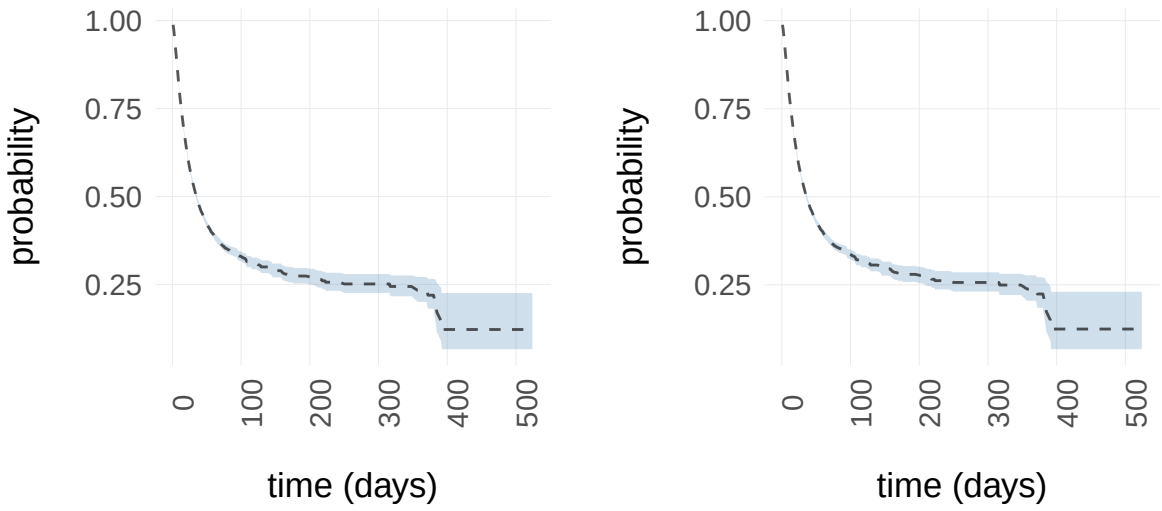

Figure 1: The null survival curves, whereby (A) is based on complete cases only, whilst (B) is based on all plausible records after multiple imputation.

The curves.

By default, citations are handled by `natbib` using a numeric citation format. To use name-date citations, sets `namedate: TRUE` in the YAML header.

Here are two sample references:

- **author (year) example:** Horvath and Raj (2018) showed some really cool things. Only seems to work properly if `namedate: TRUE`.
- **(author year) example:** This is a well known result (Ji et al. 2013).

The bibliography will appear at the end of the document.

Though not normally available in the OUP LaTeX format, CSL style files can also be used with the Rmarkdown adaptation by setting in the YAML header `citation_package: "default"` and defining the `csl` element to be the path towards the style file.

Discussion

An equation without a label for cross-referencing:

$$E = mc^2$$

An inline equation: $y = ax + b$

An equation with a label for cross-referencing:

$$\int_0^{r_2} F(r, \varphi) \mathrm{d}r \, \mathrm{d}\varphi = 1 \tag{1}$$

This equation can be referenced as follows: Eq. 1

Conclusion

The code below creates a figure.

