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casebase: An Alternative Framework For Survival Analysis

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Abstract

The abstract of the article. * joint co-authors

Keywords: keywords, not capitalized, Java.

Code formatting

Don't use markdown, instead use the more precise latex commands:

- Java
- plyr
- print("abc")

1. Introduction

The purpose of the casebase package is to provide practitioners with an easy-to-use software tool to predict the risk (or cumulative incidence (CI)) of an event, for a particular patient. The following points should be noted:

- 1. Time matching/risk set sampling (including Cox partial likelihood) eliminates the base-line hazard from the likelihood expression for the hazard ratios
- 2. If, however, the absolute risks are of interest, they have to be recovered using the semiparametric Breslow estimator

	Parameters	Density R function	dist
	(location in red)		
Exponential	rate	dexp	"exp"
Weibull (accelerated failure	shape, scale	dweibull	"weibull"
time)			
Weibull (proportional haz-	shape, scale	dweibullPH	"weibullPH"
ards)			
Gamma	shape, rate	dgamma	"gamma"
Log-normal	meanlog, sdlog	dlnorm	"lnorm"
Gompertz	shape, rate	dgompertz	"gompertz"
Log-logistic	shape, scale	dllogis	"llogis"
Generalized gamma (Pren-	<mark>mu</mark> , sigma, Q	dgengamma	"gengamma"
tice 1975)			
Generalized gamma (Stacy	shape, scale, k	dgengamma.orig	"gengamma.orig"
1962)			
Generalized F (stable)	<mark>mu</mark> , sigma, Q, P	dgenf	"genf"
Generalized F (original)	mu, sigma, s1, s2	dgenf.orig	"genf.orig"

Table 1: Built-in parametric survival distributions in **flexsurv**.

3. Alternative approaches for fitting flexible hazard models for estimating absolute risks, not requiring this two-step approach? Yes! (Hanley and Miettinen 2009)

(Hanley and Miettinen 2009) propose a fully parametric hazard model that can be fit via logistic regression. From the fitted hazard function, cumulative incidence and, thus, risk functions of time, treatment and profile can be easily derived.

2. Theoretical details

As discussed in Hanley & Miettinen (2009), the key idea behind case-base sampling is to discretize the study base into an infinite amount of *person moments*. These person moments are indexed by both an individual in the study and a time point, and therefore each person moment has a covariate profile, an exposure status and an outcome status attached to it. We note that there is only a finite number of person moments associated with the event of interest (what Hanley & Miettinen call the *case series*). The case-base sampling refers to the sampling from the base of a representative finite sample called the *base series*.

As shown by Saarela & Arjas (2015) (and further expanded in Saarela (2016)), writing the likelihood arising from this data-generating mechanism using the framework of non-homogenous Poisson processes, we eventually reach an expression where each person-moment's contribution is of the form

$$\frac{h(t)^{dN(t)}}{\rho(t) + h(t)},$$

where N(t) is the counting process associated with the event of interest, h(t) is the corresponding hazard function, and $\rho(t)$ is the hazard function for the Poisson process associated with case-base sampling. This parametric form suggests that we can readily estimate log-hazards of the form $\log(h(t)) = g(t; X)$ using logistic regression, where each observation corresponds

to a person moment, the function g(t; X) is linear in a finite number of parameters, and where we treat $-\log(\rho(t))$ as an offset.

In Hanley & Miettinen (2009), the authors suggest performing case-base samping uniformly, i.e. to sample the base series uniformly from the study base. In terms of Poisson processes, this sampling strategy corresponds essentially to a time-homogeneous Poisson process with intensity equal to b/B, where b is the number of sampled observations in the base series, and B is the total population-time for the study base. More complex examples are also available; see for example Saarela & Arjas (2015), where the probabilities of the sampling mechanism are proportional to the cardiovascular disease event rate given by the Framingham score.

