# Tutorial in biostatistics: Competing risks and multi-state models
# Analyses using the *mstate* package

Hein Putter
Department of Medical Statistics and Bioinformatics
Leiden University Medical Center
Postzone S-5-P
PO Box 9600
2300 RC Leiden
The Netherlands
E-mail: h.putter@lumc.nl

July 11, 2024

# 1 Introduction

This is a companion file both for the *mstate* package and for the Tutorial in Biostatistics: Competing risks and multi-state models (Putter et al. 2007), simply referred to henceforth as the tutorial. Emphasis in this document will be on the use of *mstate*, not on the theory of competing risks and multi-state models. The only exception is that I have added some theory about the Aalen-Johansen estimator that is implemented in *mstate* but did not appear in the tutorial. For other theory on multi-state models, and for interpretation of the results of the analyses, we will repeatedly refer to the tutorial. I will occasionally give more detail and show more analyses than in the tutorial. Also I sometimes give more details on the function in *mstate* than strictly necessary for the analyses in the tutorial, but not all features will be shown either. This file and the *mstate* package, which in turn contains all the data used in the tutorial, can be found at `https://github.com/hputter/mstate`. This file is also a vignette of the *mstate* package. Type `vignette("Tutorial")` after having installed and loaded *mstate* to access this document within R.

I do not follow the order of the tutorial. Rather, I will start with multi-state models, Section 4 of the tutorial, and finally switch back to the special case of competing risks models. Sections 2, 3 and 4 of this document will discuss data preparation, estimation and prediction, respectively in multi-state models. In Section 5 I illustrate some functions of *mstate* designed especially for competing risks.

After installation, the *mstate* package is loaded in the usual way.

```
> library(mstate)
```

The versions of `R` and *mstate* used in this document are as follows:

```
> R.version$version.string
```

```
[1] "R version 4.4.1 (2024-06-14 ucrt)"
```

```
> packageDescription("mstate", fields = "Version")
```

```
[1] "0.3.3"
```

# 2 Data preparation

The data used in Section 4 of the tutorial are 2204 patients transplanted at the EBMT between 1995 and 1998. These data are included in the *mstate* package. For (a tiny bit) more background on the data, refer to the tutorial, or type `help(ebmt3)`.

```
> data(ebmt3)
> head(ebmt3)
```

```
  id prtime prstat rfstime rfsstat dissub   age            drmatch    tcd
1  1     23      1     744       0    CML   >40    Gender mismatch No TCD
2  2     35      1     360       1    CML   >40 No gender mismatch No TCD
3  3     26      1     135       1    CML   >40 No gender mismatch No TCD
4  4     22      1     995       0    AML 20-40 No gender mismatch No TCD
5  5     29      1     422       1    AML 20-40 No gender mismatch No TCD
6  6     38      1     119       1    ALL   >40 No gender mismatch No TCD
```

Let us first have a look at the covariates. For instance disease subclassification:

```
> n <- nrow(ebmt3)
> table(ebmt3$dissub)

AML ALL CML
853 447 904

> round(100 * table(ebmt3$dissub)/n)

AML ALL CML
 39  20  41
```

The output of the other covariates is omitted.

```
> table(ebmt3$age)
> round(100 * table(ebmt3$age)/n)
> table(ebmt3$drmatch)
> round(100 * table(ebmt3$drmatch)/n)
> table(ebmt3$tcd)
> round(100 * table(ebmt3$tcd)/n)
```

The first step in a multi-state model analysis is to set up the transition matrix. The transition matrix specifies which direct transitions are possible (those with `NA` are impossible) and assigns numbers to the transitions for future reference. This can be done explicitly.

```
> tmat <- matrix(NA, 3, 3)
> tmat[1, 2:3] <- 1:2
> tmat[2, 3] <- 3
> dimnames(tmat) <- list(from = c("Tx", "PR", "RelDeath"), to = c("Tx",
+     "PR", "RelDeath"))
> tmat

          to
from       Tx PR RelDeath
  Tx       NA  1        2
  PR       NA NA        3
  RelDeath NA NA       NA
```

Steven McKinney has kindly provided a convenient function *transMat* to define transition matrices. The same transition matrix may be constructed as follows.

```
> tmat <- transMat(x = list(c(2, 3), c(3), c()), names = c("Tx",
+     "PR", "RelDeath"))
> tmat

          to
from       Tx PR RelDeath
  Tx       NA  1        2
  PR       NA NA        3
  RelDeath NA NA       NA
```

For common multi-state models, such as the illness-death model (and competing risks models, Section 5) there is a built-in function to obtain these transition matrices more easily.

```
> tmat <- trans.illdeath(names = c("Tx", "PR", "RelDeath"))
> tmat
```

```
          to
from       Tx PR RelDeath
  Tx       NA  1        2
  PR       NA NA        3
  RelDeath NA NA       NA
```

The function *paths* can be used to give a list of all possible paths through the multi-state model. This function should not be used for transition matrices specifying a multi-state model with loops, since there will be infinitely many paths. At the moment there is no check for the presence of loops, but this will be included shortly.

```
> paths(tmat)
```

```
     [,1] [,2] [,3]
[1,]    1   NA   NA
[2,]    1    2   NA
[3,]    1    2    3
[4,]    1    3   NA
```

Time in the `ebmt3` data is reported in days; before doing any analysis, we first convert this to years.

```
> ebmt3$prtime <- ebmt3$prtime/365.25
> ebmt3$rfstime <- ebmt3$rfstime/365.25
```

In order to prepare data in long format, we specify the names of the covariates that we are interested in modeling. Note that I am adding `prtime`, which is not really a covariate, but specifying the time of platelet recovery. The purpose of this will become clear later. The specified covariates are to be retained in the dataset in long format (this is the argument *keep*), which we are going to call `msbmt`. For the original dataset `ebmt3`, each row corresponds to a single patient. For the long format data `msbmt`, each row will correspond to a transition for which a patient is at risk. See the tutorial for more detailed information.

```
> covs <- c("dissub", "age", "drmatch", "tcd", "prtime")
> msbmt <- msprep(time = c(NA, "prtime", "rfstime"), status = c(NA,
+     "prstat", "rfsstat"), data = ebmt3, trans = tmat, keep = covs)
```

The result is an S3 object of class *msdata* and *data.frame*. An *msdata* object is actually only a data frame with a `trans` attribute holding the transition matrix used to define it. A *print* method has been defined for *msdata* objects, which also prints the transition matrix if requested (set argument *trans* to `TRUE`, default is `FALSE`).

```
> head(msbmt)
```

```
An object of class 'msdata'

Data:
  id from to trans     Tstart      Tstop       time status dissub age
1  1    1  2     1 0.00000000 0.06297057 0.06297057      1    CML >40
```

```
2  1    1  3     2 0.00000000 0.06297057 0.06297057      0    CML >40
3  1    2  3     3 0.06297057 2.03696099 1.97399042      0    CML >40
4  2    1  2     1 0.00000000 0.09582478 0.09582478      1    CML >40
5  2    1  3     2 0.00000000 0.09582478 0.09582478      0    CML >40
6  2    2  3     3 0.09582478 0.98562628 0.88980151      1    CML >40
             drmatch    tcd     prtime
1    Gender mismatch No TCD 0.06297057
2    Gender mismatch No TCD 0.06297057
3    Gender mismatch No TCD 0.06297057
4 No gender mismatch No TCD 0.09582478
5 No gender mismatch No TCD 0.09582478
6 No gender mismatch No TCD 0.09582478
```

In the above call of *msprep*, the *time* and *status* arguments specify the column names in the data `ebmt3` corresponding to the three states in the multi-state model. Since all the patients start in state 1 at time 0, the *time* and *status* arguments corresponding to the first state do not really have a value. In such cases, the corresponding elements of *time* and *status* may be given the value `NA`. An alternative way of specifying *time* and *status* (and *keep* as well) is as matrices of dimension $n \times S$ with $S$ the number of states (and $n \times p$ with $p$ the number of covariates for *keep*). The *data* argument doesn't need to be specified then.

The number of events in the data can be summarized with the function *events*.

```
> events(msbmt)

$Frequencies
          to
from         Tx   PR RelDeath no event total entering
  Tx          0 1169      458      577           2204
  PR          0    0      383      786           1169
  RelDeath    0    0        0      841            841

$Proportions
          to
from               Tx        PR  RelDeath  no event
  Tx       0.0000000 0.5303993 0.2078040 0.2617967
  PR       0.0000000 0.0000000 0.3276305 0.6723695
  RelDeath 0.0000000 0.0000000 0.0000000 1.0000000
```

For regression purposes, we now add transition-specific covariates to the dataset. For more details on transition-specific covariates, refer to the tutorial. For a numerical covariate `cov`, the names of the expanded (transition-specific) covariates are `cov.1`, `cov.2` etc. The extension `.i` refers to transition number $i$. First, we define these transition-specific covariates as a separate dataset, by setting *append* to `FALSE`.

```
> expcovs <- expand.covs(msbmt, covs[2:3], append = FALSE)
> head(expcovs)

  age20.40.1 age20.40.2 age20.40.3 age.40.1 age.40.2 age.40.3
1          0          0          0        1        0        0
2          0          0          0        0        1        0
3          0          0          0        0        0        1
```

```
4          0          0          0        1        0        0
5          0          0          0        0        1        0
6          0          0          0        0        0        1
  drmatchGender.mismatch.1 drmatchGender.mismatch.2 drmatchGender.mismatch.3
1                        1                        0                        0
2                        0                        1                        0
3                        0                        0                        1
4                        0                        0                        0
5                        0                        0                        0
6                        0                        0                        0
```

We see that this expanded covariates dataset is quite large, and that the covariate names are quite long. For categorical covariates, the default names of the expanded covariates are a combination of the covariate name, the level (similar to the names of the regression coefficients that you see in regression output), followed by the transition number, in such a way that the combination is allowed as column name. If these names are too long, the user may set the value of *longnames* (default=`TRUE`) to `FALSE`. In this case, the covariate name is followed by `1`, `2` etc, before the transition number. In case of a covariate with only two levels, the covariate name is just followed by the transition number. Confident that this will work out, we also set *append* to `TRUE` (default), which will append the expanded covariates to the dataset.

```
> msbmt <- expand.covs(msbmt, covs, append = TRUE, longnames = FALSE)
> head(msbmt)

An object of class 'msdata'

Data:
  id from to trans     Tstart      Tstop       time status dissub age
1  1    1  2     1 0.00000000 0.06297057 0.06297057      1    CML >40
2  1    1  3     2 0.00000000 0.06297057 0.06297057      0    CML >40
3  1    2  3     3 0.06297057 2.03696099 1.97399042      0    CML >40
4  2    1  2     1 0.00000000 0.09582478 0.09582478      1    CML >40
5  2    1  3     2 0.00000000 0.09582478 0.09582478      0    CML >40
6  2    2  3     3 0.09582478 0.98562628 0.88980151      1    CML >40
             drmatch    tcd     prtime dissub1.1 dissub1.2 dissub1.3 dissub2.1
1    Gender mismatch No TCD 0.06297057         0         0         0         1
2    Gender mismatch No TCD 0.06297057         0         0         0         0
3    Gender mismatch No TCD 0.06297057         0         0         0         0
4 No gender mismatch No TCD 0.09582478         0         0         0         1
5 No gender mismatch No TCD 0.09582478         0         0         0         0
6 No gender mismatch No TCD 0.09582478         0         0         0         0
  dissub2.2 dissub2.3 age1.1 age1.2 age1.3 age2.1 age2.2 age2.3 drmatch.1
1         0         0      0      0      0      1      0      0         1
2         1         0      0      0      0      0      1      0         0
3         0         1      0      0      0      0      0      1         0
4         0         0      0      0      0      1      0      0         0
5         1         0      0      0      0      0      1      0         0
6         0         1      0      0      0      0      0      1         0
  drmatch.2 drmatch.3 tcd.1 tcd.2 tcd.3   prtime.1   prtime.2   prtime.3
1         0         0     0     0     0 0.06297057 0.00000000 0.00000000
```

```
2         1         0     0     0     0 0.00000000 0.06297057 0.00000000
3         0         1     0     0     0 0.00000000 0.00000000 0.06297057
4         0         0     0     0     0 0.09582478 0.00000000 0.00000000
5         0         0     0     0     0 0.00000000 0.09582478 0.00000000
6         0         0     0     0     0 0.00000000 0.00000000 0.09582478
```

The names indeed are quite a bit shorter. The downside however is that we need to remember for ourselves to which category for instance the number `1` in `age1.2` corresponds (age 20-40 with $\leq 20$ as reference category).

# 3 Estimation

After having prepared the data in long format, estimation of covariate effects using Cox regression is straightforward using the ***coxph*** function of the *survival* package. This is not at all a feature of the *mstate* package, other than that ***msprep*** has facilitated preparation of the data. Let us consider the Markov model, where we assume different effects of the covariates for different transitions; hence we use the transition-specific covariates obtained by ***expand.covs***. The delayed entry aspect of this model for transition 3 (see discussion in the tutorial) is achieved by specifying *Surv(Tstart,Tstop,status)*, where (this is reflected in the long format data) `Tstart` is the time of entry in the state, and `Tstop` the event or censoring time, depending on the value of `status`. We consider first the model without any proportionality assumption on the baseline hazards; this is achieved by adding *strata(trans)* to the formula, which estimates separate baseline hazards for different values of `trans` (the transitions). The results appear in the left column of Table III of the tutorial.

```
> c1 <- coxph(Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
+     age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
+     age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
+     age1.3 + age2.3 + drmatch.3 + tcd.3 + strata(trans), data = msbmt,
+     method = "breslow")
> c1

Call:
coxph(formula = Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
    age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
    age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
    age1.3 + age2.3 + drmatch.3 + tcd.3 + strata(trans), data = msbmt,
    method = "breslow")

              coef exp(coef) se(coef)      z        p
dissub1.1 -0.04359   0.95734  0.07789 -0.560 0.575698
dissub2.1 -0.29724   0.74287  0.06800 -4.371 1.23e-05
age1.1    -0.16461   0.84822  0.07905 -2.082 0.037317
age2.1    -0.08979   0.91412  0.08647 -1.038 0.299075
drmatch.1  0.04575   1.04681  0.06660  0.687 0.492127
tcd.1      0.42907   1.53583  0.08043  5.335 9.57e-08
dissub1.2  0.25589   1.29161  0.13520  1.893 0.058411
dissub2.2  0.01675   1.01689  0.10838  0.155 0.877188
age1.2     0.25516   1.29067  0.15103  1.689 0.091127
age2.2     0.52649   1.69298  0.15790  3.334 0.000855
```

```
drmatch.2 -0.07525   0.92751  0.11028 -0.682 0.495006
tcd.2      0.29673   1.34545  0.15007  1.977 0.048006
dissub1.3  0.13646   1.14621  0.14804  0.922 0.356634
dissub2.3  0.24692   1.28007  0.11685  2.113 0.034596
age1.3     0.06156   1.06350  0.15343  0.401 0.688239
age2.3     0.58075   1.78737  0.16014  3.627 0.000287
drmatch.3  0.17280   1.18863  0.11452  1.509 0.131315
tcd.3      0.20088   1.22248  0.12636  1.590 0.111873

Likelihood ratio test=117.7  on 18 df, p=< 2.2e-16
n= 5577, number of events= 2010
```

The interpretation is discussed in the tutorial.

The next model considered is the Markov model where the transition hazards into relapse or death (these correspond to transitions 2 and 3) are assumed to be proportional. For this purpose transition 1 (transplantation → platelet recovery) belongs to one stratum and transitions 2 (transplantation → relapse/death) and 3 (platelet recovery → relapse/death) belong to a second stratum. Transitions 2 and 3 have the same receiving state, hence the same value of `to`, so the two strata can be distinguished by the variable `to` in our dataset. In order to distinguish between transitions 2 and 3, we introduce a time-dependent covariate `pr` that indicates whether or not platelet recovery has already occurred. For transition 2 (Tx → RelDeath) the value of `pr` equals 0, while for transition 3 (PR → RelDeath) the value of `pr` equals 1. Results are found in the middle of Table III of the tutorial.

```
> msbmt$pr <- 0
> msbmt$pr[msbmt$trans == 3] <- 1
> c2 <- coxph(Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
+     age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
+     age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
+     age1.3 + age2.3 + drmatch.3 + tcd.3 + pr + strata(to), data = msbmt,
+     method = "breslow")
> c2

Call:
coxph(formula = Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
    age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
    age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
    age1.3 + age2.3 + drmatch.3 + tcd.3 + pr + strata(to), data = msbmt,
    method = "breslow")

               coef exp(coef)  se(coef)      z        p
dissub1.1 -0.043592  0.957345  0.077887 -0.560 0.575698
dissub2.1 -0.297240  0.742866  0.067996 -4.371 1.23e-05
age1.1    -0.164613  0.848222  0.079054 -2.082 0.037317
age2.1    -0.089790  0.914123  0.086468 -1.038 0.299075
drmatch.1  0.045751  1.046814  0.066602  0.687 0.492127
tcd.1      0.429071  1.535831  0.080432  5.335 9.57e-08
dissub1.2  0.260968  1.298186  0.135182  1.930 0.053546
dissub2.2  0.003637  1.003644  0.108368  0.034 0.973226
age1.2     0.250894  1.285174  0.151057  1.661 0.096727
```

```
age2.2     0.525790  1.691796  0.157895  3.330 0.000868
drmatch.2 -0.072067  0.930469  0.110260 -0.654 0.513364
tcd.2      0.318537  1.375114  0.149970  2.124 0.033669
dissub1.3  0.139811  1.150056  0.147981  0.945 0.344767
dissub2.3  0.250328  1.284447  0.116788  2.143 0.032078
age1.3     0.055559  1.057131  0.153372  0.362 0.717166
age2.3     0.562484  1.755027  0.159970  3.516 0.000438
drmatch.3  0.169149  1.184297  0.114446  1.478 0.139414
tcd.3      0.211029  1.234948  0.126198  1.672 0.094484
pr        -0.378633  0.684797  0.211523 -1.790 0.073449

Likelihood ratio test=135.3  on 19 df, p=< 2.2e-16
n= 5577, number of events= 2010
```

For a discussion of the results we again refer to the tutorial. The hazard ratio of `pr` (0.685) and its $p$-value (0.073) indicate a trend-significant beneficial effect of platelet recovery on relapse-free survival. Later on we will look at the corresponding baseline transition intensities for these two models and see as a graphical check that the assumption of proportionality of the baseline hazards for transitions 2 and 3 is reasonable. This can also be tested formally using the function *cox.zph* (part of the *survival* package, not of *mstate*).

```
> cox.zph(c2)

             chisq df       p
dissub1.1 2.46e+01  1 6.9e-07
dissub2.1 9.68e+00  1 0.00187
age1.1    1.05e-01  1 0.74633
age2.1    6.48e+00  1 0.01092
drmatch.1 6.99e+00  1 0.00821
tcd.1     1.41e+01  1 0.00017
dissub1.2 5.43e+00  1 0.01975
dissub2.2 4.43e+00  1 0.03535
age1.2    4.79e+00  1 0.02863
age2.2    1.46e+00  1 0.22647
drmatch.2 1.12e-01  1 0.73759
tcd.2     1.07e+00  1 0.30179
dissub1.3 4.93e-05  1 0.99440
dissub2.3 2.41e+01  1 9.4e-07
age1.3    2.64e+00  1 0.10394
age2.3    6.80e+00  1 0.00913
drmatch.3 4.65e+00  1 0.03109
tcd.3     1.83e+01  1 1.9e-05
pr        1.64e+01  1 5.2e-05
GLOBAL    1.17e+02 19 4.8e-16
```

There is no evidence of non-proportionality of the baseline transition intensities of transitions 2 ($p$=0.496 for `pr`). There is strong evidence that the proportional hazards assumption for `dissub2` (CML vs AML) is violated, at least for the transitions into relapse and death. This makes sense, clinically, since CML and AML are two diseases with completely different biological pathways. It would have been much better to study separate multi-state models for the three

disease subclassifications. However, since the purpose of this manuscript is to illustrate the use of *mstate*, we will blatantly ignore the clear evidence of non-proportionality for the disease subclassifications.

Building on the Markov PH model, we can investigate whether the time at which a patient arrived in state 2 (PR) influences the subsequent RFS rate, that is, the transition hazard of PR $\rightarrow$ RelDeath. Here the purpose of expanding `prtime` becomes apparent. Since `prtime` only makes sense for transition 3 (PR $\rightarrow$ RelDeath), we need the transition-specific covariate of `prtime` for transition 3, which is `prtime.3`. The corresponding model is termed the "state arrival extended Markov PH" model in the tutorial, and appears on the right of Table III.

```
> c3 <- coxph(Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
+     age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
+     age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
+     age1.3 + age2.3 + drmatch.3 + tcd.3 + pr + prtime.3 + strata(to),
+     data = msbmt, method = "breslow")
> c3

Call:
coxph(formula = Surv(Tstart, Tstop, status) ~ dissub1.1 + dissub2.1 +
    age1.1 + age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 +
    age1.2 + age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 +
    age1.3 + age2.3 + drmatch.3 + tcd.3 + pr + prtime.3 + strata(to),
    data = msbmt, method = "breslow")

               coef exp(coef)  se(coef)      z        p
dissub1.1 -0.043592  0.957345  0.077887 -0.560 0.575698
dissub2.1 -0.297240  0.742866  0.067996 -4.371 1.23e-05
age1.1    -0.164613  0.848222  0.079054 -2.082 0.037317
age2.1    -0.089790  0.914123  0.086468 -1.038 0.299075
drmatch.1  0.045751  1.046814  0.066602  0.687 0.492127
tcd.1      0.429071  1.535831  0.080432  5.335 9.57e-08
dissub1.2  0.260899  1.298097  0.135182  1.930 0.053609
dissub2.2  0.003761  1.003768  0.108368  0.035 0.972315
age1.2     0.250952  1.285248  0.151056  1.661 0.096649
age2.2     0.525772  1.691764  0.157894  3.330 0.000869
drmatch.2 -0.072088  0.930449  0.110260 -0.654 0.513238
tcd.2      0.318238  1.374703  0.149971  2.122 0.033838
dissub1.3  0.132021  1.141132  0.148849  0.887 0.375109
dissub2.3  0.251811  1.286353  0.116823  2.155 0.031123
age1.3     0.058227  1.059956  0.153426  0.380 0.704306
age2.3     0.565752  1.760771  0.160011  3.536 0.000407
drmatch.3  0.166817  1.181538  0.114556  1.456 0.145334
tcd.3      0.207404  1.230480  0.126431  1.640 0.100911
pr        -0.406872  0.665729  0.219075 -1.857 0.063279
prtime.3   0.295226  1.343430  0.594952  0.496 0.619741

Likelihood ratio test=135.5  on 20 df, p=< 2.2e-16
n= 5577, number of events= 2010
```

The influence of the time at which platelet recovery occurred seems small and is not significant ($p$=0.62, last row).

The clock-reset models may be obtained very similarly to those of the clock-forward models. The only difference is that *Surv(Tstart,Tstop,status)* is replaced by *Surv(time,status)*. This reflects the fact (recall that in our long format data each row corresponds to a transition) that for each transition the time starts at 0, rather than `Tstart`, the time since start of study at which the state has been entered. We will only show the code, not the output; the reader may try this for him-or herself.

```
> c4 <- coxph(Surv(time, status) ~ dissub1.1 + dissub2.1 + age1.1 +
+     age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 + age1.2 +
+     age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 + age1.3 +
+     age2.3 + drmatch.3 + tcd.3 + strata(trans), data = msbmt,
+     method = "breslow")
> c5 <- coxph(Surv(time, status) ~ dissub1.1 + dissub2.1 + age1.1 +
+     age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 + age1.2 +
+     age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 + age1.3 +
+     age2.3 + drmatch.3 + tcd.3 + pr + strata(to), data = msbmt,
+     method = "breslow")
> c6 <- coxph(Surv(time, status) ~ dissub1.1 + dissub2.1 + age1.1 +
+     age2.1 + drmatch.1 + tcd.1 + dissub1.2 + dissub2.2 + age1.2 +
+     age2.2 + drmatch.2 + tcd.2 + dissub1.3 + dissub2.3 + age1.3 +
+     age2.3 + drmatch.3 + tcd.3 + pr + prtime.3 + strata(to),
+     data = msbmt, method = "breslow")
```

# 4 Prediction

In order to obtain prediction probabilities in the context of the Markov multi-state models discussed in the previous section, basically two steps are involved. The first is to use the estimated parameters and baseline transition hazards and the covariate values of a patient of interest, to obtain patient-specific transition hazards for that patient, for each of the transitions in the multi-state model. This is what the function ***msfit*** is designed to do. The second step is to use the resulting patient-specific transition hazards (and variances and covariances) as input for ***probtrans*** to obtain (patient-specific) transition probabilities.

I will first show how ***msfit*** can be used to obtain the baseline hazards associated with the Markov stratified and PH models. The hazards of the Markov stratified models (and their variances and covariates) are obtained by first creating a new dataset containing the (expanded) covariates along with their values (in this case 0). This is very similar to the use of ***survfit*** from the *survival* package. The important difference is that for one patient, this *newdata* data frame needs to have exactly one line for each transition. When transition-specific covariates have been used in the model, the easiest way to obtain such a data frame is to first create a data frame with the basic covariates and then using ***expand.covs*** to obtain the transition-specific covariates. Since ***expand.covs*** expects an *msdata* object, we set the class of the *newdata* data to *msdata* explicitly. We also copy the levels of the categorical covariates before expanding, although this is not really necessary here.

```
> newd <- data.frame(dissub = rep(0, 3), age = rep(0, 3), drmatch = rep(0,
+     3), tcd = rep(0, 3), trans = 1:3)
> newd$dissub <- factor(newd$dissub, levels = 0:2, labels = levels(ebmt3$dissub))
> newd$age <- factor(newd$age, levels = 0:2, labels = levels(ebmt3$age))
> newd$drmatch <- factor(newd$drmatch, levels = 0:1, labels = levels(ebmt3$drmatch))
> newd$tcd <- factor(newd$tcd, levels = 0:1, labels = levels(ebmt3$tcd))
```

```
> attr(newd, "trans") <- tmat
> class(newd) <- c("msdata", "data.frame")
> newd <- expand.covs(newd, covs[1:4], longnames = FALSE)
> newd$strata = 1:3
> newd

An object of class 'msdata'

Data:
  dissub  age            drmatch    tcd trans dissub1.1 dissub1.2 dissub1.3
1    AML <=20 No gender mismatch No TCD     1         0         0         0
2    AML <=20 No gender mismatch No TCD     2         0         0         0
3    AML <=20 No gender mismatch No TCD     3         0         0         0
  dissub2.1 dissub2.2 dissub2.3 age1.1 age1.2 age1.3 age2.1 age2.2 age2.3
1         0         0         0      0      0      0      0      0      0
2         0         0         0      0      0      0      0      0      0
3         0         0         0      0      0      0      0      0      0
  drmatch.1 drmatch.2 drmatch.3 tcd.1 tcd.2 tcd.3 strata
1         0         0         0     0     0     0      1
2         0         0         0     0     0     0      2
3         0         0         0     0     0     0      3
```

The last command where the column `strata` is added is important and points to a second major difference between *survfit* and *msfit*. The *newdata* data frame needs to have a column `strata` specifying to which stratum in the `coxph` object each transition belongs. Here each transition corresponds to a separate stratum, so we specify 1, 2, and 3.

