

```
"package"{mylongevity}
```

Calculation of life expectancies

Description

The three functions entitled mylongevity_method1 to mylongevity_method3 calculate life expectancy for a set of individuals with certain characteristics provided in a user-supplied dataset. Gompertz distribution with prespecified intercept a and slope b is assumed for baseline hazards of the form $\lambda_0(t) = a + bt$.

The four functions entitled mylongevity_double_cox_method1 to mylongevity_double_cox_method4 fit the Double Cox regression to the provided data and calculate life expectancies for patients with type 2 diabetes mellitus, on Hormone Replacement therapy, with ischemic stroke and with TIA, respectively, using the log-hazard ratio estimates from the fitted model.

Usage

```
mylongevity_method1 (data, indexes_of_variables, working_directory)  
mylongevity_method2 (data, indexes_of_variables, list_of_variables, age, a, b, working_directory)  
mylongevity_method3 (data, indexes_of_variables, list_of_variables, age, a, b, T_start_indicator,  
T_stop_indicator, status_indicator, working_directory)  
  
double_cox_longevity1(data, dist, cluster, formula.shape, formula.scale, age_of_diagnosis,  
time_past_from_diagnosis,working_directory,name_for_age_factor=NULL)  
  
double_cox_longevity2(data, dist, cluster,formula.shape,formula.scale, age_of_diagnosis,  
time_past_from_diagnosis,working_directory,name_for_age_factor=NULL)  
  
mylongevity_double_cox_method1(data,indexes_of_variables,age_of_diagnosis,time_past_from_di  
agnosis)  
  
mylongevity_double_cox_method2(data,indexes_of_variables,age_of_diagnosis,time_past_from_di  
agnosis)  
  
mylongevity_double_cox_method3(data,indexes_of_variables,age_of_diagnosis,time_past_from_di  
agnosis)  
  
mylongevity_double_cox_method4(data,indexes_of_variables,age_of_diagnosis,time_past_from_di  
agnosis)
```

Arguments

- For mylongevity_method1, user has to input arguments: data, and indexes_of_variables.
- For mylongevity_method2, user has to input arguments: data, indexes_of_variables, list_of_variables, age, a, b and working_directory.

- For mylongevity_method3, user has to input arguments: data, indexes_of_variables, list_of_variables, age, a, b, T_start_indicator, T_stop_indicator, status_indicator, working_directory.
- For double_cox_longevity1, user has to input arguments: data, dist, cluster, formula.shape, formula.scale, age_of_diagnosis, time_past_from_diagnosis, working_directory
- For double_cox_longevity2, user has to input arguments: data, dist, cluster, formula.shape, formula.scale, age_of_diagnosis, time_past_from_diagnosis, working_directory.
- mylongevity_double_cox_method1, user must input arguments: data, indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis
- mylongevity_double_cox_method2, user must input arguments: data, indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis
- mylongevity_double_cox_method3, user must input arguments: data, indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis
- mylongevity_double_cox_method4, user must input arguments: data, indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis

User must also input an argument name_for_age_factor if age is being used as a continuous variable in the model. Otherwise, an argument name_for_age_factor should not be specified.

Details

Description of mylongevity_method1

This method matches the attributes of inputted data with results of life expectancies from the landmark analysis described in Kulinskaya et al. (2020b). For a set of given attributes, this method produces a table with life expectancies similar to those provided on the website <https://mylongevity.org/>.

Description of mylongevity_method2

This method calculates life expectancies using the log-hazard ratio estimates from the landmark analysis Kulinskaya et al. (2020b) and the weights of the risk groups estimated from the given dataset.

Description of mylongevity_method3

This method fits the Cox regression to the provided data, eliminates non-significant terms, calculates weights for each combination of risk factors in the final Cox regression model and computes life expectancies based on a paper Kulinskaya et al. (2020a). At the moment, we can only include additive terms to the model without interactions. Also, in this method we can only include categorical risk factors because we need to split the population into different risk subgroups. If there is any continuous variable, then it should be factored into a categorical one. If none of the variables in the model are significant, this method does not produce any output.

For mylongevity_method2 and mylongevity_method3, user should specify the directory where all the temporary files will be stored. The directory should be specified as working_directory="E:/myproject". A folder called "temp" will be created in the specified directory. This is the folder

where all necessary/temporary files will be stored. Also for method 2 and method 3, two functions are required: - function_for_table_of_combination() and a function calculate_life_expectancy() which are separate functions within this R package.