The casebase package fits the family of hazard functions of the form

$$h(t;X) = \exp[g(t;X)]$$

where t denotes time and X, the individual's covariate profile. Different functions of t lead to different parametric hazard models. The simplest of these models is the one-parameter exponential distribution which is obtained by taking the hazard function to be constant over the range of t.

$$h(t;X) = \exp(\beta_0 + \beta_1 X)$$

The instantaneous failure rate is independent of t, so that the conditional chance of failure in a time interval of specified length is the same regardless of how long the individual has been in the study. This is also known as the *memoryless property* (Kalbfleisch and Prentice, 2002).

The Gompertz hazard model is given by including a linear term for time:

$$h(t;X) = \exp(\beta_0 + \beta_1 t + \beta_2 X)$$

Use of log(t) yields the Weibull hazard which allows for a power dependence of the hazard on time (Kalbfleisch and Prentice, 2002):

$$h(t;X) = \exp(\beta_0 + \beta_1 \log(t) + \beta_2 X)$$

For competing-risk analyses with J possible events, we can show that each person-moment's contribution of the likelihood is of the form

$$\frac{h_j(t)^{dN_j(t)}}{\rho(t) + \sum_{j=1}^J h_j(t)},$$

where $N_j(t)$ is the counting process associated with the event of type j and $h_j(t)$ is the corresponding hazard function. As may be expected, this functional form is similar to the

terms appearing in the likelihood function for multinomial regression.¹

3. Implementation details

The functions in the casebase package can be divided into two categories: 1) data visualization, in the form of population-time plots; and 2) parametric modeling. We explicitly aimed at being compatible with both data.frames and data.tables. This is evident in some of the coding choices we made, and it is also reflected in our unit tests.

3.1. Population-time plots

3.2. Parametric modeling

The parametric modeling step was separated into three parts:

- 1. case-base sampling;
- 2. estimation of the smooth hazard function;
- 3. calculation of the risk function.

By separating the sampling and estimation functions, we allowed the possibility of users implementing more complex sampling scheme, as described in Saarela (2016).

The sampling scheme selected for sampleCaseBase was described in Hanley and Miettinen (2009): we first sample along the "person" axis, proportional to each individual's total follow-up time, and then we sample a moment uniformly over their follow-up time. This sampling scheme is equivalent to the following picture: imagine representing the total follow-up time of all individuals in the study along a single dimension, where the follow-up time of the next individual would start exactly when the follow-up time of the previous individual ends. Then the base series could be sampled uniformly from this one-dimensional representation of the overall follow-up time. In any case, the output is a dataset of the same class as the input, where each row corresponds to a person-moment. The covariate profile for each such person-moment is retained, and an offset term is added to the dataset. This output could then be used to fit a smooth hazard function, or for visualization of the base series.

The fitting function fitSmoothHazard starts by looking at the class of the dataset: if it was generated from sampleCaseBase, it automatically inherited the class cbData. If the dataset supplied to fitSmoothHazard does not inherit from cbData, then the fitting function starts by calling sampleCaseBase to generate the base series. In other words, the occasional user can bypass sampleCaseBase altogether and only worry about the fitting function fitSmoothHazard.

The fitting function retains the familiar formula interface of glm. The left-hand side of the formula should be the name of the column corresponding to the event type. The right-hand

$$\log \left(\frac{P(Y=j \mid X)}{P(Y=J \mid X)} \right) = X^T \beta_j, \qquad j = 1, \dots, J-1$$

 $^{^1{\}rm Specifically},$ it corresponds to the following parametrization:

side can be any combination of the covariates, along with an explicit functional form for the time variable. Note that non-proportional hazard models can be achieved at this stage by adding an interaction term involving time. The offset term does not need to be specified by the user, as it is automatically added to the formula.