To obtain an estimate of the baseline cumulative hazard for the "stratified hazards" model, *msfit* can be called with the first Cox model, `c1`, as input model, and `newd` as *newdata* argument.

```
> msf1 <- msfit(c1, newdata = newd, trans = tmat)
```

The result is an object of class *msfit*, which is a list with three items, `Haz`, `varHaz`, and `trans`. The item `trans` records the transition matrix used when constructing the *msfit* object. `Haz` contains the estimated cumulative hazard for each of the transitions for the particular patient specified in `newd`, while `varHaz` contains the estimated variances of these cumulative hazards, as well as the covariances for each combination of two transitions. All are evaluated at the time points for which any event in any transition occurs, possibly augmented with the largest (non-event) time point in the data. The *summary* method for *msfit* objects is most conveniently used for a summary. If we also would like to have a look at the covariances, we could set the argument *variance* equal to `TRUE`.

```
> summary(msf1)

Transition 1 (head and tail):
         time          Haz        seHaz        lower       upper
1 0.002737851 0.0005277714 0.0005290102 7.400248e-05 0.003763964
2 0.008213552 0.0010560892 0.0007502708 2.624139e-04 0.004250249
3 0.010951403 0.0010560892 0.0007502708 2.624139e-04 0.004250249
4 0.016427105 0.0010560892 0.0007502708 2.624139e-04 0.004250249
5 0.019164956 0.0015857558 0.0009219748 5.073865e-04 0.004956027
6 0.021902806 0.0015857558 0.0009219748 5.073865e-04 0.004956027
```

```
...
        time       Haz      seHaz     lower    upper
500 6.253251 0.9513165 0.07182285 0.8204662 1.103035
501 6.357290 0.9513165 0.07182285 0.8204662 1.103035
502 6.362765 0.9513165 0.07182285 0.8204662 1.103035
503 6.798084 0.9513165 0.07182285 0.8204662 1.103035
504 7.110198 0.9513165 0.07182285 0.8204662 1.103035
505 7.731691 0.9513165 0.07182285 0.8204662 1.103035

Transition 2 (head and tail):
           time          Haz        seHaz        lower       upper
506 0.002737851 0.0003046955 0.0003077143 4.209506e-05 0.002205469
507 0.008213552 0.0003046955 0.0003077143 4.209506e-05 0.002205469
508 0.010951403 0.0006097444 0.0004396591 1.483833e-04 0.002505594
509 0.016427105 0.0012203981 0.0006340496 4.408243e-04 0.003378606
510 0.019164956 0.0018316171 0.0007912068 7.854882e-04 0.004271001
511 0.021902806 0.0024438486 0.0009303805 1.158829e-03 0.005153820

...
         time       Haz      seHaz     lower     upper
1005 6.253251 0.5020560 0.08219369 0.3642490 0.6919997
1006 6.357290 0.5020560 0.08219369 0.3642490 0.6919997
1007 6.362765 0.5248419 0.08821373 0.3775385 0.7296182
1008 6.798084 0.5248419 0.08821373 0.3775385 0.7296182
1009 7.110198 0.5248419 0.08821373 0.3775385 0.7296182
1010 7.731691 0.5248419 0.08821373 0.3775385 0.7296182

Transition 3 (head and tail):
            time Haz seHaz lower upper
1011 0.002737851   0     0     0     0
1012 0.008213552   0     0     0     0
1013 0.010951403   0     0     0     0
1014 0.016427105   0     0     0     0
1015 0.019164956   0     0     0     0
1016 0.021902806   0     0     0     0

...
         time       Haz      seHaz     lower     upper
1510 6.253251 0.3291154 0.05058502 0.2435110 0.4448133
1511 6.357290 0.3427115 0.05413323 0.2514645 0.4670688
1512 6.362765 0.3427115 0.05413323 0.2514645 0.4670688
1513 6.798084 0.3693677 0.06340696 0.2638388 0.5171055
1514 7.110198 0.4647197 0.12159613 0.2782724 0.7760899
1515 7.731691 0.4647197 0.12159613 0.2782724 0.7760899
```

Let us have a closer look at some of the variances and covariances as well.

```
> vH1 <- msf1$varHaz
> head(vH1[vH1$trans1 == 1 & vH1$trans2 == 1, ])
```

```
         time       varHaz trans1 trans2
1 0.002737851 2.798518e-07      1      1
2 0.008213552 5.629062e-07      1      1
3 0.010951403 5.629062e-07      1      1
4 0.016427105 5.629062e-07      1      1
5 0.019164956 8.500376e-07      1      1
6 0.021902806 8.500376e-07      1      1

> tail(vH1[vH1$trans1 == 1 & vH1$trans2 == 1, ])

        time      varHaz trans1 trans2
500 6.253251 0.005158522      1      1
501 6.357290 0.005158522      1      1
502 6.362765 0.005158522      1      1
503 6.798084 0.005158522      1      1
504 7.110198 0.005158522      1      1
505 7.731691 0.005158522      1      1

> tail(vH1[vH1$trans1 == 1 & vH1$trans2 == 2, ])

         time varHaz trans1 trans2
1005 6.253251      0      1      2
1006 6.357290      0      1      2
1007 6.362765      0      1      2
1008 6.798084      0      1      2
1009 7.110198      0      1      2
1010 7.731691      0      1      2

> tail(vH1[vH1$trans1 == 1 & vH1$trans2 == 3, ])

         time varHaz trans1 trans2
1510 6.253251      0      1      3
1511 6.357290      0      1      3
1512 6.362765      0      1      3
1513 6.798084      0      1      3
1514 7.110198      0      1      3
1515 7.731691      0      1      3

> tail(vH1[vH1$trans1 == 2 & vH1$trans2 == 3, ])

         time varHaz trans1 trans2
2520 6.253251      0      2      3
2521 6.357290      0      2      3
2522 6.362765      0      2      3
2523 6.798084      0      2      3
2524 7.110198      0      2      3
2525 7.731691      0      2      3
```

Note that the covariances of the estimated cumulative hazards are practically (apart from rounding errors) 0. Theoretically, they should be 0, because with separate strata and separate covariate

effects for the different transitions, the estimates of the three transitions could in fact have been estimated as three separate Cox models (this would give exactly the same results).

The estimated baseline cumulative hazards for the Markov PH model are obtained in mostly the same way. The only exception is the specification of the *strata* argument in `newd`. Instead of taking the values 1, 2, and 3, for the three transitions, they take values 1, 2, 2, to indicate that transition 1 corresponds to stratum 1, and both transitions 2 and 3 correspond to stratum 2 (the order of the strata as defined in the `coxph` object). Also the time-dependent covariate `pr` needs to be included, taking the value 0 for transitions 1 and 2, and 1 for transition 3.

```
> newd$strata = c(1, 2, 2)
> newd$pr <- c(0, 0, 1)
> msf2 <- msfit(c2, newdata = newd, trans = tmat)
> summary(msf2)

Transition 1 (head and tail):
         time          Haz        seHaz        lower       upper
1 0.002737851 0.0005277714 0.0005290102 7.400248e-05 0.003763964
2 0.008213552 0.0010560892 0.0007502708 2.624139e-04 0.004250249
3 0.010951403 0.0010560892 0.0007502708 2.624139e-04 0.004250249
4 0.016427105 0.0010560892 0.0007502708 2.624139e-04 0.004250249
5 0.019164956 0.0015857558 0.0009219748 5.073865e-04 0.004956027
6 0.021902806 0.0015857558 0.0009219748 5.073865e-04 0.004956027

...
        time       Haz      seHaz     lower    upper
500 6.253251 0.9513165 0.07182285 0.8204662 1.103035
501 6.357290 0.9513165 0.07182285 0.8204662 1.103035
502 6.362765 0.9513165 0.07182285 0.8204662 1.103035
503 6.798084 0.9513165 0.07182285 0.8204662 1.103035
504 7.110198 0.9513165 0.07182285 0.8204662 1.103035
505 7.731691 0.9513165 0.07182285 0.8204662 1.103035

Transition 2 (head and tail):
           time          Haz        seHaz        lower       upper
506 0.002737851 0.0003053084 0.0003083331 4.217979e-05 0.002209902
507 0.008213552 0.0003053084 0.0003083331 4.217979e-05 0.002209902
508 0.010951403 0.0006107971 0.0004404176 1.486397e-04 0.002509915
509 0.016427105 0.0012223306 0.0006350522 4.415233e-04 0.003383948
510 0.019164956 0.0018344413 0.0007924245 7.867013e-04 0.004277576
511 0.021902806 0.0024473467 0.0009317088 1.160491e-03 0.005161183

...
         time       Haz      seHaz     lower     upper
1005 6.253251 0.5040408 0.07806657 0.3720749 0.6828118
1006 6.357290 0.5146993 0.08030652 0.3790914 0.6988167
1007 6.362765 0.5255361 0.08256535 0.3862540 0.7150431
1008 6.798084 0.5476683 0.08851937 0.3989682 0.7517906
1009 7.110198 0.6357669 0.13427464 0.4202651 0.9617730
1010 7.731691 0.6357669 0.13427464 0.4202651 0.9617730
```

```
Transition 3 (head and tail):
            time          Haz        seHaz        lower       upper
1011 0.002737851 0.0002090742 0.0002116301 2.875366e-05 0.001520225
1012 0.008213552 0.0002090742 0.0002116301 2.875366e-05 0.001520225
1013 0.010951403 0.0004182719 0.0003029499 1.011445e-04 0.001729717
1014 0.016427105 0.0008370481 0.0004386272 2.997137e-04 0.002337729
1015 0.019164956 0.0012562195 0.0005493845 5.330994e-04 0.002960212
1016 0.021902806 0.0016759351 0.0006481990 7.853066e-04 0.003576640

...
         time       Haz      seHaz     lower     upper
1510 6.253251 0.3451655 0.05260815 0.2560308 0.4653317
1511 6.357290 0.3524644 0.05411648 0.2608699 0.4762189
1512 6.362765 0.3598855 0.05563688 0.2658103 0.4872555
1513 6.798084 0.3750415 0.05964162 0.2746095 0.5122042
1514 7.110198 0.4353712 0.09072076 0.2893943 0.6549820
1515 7.731691 0.4353712 0.09072076 0.2893943 0.6549820

> vH2 <- msf2$varHaz
> tail(vH2[vH2$trans1 == 1 & vH2$trans2 == 2, ])

         time varHaz trans1 trans2
1005 6.253251      0      1      2
1006 6.357290      0      1      2
1007 6.362765      0      1      2
1008 6.798084      0      1      2
1009 7.110198      0      1      2
1010 7.731691      0      1      2

> tail(vH2[vH2$trans1 == 1 & vH2$trans2 == 3, ])

         time varHaz trans1 trans2
1510 6.253251      0      1      3
1511 6.357290      0      1      3
1512 6.362765      0      1      3
1513 6.798084      0      1      3
1514 7.110198      0      1      3
1515 7.731691      0      1      3

> tail(vH2[vH2$trans1 == 2 & vH2$trans2 == 3, ])

         time       varHaz trans1 trans2
2520 6.253251 0.0004142378      2      3
2521 6.357290 0.0005227029      2      3
2522 6.362765 0.0006348311      2      3
2523 6.798084 0.0011112104      2      3
2524 7.110198 0.0088628795      2      3
2525 7.731691 0.0088628795      2      3
```

Note that the estimated cumulative hazards and variances for transition 1 are identical to those from `msf1`. We saw earlier that the estimated regression coefficients were also identical for the

Markov stratified and the Markon PH models. Note also that the variance of the cumulative hazard of transition 3 (and 2, not shown) is smaller than with `msf1`. The cumulative hazard estimates of transitions 1 and 2 are still uncorrelated (and 1 and 3), but those of transitions 2 and 3 are correlated now, because they share a common baseline.

Let us compare the baseline hazards of the Markov stratified and PH models graphically. For this we use the *plot* method for *msfit* objects. Figure 1 corresponds to Figure 14 in the tutorial.

```
> par(mfrow = c(1, 2))
> plot(msf1, cols = rep(1, 3), lwd = 2, lty = 1:3, xlab = "Years since transplant",
+     ylab = "Stratified baseline hazards", legend.pos = c(2, 0.9))
> plot(msf2, cols = rep(1, 3), lwd = 2, lty = 1:3, xlab = "Years since transplant",
+     ylab = "Proportional baseline hazards", legend.pos = c(2,
+         0.9))
> par(mfrow = c(1, 1))
```

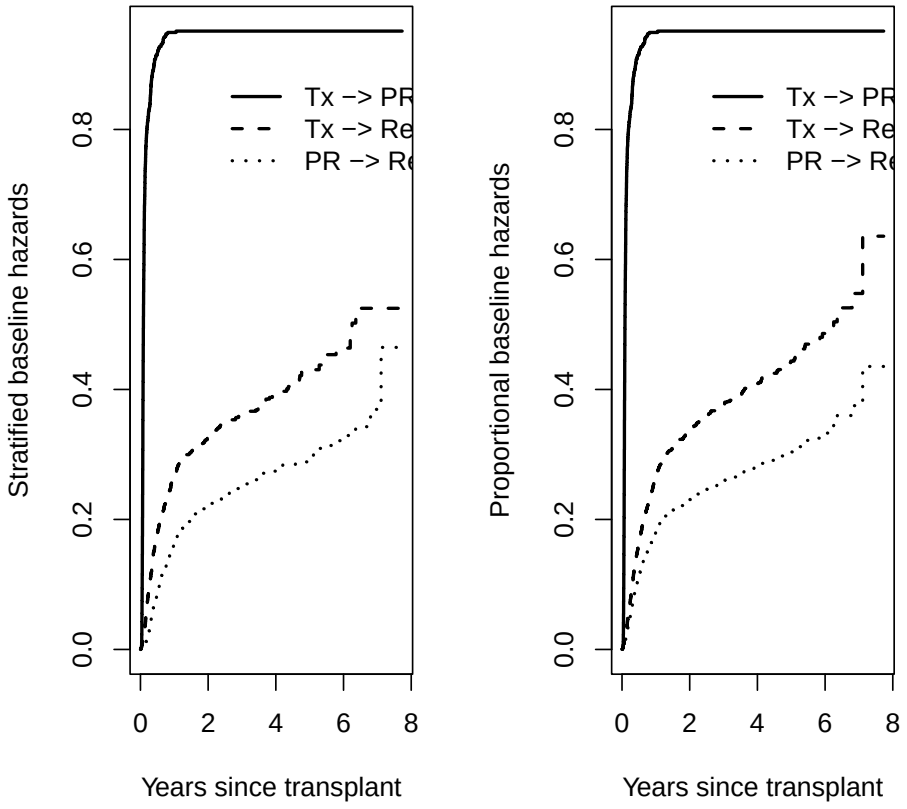


Figure 1: Baseline cumulative hazard curves for the EBMT illness-death model. On the left the Markov stratified hazards model, on the right the Markov PH model.

Define the multi-state model as $X(t)$, a random process taking values in $1, \ldots, S$ ($S$ being the number of states). We are interested in estimating so called transition probabilities $P_{gh}(s,t) = P(X(t) = h \,|\, X(s) = g)$, possibly depending on covariates. For instance, $P_{13}(0,t)$ indicates

the probability of having relapsed/died (state 3) by time $t$, given that the individual was alive without relapse or platelet recovery (state 1) at time $s = 0$. By fixing $s$ and varying $t$, we can predict the future behavior of the multi-state model given the present at time $s$. For Markov models, these probabilities will depend only on the state at time $s$, not on what happened before. For these Markov models there is a powerful relation between these transition probabilities and the transition intensities, given by

$$\mathbf{P}(s,t) = \prod_{(s,t]} (\mathbf{I} + d\mathbf{\Lambda}(u)) \tag{1}$$

Here $\mathbf{P}(s,t)$ is an $S \times S$ matrix with as $(g,h)$ element the $P_{gh}(s,t)$ in which we are interested, and $\mathbf{\Lambda}(t)$ is an $S \times S$ matrix with as off-diagonal $(g,h)$ elements the transition intensities $\Lambda_{gh}(t)$ of transition $g \to h$. If such a direct transition is not possible, then $\Lambda_{gh}(t) = 0$. The diagonal elements of $\mathbf{\Lambda}(t)$ are defined as $\Lambda_{gg}(t) = -\sum_{h \neq g} \Lambda_{gh}(t)$, i.e. as minus the sum of the transition intensities of the transitions out from state $g$. Finally, $\mathbf{I}$ is the $S \times S$ identity matrix. Equation (1) describes a theoretical relation between the true underlying transition intensities and transition probabilities. The product is a so called product integral (Andersen et al. 1993) when the transition intensities are continuous.

We already have estimates of all the transition intensities. If we gather these in a matrix and plug them in equation (1), we get

$$\hat{\mathbf{P}}(s,t) = \prod_{s<u\leq t} \left(\mathbf{I} + d\hat{\mathbf{\Lambda}}(u)\right) \tag{2}$$

as an estimate of the transition probabilities. This estimator is called the Aalen-Johansen estimator, and it is implemented in ***probtrans***. By working with matrices, we immediately get all the transition probabilities from all the starting states $g$ to all the receiving states $h$ in one go. When we fix $s$, we can calculate all these transition probabilities by forward matrix multiplications using the simple recursive relation

$$\hat{\mathbf{P}}(s,t+) = \hat{\mathbf{P}}(s,t) \cdot \left(\mathbf{I} + d\hat{\mathbf{\Lambda}}(t+)\right) \ .$$

Andersen et al. (1993) and de Wreede et al. (2009) also describe recursive formulas for the covariance matrix of $\hat{\mathbf{P}}(s,t)$, with and without covariates, which are implemented in *mstate*.

Let us see all this theory in action and let us recreate Figure 15 of the tutorial. For this we need to calculate transition probabilities for a baseline patient, based on the Markov PH model. We thus use `msf2` as input for ***probtrans***. By default, ***probtrans*** uses forward prediction, which means that $s$ is kept fixed and $t > s$. The argument *predt* specifies either $s$ or $t$. In this case (forward prediction) it specifies $s$. From version 0.2.3 on, ***probtrans*** no longer needs a *trans* argument, but takes that from the `trans` item of the *msfit* object.

```
> pt <- probtrans(msf2, predt = 0)
```

The result of ***probtrans*** is a *probtrans* object, which is a list, where item `[[i]]` contains predictions from state $i$. Each item of the list is a data frame with `time` containing all event time points, and `pstate1`, `pstate2`, etc the probabilities of being in state 1, 2, etc, and finally `se1`, `se2` etc the standard errors of these estimated probabilities. The item `[[3]]` contains predictions $\hat{P}_{3h}(0,t)$ (we chose $s = 0$) starting from the RelDeath state, which is absorbing.

```
> head(pt[[3]])
```

```
         time pstate1 pstate2 pstate3 se1 se2 se3
1 0.000000000       0       0       1   0   0   0
2 0.002737851       0       0       1   0   0   0
3 0.008213552       0       0       1   0   0   0
4 0.010951403       0       0       1   0   0   0
5 0.016427105       0       0       1   0   0   0
6 0.019164956       0       0       1   0   0   0
```

```
> tail(pt[[3]])
```

```
        time pstate1 pstate2 pstate3 se1 se2 se3
501 6.253251       0       0       1   0   0   0
502 6.357290       0       0       1   0   0   0
503 6.362765       0       0       1   0   0   0
504 6.798084       0       0       1   0   0   0
505 7.110198       0       0       1   0   0   0
506 7.731691       0       0       1   0   0   0
```

We see that these prediction probabilities are not so interesting; the probabilities are all 0 or 1, and, since there is no randomness, all the SE's are 0. Item `[[2]]` contains predictions $\hat{P}_{2h}(0,t)$ from state 2.

It is easier to use the ***summary*** method for *probtrans* objects. The user may specify a *from* argument, specifying from which state the predictions are to be printed. The ***summary*** method prints a selection, the ***head*** and ***tail*** by default unless there are fewer than 12 time points. When *complete* is set to `TRUE`, predictions for all time points are printed. If the *from* argument is missing in the function call, then predictions from all states are printed.

```
> summary(pt, from = 2)
```

```
Prediction from state 2 :
           time pstate1   pstate2      pstate3 se1          se2          se3
1   0.000000000       0 1.0000000 0.0000000000   0 0.0000000000 0.0000000000
2   0.002737851       0 0.9997909 0.0002090742   0 0.0002115858 0.0002115858
3   0.008213552       0 0.9997909 0.0002090742   0 0.0002115858 0.0002115858
4   0.010951403       0 0.9995818 0.0004182281   0 0.0003028232 0.0003028232
5   0.016427105       0 0.9991632 0.0008368292   0 0.0004382601 0.0004382601
6   0.019164956       0 0.9987444 0.0012556499   0 0.0005486946 0.0005486946
7   0.021902806       0 0.9983252 0.0016748385   0 0.0006471134 0.0006471134
8   0.024640657       0 0.9979058 0.0020941700   0 0.0007382674 0.0007382674
9   0.027378508       0 0.9979058 0.0020941700   0 0.0007382674 0.0007382674
10  0.030116359       0 0.9976960 0.0023039813   0 0.0007819551 0.0007819551
11  0.032854209       0 0.9966467 0.0033533327   0 0.0009875792 0.0009875792
12  0.035592060       0 0.9964364 0.0035635857   0 0.0010269915 0.0010269915
13  0.038329911       0 0.9951731 0.0048268856   0 0.0012554415 0.0012554415
14  0.041067762       0 0.9947501 0.0052499465   0 0.0013296997 0.0013296997
15  0.043805613       0 0.9947501 0.0052499465   0 0.0013296997 0.0013296997
16  0.046543463       0 0.9945366 0.0054633694   0 0.0013668758 0.0013668758
17  0.049281314       0 0.9943219 0.0056780509   0 0.0014040833 0.0014040833
18  0.052019165       0 0.9938905 0.0061095068   0 0.0014782696 0.0014782696
19  0.054757016       0 0.9936735 0.0063265199   0 0.0015153446 0.0015153446
```

