Dynamic prediction of survival in cystic fibrosis: A landmarking analysis using patient registry data

Example R code for obtaining estimated surival probabilities

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This document provides R code that can be used to obtain estimated survival probabilities for adults with cystic fibrosis (CF) in the UK. The code gives estimated probabilities of survival up to 10 years from ages 18 to 50, given values for a set of 15 predictor variables and conditional on survival to the current age. The results come from a dynamic prediction model developed using data from the UK Cystic Fibrosis Registry, as described in the manuscript enetitled "Dynamic prediction of survival in cystic fibrosis: A landmarking analysis using patient registry data". The manuscript is currently under review. The abstract is given below and a copy of the authors' original version of the full manuscript is available on request. A link will be provided in due course.

ABSTRACT

Cystic fibrosis (CF) is an inherited, chronic, progressive condition affecting around 10,000 individuals in the UK and over 70,000 worldwide. Survival in CF has improved considerably over recent decades and it is important to provide patients with up to date information on their prognosis, and clinicians with information to guide treatment decisions. The UK Cystic Fibrosis Registry is a secure centralized database, which collects annual data on almost all CF patients in the UK. We used Registry data from 34,872 annual records on 6071 individuals to develop a dynamic survival prediction model that provides personalised estimates of survival probabilities given a patient's current health status using 16 predictors. The model was developed using the landmarking approach, giving predicted survival curves up to 10 years from landmark ages 18 to 50. Several models were compared in terms of their predictive performance using cross-validation. The final model has good discrimination (C-indexes 0.872, 0842, 0.803 for 2-, 5-, 10-year survival prediction) and low prediction error (Brier scores 0.036, 0.076, 0.133). Our application illustrates the utility of the landmarking approach for making the best use of longitudinal and survival data and shows how models can be defined and compared in terms of predictive performance.

STEP 1

Enter values for predictor variables.

Please enter these carefully and read the notes about the values that are allowed for each predictor.

Example values are given.

```r
#Current age in years (Range: 18 to 50. This must be a whole number.)
landmark.age=30
```

```r
#Sex: Male ("M") or female ("F")
sex="M"

#Current FEV1 percent predicted (Range >0).
#This is assumed to be a value taken from a measurement when the patient is "well" (e.g. at an annual r
fev1.percent.predicted=57

#Current FVC percent predicted (Range >0).
#This is assumed to be a value taken from a measurement when the patient is "well" (e.g. at an annual r
fvc.percent.predicted=77

#Genotype: "F508del-homozygous" (2 copies of F508del),
#"F508del-heterozygous" (1 copy of F508del), "other" (0 copies of F508del)
genotype="F508del-homozygous"

#Age of diagnosis in years
#(Range 0-50. This does not have to be a whole number, e.g. you can enter 0.5.)
age.of.diagnosis=0.54

#Pseudomonas aeruginosa infection in the past year
pseudomonas.aeruginosa.infection="yes"

#Burkholderia cepacia infection in the past year
burkholderia.cepacia.infection="no"

#Staphylococcus aureus infection in the past year
staph.aureus.infection="no"

#MRSA (Methicillin-resistant Staphylococcus aureus) infection in the past year
MRSA.infection="no"

#Has the patient pancreatic insufficient: "yes" or "no"
pancreatic.insufficient="yes"

#Has the patient been diagnosed with CF-related diabetes: "yes" or "no"
cfrd="yes"

#Current weight in kilograms (kg) (Range >0)
weight=64

#height in centimetres (cm) (Range >0)
height=167

#Number of days the patient has been in hospital to receive IV antibiotics in the past year
#"0 days", "1-7 days", "8-14 days", "8-14 days", "15-21 days", "22-28 days", "29+ days"
hospital.IVs="0 days"

#In the past year, has the patient been hospitalised for reasons other than receiving IVs
#"yes" or "no"
hospital.nonIV="no"
```

STEP 2

Give the survival time of interest (in years). You can enter any time from 0 to 10.

You can also specify would you would like to see a full survivor curve up to 10 years

```r
# If you are interested in 2-year survival enter 'time.for.survival=2'. This
# will be combined with the landmark age specified above.  So, if you
# entered landmark.age=18 and time.for.survival=2, the code below will
# provide an estimate of survival to age 20 for an individual currently aged
# 18 and with the values for the predictors entered above.
time.for.survival = 10

# Specify whether you would also like to see a survival curve.  This gives a
# plot of the estimated probability of survival to up to 10 years from the
# current age.
survival.curve = "yes"  #enter 'yes' or 'no'
```