To fit the hazard function, we provide several approaches that are available via the family parameter. These approaches are:

- glm: This is the familiar logistic regression.
- glmnet: This option allows for variable selection using Lasso or elastic-net. This functionality is provided through the glmnet package (Friedman, Hastie, and Tibshirani 2010).
- gam: This option provides support for *Generalized Additive Models* via the gam package (Hastie and Tibshirani 1987).
- gbm: This option provides support for *Gradient Boosted Trees* via the gbm package. This feature is still experimental.

In the case of multiple events, the hazard is fitted via multinomial regression as performed by the **VGAM** package. This package was selected for its ability to fit multinomial regression models with an offset.

Once a model-fit object has been returned by fitSmoothHazard, all the familiar summary and diagnostic functions are available: print, summary, predict, plot, etc. Our package provides one more functionality: it computes risk functions from the model fit. For the case of a single event, it uses the familiar identity

$$S(t) = \exp\left(-\int_0^t h(u; X) du\right).$$

The integral is computed using either the stats::integrate function or Monte-Carlo integration. The risk function (or cumulative incidence function) is then defined as

$$CI(t) = 1 - S(t).$$

For the case of a competing-event analysis, the event-specific risk is computed using the following procedure: first, we compute the overall survival function (i.e. for all event types):

$$S(t) = \exp\left(-\int_0^t H(u;X)du\right), \qquad H(t;X) = \sum_{j=1}^J h_j(t;X).$$

From this, we can derive the event-specific subdensities:

$$f_i(t) = h_i(t)S(t).$$

Finally, by integrating these subdensities, we obtain the event-specific cumulative incidence functions:

$$CI_j(t) = \int_0^t f_j(u) du.$$

We created absoluteRisk as an S3 generic, with methods for the different types of outputs of fitSmoothHazard. The method dispatch system of R then takes care of matching the correct output to the correct methodology for calculating the cumulative incidence function, without the user's intervention.

In the following sections, we illustrate these functionalities in the context of three case studies.

4. Case study 1-European Randomized Study of Prostate Cancer Screening

To introduce the different features available, we make use of the European Randomized Study of Prostate Cancer Screening data; this dataset is available through the **casebase** package:

The results of this study were published by [schroder2009screening]. This data was obtained using the approach described in [liu2014recovering].

Population time plots can be extremely informative graphical displays of survival data. They should be the first step in an exploratory data analysis. We facilitate this task in the **casebase** package using the **popTime** function. We first create the necessary dataset for producing the population time plots, and we can produce the plot by using the corresponding **plot** method:

```
R> pt_object <- casebase::popTime(ERSPC, event = "DeadOfPrCa")
R> plot(pt_object)
```

We can also create exposure stratified plots by specifying the exposure argument in the popTime function:

We can also plot them side-by-side using the ncol argument:

```
R> plot(pt_object_strat, ncol = 2)
```

First, we fit a Cox model to the data, examine the hazard ratio for the screening group (relative to the control group), and plot the cumulative incidence function (CIF).

We can plot the CIF for each group:

```
R> new_data <- data.frame(ScrArm = c("Control group", "Screening group"),
R.>
                           ignore = 99)
R>
R> plot(survfit(cox_model, newdata = new_data),
        xlab = "Years since Randomization",
R>
        ylab = "Cumulative Incidence",
R>
        fun = "event",
R.>
        xlim = c(0,15), conf.int = FALSE, col = c("red","blue"),
R.>
R>
        main = sprintf("Estimated Cumulative Incidence (risk) of Death from Prostate
                        Cancer Screening group Hazard Ratio: %.2g (%.2g, %.2g)",
R>
                        exp(coef(cox_model)),
R>
R>
                        exp(confint(cox_model))[1],
                        exp(confint(cox_model))[2]))
R>
R> legend("topleft",
          legend = c("Control group", "Screening group"),
R>
          col = c("red", "blue"),
R.>
R.>
          1ty = c(1, 1),
          bg = "gray90")
R.>
```

Next we fit several models using case-base sampling. The models we fit differ in how we choose to model time.