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 20 | 0.057494867 | 0 | 0.9925813 | 0.0074187085 | 0 | 0.0016993040 | 0.0016993040 |
| 21 | 0.060232717 | 0 | 0.9921418 | 0.0078582244 | 0 | 0.0017723751 | 0.0017723751 |
| 22 | 0.062970568 | 0 | 0.9919205 | 0.0080795369 | 0 | 0.0018089881 | 0.0018089881 |
| 23 | 0.065708419 | 0 | 0.9916974 | 0.0083025976 | 0 | 0.0018457649 | 0.0018457649 |
| 24 | 0.068446270 | 0 | 0.9910234 | 0.0089765698 | 0 | 0.0019560576 | 0.0019560576 |
| 25 | 0.071184120 | 0 | 0.9907973 | 0.0092026909 | 0 | 0.0019928405 | 0.0019928405 |
| 26 | 0.073921971 | 0 | 0.9907973 | 0.0092026909 | 0 | 0.0019928405 | 0.0019928405 |
| 27 | 0.076659822 | 0 | 0.9901081 | 0.0098918633 | 0 | 0.0021043311 | 0.0021043311 |
| 28 | 0.079397673 | 0 | 0.9896456 | 0.0103544261 | 0 | 0.0021786853 | 0.0021786853 |
| 29 | 0.082135524 | 0 | 0.9882481 | 0.0117519281 | 0 | 0.0024008188 | 0.0024008188 |
| 30 | 0.084873374 | 0 | 0.9875448 | 0.0124551726 | 0 | 0.0025115528 | 0.0025115528 |
| 31 | 0.087611225 | 0 | 0.9870736 | 0.0129264204 | 0 | 0.0025853005 | 0.0025853005 |
| 32 | 0.090349076 | 0 | 0.9868370 | 0.0131630100 | 0 | 0.0026222339 | 0.0026222339 |
| 33 | 0.093086927 | 0 | 0.9865994 | 0.0134005604 | 0 | 0.0026592330 | 0.0026592330 |
| 34 | 0.095824778 | 0 | 0.9851694 | 0.0148306199 | 0 | 0.0028803426 | 0.0028803426 |
| 35 | 0.098562628 | 0 | 0.9851694 | 0.0148306199 | 0 | 0.0028803426 | 0.0028803426 |
| 36 | 0.101300479 | 0 | 0.9851694 | 0.0148306199 | 0 | 0.0028803426 | 0.0028803426 |
| 37 | 0.104038330 | 0 | 0.9849286 | 0.0150714175 | 0 | 0.0029173767 | 0.0029173767 |
| 38 | 0.106776181 | 0 | 0.9846868 | 0.0153132001 | 0 | 0.0029544905 | 0.0029544905 |
| 39 | 0.109514031 | 0 | 0.9839600 | 0.0160399907 | 0 | 0.0030656314 | 0.0030656314 |
| 40 | 0.112251882 | 0 | 0.9837167 | 0.0162832522 | 0 | 0.0031027188 | 0.0031027188 |
| 41 | 0.114989733 | 0 | 0.9837167 | 0.0162832522 | 0 | 0.0031027188 | 0.0031027188 |
| 42 | 0.117727584 | 0 | 0.9827398 | 0.0172602467 | 0 | 0.0032508677 | 0.0032508677 |
| 43 | 0.120465435 | 0 | 0.9824950 | 0.0175049699 | 0 | 0.0032878625 | 0.0032878625 |
| 44 | 0.123203285 | 0 | 0.9815155 | 0.0184844739 | 0 | 0.0034353951 | 0.0034353951 |
| 45 | 0.125941136 | 0 | 0.9810250 | 0.0189749929 | 0 | 0.0035090190 | 0.0035090190 |
| 46 | 0.128678987 | 0 | 0.9797966 | 0.0202034490 | 0 | 0.0036926352 | 0.0036926352 |
| 47 | 0.131416838 | 0 | 0.9795502 | 0.0204498364 | 0 | 0.0037293440 | 0.0037293440 |
| 48 | 0.134154689 | 0 | 0.9788101 | 0.0211898906 | 0 | 0.0038392369 | 0.0038392369 |
| 49 | 0.136892539 | 0 | 0.9783152 | 0.0216847801 | 0 | 0.0039125482 | 0.0039125482 |
| 50 | 0.139630390 | 0 | 0.9778190 | 0.0221810154 | 0 | 0.0039859200 | 0.0039859200 |
| 51 | 0.142368241 | 0 | 0.9768255 | 0.0231744814 | 0 | 0.0041323397 | 0.0041323397 |
| 52 | 0.145106092 | 0 | 0.9760795 | 0.0239204727 | 0 | 0.0042420002 | 0.0042420002 |
| 53 | 0.147843943 | 0 | 0.9748347 | 0.0251652806 | 0 | 0.0044243187 | 0.0044243187 |
| 54 | 0.150581793 | 0 | 0.9745850 | 0.0254149736 | 0 | 0.0044608200 | 0.0044608200 |
| 55 | 0.153319644 | 0 | 0.9735852 | 0.0264147803 | 0 | 0.0046065343 | 0.0046065343 |
| 56 | 0.156057495 | 0 | 0.9720825 | 0.0279175354 | 0 | 0.0048247143 | 0.0048247143 |
| 57 | 0.158795346 | 0 | 0.9713282 | 0.0286718152 | 0 | 0.0049339122 | 0.0049339122 |
| 58 | 0.161533196 | 0 | 0.9703215 | 0.0296785269 | 0 | 0.0050792896 | 0.0050792896 |
| 59 | 0.164271047 | 0 | 0.9693137 | 0.0306862643 | 0 | 0.0052245305 | 0.0052245305 |
| 60 | 0.167008898 | 0 | 0.9688092 | 0.0311908223 | 0 | 0.0052971486 | 0.0052971486 |
| 61 | 0.169746749 | 0 | 0.9683037 | 0.0316962510 | 0 | 0.0053698084 | 0.0053698084 |
| 62 | 0.172484600 | 0 | 0.9680508 | 0.0319491720 | 0 | 0.0054061539 | 0.0054061539 |
| 63 | 0.175222450 | 0 | 0.9670384 | 0.0329616059 | 0 | 0.0055513759 | 0.0055513759 |
| 64 | 0.177960301 | 0 | 0.9662780 | 0.0337220422 | 0 | 0.0056602721 | 0.0056602721 |
| 65 | 0.180698152 | 0 | 0.9657701 | 0.0342298951 | 0 | 0.0057329001 | 0.0057329001 |
| 66 | 0.183436003 | 0 | 0.9652618 | 0.0347381659 | 0 | 0.0058054936 | 0.0058054936 |
| 67 | 0.186173854 | 0 | 0.9639888 | 0.0360112363 | 0 | 0.0059869295 | 0.0059869295 |
| 68 | 0.188911704 | 0 | 0.9637336 | 0.0362664430 | 0 | 0.0060232687 | 0.0060232687 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 69 | 0.191649555 | 0 | 0.9634781 | 0.0365218674 | 0 | 0.0060596170 | 0.0060596170 |
| 70 | 0.194387406 | 0 | 0.9609225 | 0.0390775020 | 0 | 0.0064217447 | 0.0064217447 |
| 71 | 0.197125257 | 0 | 0.9601539 | 0.0398460910 | 0 | 0.0065303961 | 0.0065303961 |
| 72 | 0.199863107 | 0 | 0.9601539 | 0.0398460910 | 0 | 0.0065303961 | 0.0065303961 |
| 73 | 0.202600958 | 0 | 0.9591272 | 0.0408728032 | 0 | 0.0066752892 | 0.0066752892 |
| 74 | 0.205338809 | 0 | 0.9588700 | 0.0411299702 | 0 | 0.0067115588 | 0.0067115588 |
| 75 | 0.208076660 | 0 | 0.9580977 | 0.0419023219 | 0 | 0.0068203342 | 0.0068203342 |
| 76 | 0.210814511 | 0 | 0.9580977 | 0.0419023219 | 0 | 0.0068203342 | 0.0068203342 |
| 77 | 0.213552361 | 0 | 0.9573242 | 0.0426758306 | 0 | 0.0069290903 | 0.0069290903 |
| 78 | 0.216290212 | 0 | 0.9560317 | 0.0439682788 | 0 | 0.0071104634 | 0.0071104634 |
| 79 | 0.219028063 | 0 | 0.9557726 | 0.0442273885 | 0 | 0.0071467986 | 0.0071467986 |
| 80 | 0.221765914 | 0 | 0.9552540 | 0.0447459593 | 0 | 0.0072194379 | 0.0072194379 |
| 81 | 0.224503765 | 0 | 0.9544755 | 0.0455244976 | 0 | 0.0073283583 | 0.0073283583 |
| 82 | 0.227241615 | 0 | 0.9544755 | 0.0455244976 | 0 | 0.0073283583 | 0.0073283583 |
| 83 | 0.229979466 | 0 | 0.9534353 | 0.0465646989 | 0 | 0.0074736132 | 0.0074736132 |
| 84 | 0.232717317 | 0 | 0.9529147 | 0.0470853054 | 0 | 0.0075462452 | 0.0075462452 |
| 85 | 0.235455168 | 0 | 0.9526540 | 0.0473459855 | 0 | 0.0075826079 | 0.0075826079 |
| 86 | 0.238193018 | 0 | 0.9510878 | 0.0489122349 | 0 | 0.0078005284 | 0.0078005284 |
| 87 | 0.243668720 | 0 | 0.9495168 | 0.0504832218 | 0 | 0.0080185257 | 0.0080185257 |
| 88 | 0.246406571 | 0 | 0.9489922 | 0.0510078030 | 0 | 0.0080912638 | 0.0080912638 |
| 89 | 0.249144422 | 0 | 0.9484673 | 0.0515326757 | 0 | 0.0081639909 | 0.0081639909 |
| 90 | 0.251882272 | 0 | 0.9479417 | 0.0520583230 | 0 | 0.0082367933 | 0.0082367933 |
| 91 | 0.254620123 | 0 | 0.9474155 | 0.0525845408 | 0 | 0.0083096441 | 0.0083096441 |
| 92 | 0.257357974 | 0 | 0.9463626 | 0.0536373633 | 0 | 0.0084551519 | 0.0084551519 |
| 93 | 0.260095825 | 0 | 0.9455718 | 0.0544282418 | 0 | 0.0085643206 | 0.0085643206 |
| 94 | 0.262833676 | 0 | 0.9453078 | 0.0546922419 | 0 | 0.0086007505 | 0.0086007505 |
| 95 | 0.265571526 | 0 | 0.9445154 | 0.0554846323 | 0 | 0.0087099674 | 0.0087099674 |
| 96 | 0.268309377 | 0 | 0.9437223 | 0.0562776516 | 0 | 0.0088190979 | 0.0088190979 |
| 97 | 0.271047228 | 0 | 0.9423988 | 0.0576012113 | 0 | 0.0090009133 | 0.0090009133 |
| 98 | 0.273785079 | 0 | 0.9423988 | 0.0576012113 | 0 | 0.0090009133 | 0.0090009133 |
| 99 | 0.276522930 | 0 | 0.9416022 | 0.0583978478 | 0 | 0.0091101808 | 0.0091101808 |
| 100 | 0.279260780 | 0 | 0.9405396 | 0.0594604433 | 0 | 0.0092557441 | 0.0092557441 |
| 101 | 0.281998631 | 0 | 0.9402735 | 0.0597264915 | 0 | 0.0092921719 | 0.0092921719 |
| 102 | 0.284736482 | 0 | 0.9394744 | 0.0605255740 | 0 | 0.0094015161 | 0.0094015161 |
| 103 | 0.287474333 | 0 | 0.9386736 | 0.0613263646 | 0 | 0.0095109448 | 0.0095109448 |
| 104 | 0.290212183 | 0 | 0.9378714 | 0.0621285857 | 0 | 0.0096204190 | 0.0096204190 |
| 105 | 0.292950034 | 0 | 0.9373359 | 0.0626641040 | 0 | 0.0096934026 | 0.0096934026 |
| 106 | 0.295687885 | 0 | 0.9367997 | 0.0632002787 | 0 | 0.0097663746 | 0.0097663746 |
| 107 | 0.298425736 | 0 | 0.9357258 | 0.0642742334 | 0 | 0.0099123218 | 0.0099123218 |
| 108 | 0.301163587 | 0 | 0.9357258 | 0.0642742334 | 0 | 0.0099123218 | 0.0099123218 |
| 109 | 0.303901437 | 0 | 0.9343814 | 0.0656186158 | 0 | 0.0100946478 | 0.0100946478 |
| 110 | 0.306639288 | 0 | 0.9335736 | 0.0664264022 | 0 | 0.0102040524 | 0.0102040524 |
| 111 | 0.309377139 | 0 | 0.9327638 | 0.0672361757 | 0 | 0.0103136406 | 0.0103136406 |
| 112 | 0.312114990 | 0 | 0.9322234 | 0.0677765957 | 0 | 0.0103867089 | 0.0103867089 |
| 113 | 0.314852841 | 0 | 0.9314120 | 0.0685879956 | 0 | 0.0104962783 | 0.0104962783 |
| 114 | 0.317590691 | 0 | 0.9305994 | 0.0694005733 | 0 | 0.0106058848 | 0.0106058848 |
| 115 | 0.320328542 | 0 | 0.9297867 | 0.0702133289 | 0 | 0.0107154131 | 0.0107154131 |
| 116 | 0.323066393 | 0 | 0.9289725 | 0.0710274910 | 0 | 0.0108250407 | 0.0108250407 |
| 117 | 0.325804244 | 0 | 0.9276143 | 0.0723856612 | 0 | 0.0110075784 | 0.0110075784 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 118 | 0.328542094 | 0 | 0.9273423 | 0.0726576660 | 0 | 0.0110441415 | 0.0110441415 |
| 119 | 0.331279945 | 0 | 0.9267979 | 0.0732020747 | 0 | 0.0111172692 | 0.0111172692 |
| 120 | 0.334017796 | 0 | 0.9262528 | 0.0737471727 | 0 | 0.0111904296 | 0.0111904296 |
| 121 | 0.336755647 | 0 | 0.9246158 | 0.0753842216 | 0 | 0.0114096431 | 0.0114096431 |
| 122 | 0.339493498 | 0 | 0.9240694 | 0.0759305694 | 0 | 0.0114827458 | 0.0114827458 |
| 123 | 0.342231348 | 0 | 0.9229754 | 0.0770245945 | 0 | 0.0116289060 | 0.0116289060 |
| 124 | 0.344969199 | 0 | 0.9224276 | 0.0775724022 | 0 | 0.0117020289 | 0.0117020289 |
| 125 | 0.347707050 | 0 | 0.9216053 | 0.0783947326 | 0 | 0.0118116820 | 0.0118116820 |
| 126 | 0.353182752 | 0 | 0.9210559 | 0.0789440600 | 0 | 0.0118848941 | 0.0118848941 |
| 127 | 0.355920602 | 0 | 0.9207808 | 0.0792191515 | 0 | 0.0119215345 | 0.0119215345 |
| 128 | 0.361396304 | 0 | 0.9196785 | 0.0803215038 | 0 | 0.0120681109 | 0.0120681109 |
| 129 | 0.364134155 | 0 | 0.9185734 | 0.0814266026 | 0 | 0.0122148240 | 0.0122148240 |
| 130 | 0.366872005 | 0 | 0.9180201 | 0.0819798949 | 0 | 0.0122882164 | 0.0122882164 |
| 131 | 0.369609856 | 0 | 0.9174663 | 0.0825336692 | 0 | 0.0123616235 | 0.0123616235 |
| 132 | 0.372347707 | 0 | 0.9171892 | 0.0828107850 | 0 | 0.0123983419 | 0.0123983419 |
| 133 | 0.375085558 | 0 | 0.9166348 | 0.0833652296 | 0 | 0.0124717485 | 0.0124717485 |
| 134 | 0.377823409 | 0 | 0.9155253 | 0.0844747209 | 0 | 0.0126184156 | 0.0126184156 |
| 135 | 0.380561259 | 0 | 0.9138584 | 0.0861415776 | 0 | 0.0128382516 | 0.0128382516 |
| 136 | 0.383299110 | 0 | 0.9133019 | 0.0866981050 | 0 | 0.0129115890 | 0.0129115890 |
| 137 | 0.386036961 | 0 | 0.9121872 | 0.0878128429 | 0 | 0.0130582546 | 0.0130582546 |
| 138 | 0.388774812 | 0 | 0.9116290 | 0.0883710059 | 0 | 0.0131316259 | 0.0131316259 |
| 139 | 0.394250513 | 0 | 0.9110703 | 0.0889296503 | 0 | 0.0132049857 | 0.0132049857 |
| 140 | 0.396988364 | 0 | 0.9110703 | 0.0889296503 | 0 | 0.0132049857 | 0.0132049857 |
| 141 | 0.399726215 | 0 | 0.9110703 | 0.0889296503 | 0 | 0.0132049857 | 0.0132049857 |
| 142 | 0.405201916 | 0 | 0.9105105 | 0.0894895420 | 0 | 0.0132784384 | 0.0132784384 |
| 143 | 0.407939767 | 0 | 0.9102298 | 0.0897701517 | 0 | 0.0133152462 | 0.0133152462 |
| 144 | 0.410677618 | 0 | 0.9096685 | 0.0903315227 | 0 | 0.0133888232 | 0.0133888232 |
| 145 | 0.413415469 | 0 | 0.9088258 | 0.0911741838 | 0 | 0.0134991204 | 0.0134991204 |
| 146 | 0.416153320 | 0 | 0.9088258 | 0.0911741838 | 0 | 0.0134991204 | 0.0134991204 |
| 147 | 0.418891170 | 0 | 0.9079815 | 0.0920184741 | 0 | 0.0136095094 | 0.0136095094 |
| 148 | 0.421629021 | 0 | 0.9071358 | 0.0928641732 | 0 | 0.0137199468 | 0.0137199468 |
| 149 | 0.424366872 | 0 | 0.9062892 | 0.0937108019 | 0 | 0.0138303836 | 0.0138303836 |
| 150 | 0.427104723 | 0 | 0.9057241 | 0.0942758522 | 0 | 0.0139040401 | 0.0139040401 |
| 151 | 0.432580424 | 0 | 0.9048757 | 0.0951243062 | 0 | 0.0140145438 | 0.0140145438 |
| 152 | 0.435318275 | 0 | 0.9043095 | 0.0956904633 | 0 | 0.0140882101 | 0.0140882101 |
| 153 | 0.438056126 | 0 | 0.9040262 | 0.0959738025 | 0 | 0.0141250740 | 0.0141250740 |
| 154 | 0.440793977 | 0 | 0.9031756 | 0.0968244431 | 0 | 0.0142356150 | 0.0142356150 |
| 155 | 0.443531828 | 0 | 0.9031756 | 0.0968244431 | 0 | 0.0142356150 | 0.0142356150 |
| 156 | 0.446269678 | 0 | 0.9031756 | 0.0968244431 | 0 | 0.0142356150 | 0.0142356150 |
| 157 | 0.449007529 | 0 | 0.9026077 | 0.0973923346 | 0 | 0.0143093585 | 0.0143093585 |
| 158 | 0.451745380 | 0 | 0.9020391 | 0.0979609087 | 0 | 0.0143831280 | 0.0143831280 |
| 159 | 0.454483231 | 0 | 0.9014701 | 0.0985298976 | 0 | 0.0144568892 | 0.0144568892 |
| 160 | 0.457221081 | 0 | 0.9011854 | 0.0988146096 | 0 | 0.0144937872 | 0.0144937872 |
| 161 | 0.459958932 | 0 | 0.9003310 | 0.0996689842 | 0 | 0.0146043798 | 0.0146043798 |
| 162 | 0.465434634 | 0 | 0.8991904 | 0.1008095902 | 0 | 0.0147518995 | 0.0147518995 |
| 163 | 0.470910335 | 0 | 0.8989049 | 0.1010950968 | 0 | 0.0147888077 | 0.0147888077 |
| 164 | 0.473648186 | 0 | 0.8983336 | 0.1016664408 | 0 | 0.0148626207 | 0.0148626207 |
| 165 | 0.476386037 | 0 | 0.8977618 | 0.1022382256 | 0 | 0.0149364268 | 0.0149364268 |
| 166 | 0.479123888 | 0 | 0.8974756 | 0.1025243630 | 0 | 0.0149733593 | 0.0149733593 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 167 | 0.481861739 | 0 | 0.8971894 | 0.1028105690 | 0 | 0.0150102851 | 0.0150102851 |
| 168 | 0.484599589 | 0 | 0.8963305 | 0.1036694826 | 0 | 0.0151209708 | 0.0151209708 |
| 169 | 0.487337440 | 0 | 0.8957573 | 0.1042426559 | 0 | 0.0151947629 | 0.0151947629 |
| 170 | 0.492813142 | 0 | 0.8951836 | 0.1048164329 | 0 | 0.0152685715 | 0.0152685715 |
| 171 | 0.495550992 | 0 | 0.8948965 | 0.1051035206 | 0 | 0.0153054898 | 0.0153054898 |
| 172 | 0.498288843 | 0 | 0.8943213 | 0.1056786939 | 0 | 0.0153793953 | 0.0153793953 |
| 173 | 0.501026694 | 0 | 0.8934576 | 0.1065423515 | 0 | 0.0154902019 | 0.0154902019 |
| 174 | 0.503764545 | 0 | 0.8928811 | 0.1071188697 | 0 | 0.0155641120 | 0.0155641120 |
| 175 | 0.506502396 | 0 | 0.8925927 | 0.1074072995 | 0 | 0.0156010788 | 0.0156010788 |
| 176 | 0.509240246 | 0 | 0.8925927 | 0.1074072995 | 0 | 0.0156010788 | 0.0156010788 |
| 177 | 0.511978097 | 0 | 0.8911482 | 0.1088518115 | 0 | 0.0157858458 | 0.0157858458 |
| 178 | 0.514715948 | 0 | 0.8902805 | 0.1097195144 | 0 | 0.0158966885 | 0.0158966885 |
| 179 | 0.517453799 | 0 | 0.8899909 | 0.1100090732 | 0 | 0.0159336600 | 0.0159336600 |
| 180 | 0.520191650 | 0 | 0.8899909 | 0.1100090732 | 0 | 0.0159336600 | 0.0159336600 |
| 181 | 0.522929500 | 0 | 0.8894110 | 0.1105889641 | 0 | 0.0160076228 | 0.0160076228 |
| 182 | 0.528405202 | 0 | 0.8891208 | 0.1108791858 | 0 | 0.0160446291 | 0.0160446291 |
| 183 | 0.531143053 | 0 | 0.8885403 | 0.1114596769 | 0 | 0.0161185887 | 0.0161185887 |
| 184 | 0.533880903 | 0 | 0.8876686 | 0.1123314248 | 0 | 0.0162294864 | 0.0162294864 |
| 185 | 0.536618754 | 0 | 0.8870869 | 0.1129130610 | 0 | 0.0163034057 | 0.0163034057 |
| 186 | 0.542094456 | 0 | 0.8862137 | 0.1137863194 | 0 | 0.0164142445 | 0.0164142445 |
| 187 | 0.547570157 | 0 | 0.8859223 | 0.1140776720 | 0 | 0.0164511984 | 0.0164511984 |
| 188 | 0.550308008 | 0 | 0.8859223 | 0.1140776720 | 0 | 0.0164511984 | 0.0164511984 |
| 189 | 0.553045859 | 0 | 0.8847547 | 0.1152452801 | 0 | 0.0165990442 | 0.0165990442 |
| 190 | 0.555783710 | 0 | 0.8844626 | 0.1155374250 | 0 | 0.0166360117 | 0.0166360117 |
| 191 | 0.558521561 | 0 | 0.8838778 | 0.1161221637 | 0 | 0.0167099480 | 0.0167099480 |
| 192 | 0.561259411 | 0 | 0.8832930 | 0.1167070443 | 0 | 0.0167838110 | 0.0167838110 |
| 193 | 0.566735113 | 0 | 0.8830001 | 0.1169998674 | 0 | 0.0168207706 | 0.0168207706 |
| 194 | 0.572210815 | 0 | 0.8824143 | 0.1175856605 | 0 | 0.0168946566 | 0.0168946566 |
| 195 | 0.577686516 | 0 | 0.8815345 | 0.1184654531 | 0 | 0.0170054620 | 0.0170054620 |
| 196 | 0.580424367 | 0 | 0.8812410 | 0.1187590223 | 0 | 0.0170424238 | 0.0170424238 |
| 197 | 0.585900068 | 0 | 0.8803590 | 0.1196410416 | 0 | 0.0171534257 | 0.0171534257 |
| 198 | 0.588637919 | 0 | 0.8791816 | 0.1208184027 | 0 | 0.0173012832 | 0.0173012832 |
| 199 | 0.591375770 | 0 | 0.8782976 | 0.1217024173 | 0 | 0.0174121379 | 0.0174121379 |
| 200 | 0.599589322 | 0 | 0.8780024 | 0.1219975728 | 0 | 0.0174491265 | 0.0174491265 |
| 201 | 0.602327173 | 0 | 0.8774121 | 0.1225878949 | 0 | 0.0175230490 | 0.0175230490 |
| 202 | 0.605065024 | 0 | 0.8768216 | 0.1231783964 | 0 | 0.0175969463 | 0.0175969463 |
| 203 | 0.607802875 | 0 | 0.8762303 | 0.1237696871 | 0 | 0.0176708684 | 0.0176708684 |
| 204 | 0.610540726 | 0 | 0.8759344 | 0.1240655643 | 0 | 0.0177078464 | 0.0177078464 |
| 205 | 0.613278576 | 0 | 0.8756382 | 0.1243618263 | 0 | 0.0177448638 | 0.0177448638 |
| 206 | 0.616016427 | 0 | 0.8750454 | 0.1249546019 | 0 | 0.0178188655 | 0.0178188655 |
| 207 | 0.618754278 | 0 | 0.8744515 | 0.1255484660 | 0 | 0.0178929339 | 0.0178929339 |
| 208 | 0.621492129 | 0 | 0.8741545 | 0.1258455051 | 0 | 0.0179299737 | 0.0179299737 |
| 209 | 0.624229979 | 0 | 0.8738572 | 0.1261427591 | 0 | 0.0179670247 | 0.0179670247 |
| 210 | 0.626967830 | 0 | 0.8729645 | 0.1270355371 | 0 | 0.0180781749 | 0.0180781749 |
| 211 | 0.632443532 | 0 | 0.8723684 | 0.1276316261 | 0 | 0.0181523096 | 0.0181523096 |
| 212 | 0.635181383 | 0 | 0.8720702 | 0.1279298191 | 0 | 0.0181893867 | 0.0181893867 |
| 213 | 0.637919233 | 0 | 0.8717720 | 0.1282280273 | 0 | 0.0182264585 | 0.0182264585 |
| 214 | 0.640657084 | 0 | 0.8714738 | 0.1285262414 | 0 | 0.0182635183 | 0.0182635183 |
| 215 | 0.643394935 | 0 | 0.8711754 | 0.1288246403 | 0 | 0.0183005880 | 0.0183005880 |

```
216 0.648870637       0 0.8708767 0.1291233163   0 0.0183376680 0.0183376680
217 0.651608487       0 0.8705777 0.1294222510   0 0.0183747596 0.0183747596
218 0.662559890       0 0.8702782 0.1297218215   0 0.0184119352 0.0184119352
219 0.665297741       0 0.8699786 0.1300214181   0 0.0184490983 0.0184490983
220 0.668035592       0 0.8696786 0.1303214028   0 0.0184862912 0.0184862912
221 0.670773443       0 0.8693783 0.1306217432   0 0.0185235031 0.0185235031
222 0.673511294       0 0.8687772 0.1312228342   0 0.0185978960 0.0185978960
223 0.676249144       0 0.8684765 0.1315235087   0 0.0186350907 0.0186350907
224 0.684462697       0 0.8678737 0.1321262838   0 0.0187096098 0.0187096098
225 0.687200548       0 0.8672701 0.1327298879   0 0.0187841596 0.0187841596
226 0.689938398       0 0.8669680 0.1330319877   0 0.0188214563 0.0188214563
227 0.692676249       0 0.8663637 0.1336363458   0 0.0188960014 0.0188960014
228 0.695414100       0 0.8660611 0.1339388718   0 0.0189333078 0.0189333078
229 0.698151951       0 0.8657584 0.1342416464   0 0.0189706263 0.0189706263
230 0.703627652       0 0.8654555 0.1345445138   0 0.0190079385 0.0190079385
231 0.706365503       0 0.8648491 0.1351509243   0 0.0190825769 0.0190825769
232 0.709103354       0 0.8645452 0.1354547553   0 0.0191199517 0.0191199517
233 0.711841205       0 0.8642414 0.1357586246   0 0.0191573133 0.0191573133
234 0.714579055       0 0.8639375 0.1360625136   0 0.0191946746 0.0191946746
235 0.717316906       0 0.8636334 0.1363666499   0 0.0192320527 0.0192320527
236 0.720054757       0 0.8630242 0.1369757797   0 0.0193068224 0.0193068224
237 0.722792608       0 0.8630242 0.1369757797   0 0.0193068224 0.0193068224
238 0.725530459       0 0.8624146 0.1375854399   0 0.0193815810 0.0193815810
239 0.739219713       0 0.8621095 0.1378905005   0 0.0194189694 0.0194189694
240 0.741957563       0 0.8614983 0.1385016983   0 0.0194938046 0.0194938046
241 0.744695414       0 0.8605809 0.1394190584   0 0.0196059719 0.0196059719
242 0.747433265       0 0.8602749 0.1397251183   0 0.0196433733 0.0196433733
243 0.750171116       0 0.8599688 0.1400312176   0 0.0196807697 0.0196807697
244 0.752908966       0 0.8596625 0.1403375476   0 0.0197181790 0.0197181790
245 0.755646817       0 0.8596625 0.1403375476   0 0.0197181790 0.0197181790
246 0.758384668       0 0.8590492 0.1409507727   0 0.0197929878 0.0197929878
247 0.763860370       0 0.8587422 0.1412577730   0 0.0198304208 0.0198304208
248 0.766598220       0 0.8584349 0.1415651154   0 0.0198678766 0.0198678766
249 0.769336071       0 0.8581274 0.1418726487   0 0.0199053416 0.0199053416
250 0.772073922       0 0.8578198 0.1421802057   0 0.0199427879 0.0199427879
251 0.777549624       0 0.8568970 0.1431029711   0 0.0200550295 0.0200550295
252 0.780287474       0 0.8565890 0.1434110078   0 0.0200924667 0.0200924667
253 0.783025325       0 0.8562807 0.1437193257   0 0.0201299237 0.0201299237
254 0.785763176       0 0.8556637 0.1443362903   0 0.0202048062 0.0202048062
255 0.793976728       0 0.8553548 0.1446452304   0 0.0202422891 0.0202422891
256 0.799452430       0 0.8547366 0.1452634027   0 0.0203172184 0.0203172184
257 0.802190281       0 0.8544272 0.1455728149   0 0.0203547061 0.0203547061
258 0.804928131       0 0.8544272 0.1455728149   0 0.0203547061 0.0203547061
259 0.807665982       0 0.8541172 0.1458828305   0 0.0203922837 0.0203922837
260 0.815879535       0 0.8534968 0.1465031851   0 0.0204674053 0.0204674053
261 0.818617385       0 0.8528756 0.1471243913   0 0.0205425966 0.0205425966
262 0.821355236       0 0.8516317 0.1483682710   0 0.0206928680 0.0206928680
263 0.829568789       0 0.8513205 0.1486795139   0 0.0207304557 0.0207304557
264 0.835044490       0 0.8503861 0.1496138587   0 0.0208431442 0.0208431442
```

```
265 0.837782341       0 0.8500743 0.1499256902   0 0.0208807196 0.0208807196
266 0.845995893       0 0.8497623 0.1502376713   0 0.0209182938 0.0209182938
267 0.848733744       0 0.8494503 0.1505496524   0 0.0209558660 0.0209558660
268 0.859685147       0 0.8491379 0.1508620720   0 0.0209934672 0.0209934672
269 0.862422998       0 0.8485117 0.1514883127   0 0.0210687760 0.0210687760
270 0.865160849       0 0.8481984 0.1518015719   0 0.0211064166 0.0211064166
271 0.870636550       0 0.8478849 0.1521151397   0 0.0211440911 0.0211440911
272 0.873374401       0 0.8472577 0.1527423412   0 0.0212194079 0.0212194079
273 0.876112252       0 0.8469438 0.1530562009   0 0.0212570808 0.0212570808
274 0.878850103       0 0.8463152 0.1536847902   0 0.0213324554 0.0213324554
275 0.887063655       0 0.8460002 0.1539998345   0 0.0213702095 0.0213702095
276 0.898015058       0 0.8450542 0.1549458407   0 0.0214834599 0.0214834599
277 0.900752909       0 0.8441071 0.1558929147   0 0.0215966625 0.0215966625
278 0.903490760       0 0.8437912 0.1562087580   0 0.0216343974 0.0216343974
279 0.906228611       0 0.8434752 0.1565247549   0 0.0216721308 0.0216721308
280 0.908966461       0 0.8431592 0.1568408239   0 0.0217098491 0.0217098491
281 0.911704312       0 0.8425267 0.1574733125   0 0.0217852514 0.0217852514
282 0.919917864       0 0.8415763 0.1584237479   0 0.0218983480 0.0218983480
283 0.925393566       0 0.8412591 0.1587408994   0 0.0219360796 0.0219360796
284 0.928131417       0 0.8409416 0.1590584003   0 0.0219738232 0.0219738232
285 0.930869268       0 0.8403062 0.1596938300   0 0.0220492804 0.0220492804
286 0.933607118       0 0.8399881 0.1600119051   0 0.0220870262 0.0220870262
287 0.939082820       0 0.8393519 0.1606480997   0 0.0221624808 0.0221624808
288 0.955509925       0 0.8390334 0.1609666319   0 0.0222002338 0.0222002338
289 0.971937029       0 0.8380767 0.1619232640   0 0.0223134119 0.0223134119
290 0.974674880       0 0.8377575 0.1622424839   0 0.0223511711 0.0223511711
291 0.980150582       0 0.8374380 0.1625619611   0 0.0223889482 0.0223889482
292 0.985626283       0 0.8367979 0.1632020683   0 0.0224645606 0.0224645606
293 0.991101985       0 0.8358366 0.1641633828   0 0.0225779903 0.0225779903
294 0.996577687       0 0.8355156 0.1644844345   0 0.0226158184 0.0226158184
295 0.999315537       0 0.8351944 0.1648056097   0 0.0226536769 0.0226536769
296 1.004791239       0 0.8348725 0.1651274761   0 0.0226916249 0.0226916249
297 1.007529090       0 0.8332594 0.1667406388   0 0.0228813849 0.0228813849
298 1.010266940       0 0.8322894 0.1677105915   0 0.0229954160 0.0229954160
299 1.013004791       0 0.8316415 0.1683585006   0 0.0230714904 0.0230714904
300 1.023956194       0 0.8309925 0.1690075183   0 0.0231476086 0.0231476086
301 1.029431896       0 0.8306673 0.1693327449   0 0.0231857141 0.0231857141
302 1.032169747       0 0.8300166 0.1699833529   0 0.0232618531 0.0232618531
303 1.034907598       0 0.8296911 0.1703088559   0 0.0232999231 0.0232999231
304 1.043121150       0 0.8290384 0.1709616329   0 0.0233762216 0.0233762216
305 1.051334702       0 0.8283843 0.1716157170   0 0.0234525709 0.0234525709
306 1.054072553       0 0.8283843 0.1716157170   0 0.0234525709 0.0234525709
307 1.059548255       0 0.8280566 0.1719434167   0 0.0234907769 0.0234907769
308 1.067761807       0 0.8274002 0.1725998454   0 0.0235672389 0.0235672389
309 1.070499658       0 0.8267432 0.1732568446   0 0.0236436802 0.0236436802
310 1.081451061       0 0.8264143 0.1735856661   0 0.0236819144 0.0236819144
311 1.086926762       0 0.8254256 0.1745744212   0 0.0237966969 0.0237966969
312 1.092402464       0 0.8250957 0.1749042839   0 0.0238349782 0.0238349782
313 1.100616016       0 0.8247655 0.1752345086   0 0.0238732845 0.0238732845
```