STEP 3

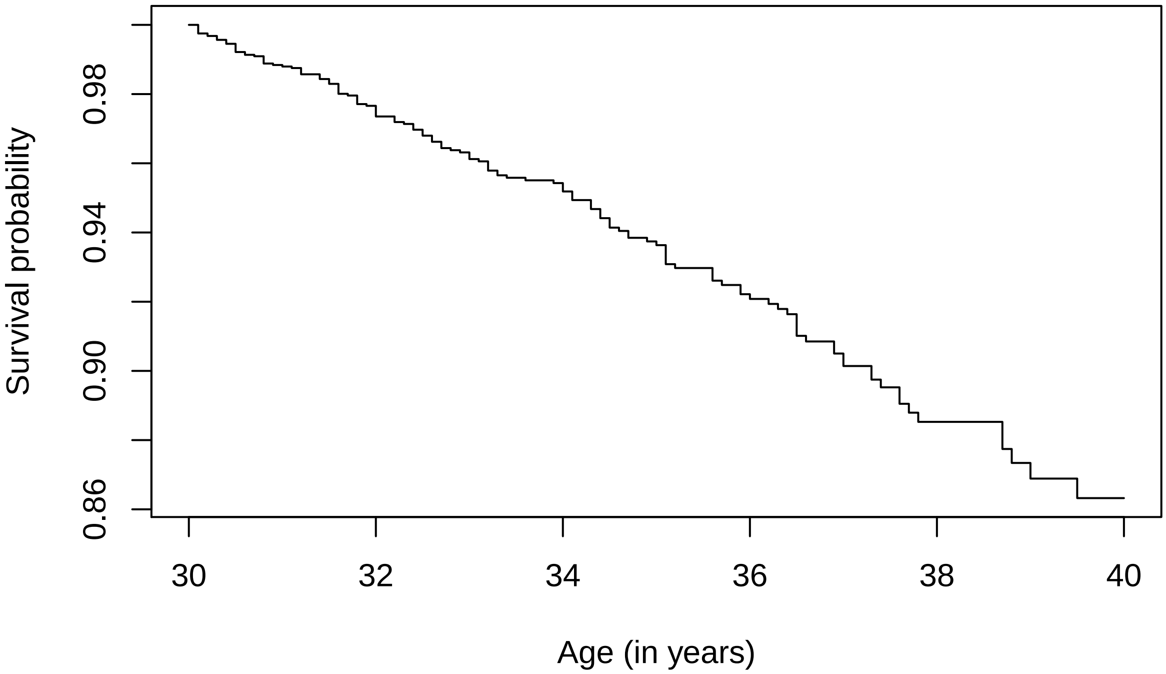
FROM THIS POINT ONWARDS, YOU DO NOT NEED TO ENTER ANY VALUES OR MAKE ANY CHANGES TO THE CODE.

RUN THE CODE BELOW TO OBTAIN ESTIMATED SURVIVAL PROBABILITIES AND AN ESTIMATED SURVIVOR CURVE, GIVEN THE DETAILED ENTERED ABOVE.

```r
#---------------------------------------
# read in the estimated baseline cumulative hazards and estimated log hazard
# ratios
#---------------------------------------

baseline.cumulative.hazards = read.table(file = "./baseline_cumulative_hazards.csv",
    sep = ",")

times = read.table(file = "./times.csv", sep = ",")

log.hazard.ratios = read.table(file = "./log_hazard_ratios.csv", sep = ",")

#---------------------------------------
# obtain estimates of the probability of survival for a given number of
# years (time.for.survival: up to 10 years from the current age)
#---------------------------------------

risk.score = log.hazard.ratios["sex", ] * (sex == "F") + log.hazard.ratios["fev1",
    ] * fev1.percent.predicted + log.hazard.ratios["fvc", ] * fvc.percent.predicted +
    log.hazard.ratios["genotype.1", ] * (genotype == "F508del-heterozygous") +
    log.hazard.ratios["genotype.0", ] * (genotype == "other") + log.hazard.ratios["age.diagnosis",
    ] * age.of.diagnosis + log.hazard.ratios["p.aeruginosa", ] * (pseudomonas.aeruginosa.infection ==
    "yes") + log.hazard.ratios["b.cepacia", ] * (burkholderia.cepacia.infection ==
    "yes") + log.hazard.ratios["s.aureus", ] * (staph.aureus.infection == "yes") +
    log.hazard.ratios["mrsa", ] * (MRSA.infection == "yes") + log.hazard.ratios["panc.insuff",
    ] * (pancreatic.insufficient == "yes") + log.hazard.ratios["cfrd", ] * (cfrd ==
    "yes") + log.hazard.ratios["weight", ] * weight + log.hazard.ratios["height",
    ] * height + log.hazard.ratios["year", ] * 10 + log.hazard.ratios["hospital.nonIV",
    ] * (hospital.nonIV == "yes") + log.hazard.ratios["hospital.IVs:1-7", ] *
    (hospital.IVs == "1-7 days") + log.hazard.ratios["hospital.IVs:8-14", ] *
    (hospital.IVs == "8-14 days") + log.hazard.ratios["hospital.IVs:15-21",
    ] * (hospital.IVs == "15-21 days") + log.hazard.ratios["hospital.IVs:22-28",
    ] * (hospital.IVs == "22-28 days") + log.hazard.ratios["hospital.IVs:29+",
    ] * (hospital.IVs == "29+ days")

baseline.cumulative.hazard.landmark = na.omit(baseline.cumulative.hazards[,
    paste0("lm", landmark.age)])
times.landmark = na.omit(times[, paste0("lm", landmark.age)])
baseline.hazard.landmark = c(baseline.cumulative.hazard.landmark[1], diff(baseline.cumulative.hazard.la
    lag = 1))

if (!is.null(time.for.survival)) {

    survival.probability = exp(-exp(risk.score) * sum(baseline.hazard.landmark[which(times.landmark <=
        landmark.age + time.for.survival)]))

    paste("Given the patient is now aged", landmark.age, ", and given the values provided for the predi
        landmark.age + time.for.survival, "is", round(survival.probability,
            3))

}
```

```
## [1] "Given the patient is now aged 30 , and given the values provided for the predictors, the patien
```

```r
#--------------------------------------
# obtain an estimated surivor curve up to 10 years from the current age
#--------------------------------------

if (survival.curve == "yes") {

    grid.times = seq(0, 10, 0.1)

    survival.probability = exp(-exp(risk.score) * sapply(grid.times, FUN = function(x) {
        sum(baseline.hazard.landmark[which(times.landmark <= landmark.age +
            x)])
    }))

    plot(landmark.age + grid.times, survival.probability, type = "s", xlab = "Age (in years)",
        ylab = "Survival probability")

}
```


Survival probability
0.86
0.90
0.94
0.98
30
32
34
36
38
40
Age (in years)