The fitSmoothHazard function provides an estimate of the hazard function h(x,t) is the hazard function, where t denotes the numerical value of a point in prognostic/prospective time and x is the realization of the vector X of variates based on the patient's profile and intervention (if any).

The absoluteRisk function provides an estimate of the cumulative incidence curves for a specific risk profile using the following equation:

$$CI(x,t) = 1 - \exp\left(-\int_0^t h(x,u)du\right)$$

In the plot below, we overlay the estimated CIF from the casebase exponential model on the Cox model CIF:

```
R> plot(survfit(cox_model, newdata = new_data),
R.>
        xlab = "Years since Randomization",
        ylab = "Cumulative Incidence",
R>
R.>
        fun = "event",
        xlim = c(0,15), conf.int = FALSE, col = c("red","blue"),
R>
        main = sprintf("Estimated Cumulative Incidence (risk) of Death from Prostate
R.>
R.>
                        Cancer Screening group Hazard Ratio: %.2g (%.2g, %.2g)",
                        exp(coef(cox_model)),
R.>
R>
                        exp(confint(cox_model))[1],
R>
                        exp(confint(cox_model))[2]))
R> lines(smooth_risk_exp[,1], smooth_risk_exp[,2], col = "red", lty = 2)
R> lines(smooth_risk_exp[,1], smooth_risk_exp[,3], col = "blue", lty = 2)
R>
R>
R> legend("topleft",
          legend = c("Control group (Cox)", "Control group (Casebase)",
R.>
                      "Screening group (Cox)", "Screening group (Casebase)"),
R>
          col = c("red", "red", "blue", "blue"),
R.>
R>
          1ty = c(1, 2, 1, 2),
          bg = "gray90")
R>
```

As we can see, the exponential model is not a good fit. Based on what we observed in the population time plot, where more events are observed later on in time, this poor fit is expected. A constant hazard model would overestimate the cumulative incidence earlier on in time, and underestimate it later on; this is what we see on the cumulative incidence plot. This example demonstrates the benefits of population time plots as an exploratory analysis tool.

Next we enter time linearly into the model:

```
R> casebase_time <- fitSmoothHazard(DeadOfPrCa ~ Follow.Up.Time + ScrArm,</pre>
R>
                                      data = ERSPC,
R>
                                      ratio = 100)
R.>
R> summary(casebase_time)
R> exp(coef(casebase_time))
R> exp(confint(casebase_time))
R> smooth_risk_time <- casebase::absoluteRisk(object = casebase_time,
R>
                                               time = seq(0,15,0.1),
R.>
                                               newdata = new_data)
R.>
R> plot(survfit(cox_model, newdata = new_data),
R>
        xlab = "Years since Randomization",
        ylab = "Cumulative Incidence",
R.>
        fun = "event",
R>
        xlim = c(0,15), conf.int = FALSE, col = c("red","blue"),
R.>
```

```
R>
        main = sprintf("Estimated Cumulative Incidence (risk) of Death from Prostate
R.>
                        Cancer Screening group Hazard Ratio: %.2g (%.2g, %.2g)",
R>
                        exp(coef(cox_model)),
R.>
                        exp(confint(cox_model))[1],
                        exp(confint(cox_model))[2]))
R.>
R> lines(smooth_risk_time[,1], smooth_risk_time[,2], col = "red", lty = 2)
R> lines(smooth_risk_time[,1], smooth_risk_time[,3], col = "blue", lty = 2)
R>
R> legend("topleft",
R>
          legend = c("Control group (Cox)", "Control group (Casebase)",
                      "Screening group (Cox)", "Screening group (Casebase)"),
R>
R>
          col = c("red", "red", "blue", "blue"),
          1ty = c(1, 2, 1, 2),
R>
R.>
          bg = "gray90")
```

We see that the Weibull model leads to a better fit.