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 314 | 1.103353867 | 0 | 0.8244351 | 0.1755649062 | 0 | 0.0239115887 | 0.0239115887 |
| 315 | 1.111567420 | 0 | 0.8241043 | 0.1758956696 | 0 | 0.0239499127 | 0.0239499127 |
| 316 | 1.114305270 | 0 | 0.8234413 | 0.1765587336 | 0 | 0.0240266809 | 0.0240266809 |
| 317 | 1.122518823 | 0 | 0.8231096 | 0.1768904244 | 0 | 0.0240650654 | 0.0240650654 |
| 318 | 1.138945927 | 0 | 0.8227758 | 0.1772241538 | 0 | 0.0241036689 | 0.0241036689 |
| 319 | 1.141683778 | 0 | 0.8224421 | 0.1775578910 | 0 | 0.0241422565 | 0.0241422565 |
| 320 | 1.149897331 | 0 | 0.8221074 | 0.1778925667 | 0 | 0.0241809280 | 0.0241809280 |
| 321 | 1.155373032 | 0 | 0.8217727 | 0.1782272502 | 0 | 0.0242195835 | 0.0242195835 |
| 322 | 1.158110883 | 0 | 0.8214381 | 0.1785619415 | 0 | 0.0242582232 | 0.0242582232 |
| 323 | 1.166324435 | 0 | 0.8211029 | 0.1788971416 | 0 | 0.0242968977 | 0.0242968977 |
| 324 | 1.171800137 | 0 | 0.8207673 | 0.1792327011 | 0 | 0.0243355913 | 0.0243355913 |
| 325 | 1.177275838 | 0 | 0.8204315 | 0.1795684625 | 0 | 0.0243742849 | 0.0243742849 |
| 326 | 1.182751540 | 0 | 0.8200955 | 0.1799044693 | 0 | 0.0244129814 | 0.0244129814 |
| 327 | 1.185489391 | 0 | 0.8197589 | 0.1802410621 | 0 | 0.0244517106 | 0.0244517106 |
| 328 | 1.193702943 | 0 | 0.8194221 | 0.1805778717 | 0 | 0.0244904416 | 0.0244904416 |
| 329 | 1.201916496 | 0 | 0.8190853 | 0.1809146892 | 0 | 0.0245291564 | 0.0245291564 |
| 330 | 1.204654346 | 0 | 0.8187484 | 0.1812515789 | 0 | 0.0245678748 | 0.0245678748 |
| 331 | 1.221081451 | 0 | 0.8184110 | 0.1815890481 | 0 | 0.0246066202 | 0.0246066202 |
| 332 | 1.245722108 | 0 | 0.8180718 | 0.1819282279 | 0 | 0.0246455344 | 0.0246455344 |
| 333 | 1.248459959 | 0 | 0.8173931 | 0.1826069010 | 0 | 0.0247233318 | 0.0247233318 |
| 334 | 1.251197810 | 0 | 0.8167143 | 0.1832856761 | 0 | 0.0248011111 | 0.0248011111 |
| 335 | 1.256673511 | 0 | 0.8163746 | 0.1836254406 | 0 | 0.0248400301 | 0.0248400301 |
| 336 | 1.262149213 | 0 | 0.8160347 | 0.1839653291 | 0 | 0.0248789397 | 0.0248789397 |
| 337 | 1.264887064 | 0 | 0.8156947 | 0.1843053037 | 0 | 0.0249178306 | 0.0249178306 |
| 338 | 1.270362765 | 0 | 0.8153545 | 0.1846454881 | 0 | 0.0249567217 | 0.0249567217 |
| 339 | 1.275838467 | 0 | 0.8150140 | 0.1849859988 | 0 | 0.0249956103 | 0.0249956103 |
| 340 | 1.281314168 | 0 | 0.8146733 | 0.1853266757 | 0 | 0.0250345025 | 0.0250345025 |
| 341 | 1.286789870 | 0 | 0.8143318 | 0.1856681553 | 0 | 0.0250734593 | 0.0250734593 |
| 342 | 1.295003422 | 0 | 0.8139900 | 0.1860100278 | 0 | 0.0251124367 | 0.0251124367 |
| 343 | 1.308692676 | 0 | 0.8136474 | 0.1863526397 | 0 | 0.0251514725 | 0.0251514725 |
| 344 | 1.322381930 | 0 | 0.8133042 | 0.1866957657 | 0 | 0.0251905560 | 0.0251905560 |
| 345 | 1.338809035 | 0 | 0.8129610 | 0.1870390187 | 0 | 0.0252296299 | 0.0252296299 |
| 346 | 1.344284736 | 0 | 0.8126175 | 0.1873824850 | 0 | 0.0252687036 | 0.0252687036 |
| 347 | 1.355236140 | 0 | 0.8122736 | 0.1877264064 | 0 | 0.0253078038 | 0.0253078038 |
| 348 | 1.360711841 | 0 | 0.8119293 | 0.1880706724 | 0 | 0.0253469243 | 0.0253469243 |
| 349 | 1.368925394 | 0 | 0.8115849 | 0.1884150664 | 0 | 0.0253860350 | 0.0253860350 |
| 350 | 1.385352498 | 0 | 0.8112395 | 0.1887605336 | 0 | 0.0254252419 | 0.0254252419 |
| 351 | 1.393566051 | 0 | 0.8108938 | 0.1891061853 | 0 | 0.0254644451 | 0.0254644451 |
| 352 | 1.434633812 | 0 | 0.8105472 | 0.1894528109 | 0 | 0.0255037200 | 0.0255037200 |
| 353 | 1.451060917 | 0 | 0.8101995 | 0.1898005460 | 0 | 0.0255431066 | 0.0255431066 |
| 354 | 1.472963723 | 0 | 0.8095025 | 0.1904974570 | 0 | 0.0256219433 | 0.0256219433 |
| 355 | 1.475701574 | 0 | 0.8091537 | 0.1908463111 | 0 | 0.0256613637 | 0.0256613637 |
| 356 | 1.486652977 | 0 | 0.8088043 | 0.1911956569 | 0 | 0.0257008192 | 0.0257008192 |
| 357 | 1.489390828 | 0 | 0.8084542 | 0.1915458021 | 0 | 0.0257403327 | 0.0257403327 |
| 358 | 1.492128679 | 0 | 0.8081039 | 0.1918960618 | 0 | 0.0257798427 | 0.0257798427 |
| 359 | 1.494866530 | 0 | 0.8077536 | 0.1922463758 | 0 | 0.0258193348 | 0.0258193348 |
| 360 | 1.503080082 | 0 | 0.8074028 | 0.1925971659 | 0 | 0.0258588638 | 0.0258588638 |
| 361 | 1.508555784 | 0 | 0.8070518 | 0.1929481817 | 0 | 0.0258983924 | 0.0258983924 |
| 362 | 1.511293634 | 0 | 0.8067004 | 0.1932996438 | 0 | 0.0259379330 | 0.0259379330 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 363 | 1.524982888 | 0 | 0.8063489 | 0.1936511494 | 0 | 0.0259774756 | 0.0259774756 |
| 364 | 1.535934292 | 0 | 0.8056456 | 0.1943544294 | 0 | 0.0260564931 | 0.0260564931 |
| 365 | 1.549623546 | 0 | 0.8052931 | 0.1947068783 | 0 | 0.0260960696 | 0.0260960696 |
| 366 | 1.566050650 | 0 | 0.8049403 | 0.1950596729 | 0 | 0.0261356701 | 0.0261356701 |
| 367 | 1.571526352 | 0 | 0.8045869 | 0.1954131472 | 0 | 0.0261753114 | 0.0261753114 |
| 368 | 1.585215606 | 0 | 0.8042330 | 0.1957670394 | 0 | 0.0262149747 | 0.0262149747 |
| 369 | 1.587953457 | 0 | 0.8038785 | 0.1961214789 | 0 | 0.0262546720 | 0.0262546720 |
| 370 | 1.590691307 | 0 | 0.8035237 | 0.1964762649 | 0 | 0.0262943904 | 0.0262943904 |
| 371 | 1.631759069 | 0 | 0.8028096 | 0.1971903624 | 0 | 0.0263742328 | 0.0263742328 |
| 372 | 1.639972621 | 0 | 0.8024520 | 0.1975479713 | 0 | 0.0264141843 | 0.0264141843 |
| 373 | 1.648186174 | 0 | 0.8020941 | 0.1979058899 | 0 | 0.0264541497 | 0.0264541497 |
| 374 | 1.702943190 | 0 | 0.8017330 | 0.1982669932 | 0 | 0.0264944830 | 0.0264944830 |
| 375 | 1.708418891 | 0 | 0.8013715 | 0.1986284615 | 0 | 0.0265348303 | 0.0265348303 |
| 376 | 1.790554415 | 0 | 0.8010073 | 0.1989927064 | 0 | 0.0265754351 | 0.0265754351 |
| 377 | 1.796030116 | 0 | 0.8006427 | 0.1993572872 | 0 | 0.0266160648 | 0.0266160648 |
| 378 | 1.809719370 | 0 | 0.8002767 | 0.1997232636 | 0 | 0.0266567962 | 0.0266567962 |
| 379 | 1.815195072 | 0 | 0.7999103 | 0.2000896865 | 0 | 0.0266975719 | 0.0266975719 |
| 380 | 1.826146475 | 0 | 0.7995430 | 0.2004569500 | 0 | 0.0267384304 | 0.0267384304 |
| 381 | 1.831622177 | 0 | 0.7991754 | 0.2008246128 | 0 | 0.0267793109 | 0.0267793109 |
| 382 | 1.839835729 | 0 | 0.7988070 | 0.2011929953 | 0 | 0.0268202449 | 0.0268202449 |
| 383 | 1.861738535 | 0 | 0.7980670 | 0.2019329682 | 0 | 0.0269024056 | 0.0269024056 |
| 384 | 1.869952088 | 0 | 0.7976967 | 0.2023032832 | 0 | 0.0269434799 | 0.0269434799 |
| 385 | 1.894592745 | 0 | 0.7969556 | 0.2030444001 | 0 | 0.0270255874 | 0.0270255874 |
| 386 | 1.921971253 | 0 | 0.7965827 | 0.2034172676 | 0 | 0.0270668650 | 0.0270668650 |
| 387 | 1.943874059 | 0 | 0.7962076 | 0.2037924478 | 0 | 0.0271083723 | 0.0271083723 |
| 388 | 1.971252567 | 0 | 0.7954503 | 0.2045496588 | 0 | 0.0271920049 | 0.0271920049 |
| 389 | 1.973990418 | 0 | 0.7946920 | 0.2053079663 | 0 | 0.0272756318 | 0.0272756318 |
| 390 | 1.982203970 | 0 | 0.7943117 | 0.2056883240 | 0 | 0.0273175420 | 0.0273175420 |
| 391 | 2.006844627 | 0 | 0.7939286 | 0.2060713842 | 0 | 0.0273598015 | 0.0273598015 |
| 392 | 2.012320329 | 0 | 0.7935454 | 0.2064545837 | 0 | 0.0274020450 | 0.0274020450 |
| 393 | 2.026009582 | 0 | 0.7931589 | 0.2068410719 | 0 | 0.0274446664 | 0.0274446664 |
| 394 | 2.031485284 | 0 | 0.7927721 | 0.2072279093 | 0 | 0.0274873032 | 0.0274873032 |
| 395 | 2.039698836 | 0 | 0.7923839 | 0.2076161218 | 0 | 0.0275300481 | 0.0275300481 |
| 396 | 2.050650240 | 0 | 0.7919950 | 0.2080050204 | 0 | 0.0275728345 | 0.0275728345 |
| 397 | 2.069815195 | 0 | 0.7916046 | 0.2083954077 | 0 | 0.0276157395 | 0.0276157395 |
| 398 | 2.072553046 | 0 | 0.7912139 | 0.2087860801 | 0 | 0.0276586427 | 0.0276586427 |
| 399 | 2.105407255 | 0 | 0.7908209 | 0.2091790545 | 0 | 0.0277018066 | 0.0277018066 |
| 400 | 2.121834360 | 0 | 0.7904268 | 0.2095732185 | 0 | 0.0277450877 | 0.0277450877 |
| 401 | 2.124572211 | 0 | 0.7900325 | 0.2099675309 | 0 | 0.0277883633 | 0.0277883633 |
| 402 | 2.168377823 | 0 | 0.7896363 | 0.2103636984 | 0 | 0.0278317951 | 0.0278317951 |
| 403 | 2.184804928 | 0 | 0.7892387 | 0.2107612530 | 0 | 0.0278753703 | 0.0278753703 |
| 404 | 2.190280630 | 0 | 0.7888409 | 0.2111591289 | 0 | 0.0279189558 | 0.0279189558 |
| 405 | 2.195756331 | 0 | 0.7884425 | 0.2115575030 | 0 | 0.0279625902 | 0.0279625902 |
| 406 | 2.201232033 | 0 | 0.7880436 | 0.2119563536 | 0 | 0.0280062497 | 0.0280062497 |
| 407 | 2.212183436 | 0 | 0.7876429 | 0.2123570793 | 0 | 0.0280500821 | 0.0280500821 |
| 408 | 2.242299795 | 0 | 0.7872402 | 0.2127597890 | 0 | 0.0280941257 | 0.0280941257 |
| 409 | 2.253251198 | 0 | 0.7868356 | 0.2131643814 | 0 | 0.0281383357 | 0.0281383357 |
| 410 | 2.275154004 | 0 | 0.7864287 | 0.2135713211 | 0 | 0.0281827682 | 0.0281827682 |
| 411 | 2.318959617 | 0 | 0.7860197 | 0.2139802542 | 0 | 0.0282274326 | 0.0282274326 |

```
412 2.351813826       0 0.7856086 0.2143913760   0 0.0282723587 0.0282723587
413 2.360027379       0 0.7851970 0.2148029791   0 0.0283173010 0.0283173010
414 2.390143737       0 0.7839582 0.2160417734   0 0.0284523894 0.0284523894
415 2.395619439       0 0.7835447 0.2164552766   0 0.0284974379 0.0284974379
416 2.406570842       0 0.7831305 0.2168695287   0 0.0285425223 0.0285425223
417 2.412046543       0 0.7827158 0.2172841721   0 0.0285876073 0.0285876073
418 2.414784394       0 0.7823011 0.2176988780   0 0.0286326941 0.0286326941
419 2.442162902       0 0.7818844 0.2181156202   0 0.0286779593 0.0286779593
420 2.507871321       0 0.7814637 0.2185362589   0 0.0287236233 0.0287236233
421 2.551676934       0 0.7810366 0.2189633780   0 0.0287700484 0.0287700484
422 2.554414784       0 0.7806089 0.2193910607   0 0.0288164930 0.0288164930
423 2.559890486       0 0.7801812 0.2198188272   0 0.0288629081 0.0288629081
424 2.570841889       0 0.7797527 0.2202473105   0 0.0289093732 0.0289093732
425 2.603696099       0 0.7793188 0.2206812016   0 0.0289563870 0.0289563870
426 2.614647502       0 0.7788839 0.2211160719   0 0.0290034587 0.0290034587
427 2.625598905       0 0.7784485 0.2215515006   0 0.0290505207 0.0290505207
428 2.628336756       0 0.7780124 0.2219876015   0 0.0290976000 0.0290976000
429 2.636550308       0 0.7775751 0.2224249362   0 0.0291447665 0.0291447665
430 2.740588638       0 0.7771271 0.2228729033   0 0.0291932247 0.0291932247
431 2.800821355       0 0.7766740 0.2233260347   0 0.0292422111 0.0292422111
432 2.803559206       0 0.7762208 0.2237791662   0 0.0292911911 0.0292911911
433 2.819986311       0 0.7757657 0.2242343124   0 0.0293403490 0.0293403490
434 2.839151266       0 0.7753082 0.2246918289   0 0.0293897436 0.0293897436
435 2.866529774       0 0.7748465 0.2251534881   0 0.0294395750 0.0294395750
436 2.899383984       0 0.7743816 0.2256184194   0 0.0294897662 0.0294897662
437 2.948665298       0 0.7739106 0.2260894374   0 0.0295406345 0.0295406345
438 2.954140999       0 0.7734379 0.2265621250   0 0.0295916413 0.0295916413
439 2.997946612       0 0.7729569 0.2270430518   0 0.0296434917 0.0296434917
440 3.008898015       0 0.7724711 0.2275288531   0 0.0296958695 0.0296958695
441 3.028062971       0 0.7719809 0.2280190679   0 0.0297486683 0.0297486683
442 3.033538672       0 0.7714904 0.2285095579   0 0.0298014415 0.0298014415
443 3.036276523       0 0.7709994 0.2290005692   0 0.0298541917 0.0298541917
444 3.041752225       0 0.7705069 0.2294930915   0 0.0299070267 0.0299070267
445 3.110198494       0 0.7700041 0.2299959479   0 0.0299609338 0.0299609338
446 3.186858316       0 0.7694936 0.2305064120   0 0.0300157400 0.0300157400
447 3.189596167       0 0.7689815 0.2310184775   0 0.0300706571 0.0300706571
448 3.227926078       0 0.7684644 0.2315356396   0 0.0301261404 0.0301261404
449 3.266255989       0 0.7679403 0.2320596694   0 0.0301822535 0.0301822535
450 3.285420945       0 0.7674158 0.2325842057   0 0.0302383730 0.0302383730
451 3.290896646       0 0.7668907 0.2331092832   0 0.0302945219 0.0302945219
452 3.411362081       0 0.7663436 0.2336563703   0 0.0303530707 0.0303530707
453 3.474332649       0 0.7657848 0.2342151809   0 0.0304129612 0.0304129612
454 3.498973306       0 0.7652192 0.2347808460   0 0.0304734924 0.0304734924
455 3.531827515       0 0.7646447 0.2353552651   0 0.0305350014 0.0305350014
456 3.534565366       0 0.7634946 0.2365053608   0 0.0306579709 0.0306579709
457 3.550992471       0 0.7629159 0.2370840729   0 0.0307197467 0.0307197467
458 3.553730322       0 0.7623367 0.2376633361   0 0.0307815000 0.0307815000
459 3.570157426       0 0.7617526 0.2382473599   0 0.0308437265 0.0308437265
460 3.592060233       0 0.7611656 0.2388344197   0 0.0309061937 0.0309061937
```

```
461 3.603011636       0 0.7605776 0.2394224316   0 0.0309686631 0.0309686631
462 3.619438741       0 0.7599852 0.2400148375   0 0.0310314629 0.0310314629
463 3.627652293       0 0.7593926 0.2406074465   0 0.0310941632 0.0310941632
464 3.671457906       0 0.7587890 0.2412110115   0 0.0311580634 0.0311580634
465 3.701574264       0 0.7581791 0.2418208758   0 0.0312227202 0.0312227202
466 3.707049966       0 0.7575666 0.2424333955   0 0.0312876442 0.0312876442
467 3.811088296       0 0.7569298 0.2430702467   0 0.0313553308 0.0313553308
468 3.898699521       0 0.7562642 0.2437358409   0 0.0314260230 0.0314260230
469 3.961670089       0 0.7555758 0.2444242332   0 0.0314993320 0.0314993320
470 4.030116359       0 0.7548408 0.2451591733   0 0.0315779213 0.0315779213
471 4.095824778       0 0.7540745 0.2459255109   0 0.0316601133 0.0316601133
472 4.109514031       0 0.7532997 0.2467003208   0 0.0317429918 0.0317429918
473 4.114989733       0 0.7525212 0.2474788003   0 0.0318262610 0.0318262610
474 4.125941136       0 0.7517361 0.2482638572   0 0.0319102558 0.0319102558
475 4.136892539       0 0.7509428 0.2490571828   0 0.0319949778 0.0319949778
476 4.205338809       0 0.7501240 0.2498760372   0 0.0320824434 0.0320824434
477 4.320328542       0 0.7492526 0.2507473745   0 0.0321757314 0.0321757314
478 4.369609856       0 0.7483593 0.2516407043   0 0.0322713478 0.0322713478
479 4.394250513       0 0.7474598 0.2525401691   0 0.0323674067 0.0323674067
480 4.574948665       0 0.7464916 0.2535083508   0 0.0324716715 0.0324716715
481 4.577686516       0 0.7455192 0.2544808409   0 0.0325760464 0.0325760464
482 4.613278576       0 0.7445371 0.2554628516   0 0.0326811149 0.0326811149
483 4.698151951       0 0.7435011 0.2564988806   0 0.0327922805 0.0327922805
484 4.706365503       0 0.7424575 0.2575424857   0 0.0329039246 0.0329039246
485 4.761122519       0 0.7413766 0.2586234320   0 0.0330206694 0.0330206694
486 4.763860370       0 0.7402926 0.2597073552   0 0.0331376299 0.0331376299
487 4.947296372       0 0.7391108 0.2608891877   0 0.0332665789 0.0332665789
488 4.985626283       0 0.7378970 0.2621029906   0 0.0333991056 0.0333991056
489 5.084188912       0 0.7364541 0.2635459216   0 0.0335621736 0.0335621736
490 5.111567420       0 0.7349827 0.2650172899   0 0.0337284826 0.0337284826
491 5.152635181       0 0.7334618 0.2665382483   0 0.0339005315 0.0339005315
492 5.190965092       0 0.7319004 0.2680996370   0 0.0340774941 0.0340774941
493 5.281314168       0 0.7302609 0.2697390924   0 0.0342646553 0.0342646553
494 5.349760438       0 0.7285100 0.2714900347   0 0.0344652600 0.0344652600
495 5.399041752       0 0.7266961 0.2733038710   0 0.0346740793 0.0346740793
496 5.412731006       0 0.7248492 0.2751507563   0 0.0348862697 0.0348862697
497 5.779603012       0 0.7223610 0.2776389820   0 0.0352051052 0.0352051052
498 5.848049281       0 0.7196580 0.2803419666   0 0.0355569948 0.0355569948
499 5.921971253       0 0.7167290 0.2832710030   0 0.0359419225 0.0359419225
500 6.198494182       0 0.7125818 0.2874181508   0 0.0365481818 0.0365481818
501 6.253251198       0 0.7079572 0.2920427816   0 0.0372443177 0.0372443177
502 6.357289528       0 0.7027899 0.2972100955   0 0.0380325159 0.0380325159
503 6.362765229       0 0.6975745 0.3024255054   0 0.0388108714 0.0388108714
504 6.798083504       0 0.6870020 0.3129979816   0 0.0409739118 0.0409739118
505 7.110198494       0 0.6455554 0.3544445695   0 0.0585652812 0.0585652812
506 7.731690623       0 0.6455554 0.3544445695   0 0.0585652812 0.0585652812
    lower1    lower2       lower3 upper1    upper2      upper3
1        0 1.0000000 0.000000e+00      0 1.0000000 0.000000000
2        0 0.9993763 2.876559e-05      0 1.0000000 0.001519594
```

```
3        0 0.9993763 2.876559e-05      0 1.0000000 0.001519594
4        0 0.9989884 1.011790e-04      0 1.0000000 0.001728766
5        0 0.9983046 2.998125e-04      0 1.0000000 0.002335737
6        0 0.9976695 5.332244e-04      0 0.9998204 0.002956835
7        0 0.9970576 7.854004e-04      0 0.9995943 0.003571534
8        0 0.9964599 1.049383e-03      0 0.9993539 0.004179169
9        0 0.9964599 1.049383e-03      0 0.9993539 0.004179169
10       0 0.9961646 1.184642e-03      0 0.9992298 0.004480957
11       0 0.9947129 1.882747e-03      0 0.9985842 0.005972570
12       0 0.9944256 2.025718e-03      0 0.9984513 0.006268958
13       0 0.9927155 2.899179e-03      0 0.9976368 0.008036353
14       0 0.9921473 3.195683e-03      0 0.9973596 0.008624742
15       0 0.9921473 3.195683e-03      0 0.9973596 0.008624742
16       0 0.9918612 3.345794e-03      0 0.9972193 0.008921173
17       0 0.9915738 3.497131e-03      0 0.9970777 0.009219060
18       0 0.9909974 3.802310e-03      0 0.9967921 0.009816682
19       0 0.9907079 3.956242e-03      0 0.9966479 0.010116887
20       0 0.9892563 4.735382e-03      0 0.9959175 0.011622555
21       0 0.9886741 5.050578e-03      0 0.9956217 0.012226659
22       0 0.9883812 5.209602e-03      0 0.9954724 0.012530499
23       0 0.9880864 5.370094e-03      0 0.9953216 0.012836484
24       0 0.9871970 5.856358e-03      0 0.9948647 0.013759201
25       0 0.9868991 6.019873e-03      0 0.9947109 0.014068323
26       0 0.9868991 6.019873e-03      0 0.9947109 0.014068323
27       0 0.9859923 6.519270e-03      0 0.9942412 0.015009189
28       0 0.9853846 6.855259e-03      0 0.9939249 0.015639693
29       0 0.9835537 7.874371e-03      0 0.9929648 0.017538900
30       0 0.9826345 8.388942e-03      0 0.9924797 0.018492358
31       0 0.9820195 8.734477e-03      0 0.9921537 0.019130207
32       0 0.9817109 8.908106e-03      0 0.9919899 0.019450244
33       0 0.9814012 9.082573e-03      0 0.9918252 0.019771382
34       0 0.9795402 1.013544e-02      0 0.9908310 0.021700823
35       0 0.9795402 1.013544e-02      0 0.9908310 0.021700823
36       0 0.9795402 1.013544e-02      0 0.9908310 0.021700823
37       0 0.9792272 1.031304e-02      0 0.9906632 0.022025274
38       0 0.9789131 1.049149e-02      0 0.9904946 0.022350881
39       0 0.9779698 1.102856e-02      0 0.9899869 0.023328638
40       0 0.9776543 1.120850e-02      0 0.9898168 0.023655642
41       0 0.9776543 1.120850e-02      0 0.9898168 0.023655642
42       0 0.9763888 1.193241e-02      0 0.9891320 0.024966973
43       0 0.9760720 1.211392e-02      0 0.9889603 0.025295187
44       0 0.9748053 1.284129e-02      0 0.9882719 0.026607585
45       0 0.9741715 1.320596e-02      0 0.9879267 0.027264224
46       0 0.9725858 1.412047e-02      0 0.9870608 0.028906916
47       0 0.9722680 1.430408e-02      0 0.9868869 0.029236111
48       0 0.9713142 1.485614e-02      0 0.9863639 0.030223971
49       0 0.9706767 1.522559e-02      0 0.9860138 0.030884166
50       0 0.9700378 1.559627e-02      0 0.9856625 0.031545834
51       0 0.9687598 1.633912e-02      0 0.9849584 0.032869369
```

```
52      0 0.9678007 1.689739e-02      0 0.9844292 0.033862563
53      0 0.9662017 1.783001e-02      0 0.9835449 0.035518276
54      0 0.9658811 1.801720e-02      0 0.9833674 0.035850236
55      0 0.9645983 1.876740e-02      0 0.9826559 0.037178340
56      0 0.9626720 1.989630e-02      0 0.9815849 0.039172555
57      0 0.9617059 2.046343e-02      0 0.9810468 0.040172783
58      0 0.9604171 2.122094e-02      0 0.9803279 0.041506874
59      0 0.9591277 2.197969e-02      0 0.9796079 0.042841677
60      0 0.9584824 2.235975e-02      0 0.9792472 0.043509760
61      0 0.9578361 2.274060e-02      0 0.9788858 0.044178797
62      0 0.9575127 2.293120e-02      0 0.9787049 0.044513561
63      0 0.9562189 2.369460e-02      0 0.9779803 0.045852949
64      0 0.9552475 2.426828e-02      0 0.9774358 0.046858538
65      0 0.9545989 2.465156e-02      0 0.9770720 0.047529881
66      0 0.9539501 2.503530e-02      0 0.9767077 0.048201543
67      0 0.9523257 2.599707e-02      0 0.9757946 0.049882905
68      0 0.9520002 2.618992e-02      0 0.9756115 0.050219889
69      0 0.9516744 2.638297e-02      0 0.9754283 0.050557106
70      0 0.9484182 2.831691e-02      0 0.9735917 0.053927187
71      0 0.9474395 2.889894e-02      0 0.9730389 0.054940116
72      0 0.9474395 2.889894e-02      0 0.9730389 0.054940116
73      0 0.9461327 2.967682e-02      0 0.9723002 0.056292621
74      0 0.9458054 2.987170e-02      0 0.9721151 0.056631341
75      0 0.9448229 3.045721e-02      0 0.9715590 0.057648232
76      0 0.9448229 3.045721e-02      0 0.9715590 0.057648232
77      0 0.9438393 3.104388e-02      0 0.9710017 0.058666192
78      0 0.9421966 3.202468e-02      0 0.9700700 0.060366236
79      0 0.9418673 3.222136e-02      0 0.9698832 0.060707001
80      0 0.9412085 3.261509e-02      0 0.9695092 0.061388787
81      0 0.9402197 3.320642e-02      0 0.9689474 0.062412030
82      0 0.9402197 3.320642e-02      0 0.9689474 0.062412030
83      0 0.9388992 3.399690e-02      0 0.9681964 0.063778494
84      0 0.9382385 3.439263e-02      0 0.9678204 0.064462234
85      0 0.9379077 3.459080e-02      0 0.9676322 0.064804588
86      0 0.9359212 3.578226e-02      0 0.9665001 0.066860130
87      0 0.9339301 3.697823e-02      0 0.9653636 0.068920442
88      0 0.9332654 3.737767e-02      0 0.9649840 0.069608293
89      0 0.9326004 3.777742e-02      0 0.9646042 0.070296400
90      0 0.9319345 3.817781e-02      0 0.9642237 0.070985449
91      0 0.9312680 3.857868e-02      0 0.9638429 0.071675174
92      0 0.9299351 3.938110e-02      0 0.9630804 0.073054503
93      0 0.9289341 3.998409e-02      0 0.9625074 0.074090315
94      0 0.9286000 4.018538e-02      0 0.9623161 0.074436051
95      0 0.9275975 4.078977e-02      0 0.9617418 0.075473445
96      0 0.9265946 4.139490e-02      0 0.9611667 0.076511223
97      0 0.9249214 4.240535e-02      0 0.9602064 0.078242471
98      0 0.9249214 4.240535e-02      0 0.9602064 0.078242471
99      0 0.9239148 4.301379e-02      0 0.9596282 0.079284078
100     0 0.9225725 4.382564e-02      0 0.9588566 0.080672972
```

```
101      0 0.9222364 4.402893e-02      0 0.9586634 0.081020676
102      0 0.9212273 4.463964e-02      0 0.9580830 0.082064846
103      0 0.9202164 4.525188e-02      0 0.9575011 0.083110871
104      0 0.9192040 4.586544e-02      0 0.9569179 0.084158384
105      0 0.9185284 4.627516e-02      0 0.9565285 0.084857403
106      0 0.9178522 4.668554e-02      0 0.9561384 0.085557019
107      0 0.9164983 4.750784e-02      0 0.9553566 0.086957799
108      0 0.9164983 4.750784e-02      0 0.9553566 0.086957799
109      0 0.9148042 4.853777e-02      0 0.9543775 0.088710362
110      0 0.9137867 4.915683e-02      0 0.9537889 0.089763040
111      0 0.9127669 4.977756e-02      0 0.9531988 0.090818097
112      0 0.9120865 5.019192e-02      0 0.9528049 0.091522043
113      0 0.9110652 5.081425e-02      0 0.9522132 0.092578615
114      0 0.9100427 5.143768e-02      0 0.9516205 0.093636414
115      0 0.9090203 5.206139e-02      0 0.9510275 0.094694190
116      0 0.9079963 5.268633e-02      0 0.9504333 0.095753574
117      0 0.9062888 5.372935e-02      0 0.9494416 0.097519953
118      0 0.9059469 5.393824e-02      0 0.9492431 0.097873731
119      0 0.9052626 5.435639e-02      0 0.9488455 0.098581673
120      0 0.9045776 5.477516e-02      0 0.9484474 0.099290360
121      0 0.9025215 5.603358e-02      0 0.9472509 0.101417414
122      0 0.9018355 5.645366e-02      0 0.9468515 0.102127157
123      0 0.9004623 5.729516e-02      0 0.9460514 0.103547800
124      0 0.8997748 5.771663e-02      0 0.9456507 0.104258996
125      0 0.8987431 5.834947e-02      0 0.9450490 0.105326306
126      0 0.8980541 5.877228e-02      0 0.9446470 0.106039191
127      0 0.8977090 5.898404e-02      0 0.9444456 0.106396131
128      0 0.8963270 5.983301e-02      0 0.9436383 0.107825827
129      0 0.8949421 6.068444e-02      0 0.9428287 0.109258507
130      0 0.8942488 6.111083e-02      0 0.9424233 0.109975654
131      0 0.8935551 6.153766e-02      0 0.9420174 0.110693301
132      0 0.8932080 6.175127e-02      0 0.9418143 0.111052383
133      0 0.8925136 6.217876e-02      0 0.9414078 0.111770674
134      0 0.8911247 6.303453e-02      0 0.9405940 0.113207458
135      0 0.8890392 6.432097e-02      0 0.9393706 0.115364727
136      0 0.8883430 6.475058e-02      0 0.9389620 0.116084843
137      0 0.8869492 6.561145e-02      0 0.9381433 0.117526663
138      0 0.8862514 6.604260e-02      0 0.9377333 0.118248436
139      0 0.8855532 6.647424e-02      0 0.9373228 0.118970640
140      0 0.8855532 6.647424e-02      0 0.9373228 0.118970640
141      0 0.8855532 6.647424e-02      0 0.9373228 0.118970640
142      0 0.8848536 6.690694e-02      0 0.9369112 0.119694276
143      0 0.8845030 6.712382e-02      0 0.9367050 0.120056939
144      0 0.8838018 6.755777e-02      0 0.9362923 0.120782312
145      0 0.8827494 6.820939e-02      0 0.9356725 0.121870776
146      0 0.8827494 6.820939e-02      0 0.9356725 0.121870776
147      0 0.8816954 6.886246e-02      0 0.9350513 0.122961039
148      0 0.8806399 6.951682e-02      0 0.9344290 0.124052777
149      0 0.8795835 7.017209e-02      0 0.9338057 0.125145407
```

```
150      0 0.8788786 7.060950e-02      0 0.9333897 0.125874516
151      0 0.8778204 7.126644e-02      0 0.9327648 0.126969073
152      0 0.8771145 7.170491e-02      0 0.9323478 0.127699272
153      0 0.8767612 7.192435e-02      0 0.9321391 0.128064701
154      0 0.8757008 7.258336e-02      0 0.9315123 0.129161454
155      0 0.8757008 7.258336e-02      0 0.9315123 0.129161454
156      0 0.8757008 7.258336e-02      0 0.9315123 0.129161454
157      0 0.8749931 7.302340e-02      0 0.9310938 0.129893516
158      0 0.8742846 7.346407e-02      0 0.9306746 0.130626300
159      0 0.8735758 7.390515e-02      0 0.9302551 0.131359460
160      0 0.8732212 7.412588e-02      0 0.9300452 0.131726294
161      0 0.8721572 7.478844e-02      0 0.9294150 0.132826766
162      0 0.8707371 7.567316e-02      0 0.9285735 0.134295611
163      0 0.8703817 7.589465e-02      0 0.9283628 0.134663237
164      0 0.8696706 7.633794e-02      0 0.9279412 0.135398797
165      0 0.8689591 7.678167e-02      0 0.9275192 0.136134762
166      0 0.8686030 7.700373e-02      0 0.9273080 0.136503056
167      0 0.8682469 7.722587e-02      0 0.9270967 0.136871400
168      0 0.8671786 7.789271e-02      0 0.9264625 0.137976478
169      0 0.8664658 7.833781e-02      0 0.9260391 0.138713743
170      0 0.8657524 7.878348e-02      0 0.9256152 0.139451630
171      0 0.8653955 7.900649e-02      0 0.9254031 0.139820801
172      0 0.8646806 7.945336e-02      0 0.9249781 0.140560274
173      0 0.8636074 8.012463e-02      0 0.9243396 0.141670212
174      0 0.8628912 8.057280e-02      0 0.9239133 0.142410989
175      0 0.8625330 8.079704e-02      0 0.9237000 0.142781571
176      0 0.8625330 8.079704e-02      0 0.9237000 0.142781571
177      0 0.8607394 8.192061e-02      0 0.9226312 0.144636575
178      0 0.8596624 8.259575e-02      0 0.9219890 0.145750493
179      0 0.8593031 8.282108e-02      0 0.9217747 0.146122172
180      0 0.8593031 8.282108e-02      0 0.9217747 0.146122172
181      0 0.8585836 8.327245e-02      0 0.9213453 0.146866321
182      0 0.8582235 8.349837e-02      0 0.9211304 0.147238724
183      0 0.8575035 8.395033e-02      0 0.9207005 0.147983443
184      0 0.8564226 8.462932e-02      0 0.9200546 0.149101382
185      0 0.8557015 8.508246e-02      0 0.9196235 0.149847097
186      0 0.8546193 8.576300e-02      0 0.9189761 0.150966338
187      0 0.8542583 8.599010e-02      0 0.9187600 0.151339694
188      0 0.8542583 8.599010e-02      0 0.9187600 0.151339694
189      0 0.8528121 8.690057e-02      0 0.9178938 0.152835300
190      0 0.8524503 8.712841e-02      0 0.9176770 0.153209451
191      0 0.8517263 8.758454e-02      0 0.9172431 0.153958188
192      0 0.8510023 8.804091e-02      0 0.9168088 0.154706874
193      0 0.8506399 8.826943e-02      0 0.9165914 0.155081656
194      0 0.8499150 8.872665e-02      0 0.9161564 0.155831277
195      0 0.8488267 8.941360e-02      0 0.9155027 0.156956707
196      0 0.8484636 8.964283e-02      0 0.9152846 0.157332212
197      0 0.8473727 9.033165e-02      0 0.9146293 0.158460285
198      0 0.8459173 9.125158e-02      0 0.9137539 0.159965295
```

```
199      0 0.8448249 9.194256e-02      0 0.9130964 0.161094911
200      0 0.8444603 9.217330e-02      0 0.9128769 0.161472008
201      0 0.8437310 9.263487e-02      0 0.9124377 0.162226076
202      0 0.8430017 9.309666e-02      0 0.9119983 0.162980254
203      0 0.8422716 9.355918e-02      0 0.9115582 0.163735253
204      0 0.8419063 9.379063e-02      0 0.9113379 0.164113019
205      0 0.8415405 9.402241e-02      0 0.9111174 0.164491255
206      0 0.8408088 9.448625e-02      0 0.9106760 0.165247884
207      0 0.8400759 9.495105e-02      0 0.9102338 0.166005727
208      0 0.8397094 9.518354e-02      0 0.9100125 0.166384767
209      0 0.8393426 9.541623e-02      0 0.9097911 0.166764042
210      0 0.8382413 9.611528e-02      0 0.9091259 0.167902835
211      0 0.8375062 9.658214e-02      0 0.9086817 0.168662986
212      0 0.8371385 9.681570e-02      0 0.9084595 0.169043231
213      0 0.8367708 9.704928e-02      0 0.9082372 0.169423477
214      0 0.8364031 9.728289e-02      0 0.9080149 0.169803698
215      0 0.8360352 9.751666e-02      0 0.9077925 0.170184123
216      0 0.8356671 9.775069e-02      0 0.9075698 0.170564840
217      0 0.8352986 9.798495e-02      0 0.9073469 0.170945834
218      0 0.8349294 9.821970e-02      0 0.9071235 0.171327653
219      0 0.8345602 9.845450e-02      0 0.9069001 0.171709466
220      0 0.8341905 9.868963e-02      0 0.9066764 0.172091727
221      0 0.8338205 9.892507e-02      0 0.9064524 0.172474377
222      0 0.8330801 9.939640e-02      0 0.9060039 0.173239993
223      0 0.8327097 9.963220e-02      0 0.9057795 0.173622920
224      0 0.8319675 1.001050e-01      0 0.9053296 0.174390475
225      0 0.8312243 1.005785e-01      0 0.9048790 0.175158904
226      0 0.8308524 1.008155e-01      0 0.9046535 0.175543460
227      0 0.8301086 1.012898e-01      0 0.9042021 0.176312603
228      0 0.8297363 1.015273e-01      0 0.9039762 0.176697594
229      0 0.8293637 1.017649e-01      0 0.9037501 0.177082855
230      0 0.8289911 1.020027e-01      0 0.9035238 0.177468189
231      0 0.8282451 1.024788e-01      0 0.9030707 0.178239542
232      0 0.8278714 1.027174e-01      0 0.9028437 0.178625961
233      0 0.8274977 1.029560e-01      0 0.9026166 0.179012383
234      0 0.8271240 1.031947e-01      0 0.9023895 0.179398824
235      0 0.8267500 1.034336e-01      0 0.9021622 0.179785546
236      0 0.8260011 1.039122e-01      0 0.9017067 0.180559846
237      0 0.8260011 1.039122e-01      0 0.9017067 0.180559846
238      0 0.8252518 1.043913e-01      0 0.9012508 0.181334627
239      0 0.8248769 1.046310e-01      0 0.9010226 0.181722263
240      0 0.8241260 1.051115e-01      0 0.9005654 0.182498716
241      0 0.8229992 1.058330e-01      0 0.8998788 0.183663722
242      0 0.8226234 1.060737e-01      0 0.8996497 0.184052352
243      0 0.8222475 1.063144e-01      0 0.8994206 0.184441008
244      0 0.8218714 1.065554e-01      0 0.8991912 0.184829918
245      0 0.8218714 1.065554e-01      0 0.8991912 0.184829918
246      0 0.8211186 1.070379e-01      0 0.8987320 0.185608256
247      0 0.8207418 1.072795e-01      0 0.8985021 0.185997871
```

```
248      0 0.8203646 1.075214e-01      0 0.8982719 0.186387872
249      0 0.8199872 1.077634e-01      0 0.8980416 0.186778080
250      0 0.8196098 1.080055e-01      0 0.8978111 0.187168264
251      0 0.8184778 1.087321e-01      0 0.8971196 0.188338662
252      0 0.8181000 1.089747e-01      0 0.8968888 0.188729284
253      0 0.8177219 1.092175e-01      0 0.8966577 0.189120228
254      0 0.8169654 1.097036e-01      0 0.8961951 0.189902351
255      0 0.8165867 1.099470e-01      0 0.8959634 0.190293959
256      0 0.8158289 1.104341e-01      0 0.8954998 0.191077363
257      0 0.8154497 1.106779e-01      0 0.8952677 0.191469437
258      0 0.8154497 1.106779e-01      0 0.8952677 0.191469437
259      0 0.8150698 1.109222e-01      0 0.8950352 0.191862321
260      0 0.8143096 1.114112e-01      0 0.8945699 0.192648314
261      0 0.8135484 1.119009e-01      0 0.8941039 0.193435304
262      0 0.8120250 1.128819e-01      0 0.8931702 0.195010412
263      0 0.8116439 1.131274e-01      0 0.8929366 0.195404504
264      0 0.8105000 1.138645e-01      0 0.8922351 0.196587183
265      0 0.8101184 1.141106e-01      0 0.8920009 0.196981810
266      0 0.8097366 1.143568e-01      0 0.8917666 0.197376578
267      0 0.8093548 1.146030e-01      0 0.8915323 0.197771342
268      0 0.8089725 1.148496e-01      0 0.8912976 0.198166601
269      0 0.8082064 1.153441e-01      0 0.8908270 0.198958735
270      0 0.8078232 1.155914e-01      0 0.8905916 0.199354901
271      0 0.8074397 1.158390e-01      0 0.8903560 0.199751450
272      0 0.8066726 1.163344e-01      0 0.8898846 0.200544531
273      0 0.8062888 1.165823e-01      0 0.8896487 0.200941359
274      0 0.8055204 1.170789e-01      0 0.8891761 0.201735922
275      0 0.8051353 1.173278e-01      0 0.8889392 0.202134093
276      0 0.8039792 1.180755e-01      0 0.8882276 0.203329419
277      0 0.8028222 1.188242e-01      0 0.8875150 0.204525653
278      0 0.8024364 1.190740e-01      0 0.8872774 0.204924547
279      0 0.8020505 1.193238e-01      0 0.8870396 0.205323585
280      0 0.8016645 1.195738e-01      0 0.8868017 0.205722654
281      0 0.8008923 1.200742e-01      0 0.8863255 0.206521043
282      0 0.7997324 1.208264e-01      0 0.8856095 0.207720246
283      0 0.7993453 1.210774e-01      0 0.8853706 0.208120391
284      0 0.7989579 1.213287e-01      0 0.8851314 0.208520903
285      0 0.7981828 1.218319e-01      0 0.8846525 0.209322261
286      0 0.7977949 1.220837e-01      0 0.8844128 0.209723331
287      0 0.7970191 1.225876e-01      0 0.8839332 0.210525421
288      0 0.7966307 1.228400e-01      0 0.8836930 0.210926949
289      0 0.7954647 1.235981e-01      0 0.8829714 0.212132325
290      0 0.7950757 1.238510e-01      0 0.8827306 0.212534532
291      0 0.7946864 1.241043e-01      0 0.8824896 0.212937032
292      0 0.7939065 1.246117e-01      0 0.8820066 0.213743288
293      0 0.7927356 1.253740e-01      0 0.8812810 0.214953813
294      0 0.7923447 1.256286e-01      0 0.8810386 0.215357957
295      0 0.7919536 1.258834e-01      0 0.8807962 0.215762299
296      0 0.7915616 1.261387e-01      0 0.8805532 0.216167532
```

```
297      0 0.7895982 1.274187e-01      0 0.8793348 0.218197434
298      0 0.7884178 1.281885e-01      0 0.8786022 0.219417804
299      0 0.7876296 1.287029e-01      0 0.8781127 0.220232747
300      0 0.7868402 1.292182e-01      0 0.8776223 0.221048868
301      0 0.7864448 1.294765e-01      0 0.8773764 0.221457736
302      0 0.7856538 1.299934e-01      0 0.8768845 0.222275439
303      0 0.7852582 1.302520e-01      0 0.8766383 0.222684484
304      0 0.7844648 1.307708e-01      0 0.8761446 0.223504679
305      0 0.7836701 1.312907e-01      0 0.8756497 0.224326259
306      0 0.7836701 1.312907e-01      0 0.8756497 0.224326259
307      0 0.7832721 1.315513e-01      0 0.8754017 0.224737761
308      0 0.7824749 1.320733e-01      0 0.8749048 0.225561882
309      0 0.7816772 1.325960e-01      0 0.8744073 0.226386501
310      0 0.7812780 1.328576e-01      0 0.8741583 0.226799156
311      0 0.7800782 1.336445e-01      0 0.8734091 0.228039523
312      0 0.7796779 1.339071e-01      0 0.8731592 0.228453300
313      0 0.7792772 1.341699e-01      0 0.8729090 0.228867488
314      0 0.7788764 1.344330e-01      0 0.8726586 0.229281838
315      0 0.7784752 1.346963e-01      0 0.8724079 0.229696590
316      0 0.7776711 1.352244e-01      0 0.8719053 0.230527877
317      0 0.7772689 1.354885e-01      0 0.8716538 0.230943676
318      0 0.7768642 1.357544e-01      0 0.8714008 0.231361988
319      0 0.7764596 1.360202e-01      0 0.8711477 0.231780269
320      0 0.7760539 1.362869e-01      0 0.8708939 0.232199663
321      0 0.7756482 1.365535e-01      0 0.8706401 0.232619026
322      0 0.7752426 1.368203e-01      0 0.8703862 0.233038357
323      0 0.7748364 1.370874e-01      0 0.8701319 0.233458266
324      0 0.7744298 1.373549e-01      0 0.8698773 0.233878569
325      0 0.7740231 1.376225e-01      0 0.8696225 0.234299067
326      0 0.7736161 1.378904e-01      0 0.8693675 0.234719808
327      0 0.7732084 1.381589e-01      0 0.8691120 0.235141196
328      0 0.7728006 1.384275e-01      0 0.8688563 0.235562797
329      0 0.7723928 1.386962e-01      0 0.8686005 0.235984365
330      0 0.7719849 1.389649e-01      0 0.8683447 0.236406014
331      0 0.7715764 1.392341e-01      0 0.8680884 0.236828287
332      0 0.7711659 1.395048e-01      0 0.8678307 0.237252632
333      0 0.7703446 1.400465e-01      0 0.8673151 0.238101548
334      0 0.7695233 1.405883e-01      0 0.8667993 0.238950520
335      0 0.7691123 1.408595e-01      0 0.8665411 0.239375444
336      0 0.7687011 1.411308e-01      0 0.8662828 0.239800464
337      0 0.7682899 1.414023e-01      0 0.8660244 0.240225521
338      0 0.7678785 1.416740e-01      0 0.8657658 0.240650780
339      0 0.7674669 1.419460e-01      0 0.8655069 0.241076347
340      0 0.7670550 1.422181e-01      0 0.8652478 0.241502083
341      0 0.7666422 1.424910e-01      0 0.8649880 0.241928756
342      0 0.7662290 1.427642e-01      0 0.8647280 0.242355858
343      0 0.7658150 1.430380e-01      0 0.8644673 0.242783820
344      0 0.7654004 1.433122e-01      0 0.8642062 0.243212397
345      0 0.7649857 1.435866e-01      0 0.8639450 0.243641073
```

```
346      0 0.7645708 1.438612e-01      0 0.8636836 0.244069954
347      0 0.7641554 1.441362e-01      0 0.8634218 0.244499340
348      0 0.7637396 1.444115e-01      0 0.8631597 0.244929110
349      0 0.7633237 1.446869e-01      0 0.8628975 0.245358979
350      0 0.7629066 1.449633e-01      0 0.8626344 0.245790123
351      0 0.7624893 1.452398e-01      0 0.8623711 0.246221437
352      0 0.7620709 1.455171e-01      0 0.8621071 0.246653868
353      0 0.7616513 1.457954e-01      0 0.8618421 0.247087648
354      0 0.7608104 1.463533e-01      0 0.8613110 0.247956757
355      0 0.7603896 1.466326e-01      0 0.8610451 0.248391701
356      0 0.7599682 1.469123e-01      0 0.8607787 0.248827207
357      0 0.7595460 1.471927e-01      0 0.8605117 0.249263629
358      0 0.7591236 1.474733e-01      0 0.8602446 0.249700154
359      0 0.7587012 1.477539e-01      0 0.8599774 0.250136686
360      0 0.7582783 1.480349e-01      0 0.8597098 0.250573770
361      0 0.7578552 1.483162e-01      0 0.8594420 0.251011071
362      0 0.7574317 1.485978e-01      0 0.8591738 0.251448832
363      0 0.7570081 1.488795e-01      0 0.8589056 0.251886641
364      0 0.7561608 1.494433e-01      0 0.8583688 0.252762349
365      0 0.7557362 1.497259e-01      0 0.8580997 0.253201154
366      0 0.7553113 1.500088e-01      0 0.8578304 0.253640352
367      0 0.7548856 1.502922e-01      0 0.8575604 0.254080308
368      0 0.7544594 1.505761e-01      0 0.8572902 0.254520723
369      0 0.7540327 1.508604e-01      0 0.8570194 0.254961750
370      0 0.7536056 1.511450e-01      0 0.8567484 0.255403165
371      0 0.7527462 1.517181e-01      0 0.8562027 0.256291372
372      0 0.7523159 1.520051e-01      0 0.8559294 0.256736092
373      0 0.7518852 1.522924e-01      0 0.8556558 0.257181147
374      0 0.7514507 1.525823e-01      0 0.8553798 0.257630194
375      0 0.7510159 1.528725e-01      0 0.8551035 0.258079629
376      0 0.7505778 1.531649e-01      0 0.8548250 0.258532384
377      0 0.7501393 1.534577e-01      0 0.8545462 0.258985526
378      0 0.7496993 1.537517e-01      0 0.8542663 0.259440267
379      0 0.7492588 1.540460e-01      0 0.8539860 0.259895551
380      0 0.7488173 1.543411e-01      0 0.8537051 0.260351854
381      0 0.7483753 1.546365e-01      0 0.8534238 0.260808598
382      0 0.7479326 1.549325e-01      0 0.8531419 0.261266169
383      0 0.7470434 1.555272e-01      0 0.8525756 0.262185140
384      0 0.7465985 1.558249e-01      0 0.8522922 0.262644928
385      0 0.7457083 1.564208e-01      0 0.8517247 0.263564871
386      0 0.7452606 1.567207e-01      0 0.8514392 0.264027630
387      0 0.7448101 1.570224e-01      0 0.8511518 0.264493194
388      0 0.7439012 1.576317e-01      0 0.8505716 0.265432472
389      0 0.7429912 1.582420e-01      0 0.8499904 0.266372795
390      0 0.7425349 1.585482e-01      0 0.8496988 0.266844361
391      0 0.7420753 1.588565e-01      0 0.8494053 0.267319410
392      0 0.7416155 1.591649e-01      0 0.8491116 0.267794554
393      0 0.7411518 1.594760e-01      0 0.8488154 0.268273816
394      0 0.7406877 1.597874e-01      0 0.8485189 0.268753454
```

```
395      0 0.7402221 1.600999e-01      0 0.8482214 0.269234689
396      0 0.7397558 1.604131e-01      0 0.8479232 0.269716690
397      0 0.7392877 1.607275e-01      0 0.8476238 0.270200423
398      0 0.7388194 1.610422e-01      0 0.8473241 0.270684426
399      0 0.7383483 1.613588e-01      0 0.8470227 0.271171304
400      0 0.7378758 1.616763e-01      0 0.8467204 0.271659623
401      0 0.7374032 1.619940e-01      0 0.8464179 0.272148072
402      0 0.7369285 1.623133e-01      0 0.8461139 0.272638701
403      0 0.7364522 1.626337e-01      0 0.8458089 0.273131028
404      0 0.7359755 1.629544e-01      0 0.8455036 0.273623691
405      0 0.7354983 1.632755e-01      0 0.8451979 0.274116959
406      0 0.7350205 1.635970e-01      0 0.8448918 0.274610749
407      0 0.7345406 1.639201e-01      0 0.8445842 0.275106782
408      0 0.7340583 1.642448e-01      0 0.8442751 0.275605257
409      0 0.7335739 1.645711e-01      0 0.8439645 0.276105964
410      0 0.7330867 1.648993e-01      0 0.8436520 0.276609491
411      0 0.7325971 1.652291e-01      0 0.8433380 0.277115524
412      0 0.7321049 1.655606e-01      0 0.8430225 0.277624324
413      0 0.7316122 1.658926e-01      0 0.8427065 0.278133630
414      0 0.7301298 1.668921e-01      0 0.8417552 0.279666049
415      0 0.7296350 1.672258e-01      0 0.8414376 0.280177457
416      0 0.7291395 1.675601e-01      0 0.8411193 0.280689677
417      0 0.7286436 1.678948e-01      0 0.8408007 0.281202277
418      0 0.7281477 1.682296e-01      0 0.8404821 0.281714943
419      0 0.7276494 1.685661e-01      0 0.8401618 0.282230020
420      0 0.7271465 1.689058e-01      0 0.8398384 0.282749852
421      0 0.7266358 1.692507e-01      0 0.8395103 0.283277842
422      0 0.7261245 1.695960e-01      0 0.8391816 0.283806424
423      0 0.7256132 1.699415e-01      0 0.8388528 0.284335015
424      0 0.7251011 1.702876e-01      0 0.8385235 0.284864422
425      0 0.7245826 1.706381e-01      0 0.8381899 0.285400418
426      0 0.7240630 1.709895e-01      0 0.8378555 0.285937504
427      0 0.7235430 1.713415e-01      0 0.8375205 0.286475104
428      0 0.7230222 1.716941e-01      0 0.8371849 0.287013395
429      0 0.7225001 1.720477e-01      0 0.8368483 0.287553096
430      0 0.7219651 1.724097e-01      0 0.8365038 0.288106287
431      0 0.7214239 1.727760e-01      0 0.8361553 0.288665781
432      0 0.7208828 1.731423e-01      0 0.8358069 0.289225261
433      0 0.7203394 1.735102e-01      0 0.8354568 0.289787130
434      0 0.7197932 1.738801e-01      0 0.8351049 0.290351878
435      0 0.7192420 1.742534e-01      0 0.8347497 0.290921716
436      0 0.7186870 1.746293e-01      0 0.8343922 0.291495613
437      0 0.7181248 1.750101e-01      0 0.8340300 0.292077075
438      0 0.7175606 1.753923e-01      0 0.8336664 0.292660495
439      0 0.7169867 1.757812e-01      0 0.8332965 0.293253973
440      0 0.7164069 1.761741e-01      0 0.8329228 0.293853473
441      0 0.7158221 1.765707e-01      0 0.8325456 0.294458283
442      0 0.7152370 1.769675e-01      0 0.8321682 0.295063295
443      0 0.7146515 1.773649e-01      0 0.8317902 0.295668753
```

```
444      0 0.7140644 1.777636e-01      0 0.8314109 0.296275881
445      0 0.7134650 1.781708e-01      0 0.8310236 0.296895659
446      0 0.7128564 1.785840e-01      0 0.8306306 0.297525027
447      0 0.7122461 1.789986e-01      0 0.8302363 0.298156218
448      0 0.7116297 1.794173e-01      0 0.8298382 0.298793744
449      0 0.7110053 1.798417e-01      0 0.8294346 0.299439469
450      0 0.7103804 1.802665e-01      0 0.8290305 0.300085699
451      0 0.7097549 1.806919e-01      0 0.8286260 0.300732528
452      0 0.7091032 1.811351e-01      0 0.8282046 0.301406590
453      0 0.7084374 1.815876e-01      0 0.8277745 0.302095320
454      0 0.7077636 1.820458e-01      0 0.8273389 0.302792264
455      0 0.7070794 1.825110e-01      0 0.8268966 0.303500101
456      0 0.7057098 1.834427e-01      0 0.8260110 0.304916873
457      0 0.7050209 1.839117e-01      0 0.8255652 0.305629523
458      0 0.7043315 1.843813e-01      0 0.8251188 0.306342651
459      0 0.7036366 1.848548e-01      0 0.8246687 0.307061556
460      0 0.7029382 1.853309e-01      0 0.8242162 0.307783993
461      0 0.7022389 1.858079e-01      0 0.8237627 0.308507355
462      0 0.7015347 1.862887e-01      0 0.8233056 0.309235782
463      0 0.7008304 1.867698e-01      0 0.8228482 0.309964157
464      0 0.7001131 1.872598e-01      0 0.8223824 0.310706105
465      0 0.6993882 1.877547e-01      0 0.8219120 0.311456027
466      0 0.6986603 1.882518e-01      0 0.8214395 0.312209182
467      0 0.6979031 1.887684e-01      0 0.8209488 0.312992723
468      0 0.6971118 1.893084e-01      0 0.8204358 0.313811508
469      0 0.6962932 1.898666e-01      0 0.8199057 0.314658836
470      0 0.6954186 1.904621e-01      0 0.8193405 0.315564279
471      0 0.6945063 1.910826e-01      0 0.8187518 0.316509028
472      0 0.6935844 1.917103e-01      0 0.8181562 0.317463667
473      0 0.6926582 1.923410e-01      0 0.8175578 0.318422829
474      0 0.6917242 1.929770e-01      0 0.8169545 0.319390156
475      0 0.6907807 1.936199e-01      0 0.8163446 0.320367280
476      0 0.6898069 1.942835e-01      0 0.8157151 0.321375897
477      0 0.6887704 1.949893e-01      0 0.8150459 0.322449712
478      0 0.6877078 1.957130e-01      0 0.8143598 0.323550571
479      0 0.6866384 1.964419e-01      0 0.8136687 0.324658458
480      0 0.6854859 1.972253e-01      0 0.8129267 0.325853177
481      0 0.6843289 1.980126e-01      0 0.8121808 0.327052330
482      0 0.6831613 1.988082e-01      0 0.8114270 0.328262403
483      0 0.6819291 1.996471e-01      0 0.8106326 0.329539848
484      0 0.6806885 2.004926e-01      0 0.8098318 0.330825801
485      0 0.6794017 2.013667e-01      0 0.8090048 0.332160560
486      0 0.6781116 2.022434e-01      0 0.8081755 0.333498738
487      0 0.6767027 2.031971e-01      0 0.8072745 0.334961384
488      0 0.6752556 2.041764e-01      0 0.8063495 0.336463831
489      0 0.6735257 2.053322e-01      0 0.8052620 0.338263802
490      0 0.6717619 2.065107e-01      0 0.8041534 0.340099324
491      0 0.6699386 2.077288e-01      0 0.8030081 0.341997056
492      0 0.6680666 2.089787e-01      0 0.8018334 0.343946099
```

```
493      0 0.6660989 2.102891e-01      0 0.8006033 0.345995995
494      0 0.6639965 2.116874e-01      0 0.7992915 0.348187099
495      0 0.6618172 2.131345e-01      0 0.7979353 0.350459451
496      0 0.6595993 2.146086e-01      0 0.7965539 0.352772125
497      0 0.6565533 2.165442e-01      0 0.7947648 0.355970720
498      0 0.6532356 2.186384e-01      0 0.7928344 0.359459298
499      0 0.6496353 2.209023e-01      0 0.7907520 0.363248699
500      0 0.6444316 2.240140e-01      0 0.7879392 0.368768014
501      0 0.6385970 2.274534e-01      0 0.7848509 0.374973439
502      0 0.6320646 2.312807e-01      0 0.7814290 0.381933398
503      0 0.6255073 2.351701e-01      0 0.7779448 0.388915109
504      0 0.6112107 2.421656e-01      0 0.7721916 0.404548460
505      0 0.5403957 2.563913e-01      0 0.7711790 0.489996898
506      0 0.5403957 2.563913e-01      0 0.7711790 0.489996898
```