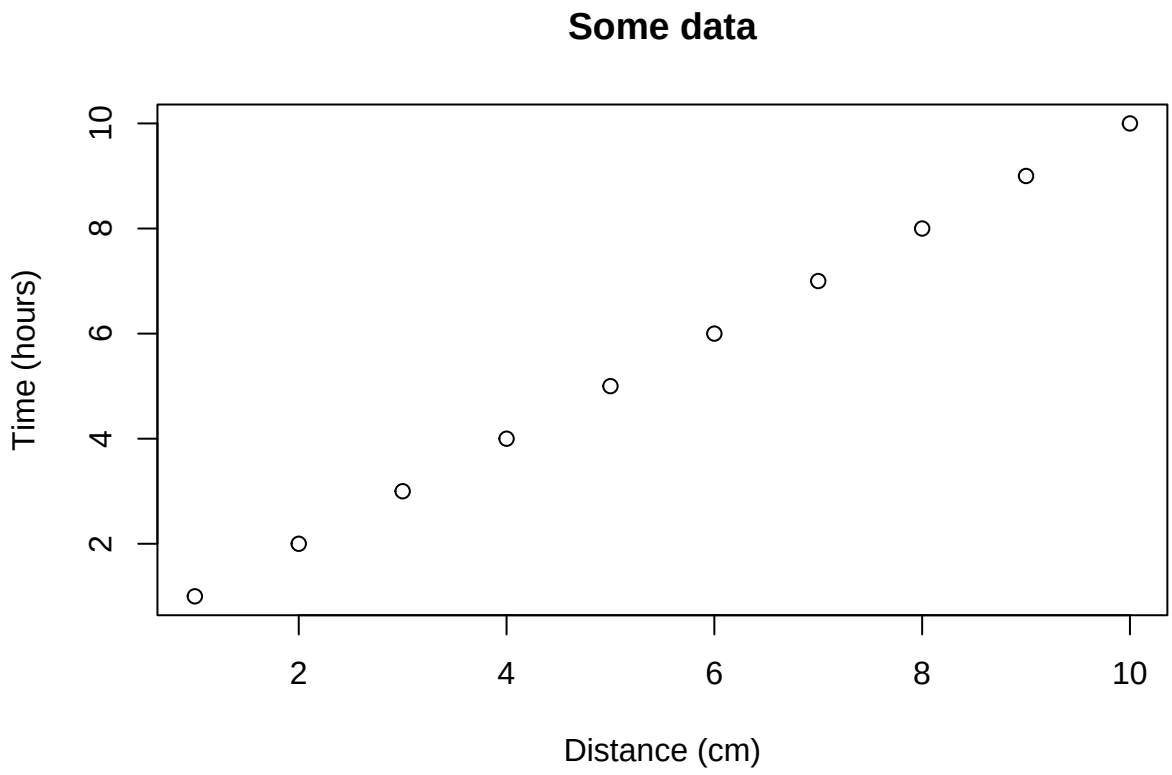

Figure 2: This is the first figure.

You can reference this figure as follows: Fig. **??**.

Figures can span two columns be setting `fig.env="figure*"`.

Reference to second figure: Fig. 3

Generate a table using `xtable`

```
df <- data.frame(ID=1:3,code=letters[1:3])

# Creates tables that follow OUP guidelines
# using xtable

print(xtable::xtable(df,caption="This is a xtable table.", label="tab:tab1"), comment=FALSE,caption.pla
```

You can reference this table as follows: Table 1.