Next we try to enter a smooth function of time into the model using the splines package:

```
R> casebase_splines <- fitSmoothHazard(DeadOfPrCa ~ bs(Follow.Up.Time) + ScrArm,
R>
                                        data = ERSPC,
                                        ratio = 100)
R>
R>
R> summary(casebase_splines)
R> exp(coef(casebase_splines))
R> exp(confint(casebase_splines))
R> smooth_risk_splines <- absoluteRisk(object = casebase_splines,</pre>
R>
                                        time = seq(0,15,0.1),
R>
                                        newdata = new_data)
R.>
R> plot(survfit(cox_model, newdata = new_data),
R.>
        xlab = "Years since Randomization",
        ylab = "Cumulative Incidence",
R>
R>
        fun = "event",
        xlim = c(0,15), conf.int = FALSE, col = c("red","blue"),
R>
        main = sprintf("Estimated Cumulative Incidence (risk) of Death from Prostate
R.>
                        Cancer Screening group Hazard Ratio: %.2g (%.2g, %.2g)",
R>
R>
                        exp(coef(cox_model)),
R>
                        exp(confint(cox_model))[1],
                        exp(confint(cox_model))[2]))
R>
R> lines(smooth_risk_splines[,1], smooth_risk_splines[,2], col = "red", lty = 2)
R> lines(smooth_risk_splines[,1], smooth_risk_splines[,3], col = "blue", lty = 2)
R>
R> legend("topleft",
          legend = c("Control group (Cox)", "Control group (Casebase)",
R.>
                      "Screening group (Cox)", "Screening group (Casebase)"),
R.>
```

```
R> col = c("red", "red", "blue", "blue"),
R> lty = c(1, 2, 1, 2),
R> bg = "gray90")
```

It looks like the best fit.

Since we are within the GLM framework, we can easily test for which model better fits the data using a Likelihood Ratio Test (LRT). The null hypothesis here is that the linear model is just as good as the larger (in terms of number of parameters) splines model.

```
R> anova(casebase_time, casebase_splines, test = "LRT")
```

As espected, we see that splines model provides a better fit.

5. Case study 2–Bone-marrow transplant

The next example shows how case-base sampling can also be used in the context of a competing risk analysis. For illustrative purposes, we will use the same data that was used in Scrucca et al (2010). The data was downloaded from the main author's website, and it is also available as part of the **casebase** package.

```
R> data(bmtcrr)
```

The data contains information on 177 patients who received a stem-cell transplant for acute leukemia. The event of interest is relapse, but other competing causes (e.g. transplant-related death) were also recorded Several covariates were also captured at baseline: sex, disease type (acute lymphoblastic or myeloblastic leukemia, abbreviated as ALL and AML, respectively), disease phase at transplant (Relapse, CR1, CR2, CR3), source of stem cells (bone marrow and peripheral blood, coded as BM+PB, or only peripheral blood, coded as PB), and age. A summary of these baseline characteristics appear in Table 2. We note that the statistical summaries were generated differently for different variable types: for continuous variables, we gave the range, followed by the mean and standard deviation; for categorical variables, we gave the counts for each category.

In order to try and visualize the incidence density of relapse, we can look at the corresponding population-time plot. In Figure ??, failure times associated with relapse are highlighted on the plot using red points, while Figure ?? provides a similar population-time plot for competing events.

Our main objective is to compute the absolute risk of relapse for a given set of covariates. First, we fit a smooth hazard to the data; for the sake of this example, we opted for a linear term for time:

```
R> model_cb <- fitSmoothHazard(
R> Status ~ ftime + Sex + D + Phase + Source + Age,
R> data = bmtcrr,
R> ratio = 100,
R> time = "ftime")
```

Variable	Description	Statistical summary
Sex	Sex	M=Male (100)
		F=Female (77)
D	Disease	ALL (73)
		AML (104)
Phase	Phase	CR1 (47)
		CR2 (45)
		CR3 (12)
		Relapse (73)
Source	Type of transplant	BM+PB (21)
		PB (156)
Age	Age of patient (years)	4-62
		$30.47 \ (13.04)$
Ftime	Failure time (months)	0.13 – 131.77
		20.28 (30.78)
Status	Status indicator	0 = censored (46)
		1 = relapse (56)
		2=competing event (75)

Table 2: Baseline characteristics of patients in the stem-cell transplant study.