From state 2 it is only possible to visit state 3 or to remain in state 2. The probability of going to state 1 is 0. The predictions $\hat{P}_{1h}(0,t)$ from state 1 in `[[1]]` are perhaps of most interest here.

```
> summary(pt, from = 1)

Prediction from state 1 (head and tail):
         time   pstate1      pstate2      pstate3          se1          se2
1 0.000000000 1.0000000 0.0000000000 0.0000000000 0.0000000000 0.0000000000
2 0.002737851 0.9991669 0.0005277714 0.0003053084 0.0006117979 0.0005285695
3 0.008213552 0.9986390 0.0010556490 0.0003053084 0.0008100529 0.0007492497
4 0.010951403 0.9983340 0.0010554282 0.0006106022 0.0008685356 0.0007490930
5 0.016427105 0.9977235 0.0010549862 0.0012215589 0.0009807157 0.0007487794
6 0.019164956 0.9965843 0.0015830048 0.0018327183 0.0012115670 0.0009191199
           se3    lower1       lower2       lower3    upper1      upper2
1 0.0000000000 1.0000000 0.000000e+00 0.000000e+00 1.0000000 0.000000000
2 0.0003082357 0.9979685 7.412369e-05 4.220615e-05 1.0000000 0.003757809
3 0.0003082357 0.9970526 2.626497e-04 4.220615e-05 1.0000000 0.004242894
4 0.0004401329 0.9966331 2.625948e-04 1.486610e-04 1.0000000 0.004242006
5 0.0006342283 0.9958031 2.624848e-04 4.415441e-04 0.9996475 0.004240230
6 0.0007908588 0.9942125 5.072942e-04 7.866531e-04 0.9989617 0.004939745
       upper3
1 0.000000000
2 0.002208522
3 0.002208522
4 0.002507954
5 0.003379518
6 0.004269806

...
        time   pstate1   pstate2   pstate3        se1        se2        se3
501 6.253251 0.2308531 0.4336481 0.3354989 0.02448884 0.02974526 0.03063866
502 6.357290 0.2283925 0.4304829 0.3411246 0.02460675 0.03002904 0.03150500
503 6.362765 0.2259175 0.4272883 0.3467942 0.02472281 0.03031296 0.03234850
504 6.798084 0.2209174 0.4208123 0.3582703 0.02518284 0.03119272 0.03507050
505 7.110198 0.2014549 0.3954248 0.4031203 0.03067690 0.03987257 0.05867417
```

```
506 7.731691 0.2014549 0.3954248 0.4031203 0.03067690 0.03987257 0.05867417
       lower1    lower2    lower3    upper1    upper2    upper3
501 0.1875169 0.3790974 0.2805156 0.2842045 0.4960483 0.4012593
502 0.1849160 0.3754732 0.2846421 0.2820911 0.4935519 0.4088150
503 0.1823058 0.3718215 0.2888504 0.2799621 0.4910294 0.4163617
504 0.1766850 0.3639092 0.2957250 0.2762233 0.4866130 0.4340438
505 0.1494719 0.3245138 0.3030695 0.2715164 0.4818309 0.5362003
506 0.1494719 0.3245138 0.3030695 0.2715164 0.4818309 0.5362003
```