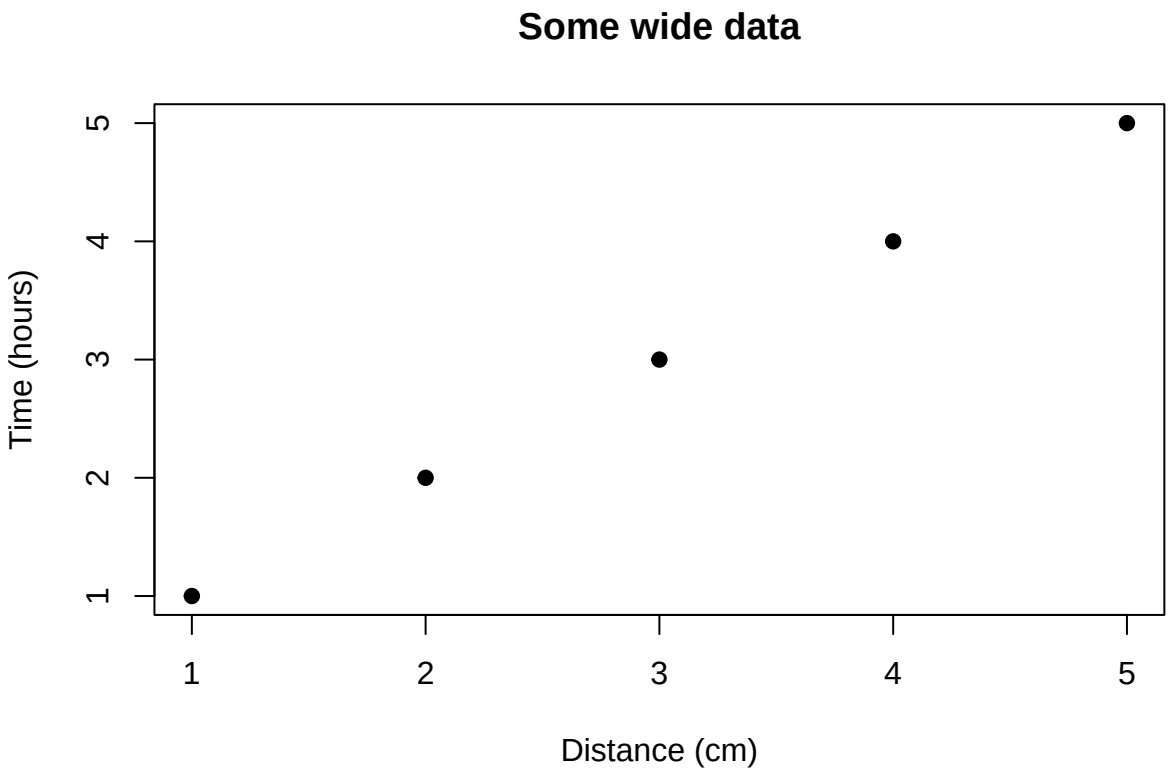

Figure 3: This is a wide figure.

Table 1: This is a xtable table.

	ID	code
1	1	a
2	2	b
3	3	c

Table 2: This is a kable table.

ID	code
1	a
2	b
3	c

Generate a table using `kable`

```
df <- data.frame(ID=1:3,code=letters[1:3])

# kable can alse be used for creating tables
knitr::kable(df,caption="This is a kable table.",
             booktabs=TRUE,label="tab2")
```

You can reference this table as follows: Table 2.

Table spanning two columns

Tables can span two columns be setting `table.envir = "table*"` in `knitr::kable`.

```
df <- data.frame(ID=1:3,code1=letters[1:3],
                 code2=letters[4:6],
                 code3=letters[7:9],
                 code4=letters[10:12],
                 code5=letters[13:15])

# kable can alse be used for creating tables
knitr::kable(df,caption="This is a wide kable table.",
             #format="latex",
             table.envir="table*",
             booktabs=TRUE,label="tab3")
```

Table 3: This is a wide kable table.

ID	code1	code2	code3	code4	code5
1	a	d	g	j	m
2	b	e	h	k	n
3	c	f	i	l	o

Appendices

Exploratory Analysis

Graphs

Missing Data

Clusters, patterns, associations.

References

Horvath, Steve, and Kenneth Raj. 2018. "DNA Methylation-Based Biomarkers and the Epigenetic Clock Theory of Ageing." *Nature Reviews Genetics* 19 (6): 371–84. https://doi.org/10.1038/s41576-018-0004-3.

Ji, Shuiwang, Wei Xu, Ming Yang, and Kai Yu. 2013. "3d Convolutional Neural Networks for Human Action Recognition." *IEEE Transactions on Pattern Analysis and Machine Intelligence* 35 (1): 221–31. https://doi.org/10.1109/TPAMI.2012.59.

Riley, Jill A. AND Steyerberg, Richard D. AND Hayden. 2013. "Prognosis Research Strategy (PROGRESS) 2: Prognostic Factor Research." *PLOS Medicine* 10 (2): 1–9. https://doi.org/10.1371/journal.pmed.1001380.