From the fit object, we can extract both the hazard ratios and their corresponding confidence intervals:

As we can see, the only significant hazard ratio is the one associated with the phase of the disease at transplant. More precisely, being in relapse at transplant is associated with a hazard ratio of 3.92 when compared to CR1.

Given our estimate of the hazard function, we can compute the absolute risk curve for a fixed covariate profile. We performed this computation for a 35 year old woman who received a stem-cell transplant from peripheral blood at relapse. We compared the absolute risk curve for such a woman with acute lymphoblastic leukemia with that for a similar woman with acute myeloblastic leukemia. Figure ?? shows these two curves as a function of time. This figure also shows the Kaplan-Meier estimate fitted to the two disease groups (ignoring the other covariates).

```
R> # Pick 100 equidistant points between 0 and 60 months
R> time_points <- seq(0, 60, length.out = 50)
R> # Data.frame containing risk profile
R> newdata <- data.frame("Sex" = factor(c("F", "F"),</pre>
                                          levels = levels(bmtcrr[,"Sex"])),
R>
                          "D" = c("ALL", "AML"),
R>
                          "Phase" = factor(c("Relapse", "Relapse"),
R.>
                                            levels = levels(bmtcrr[, "Phase"])),
R>
                          "Age" = c(35, 35),
R>
                          "Source" = factor(c("PB", "PB"),
R.>
                                             levels = levels(bmtcrr[, "Source"])))
R>
```

6. Case study 3-The Cancer Genome Atlas

• Glmnet and TCGA data

7. Discussion

In the following table we provide a comparison between the Cox model and case-base sampling:

8. Environment Details

This report was generated on 2019-07-25 16:51:47 using the following computational environment and dependencies:

```
R> # which R packages and versions?
R> devtools::session_info()
#> - Session info ------
  setting value
#>
  version R version 3.6.1 (2019-07-05)
#>
  os
          Ubuntu 18.04.2 LTS
#>
  system x86_64, linux-gnu
#>
  ui
          X11
#> language en_CA:en
#>
   collate en_CA.UTF-8
          en_CA.UTF-8
#>
   ctype
#>
   tz
          America/Winnipeg
          2019-07-25
#>
   date
#>
#>
   package
             * version
                        date
                                 lib source
              0.2.1
                        2019-03-21 [1] CRAN (R 3.6.1)
#>
   assertthat
                       2019-04-10 [1] CRAN (R 3.6.1)
#> backports
              1.1.4
                        2019-04-07 [1] CRAN (R 3.6.1)
#> broom
             0.5.2
#> callr
              3.3.1
                        2019-07-18 [1] CRAN (R 3.6.1)
#> casebase * 0.2.1.9000 2019-07-25 [1] local
#> cellranger
              1.1.0
                        2016-07-27 [1] CRAN (R 3.6.1)
#> cli
                       2019-03-19 [1] CRAN (R 3.6.1)
              1.1.0
                      2019-03-18 [1] CRAN (R 3.6.1)
  colorspace 1.4-1
#>
```