But we see that we do not have enough information to create Figure 15 of the tutorial, since the probability of the relapse/death state (`pstate3`) does not distinguish between relapse/death before or after platelet recovery. The remedy is actually easy in this case. Consider a different multi-state model with two RelDeath states, the first one (state 3) after platelet recovery, the second one (state 4) without platelet recovery. The transition matrix of this multi-state model is defined as

```
> tmat2 <- transMat(x = list(c(2, 4), c(3), c(), c()))
> tmat2
```

```
         to
from      State 1 State 2 State 3 State 4
  State 1      NA       1      NA       2
  State 2      NA      NA       3      NA
  State 3      NA      NA      NA      NA
  State 4      NA      NA      NA      NA
```

The multi-state model has four states and the same three transitions as before. If we apply *probtrans* to this new multi-state model with the same estimated cumulative hazards and standard errors as before, we get exactly what we want. Thus, we just have to call *probtrans* with the old `msf2` and the new `tmat2`. From version 0.2.3 on, since the transition matrix is in the *msfit* object, we just need to replace the `trans` item of `msf2` by `tmat2`. In the elements of the resulting lists, `pstate3` will indicate the probability of relapse/death after platelet recovery and `pstate4` the probability of relapse/death without platelet recovery.

```
> msf2$trans <- tmat2
> pt <- probtrans(msf2, predt = 0)
> summary(pt, from = 1)
```

```
Prediction from state 1 (head and tail):
         time   pstate1      pstate2      pstate3      pstate4          se1
1 0.000000000 1.0000000 0.0000000000 0.000000e+00 0.0000000000 0.0000000000
2 0.002737851 0.9991669 0.0005277714 0.000000e+00 0.0003053084 0.0006117979
3 0.008213552 0.9986390 0.0010556490 0.000000e+00 0.0003053084 0.0008100529
4 0.010951403 0.9983340 0.0010554282 2.208393e-07 0.0006103813 0.0008685356
5 0.016427105 0.9977235 0.0010549862 6.628276e-07 0.0012208961 0.0009807157
6 0.019164956 0.9965843 0.0015830048 1.105048e-06 0.0018316132 0.0012115670
           se2          se3          se4    lower1       lower2       lower3
1 0.0000000000 0.000000e+00 0.0000000000 1.0000000 0.000000e+00 0.000000e+00
2 0.0005285695 1.116923e-07 0.0003080762 0.9979685 7.412369e-05 0.000000e+00
3 0.0007492497 1.116923e-07 0.0003080762 0.9970526 2.626497e-04 0.000000e+00
4 0.0007490930 2.989514e-07 0.0004397978 0.9966331 2.625948e-04 1.555250e-08
```

```
5 0.0007487794 6.308958e-07 0.0006336859 0.9958031 2.624848e-04 1.026138e-07
6 0.0009191199 1.032427e-06 0.0007900509 0.9942125 5.072942e-04 1.770590e-07
        lower4    upper1      upper2       upper3      upper4
1 0.0000000000 1.0000000 0.000000000 0.000000e+00 0.000000000
2 0.0000422494 1.0000000 0.003757809          NaN 0.002206261
3 0.0000422494 1.0000000 0.004242894          NaN 0.002206261
4 0.0001486912 1.0000000 0.004242006 3.135832e-06 0.002505631
5 0.0004414450 0.9996475 0.004240230 4.281495e-06 0.003376609
6 0.0007864573 0.9989617 0.004939745 6.896741e-06 0.004265720

...
        time   pstate1   pstate2   pstate3   pstate4        se1        se2
501 6.253251 0.2308531 0.4336481 0.1681264 0.1673724 0.02448884 0.02974526
502 6.357290 0.2283925 0.4304829 0.1712916 0.1698330 0.02460675 0.03002904
503 6.362765 0.2259175 0.4272883 0.1744862 0.1723080 0.02472281 0.03031296
504 6.798084 0.2209174 0.4208123 0.1809622 0.1773081 0.02518284 0.03119272
505 7.110198 0.2014549 0.3954248 0.2063497 0.1967706 0.03067690 0.03987257
506 7.731691 0.2014549 0.3954248 0.2063497 0.1967706 0.03067690 0.03987257
           se3        se4    lower1    lower2    lower3    lower4    upper1
501 0.02379684 0.02100629 0.1875169 0.3790974 0.1273960 0.1308738 0.2842045
502 0.02430502 0.02136056 0.1849160 0.3754732 0.1297050 0.1327282 0.2820911
503 0.02480762 0.02170882 0.1823058 0.3718215 0.1320509 0.1346059 0.2799621
504 0.02616939 0.02264879 0.1766850 0.3639092 0.1362993 0.1380380 0.2762233
505 0.03690104 0.02987965 0.1494719 0.3245138 0.1453401 0.1461185 0.2715164
506 0.03690104 0.02987965 0.1494719 0.3245138 0.1453401 0.1461185 0.2715164
       upper2    upper3    upper4
501 0.4960483 0.2218790 0.2140499
502 0.4935519 0.2262118 0.2173106
503 0.4910294 0.2305584 0.2205703
504 0.4866130 0.2402604 0.2277500
505 0.4818309 0.2929694 0.2649813
506 0.4818309 0.2929694 0.2649813
```

The reader may check that the `pstate3` and `pstate4` probabilities of this new Aalen-Johansen estimator sum up to the `pstate3` probability of the result of the previous call to *probtrans*, and that the `pstate1` and `pstate2` probabilities are unchanged.

Figure 2 contains a plot of `pt1`. For this we use the *plot* method for *probtrans* objects.

```
> plot(pt, ord = c(2, 3, 4, 1), lwd = 2, xlab = "Years since transplant",
+     ylab = "Prediction probabilities", cex = 0.75, legend = c("Alive in remission, no PR",
+         "Alive in remission, PR", "Relapse or death after PR",
+         "Relapse or death without PR"))
```

The argument *from* determines from which state the transition probabilities are to be plotted. The default is from state 1, which is what we want, so the *from* argument is omitted here. The default *type* of the *plot* method for *probtrans* objects is a "stacked" plot, for which the difference between two adjacent lines represents the probability of being in a state. The argument *ord* specifies the order of the states of which the probabilities are stacked. The present order, 2, 3, 4, 1, allows states 2 and 3 to be combined visually (states with platelet recovery) and states 3 and 4 (death states). Other plot types are "filled", which is like "stacked", but uses colors

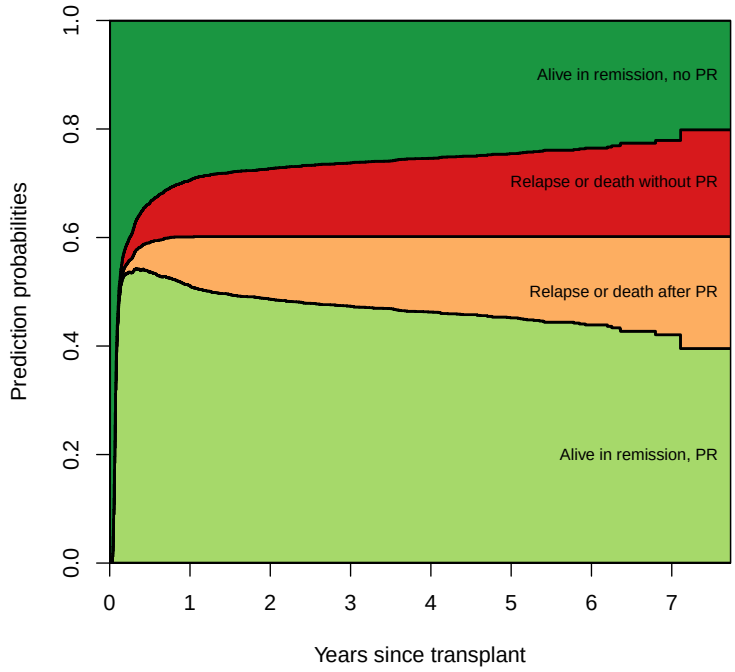


Figure 2: Stacked prediction probabilities at $s = 0$ for a reference patient. PR stands for platelet recovery

to fill the space between adjacent lines, "single", which simply plots the transition probabilities as different lines in a single plot, and "separate", which uses separate plots for the transition probabilities.