#>	crayon		1.3.4	2017-09-16	[1]	CRAN	(R 3.6.1)
#>	data.table		1.12.2	2019-04-07	[1]	CRAN	(R 3.6.1)
#>	desc		1.2.0	2018-05-01	[1]	CRAN	(R 3.6.1)
#>	devtools		2.1.0	2019-07-06	[1]	CRAN	(R 3.6.1)
#>	digest		0.6.20	2019-07-04	[1]	CRAN	(R 3.6.1)
#>	dplyr	*	0.8.3	2019-07-04	[1]	CRAN	(R 3.6.1)
#>	evaluate		0.14	2019-05-28	[1]	CRAN	(R 3.6.1)
#>	forcats	*	0.4.0	2019-02-17	[1]	CRAN	(R 3.6.1)
#>	fs		1.3.1	2019-05-06	[1]	CRAN	(R 3.6.1)
#>	generics		0.0.2	2018-11-29	[1]	CRAN	(R 3.6.1)
#>	ggplot2	*	3.2.0	2019-06-16	[1]	CRAN	(R 3.6.1)
#>	glue		1.3.1	2019-03-12	[1]	CRAN	(R 3.6.1)
#>	gtable		0.3.0	2019-03-25	[1]	CRAN	(R 3.6.1)
#>	haven		2.1.1	2019-07-04	[1]	CRAN	(R 3.6.1)
#>	hms		0.5.0	2019-07-09	[1]	CRAN	(R 3.6.1)
#>	htmltools		0.3.6	2017-04-28	[1]	CRAN	(R 3.6.1)
#>	httr		1.4.0	2018-12-11	[1]	CRAN	(R 3.6.1)
#>	jsonlite		1.6	2018-12-07	[1]	CRAN	(R 3.6.1)
#>	knitr		1.23	2019-05-18	[1]	CRAN	(R 3.6.1)
#>	lattice		0.20-38	2018-11-04	[4]	CRAN	(R 3.5.1)
#>	lazyeval		0.2.2	2019-03-15	[1]	CRAN	(R 3.6.1)
#>	lubridate		1.7.4	2018-04-11	[1]	CRAN	(R 3.6.1)
#>	${ t magrittr}$	*	1.5	2014-11-22	[1]	CRAN	(R 3.6.1)
#>	Matrix		1.2-17	2019-03-22	[4]	CRAN	(R 3.5.3)
#>	memoise		1.1.0	2017-04-21	[1]	CRAN	(R 3.6.1)
#>	mgcv		1.8-28	2019-03-21	[4]	CRAN	(R 3.5.3)
#>	modelr		0.1.4	2019-02-18	[1]	CRAN	(R 3.6.1)
#>	munsell		0.5.0	2018-06-12	[1]	CRAN	(R 3.6.1)
#>	nlme		3.1-140	2019-05-12	[4]	CRAN	(R 3.6.0)
#>	pillar		1.4.2	2019-06-29	[1]	CRAN	(R 3.6.1)
#>	pkgbuild		1.0.3	2019-03-20	[1]	CRAN	(R 3.6.1)
#>	pkgconfig		2.0.2	2018-08-16	[1]	CRAN	(R 3.6.1)
#>	pkgload		1.0.2	2018-10-29	[1]	CRAN	(R 3.6.1)
#>	prettyunits		1.0.2	2015-07-13	[1]		(R 3.6.1)
#>	processx		3.4.1	2019-07-18	[1]	CRAN	(R 3.6.1)
#>	ps		1.3.0	2018-12-21	[1]	CRAN	(R 3.6.1)
#>	purrr	*	0.3.2	2019-03-15	[1]	CRAN	(R 3.6.1)
#>	R6		2.4.0	2019-02-14	[1]	CRAN	(R 3.6.1)
#>	Rcpp		1.0.1	2019-03-17	[1]	CRAN	(R 3.6.1)
#>	readr	*	1.3.1	2018-12-21	[1]	CRAN	(R 3.6.1)
#>	readxl		1.3.1	2019-03-13	[1]	CRAN	(R 3.6.1)
#>	remotes		2.1.0	2019-06-24	[1]	CRAN	(R 3.6.1)
#>	rlang		0.4.0	2019-06-25	[1]	CRAN	
#>	rmarkdown		1.14	2019-07-12			
#>	rprojroot		1.3-2	2018-01-03	[1]	CRAN	(R 3.6.1)
#>	rstudioapi		0.10	2019-03-19	[1]	CRAN	(R 3.6.1)
#>	rticles		0.9	2019-07-12	[1]	CRAN	(R 3.6.1)

```
#>
                  0.3.4
                             2019-05-15 [1] CRAN (R 3.6.1)
   rvest
#>
                  1.0.0
                             2018-08-09 [1] CRAN (R 3.6.1)
   scales
                             2018-11-05 [1] CRAN (R 3.6.1)
#>
   sessioninfo
                  1.1.1
#>
   stringi
                  1.4.3
                             2019-03-12 [1] CRAN (R 3.6.1)
                             2019-02-10 [1] CRAN (R 3.6.1)
#>
   stringr
                * 1.4.0
                * 2.43-3
                             2018-11-26 [4] CRAN (R 3.5.1)
#>
   survival
   testthat
#>
                  2.2.0
                             2019-07-22 [1] CRAN (R 3.6.1)
#>
   tibble
                * 2.1.3
                             2019-06-06 [1] CRAN (R 3.6.1)
#>
   tidyr
                * 0.8.3
                             2019-03-01 [1] CRAN (R 3.6.1)
#>
   tidyselect
                  0.2.5
                             2018-10-11 [1] CRAN (R 3.6.1)
                * 1.2.1
                             2017-11-14 [1] CRAN (R 3.6.1)
#>
   tidyverse
#>
   usethis
                  1.5.1
                             2019-07-04 [1] CRAN (R 3.6.1)
#>
                  0.2.0
                             2019-07-05 [1] CRAN (R 3.6.1)
   vctrs
#>
   VGAM
                  1.1-1
                             2019-02-18 [1] CRAN (R 3.6.1)
                             2018-03-15 [1] CRAN (R 3.6.1)
#>
   withr
                  2.1.2
#>
   xfun
                  0.8
                             2019-06-25 [1] CRAN (R 3.6.1)
#>
   xm12
                  1.2.0
                             2018-01-24 [1] CRAN (R 3.6.1)
                  2.2.0
                             2018-07-25 [1] CRAN (R 3.6.1)
#>
   yaml
#>
                  0.1.0
                             2018-01-28 [1] CRAN (R 3.6.1)
   zeallot
#>
```

- #> [1] /home/turgeonm/R/x86_64-pc-linux-gnu-library/3.6
- #> [2] /usr/local/lib/R/site-library
- #> [3] /usr/lib/R/site-library
- #> [4] /usr/lib/R/library

The current Git commit details are:

```
R> # what commit is this file at?
R> git2r::repository(here::here())
```

#> Local: review-max /home/turgeonm/Documents/git_repos/cbpaper

#> Head: [c0cb26d] 2019-07-23: Merge pull request #6 from sahirbhatnagar/fixdocker

References

- Friedman J, Hastie T, Tibshirani R (2010). "Regularization Paths for Generalized Linear Models via Coordinate Descent." *Journal of Statistical Software*, **33**(1). ISSN 1548-7660. doi:10.18637/jss.v033.i01.
- Hanley JA, Miettinen OS (2009). "Fitting smooth-in-time prognostic risk functions via logistic regression." The International Journal of Biostatistics, 5(1).
- Hastie T, Tibshirani R (1987). "Generalized additive models: some applications." *Journal of the American Statistical Association*, **82**(398), 371–386.

Saarela O (2016). "A case-base sampling method for estimating recurrent event intensities." *Lifetime data analysis*, **22**(4), 589–605.

Saarela O, Arjas E (2015). "Non-parametric Bayesian Hazard Regression for Chronic Disease Risk Assessment." Scandinavian Journal of Statistics, 42(2), 609–626.

Scrucca L, Santucci A, Aversa F (2010). "Regression modeling of competing risk using R: an in depth guide for clinicians." *Bone marrow transplantation*, **45**(9), 1388.

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