To obtain the predictions $\hat{P}_{1h}(s,t)$ for $s = 0.5$, which are plotted in Figure 16 of the tutorial, we simply change the value of *predt* in the call to ***probtrans***.

```
> pt <- probtrans(msf2, predt = 0.5)
> summary(pt, from = 1)

Prediction from state 1 (head and tail):
       time   pstate1     pstate2      pstate3     pstate4         se1
1 0.5000000 1.0000000 0.000000000 0.000000e+00 0.000000000 0.000000000
2 0.5010267 0.9985898 0.000000000 0.000000e+00 0.001410218 0.003237571
3 0.5037645 0.9976488 0.000000000 0.000000e+00 0.002351164 0.004183373
4 0.5065024 0.9955387 0.001639506 0.000000e+00 0.002821775 0.006169060
5 0.5092402 0.9938957 0.003282495 0.000000e+00 0.002821775 0.007422321
6 0.5119781 0.9915469 0.003277183 5.312169e-06 0.005170580 0.008513835
          se2          se3         se4    lower1       lower2     lower3
1 0.000000000 0.000000e+00 0.000000000 1.0000000 0.000000e+00 0.0000e+00
2 0.000000000 0.000000e+00 0.003237571 0.9922644 0.000000e+00 0.0000e+00
3 0.000000000 0.000000e+00 0.004183373 0.9894832 0.000000e+00 0.0000e+00
4 0.004136138 2.101143e-06 0.004583357 0.9835207 1.167630e-05 0.0000e+00
5 0.005848968 2.101143e-06 0.004583357 0.9794542 9.987955e-05 0.0000e+00
6 0.005839510 1.353036e-05 0.006209919 0.9749997 9.971745e-05 3.6076e-08
```

```
        lower4 upper1    upper2       upper3     upper4
1 0.000000e+00      1 0.0000000 0.0000000000 0.00000000
2 1.567120e-05      1 0.0000000 0.0000000000 0.12690255
3 7.190497e-05      1 0.0000000 0.0000000000 0.07687883
4 1.169315e-04      1 0.2302081          NaN 0.06809471
5 1.169315e-04      1 0.1078777          NaN 0.06809471
6 4.911765e-04      1 0.1077036 0.0007822136 0.05443032

...
        time   pstate1    pstate2     pstate3   pstate4        se1        se2
330 6.253251 0.6872018 0.02597812 0.005991102 0.2808290 0.05248379 0.01448894
331 6.357290 0.6798772 0.02578851 0.006180714 0.2881535 0.05348008 0.01438691
332 6.362765 0.6725095 0.02559713 0.006372091 0.2955212 0.05445049 0.01428397
333 6.798084 0.6576254 0.02520918 0.006760043 0.3104053 0.05723289 0.01407791
334 7.110198 0.5996895 0.02368832 0.008280903 0.3683412 0.07993696 0.01332734
335 7.731691 0.5996895 0.02368832 0.008280903 0.3683412 0.07993696 0.01332734
            se3        se4    lower1      lower2      lower3    lower4
330 0.003565503 0.05117341 0.5916642 0.008706862 0.001866073 0.1964870
331 0.003675647 0.05224080 0.5827386 0.008640867 0.001926781 0.2019786
332 0.003786522 0.05327926 0.5738257 0.008574230 0.001988236 0.2075517
333 0.004019125 0.05620683 0.5544966 0.008437438 0.002108021 0.2176694
334 0.005060910 0.07944552 0.4618104 0.007863898 0.002499552 0.2413567
335 0.005060910 0.07944552 0.4618104 0.007863898 0.002499552 0.2413567
       upper1     upper2     upper3    upper4
330 0.7981661 0.07750930 0.01923468 0.4013749
331 0.7932082 0.07696533 0.01982645 0.4110953
332 0.7881646 0.07641656 0.02042190 0.4207761
333 0.7799349 0.07531940 0.02167824 0.4426505
334 0.7787343 0.07135602 0.02743426 0.5621360
335 0.7787343 0.07135602 0.02743426 0.5621360
```

The result now contains only time points $t \geq 0.5$. Figure 3 contains a plot of `pt1`.

```
> plot(pt, ord = c(2, 3, 4, 1), lwd = 2, xlab = "Years since transplant",
+     ylab = "Prediction probabilities", cex = 0.75, legend = c("Alive in remission, no PR",
+         "Alive in remission, PR", "Relapse or death after PR",
+         "Relapse or death without PR"))
```

Figure 17 of the tutorial distinguishes between three patients, one being the good old (or rather young) reference patient, for which we have already calculated the probabilities, one for a patient in the age category 20-40, and one for a patient older than 40. To obtain prediction probabilities for the latter two patients as well, we have to repeat part of the calculations, changing only the value of age in the `newdata` data frame.

```
> msf2$trans <- tmat
> msf.20 <- msf2 # copy msfit result for reference (young) patient
> newd <- newd[,1:5] # use the basic covariates of the reference patient
> newd2 <- newd
> newd2$age <- 1
> newd2$age <- factor(newd2$age,levels=0:2,labels=levels(ebmt3$age))
> attr(newd2, "trans") <- tmat
```

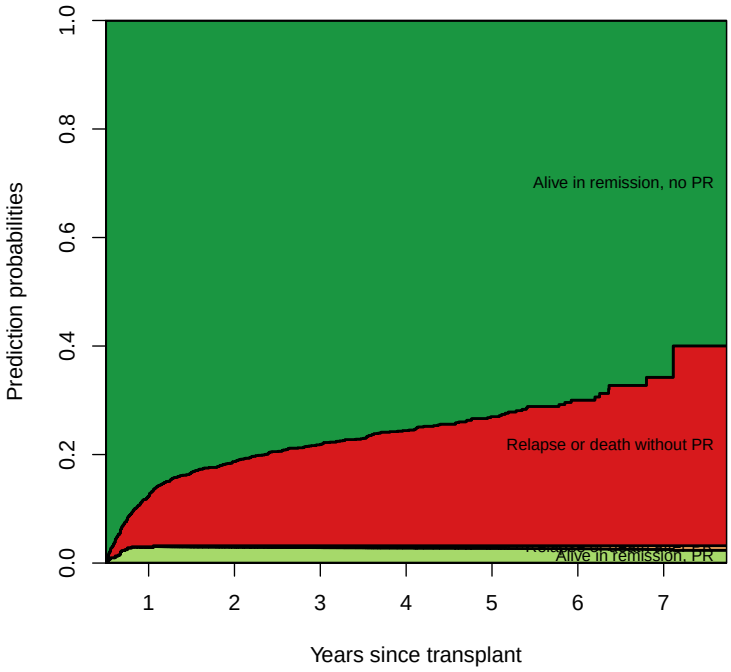


Figure 3: Stacked prediction probabilities at $s = 0.5$ for a reference patient

```
> class(newd2) <- c("msdata","data.frame")
> newd2 <- expand.covs(newd2,covs[1:4],longnames=FALSE)
> newd2$strata=c(1,2,2)
> newd2$pr <- c(0,0,1)
> msf.2040 <- msfit(c2, newdata=newd2, trans=tmat)
> newd3 <- newd
> newd3$age <- 2
> newd3$age <- factor(newd3$age,levels=0:2,labels=levels(ebmt3$age))
> attr(newd3, "trans") <- tmat
> class(newd3) <- c("msdata","data.frame")
> newd3 <- expand.covs(newd3,covs[1:4],longnames=FALSE)
> newd3$strata=c(1,2,2)
> newd3$pr <- c(0,0,1)
> msf.40 <- msfit(c2, newdata=newd3, trans=tmat)
> pt.20 <- probtrans(msf.20,predt=0) # original young (<= 20) patient
> pt.201 <- pt.20[[1]]; pt.202 <- pt.20[[2]]
> pt.2040 <- probtrans(msf.2040,predt=0) # patient 20-40
> pt.20401 <- pt.2040[[1]]; pt.20402 <- pt.2040[[2]]
> pt.40 <- probtrans(msf.40,predt=0) # patient > 40
> pt.401 <- pt.40[[1]]; pt.402 <- pt.40[[2]]
```

The 5-years transition probabilities $P_{13}(0, 5)$ and $P_{23}(0, 5)$ are estimated as 0.30275 and 0.26210 respectively.

```
> pt.201[488:489,] # 5 years falls between 488th and 489th time point
```

```
        time   pstate1   pstate2   pstate3        se1        se2        se3
488 4.985626 0.2452605 0.4519872 0.3027523 0.02411439 0.02853645 0.02693539
489 5.084189 0.2445602 0.4511034 0.3043365 0.02412385 0.02858110 0.02707436
```

```
> pt.202[488:489,] # 5-years probabilities
```

```
        time pstate1   pstate2   pstate3 se1        se2        se3
488 4.985626       0 0.7378970 0.2621030   0 0.03339911 0.03339911
489 5.084189       0 0.7364541 0.2635459   0 0.03356217 0.03356217
```

Figure 4 shows relapse-free survival probabilities without distinction between before or after platelet recovery, so we can use the first transition matrix `tmat`. The probabilities we want are $1 - \hat{P}_{13}(0,t)$ and $1 - \hat{P}_{23}(0,t)$, the first one conditioning on being in state 1 (transplantation, i.e. no PR), the second in being in state 2 (PR).

```
> plot(pt.201$time, 1 - pt.201$pstate3, ylim = c(0.425, 1), type = "s",
+     lwd = 2, col = "red", xlab = "Years since transplant", ylab = "Relapse-free survival")
> lines(pt.20401$time, 1 - pt.20401$pstate3, type = "s", lwd = 2,
+     col = "blue")
> lines(pt.401$time, 1 - pt.401$pstate3, type = "s", lwd = 2, col = "green")
> lines(pt.202$time, 1 - pt.202$pstate3, type = "s", lwd = 2, col = "red",
+     lty = 2)
> lines(pt.20402$time, 1 - pt.20402$pstate3, type = "s", lwd = 2,
+     col = "blue", lty = 2)
> lines(pt.402$time, 1 - pt.402$pstate3, type = "s", lwd = 2, col = "green",
+     lty = 2)
> legend(6, 1, c("no PR", "PR"), lwd = 2, lty = 1:2, xjust = 1,
+     bty = "n")
> legend("topright", c("<=20", "20-40", ">40"), lwd = 2, col = c("red",
+     "blue", "green"), bty = "n")
```

It is also possible to do prediction with a fixed horizon. This should not be understood as attempting to predict the past. It means that in our prediction probabilities $P_{gh}(s,t)$, we fix $t$, a time horizon, and we want to study how $P_{gh}(s,t)$ changes as more and more information on a patient becomes available. From a computational point of view this just means that the order of the matrix multiplication in (2) is reversed. We will plot $1 - \hat{P}_{13}(s,5)$ and $1 - \hat{P}_{23}(s,5)$, the 5-years relapse-free survival probabilities given that the patient is in state 1 (no PR) and in state 2 (PR), respectively, for the same three patients as before.

```
> pt.20 <- probtrans(msf.20, direction = "fixedhorizon", predt = 5)
> pt.201 <- pt.20[[1]]
> pt.202 <- pt.20[[2]]
> head(pt.201)
```

```
         time   pstate1   pstate2   pstate3        se1        se2        se3
1 0.000000000 0.2452605 0.4519872 0.3027523 0.02411439 0.02853645 0.02693539
2 0.002737851 0.2454650 0.4519742 0.3025608 0.02413403 0.02854695 0.02694328
3 0.008213552 0.2455948 0.4518230 0.3025823 0.02414644 0.02854909 0.02694380
4 0.010951403 0.2456698 0.4519611 0.3023691 0.02415369 0.02855746 0.02695114
5 0.016427105 0.2458201 0.4522376 0.3019422 0.02416821 0.02857418 0.02696574
6 0.019164956 0.2461011 0.4523628 0.3015361 0.02419520 0.02859303 0.02698076
```

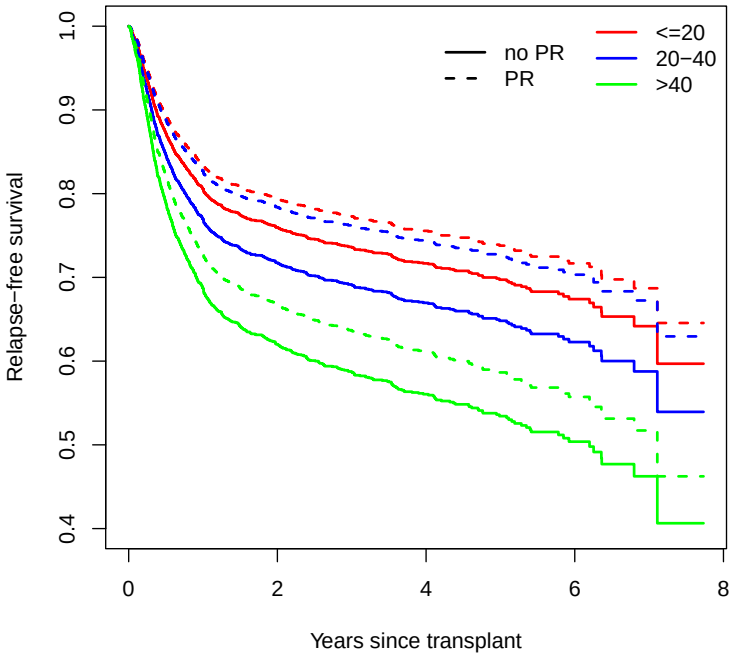


Figure 4: Predicted relapse-free survival probabilities for three patients in different age categories, given platelet recovery (dashed) and given no platelet recovery (solid). The time of prediction was at transplant (note: in the tutorial this was at 1 month after transplant).

```
> head(pt.202)
```

```
         time pstate1   pstate2   pstate3 se1        se2        se3
1 0.000000000       0 0.7378970 0.2621030   0 0.03339911 0.03339911
2 0.002737851       0 0.7380513 0.2619487   0 0.03340572 0.03340572
3 0.008213552       0 0.7380513 0.2619487   0 0.03340572 0.03340572
4 0.010951403       0 0.7382057 0.2617943   0 0.03341233 0.03341233
5 0.016427105       0 0.7385150 0.2614850   0 0.03342551 0.03342551
6 0.019164956       0 0.7388247 0.2611753   0 0.03343863 0.03343863
```

Here item `[[1]]` gives estimates $\hat{P}_{1h}(s,5)$ and `[[2]]` gives estimates $\hat{P}_{2h}(s,5)$. For item `[[g]]`, the column `time` gives the different values of $s$ and `pstate1` etc give the estimated probabilities of being in state 1 etc at 5 years, conditional on being in state $g$ at time $s$. In `pt.201` we recognize at `time` ($s$)=0) 0.30275 as $\hat{P}_{1h}(0,5)$ and in `pt.202` we see 0.26210 as $\hat{P}_{2h}(0,5)$. The backward transition probabilities for the other two patients are calculated similarly.

```
> pt.2040 <- probtrans(msf.2040, direction = "fixedhorizon", predt = 5)
> pt.20401 <- pt.2040[[1]]
> pt.20402 <- pt.2040[[2]]
> pt.40 <- probtrans(msf.40, direction = "fixedhorizon", predt = 5)
> pt.401 <- pt.40[[1]]
> pt.402 <- pt.40[[2]]
```

As mentioned before, in $s = 0$, these probabilities are the same as the five-years probabilities of Figure 4, and as $s$ approaches 5, the probabilities approach 1, since both $\hat{P}_{13}(s,5)$ and $\hat{P}_{23}(s,5)$ approach 0. Figure 5 shows 5-years relapse-free survival probabilities, both with and without platelet recovery, with the prediction time $s$ varying.

```
> plot(pt.201$time, 1 - pt.201$pstate3, ylim = c(0.425, 1), type = "s",
+     lwd = 2, col = "red", xlab = "Years since transplant", ylab = "Relapse-free survival")
> lines(pt.20401$time, 1 - pt.20401$pstate3, type = "s", lwd = 2,
+     col = "blue")
> lines(pt.401$time, 1 - pt.401$pstate3, type = "s", lwd = 2, col = "green")
> lines(pt.202$time, 1 - pt.202$pstate3, type = "s", lwd = 2, col = "red",
+     lty = 2)
> lines(pt.20402$time, 1 - pt.20402$pstate3, type = "s", lwd = 2,
+     col = "blue", lty = 2)
> lines(pt.402$time, 1 - pt.402$pstate3, type = "s", lwd = 2, col = "green",
+     lty = 2)
> legend("topleft", c("<=20", "20-40", ">40"), lwd = 2, col = c("red",
+     "blue", "green"), bty = "n")
> legend(1, 1, c("no PR", "PR"), lwd = 2, lty = 1:2, bty = "n")
> title(main = "Backward prediction")
```

# 5 Competing risks

The data used in Section 3 of the tutorial is available in *mstate* under the name `aidssi`. See the help file for more information.

```
> data(aidssi)
> si <- aidssi # Just a shorter name
> head(si)
```

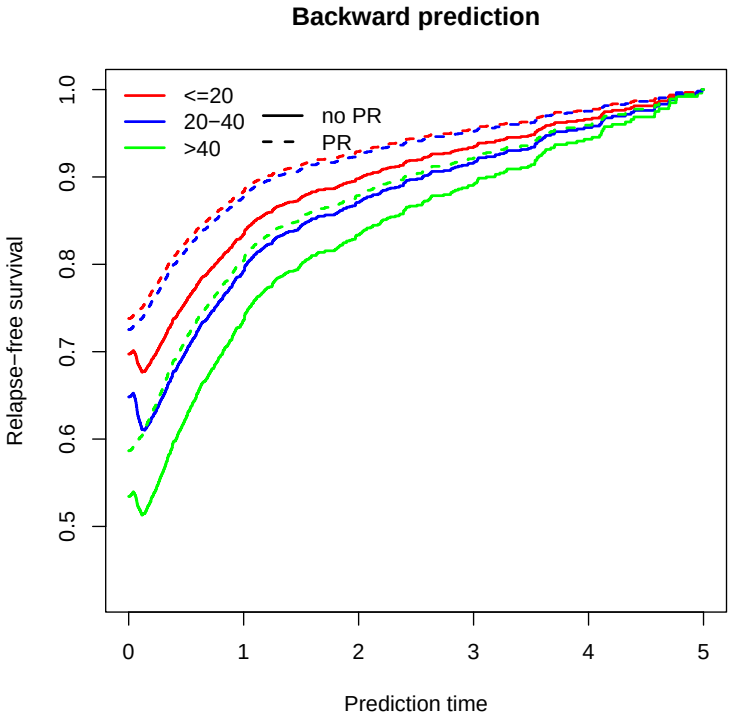


Figure 5: Predicted probabilities of 5-years relapse-free survival, conditional on being alive without relapse with (PR) and without platelet recovery (no PR). Patients in three age categories.

```
  patnr   time status      cause ccr5
1     1  9.106      1       AIDS   WW
2     2 11.039      0 event-free   WM
3     3  2.234      1       AIDS   WW
4     4  9.878      2         SI   WM
5     5  3.819      1       AIDS   WW
6     6  6.801      1       AIDS   WW
```

```
> table(si$status)

  0   1   2
107 114 108
```

To prepare data in long format, it is possible to use ***msprep***. In this case there is not a huge advantage in using ***msprep***; the long data may just as easily be prepared directly. Nevertheless we will illustrate the use of ***msprep*** to obtain data in long format. The function ***trans.comprisk*** prepares a transition matrix for competing risks models. The first argument is the number of causes of failure; in the *names* argument a character vector of length three (the total number of states in the multi-state model including the failure-free state) may be given. The transition matrix has three states with stte 1 being the failure-free state and the subsequent sttes representing the different causes of failure.

```
> tmat <- trans.comprisk(2, names = c("event-free", "AIDS", "SI"))
> tmat
```

```
            to
from         event-free AIDS SI
  event-free         NA    1  2
  AIDS               NA   NA NA
  SI                 NA   NA NA
```

Now follows the actual call to *msprep*.

```
> si$stat1 <- as.numeric(si$status == 1)
> si$stat2 <- as.numeric(si$status == 2)
> silong <- msprep(time = c(NA, "time", "time"), status = c(NA,
+     "stat1", "stat2"), data = si, keep = "ccr5", trans = tmat)
```

We can use *events* to check whether the number of events from original data (si) corresponds with long data.

```
> events(silong)

$Frequencies
            to
from         event-free AIDS  SI no event total entering
  event-free          0  114 108      107             329
  AIDS                0    0   0      114             114
  SI                  0    0   0      108             108

$Proportions
            to
from         event-free      AIDS        SI  no event
  event-free  0.0000000 0.3465046 0.3282675 0.3252280
  AIDS        0.0000000 0.0000000 0.0000000 1.0000000
  SI          0.0000000 0.0000000 0.0000000 1.0000000
```

For the regression analyses to be performed later we add transition-specific covariates. In the context of competing risks one could call them cause-specific covariates. Since the factor levels of CCR5 are quite short we keep the default setting (TRUE) of *longnames*.

```
> silong <- expand.covs(silong, "ccr5")
> silong[1:8, ]

An object of class 'msdata'

Data:
  id from to trans Tstart  Tstop   time status ccr5 ccr5WM.1 ccr5WM.2
1  1    1  2     1      0  9.106  9.106      1   WW        0        0
2  1    1  3     2      0  9.106  9.106      0   WW        0        0
3  2    1  2     1      0 11.039 11.039      0   WM        1        0
4  2    1  3     2      0 11.039 11.039      0   WM        0        1
5  3    1  2     1      0  2.234  2.234      1   WW        0        0
6  3    1  3     2      0  2.234  2.234      0   WW        0        0
7  4    1  2     1      0  9.878  9.878      0   WM        1        0
8  4    1  3     2      0  9.878  9.878      1   WM        0        1
```

To illustrate the fact that naive Kaplan-Meiers are biased estimators of the probabilities of failing from the different causes of failure, we just make use of the functions in the *survival* package. I am using *coxph* below, probably this could be done quicker.

```
> c1 <- coxph(Surv(time, status) ~ 1, data = silong, subset = (trans ==
+     1), method = "breslow")
> c2 <- coxph(Surv(time, status) ~ 1, data = silong, subset = (trans ==
+     2), method = "breslow")
> h1 <- survfit(c1)
> h1 <- data.frame(time = h1$time, surv = h1$surv)
> h2 <- survfit(c2)
> h2 <- data.frame(time = h2$time, surv = h2$surv)
```

These naive Kaplan-Meier curves are shown in Figure 6 (Figure 2 in the tutorial). The Kaplan-Meier estimate of AIDS is plotted as a survival curve, while that of SI appearance is shown as a distribution function. There is some extra code to chop the time at 13 years. This was just done to make the picture prettier.

```
> idx1 <- (h1$time<13) # this restricts the plot to the first 13 years
> plot(c(0,h1$time[idx1],13),c(1,h1$surv[idx1],min(h1$surv[idx1])),type="s",
+     xlim=c(0,13),ylim=c(0,1),xlab="Years from HIV infection",ylab="Probability",lwd=2)
> idx2 <- (h2$time<13)
> lines(c(0,h2$time[idx2],13),c(0,1-h2$surv[idx2],max(1-h2$surv[idx2])),type="s",lwd=2)
> text(8,0.71,adj=0,"AIDS")
> text(8,0.32,adj=0,"SI")
```

Cumulative incidence functions can be computed using the function *Cuminc*. It takes as main arguments *time* and *status*, which can be provided as vectors

```
> ci <- Cuminc(time = si$time, status = si$status)
```

or, alternatively, as column names representing time and status, along with a *data* argument containing these column names.

```
> ci <- Cuminc(time = "time", status = "status", data = aidssi)
```

The result is a data frame containing the failure-free probabilities (`Surv`) and the cumulative incidence functions with their standard errors. Other arguments allow to specify the codes for the causes of failure and a group identifier.

```
> head(ci)
```

```
   time      Surv CI.1        CI.2      seSurv seCI.1      seCI.2
1 0.112 0.9969605    0 0.003039514 0.003034891      0 0.003034891
2 0.137 0.9939210    0 0.006079027 0.004285436      0 0.004285436
3 0.474 0.9908628    0 0.009137246 0.005251290      0 0.005251290
4 0.824 0.9877760    0 0.012224046 0.006074796      0 0.006074796
5 0.884 0.9846795    0 0.015320522 0.006799283      0 0.006799283
6 0.969 0.9815830    0 0.018416998 0.007449696      0 0.007449696
```

```
> tail(ci)
```

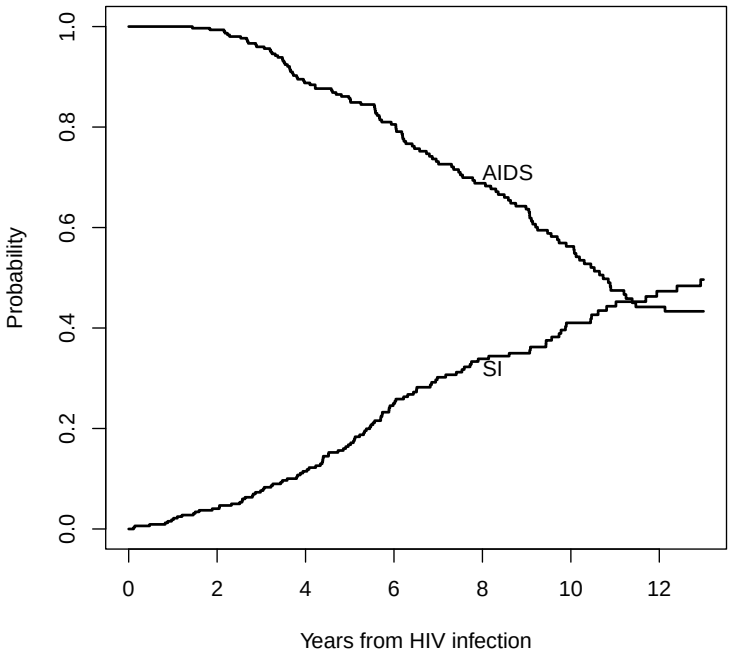


Figure 6: Estimated survival curve for AIDS and probability of SI appearance, based on the naive Kaplan-Meier estimator.

```
      time      Surv      CI.1      CI.2     seSurv     seCI.1     seCI.2
211 11.943 0.2312339 0.4035707 0.3651954 0.02638091 0.02978948 0.02881464
212 12.129 0.2266092 0.4081954 0.3651954 0.02625552 0.02989297 0.02881464
213 12.400 0.2219845 0.4081954 0.3698201 0.02612382 0.02989297 0.02896110
214 12.936 0.2165702 0.4081954 0.3752344 0.02604167 0.02989297 0.02919663
215 13.361 0.2067261 0.4180395 0.3752344 0.02665370 0.03089977 0.02919663
216 13.936 0.0000000 0.4180395 0.5819605 0.00000000 0.03089977 0.03089977
```

The cumulative incidence functions just obtained can be used to reproduce Figure 3 of the tutorial. The plots are shown in Figure 7.

```
> idx0 <- (ci$time < 13)
> plot(c(0, ci$time[idx0], 13), c(1, 1 - ci$CI.1[idx0], min(1 -
+     ci$CI.1[idx0])), type = "s", xlim = c(0, 13), ylim = c(0,
+     1), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> idx1 <- (h1$time < 13)
> lines(c(0, h1$time[idx1], 13), c(1, h1$surv[idx1], min(h1$surv[idx1])),
+     type = "s", lwd = 2, col = 8)
> lines(c(0, ci$time[idx0], 13), c(0, ci$CI.2[idx0], max(ci$CI.2[idx0])),
+     type = "s", lwd = 2)
> idx2 <- (h2$time < 13)
> lines(c(0, h2$time[idx2], 13), c(0, 1 - h2$surv[idx2], max(1 -
+     h2$surv[idx2])), type = "s", lwd = 2, col = 8)
```

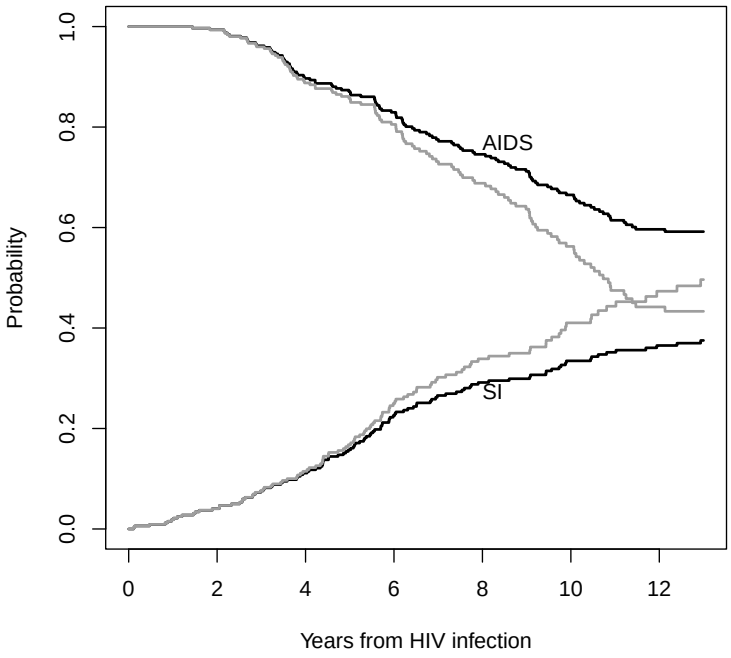


Figure 7: Estimates of probabilities of AIDS and SI appearance, based on the naive Kaplan-Meier (grey) and on cumulative incidence functions (black).

```
> text(8, 0.77, adj = 0, "AIDS")
> text(8, 0.275, adj = 0, "SI")
```

The stacked plots of Figure 4 of the tutorial are shown in Figure 8.

```
> idx0 <- (ci$time < 13)
> plot(c(0, ci$time[idx0]), c(0, ci$CI.1[idx0]), type = "s", xlim = c(0,
+     13), ylim = c(0, 1), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> lines(c(0, ci$time[idx0]), c(0, ci$CI.1[idx0] + ci$CI.2[idx0]),
+     type = "s", lwd = 2)
> text(13, 0.5 * max(ci$CI.1[idx0]), adj = 1, "AIDS")
> text(13, max(ci$CI.1[idx0]) + 0.5 * max(ci$CI.2[idx0]), adj = 1,
+     "SI")
> text(13, 0.5 + 0.5 * max(ci$CI.1[idx0]) + 0.5 * max(ci$CI.2[idx0]),
+     adj = 1, "Event-free")
```

## Regression

The section on regression in the tutorial already shows some R code and occasional output. Because of the fact that I used *msprep* to prepare the long data, occasionally there will be very small differences with the code in the tutorial. We start with regression on cause-specific hazards. Using the original dataset, we can apply ordinary Cox regression for cause 1 (AIDS), taking only the AIDS cases as events. This is done by specifying `status==1` below (observations

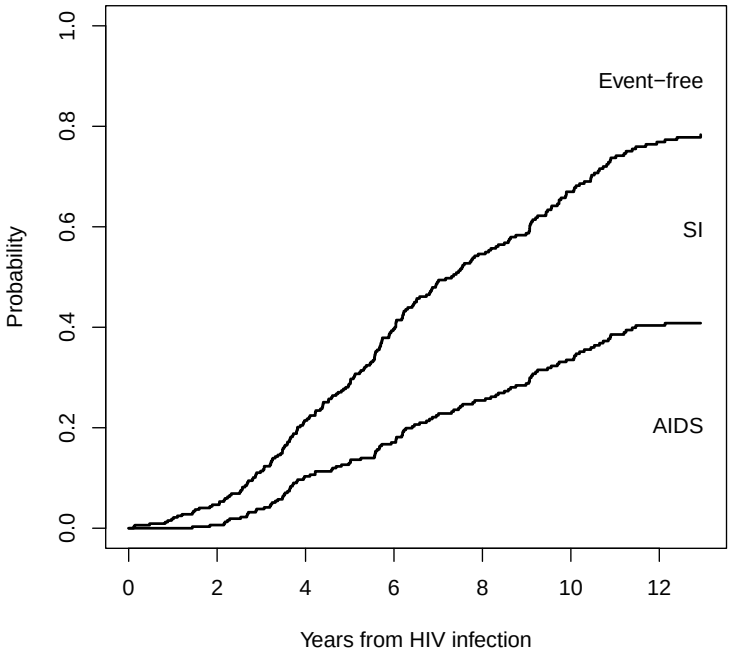


Figure 8: Cumulative incidence curves of AIDS and SI appearance. The cumulative incidence functions are stacked; the distances between two curves represent the probabilities of the different events.

with status=0 (true censorings) and status=2 (SI) are treated as censorings). Similarly for cause 2 (SI appearance), where `status==2` indicates that only failures due to SI appearance are to be treated as events.

```
> coxph(Surv(time, status == 1) ~ ccr5, data = si) # AIDS

Call:
coxph(formula = Surv(time, status == 1) ~ ccr5, data = si)

          coef exp(coef) se(coef)      z        p
ccr5WM -1.2358    0.2906   0.3071 -4.024 5.72e-05

Likelihood ratio test=21.98  on 1 df, p=2.756e-06
n= 324, number of events= 113
   (5 observations deleted due to missingness)

> coxph(Surv(time, status == 2) ~ ccr5, data = si) # SI appearance

Call:
coxph(formula = Surv(time, status == 2) ~ ccr5, data = si)

          coef exp(coef) se(coef)      z     p
ccr5WM -0.2542    0.7755   0.2380 -1.068 0.286

Likelihood ratio test=1.19  on 1 df, p=0.2748
n= 324, number of events= 107
   (5 observations deleted due to missingness)
```

The same analysis can be performed using the long format dataset `silong` in several ways. For instance, as separate Cox regressions.

```
> coxph(Surv(time, status) ~ ccr5, data = silong, subset = (trans ==
+     1), method = "breslow")

Call:
coxph(formula = Surv(time, status) ~ ccr5, data = silong, subset = (trans ==
    1), method = "breslow")

          coef exp(coef) se(coef)      z        p
ccr5WM -1.2358    0.2906   0.3071 -4.024 5.73e-05

Likelihood ratio test=21.98  on 1 df, p=2.758e-06
n= 324, number of events= 113
   (5 observations deleted due to missingness)

> coxph(Surv(time, status) ~ ccr5, data = silong, subset = (trans ==
+     2), method = "breslow")

Call:
coxph(formula = Surv(time, status) ~ ccr5, data = silong, subset = (trans ==
    2), method = "breslow")
```

```
          coef exp(coef) se(coef)      z     p
ccr5WM -0.2542    0.7755   0.2380 -1.068 0.286

Likelihood ratio test=1.19  on 1 df, p=0.2748
n= 324, number of events= 107
   (5 observations deleted due to missingness)
```

And in a single analysis, using the expanded covariates.

```
> coxph(Surv(time, status) ~ ccr5WM.1 + ccr5WM.2 + strata(trans),
+     data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5WM.1 + ccr5WM.2 + strata(trans),
    data = silong)

            coef exp(coef) se(coef)      z        p
ccr5WM.1 -1.2358    0.2906   0.3071 -4.024 5.72e-05
ccr5WM.2 -0.2542    0.7755   0.2380 -1.068    0.286

Likelihood ratio test=23.17  on 2 df, p=9.294e-06
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

The same model, but now using a covariate by cause interaction.

```
> coxph(Surv(time, status) ~ ccr5 * factor(trans) + strata(trans),
+     data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5 * factor(trans) + strata(trans),
    data = silong)

                        coef exp(coef) se(coef)      z        p
ccr5WM                -1.2358    0.2906   0.3071 -4.024 5.72e-05
factor(trans)2            NA        NA   0.0000     NA       NA
ccr5WM:factor(trans)2  0.9816    2.6688   0.3886  2.526   0.0115

Likelihood ratio test=23.17  on 2 df, p=9.294e-06
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

In the model below we assume that the effect of CCR5 on the two cause-specific hazards is equal. The significant effect of the interaction in the model we just saw indicates that this is not a good idea. But, again, this is just for educational purposes.

```
> coxph(Surv(time, status) ~ ccr5 + strata(trans), data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5 + strata(trans), data = silong)
```

```
          coef exp(coef) se(coef)     z        p
ccr5WM -0.7012    0.4960   0.1860 -3.77 0.000163

Likelihood ratio test=16.46  on 1 df, p=4.972e-05
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

There are two alternative ways yielding the same result. First, we can actually leave out the *strata* term.

```
> coxph(Surv(time, status) ~ ccr5, data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5, data = silong)

          coef exp(coef) se(coef)      z        p
ccr5WM -0.7012    0.4960   0.1860 -3.771 0.000163

Likelihood ratio test=16.46  on 1 df, p=4.964e-05
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

Second, since the *strata* term is not needed we can use `si`.

```
> coxph(Surv(time, status != 0) ~ ccr5, data = si)

Call:
coxph(formula = Surv(time, status != 0) ~ ccr5, data = si)

          coef exp(coef) se(coef)      z        p
ccr5WM -0.7013    0.4959   0.1860 -3.771 0.000163

Likelihood ratio test=16.47  on 1 df, p=4.953e-05
n= 324, number of events= 220
   (5 observations deleted due to missingness)
```

Note: the actual estimated baseline hazards may be different, whether or not the strata term is used.

Assuming that baseline hazards for AIDS and SI are proportional (this is generally not a realistic assumption by the way, but just for illustration purposes).

```
> coxph(Surv(time, status) ~ ccr5WM.1 + ccr5WM.2 + factor(trans),
+     data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5WM.1 + ccr5WM.2 + factor(trans),
    data = silong)

                  coef exp(coef) se(coef)      z       p
ccr5WM.1       -1.1664    0.3115   0.3063 -3.808 0.00014
```

```
ccr5WM.2       -0.3316    0.7178   0.2366 -1.401 0.16112
factor(trans)2 -0.1843    0.8317   0.1477 -1.248 0.21201

Likelihood ratio test=21.54  on 3 df, p=8.124e-05
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

Or, again using covariate by cause (transition) interaction.

```
> coxph(Surv(time, status) ~ ccr5 * factor(trans), data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5 * factor(trans), data = silong)

                          coef exp(coef) se(coef)      z       p
ccr5WM                -1.1664    0.3115   0.3063 -3.808 0.00014
factor(trans)2        -0.1843    0.8317   0.1477 -1.248 0.21201
ccr5WM:factor(trans)2  0.8348    2.3044   0.3855  2.165 0.03035

Likelihood ratio test=21.54  on 3 df, p=8.124e-05
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

Note that, even though patients are replicated in the long format, it is not necessary to use robust standard errors. Any of the previous analyses with the `silong` dataset gives identical results when a `cluster(id)` term is added. For instance,

```
> coxph(Surv(time, status) ~ ccr5 * factor(trans) + cluster(id),
+     data = silong)

Call:
coxph(formula = Surv(time, status) ~ ccr5 + factor(trans) + ccr5:factor(trans),
    data = silong, cluster = id)

                          coef exp(coef) se(coef) robust se      z        p
ccr5WM                -1.1664    0.3115   0.3063    0.2928 -3.983 6.81e-05
factor(trans)2        -0.1843    0.8317   0.1477    0.1477 -1.248   0.2121
ccr5WM:factor(trans)2  0.8348    2.3044   0.3855    0.3855  2.165   0.0304

Likelihood ratio test=21.54  on 3 df, p=8.124e-05
n= 648, number of events= 220
   (10 observations deleted due to missingness)
```

gives the same result as before.

So far in the regression context we have just used the *coxph* function of the *survival* package. In order to obtain predicted cumulative incidences, *msprep* is useful. First let us store our analysis with separate covariate effects for the two causes.

```
> c1 <- coxph(Surv(time, status) ~ ccr5WM.1 + ccr5WM.2 + strata(trans),
+     data = silong, method = "breslow")
```

If we want the predicted cumulative incidences for an individual with CCR5 wild-type (WW), we make a *newdata* data frame containing the (transition-specific) covariate values for each of the transitions for the individual of interest. Then we apply `msfit` as illustrated earlier in the context of multi-state models.

```
> WW <- data.frame(ccr5WM.1 = c(0, 0), ccr5WM.2 = c(0, 0), trans = c(1,
+     2), strata = c(1, 2))
> msf.WW <- msfit(c1, WW, trans = tmat)
```

And finally, to obtain the cumulative incidences we apply `probtrans`. Item `[[1]]` is selected because the prediction starts from state 1 (event-free) at time $s = 0$.

```
> pt.WW <- probtrans(msf.WW, 0)[[1]]
```

Similarly for an individual with the CCR5 mutant (WM) genotype.

```
> WM <- data.frame(ccr5WM.1 = c(1, 0), ccr5WM.2 = c(0, 1), trans = c(1,
+     2), strata = c(1, 2))
> msf.WM <- msfit(c1, WM, trans = tmat)
> pt.WM <- probtrans(msf.WM, 0)[[1]]
```

We now plot these cumulative incidence curves for AIDS (`pstate2`) and SI appearance (`pstate3`), for wild-type (WW) and mutant (WM) in Figure 9 (Figure 5 in the tutorial).

```
> idx1 <- (pt.WW$time < 13)
> idx2 <- (pt.WM$time < 13)
> plot(c(0, pt.WW$time[idx1]), c(0, pt.WW$pstate2[idx1]), type = "s",
+     ylim = c(0, 0.5), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> lines(c(0, pt.WM$time[idx2]), c(0, pt.WM$pstate2[idx2]), type = "s",
+     lwd = 2, col = 8)
> title(main = "AIDS")
> text(9.2, 0.345, "WW", adj = 0, cex = 0.75)
> text(9.2, 0.125, "WM", adj = 0, cex = 0.75)
> plot(c(0, pt.WW$time[idx1]), c(0, pt.WW$pstate3[idx1]), type = "s",
+     ylim = c(0, 0.5), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> lines(c(0, pt.WM$time[idx2]), c(0, pt.WM$pstate3[idx2]), type = "s",
+     lwd = 2, col = 8)
> title(main = "SI appearance")
> text(7.5, 0.31, "WW", adj = 0, cex = 0.75)
> text(7.5, 0.245, "WM", adj = 0, cex = 0.75)
```

The illustration of the phenomenon that the same cause-specific hazard ratio may have different effects on the cumulative incidences (Figure 7 in the tutorial) may be performed as well, by replacing the appropriate parts of the cumulative hazard of AIDS (`trans`=1), and calling `probtrans`. We are interested in SI appearance and adjust the hazards of the competing risk (AIDS) while keeping the remainder the same (Figure 7 in the tutorial). The result is shown in Figure 10. We multiply the baseline hazard of AIDS with factors (`ff` = 0, 0.5, 1, 1.5, 2, 4).

```
> ffs <- c(0, 0.5, 1, 1.5, 2, 4)
> newmsf.WW <- msf.WW
> newmsf.WM <- msf.WM
```

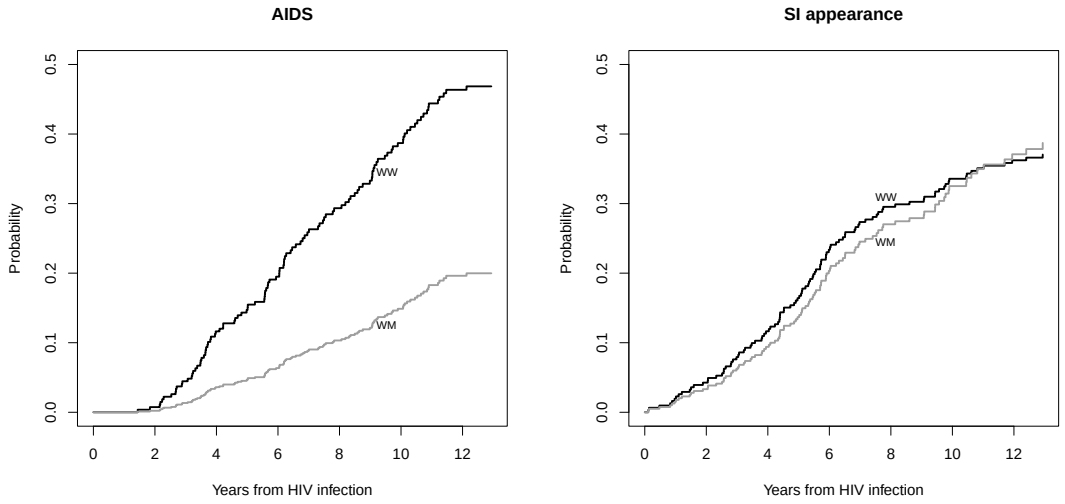


Figure 9: Cumulative incidence functions for AIDS (left) and SI appearance (right), for wild-type (WW) and mutant (WM) CCR5 genotype, based on a proportional hazards model on the cause-specific hazards.

```
> par(mfrow = c(2, 3))
> for (ff in ffs) {
+     newmsf.WW$Haz$Haz[newmsf.WW$Haz$trans == 1] <- ff * msf.WW$Haz$Haz[msf.WW$Haz$trans ==
+         1]
+     pt.WW <- probtrans(newmsf.WW, 0, variance = FALSE)[[1]]
+     newmsf.WM$Haz$Haz[newmsf.WM$Haz$trans == 1] <- ff * msf.WM$Haz$Haz[msf.WM$Haz$trans ==
+         1]
+     pt.WM <- probtrans(newmsf.WM, 0, variance = FALSE)[[1]]
+     idx1 <- (pt.WW$time < 13)
+     idx2 <- (pt.WM$time < 13)
+     plot(c(0, pt.WW$time[idx1]), c(0, pt.WW$pstate3[idx1]), type = "s",
+         ylim = c(0, 0.52), xlab = "Years from HIV infection",
+         ylab = "Probability", lwd = 2)
+     lines(c(0, pt.WM$time[idx2]), c(0, pt.WM$pstate3[idx2]),
+         type = "s", lwd = 2, col = 8)
+     title(main = paste("Factor =", ff))
+ }
> par(mfrow = c(1, 1))
```

Fine and Gray regression on cumulative incidence functions is not implemented in *mstate*, but in the R package *cmprsk*. Since our main purpose here is illustration of *mstate*, we just give the code and the output.

```
> library(cmprsk)
> sic <- si[!is.na(si$ccr5),]
> ftime <- sic$time
> fstatus <- sic$status
> cov <- as.numeric(sic$ccr5)-1
> # for failures of type 1 (AIDS)
> z1 <- crr(ftime,fstatus,cov)
```

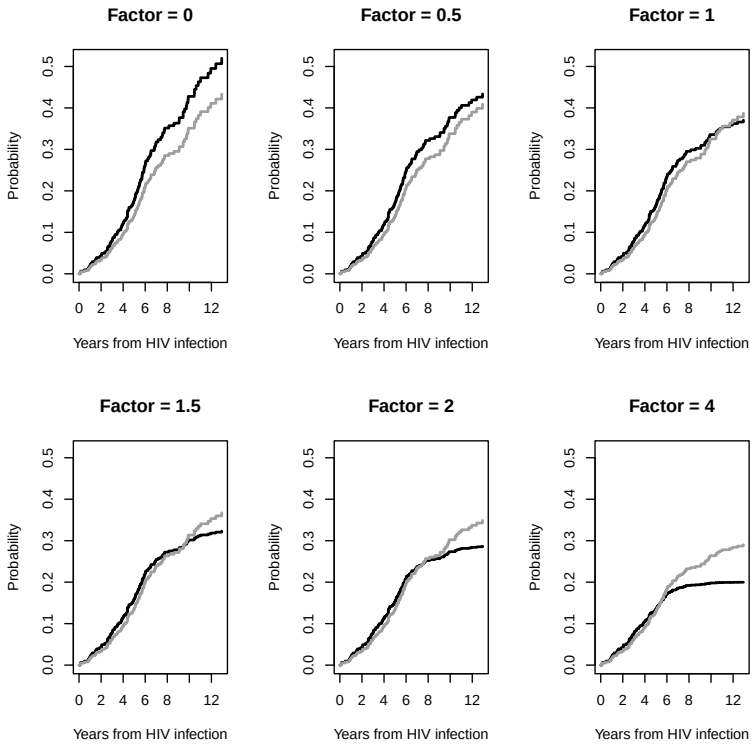


Figure 10: Cumulative incidence functions for Si appearance, for CCR5 wild-type `WW` (black) and mutant `WM` (grey). The baseline hazard of AIDS was multiplied with different factors, while keeping everything else the same.

```
> z1

convergence:  TRUE
coefficients:
  cov1
-1.004
standard errors:
[1] 0.295
two-sided p-values:
   cov1
0.00066

> # for failures of type 2 (SI)
> z2 <- crr(ftime,fstatus,cov,failcode=2)
> z2

convergence:  TRUE
coefficients:
   cov1
0.02359
standard errors:
[1] 0.2266
two-sided p-values:
cov1
0.92
```

The result (Figure 8 in the tutorial) is shown in Figure 11.

```
> z1.pr <- predict(z1,matrix(c(0,1),2,1))
> # this will contain predicted cum inc curves, both for WW (2nd column) and WM (3rd)
> z2.pr <- predict(z2,matrix(c(0,1),2,1))
> # Standard plots, not shown
> par(mfrow=c(1,2))
> plot(z1.pr,lty=1,lwd=2,color=c(8,1))
> plot(z2.pr,lty=1,lwd=2,color=c(8,1))
> par(mfrow=c(1,1))
> ## AIDS
> n1 <- nrow(z1.pr) # remove last jump
> plot(c(0,z1.pr[-n1,1]),c(0,z1.pr[-n1,2]),type="s",ylim=c(0,0.5),
+     xlab="Years from HIV infection",ylab="Probability",lwd=2)
> lines(c(0,z1.pr[-n1,1]),c(0,z1.pr[-n1,3]),type="s",lwd=2,col=8)
> title(main="AIDS")
> text(9.3,0.35,"WW",adj=0,cex=0.75)
> text(9.3,0.14,"WM",adj=0,cex=0.75)
> ## SI appearance
> n2 <- nrow(z2.pr) # again remove last jump
> plot(c(0,z2.pr[-n2,1]),c(0,z2.pr[-n2,2]),type="s",ylim=c(0,0.5),
+     xlab="Years from HIV infection",ylab="Probability",lwd=2)
> lines(c(0,z2.pr[-n2,1]),c(0,z2.pr[-n2,3]),type="s",lwd=2,col=8)
> title(main="SI appearance")
> text(7.9,0.28,"WW",adj=0,cex=0.75)
> text(7.9,0.31,"WM",adj=0,cex=0.75)
```

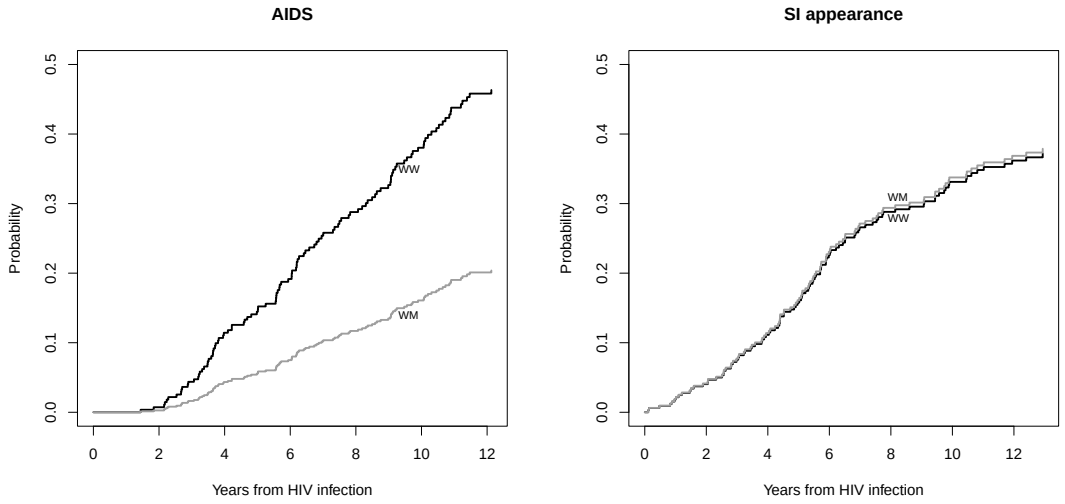


Figure 11: Cumulative incidence functions for AIDS (left) and SI appearance (right), for CCR5 wild-type WW and mutant WM, based on the Fine and Gray model.

To judge the "fit" of the cause-specific and Fine & Gray regression models we estimate cumulative incidence curves nonparametrically, i.e., for two subgroups of WW and WM CCR5-genotypes. Here we can use the *group* argument of `Cuminc`.

```
> ci <- Cuminc(si$time, si$status, group = si$ccr5)
> ci.WW <- ci[ci$group == "WW", ]
> ci.WM <- ci[ci$group == "WM", ]
```

We show these nonparametric estimates in Figure 12 (Figure 9 in the tutorial).

```
> idx1 <- (ci.WW$time < 13)
> idx2 <- (ci.WM$time < 13)
> plot(c(0, ci.WW$time[idx1]), c(0, ci.WW$CI.1[idx1]), type = "s",
+     ylim = c(0, 0.5), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> lines(c(0, ci.WM$time[idx2]), c(0, ci.WM$CI.1[idx2]), type = "s",
+     lwd = 2, col = 8)
> title(main = "AIDS")
> text(9.3, 0.35, "WW", adj = 0, cex = 0.75)
> text(9.3, 0.11, "WM", adj = 0, cex = 0.75)
> plot(c(0, ci.WW$time[idx1]), c(0, ci.WW$CI.2[idx1]), type = "s",
+     ylim = c(0, 0.5), xlab = "Years from HIV infection", ylab = "Probability",
+     lwd = 2)
> lines(c(0, ci.WM$time[idx2]), c(0, ci.WM$CI.2[idx2]), type = "s",
+     lwd = 2, col = 8)
> title(main = "SI appearance")
> text(7.9, 0.32, "WW", adj = 0, cex = 0.75)
> text(7.9, 0.245, "WM", adj = 0, cex = 0.75)
```

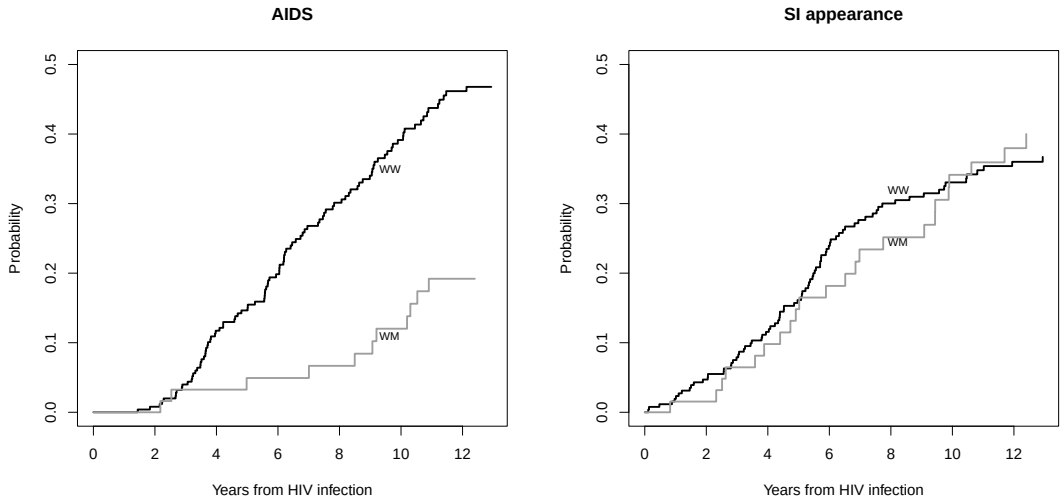


Figure 12: Non-parametric cumulative incidence functions for AIDS (left) and SI appearance (right), for CCR5 wild-type `WW` and mutant `WM`.

# References

Andersen, P. K., Borgan, Ø., Gill, R. D. & Keiding, N. (1993), *Statistical Models Based on Counting Processes*, Springer-Verlag.

de Wreede, L., Fiocco, M. & Putter, H. (2009), 'The mstate package for estimation and prediction in non- and semi-parametric multi-state models'. Submitted.

Putter, H., Fiocco, M. & Geskus, R. B. (2007), 'Tutorial in biostatistics: Competing risks and multi-state models', *Statist Med* **26**, 2389–2430.