For mylongevity_method1, user has to specify the data and columns using the argument "indexes_of_variables" in following order:
"age","gender","townsend","smokerCategory","htn","diabetesCategory","hcl","bmiCategory","qRiskCategory","statins",

The definition of columns are:

- age is a variable with numeric value which stands for number of years from the date of birth.
age should only take values between 60 and 85
- Gender is a string variable which stands for gender of individual with possible values "M" for males and "F" for females
- Townsend is a deprivation index which takes values 1, 2, 3, 4, 5. The Townsend variable measures the prosperity of area where individual lives.
- smokerCategory is a categorical variable with numeric value which defines if individual is smoker or not: (1 - no smoker, 2 - ex smoker, 3 – smoker)
- htn is a categorical variable with numeric value for treated hypertension status. 1 – no--hypertension, 2 - treated hypertension, 3 – untreated hypertension
- diabetesCategory is a categorical variable with numeric value for diabetes status. 0 – no diabetes, 1 – diabetes
- hcl is a categorical variable with numeric value for hypercholesterolemia. 0 – no hypercholesterolemia, 1 – hypercholesterolemia
- bmiCategory is a categorical variable with numeric value for Body Mass Index categories [1 – Healthy weight ($BMI < 25$), 2 – Overweight ($BMI \geq 25$ and $BMI < 30$), 3 – Obese ($BMI \geq 30$)]
- qRiskCategory is a categorical variable with numeric value for cardiovascular disease risk measured by QRISK2 <https://qrisk.org/2017/> [2 – for low risk ($QRISK2 < 20$), 0 – for moderate risk ($QRISK2 \geq 20$ and $QRISK2 < 40$), 1 - for high risk ($QRISK2 \geq 40$ or diagnosis of CVD)]
- statins is a categorical variable with numeric value for statin prescription status (0 - no statin intake, 1 – on statin/prescribed statin)

mylongevity_method2 uses log-hazard ratio coefficients from website "mylongevity.org" with inputted data. mylongevity_method2 takes the log-hazard ratio coefficients and calculates the weights from data.

For mylongevity_method2, user has to input the data with columns of interest using the argument "indexes_of_variables". Also, user has to specify the particular age of interest for a given data to select the corresponding log-hazard ratio coefficients from landmark model for a particular age. User also has to specify values for a and b from $\lambda(t) = a + bt$ assumption for Gompertz distribution. User has to specify the names of variables which will be used in calculation with the same names as in inputted data using the variable "list_of_variables"

For mylongevity_method2, user can only input columns for variables ("statins","cvd_risk","diabetes","HTN_diag_treat","hypercholesterolaemia","BMI","Smoking")
User has to specify the variables of interest using the argument "list_of_variables".

The order of specified columns using the argument "indexes_of_variables" should match the variables of interest "list_of_variables" by names.

mylongevity_method3 fits the proportional hazards Cox regression from the package "survival" and seeks the best model using the backward elimination with the AIC criterion.

User has to input the data and specify the columns for independent variables to put in cox regression using the argument "indexes_of_variables" and state the list of variables "list_of_variables". In the argument "indexes_of_variables", the column indices for "T_start_indicator", "T_stop_indicator" and "status_indicator" should be specified. Since we are fitting the cox regression to time to event data, user has to include either time to death and status using the variables T_start_indicator and status_indicator to fit models with non-interval data as "Surv(time=", T_start_indicator, ",event=", status_indicator, ")~" or using the variables T_start_indicator, T_stop_indicator and status_indicator for interval censored or counting process data as "Surv(time=", T_start_indicator, ",time2=", T_stop_indicator, ",event=", status_indicator, ")~". T_start_indicator, T_stop_indicator and status_indicator are the names of columns in inputted data. The columns for T_start_indicator, T_stop_indicator and status_indicator also should be specified.

Description of double_cox_method1

This method fits the Double Cox regression model introduced in Begun et al. (2019) to the provided dataset and calculates life expectancies using the log-hazard ratio estimates from fitted model. This method returns a data frame with all possible combinations of categorical variables from double-Cox regression model and resulting life expectancies.

Description of double_cox_method2

This method fits the Double Cox regression model to the provided data and calculates life expectancies using the log-hazard ratio estimates from fitted model. This method returns a data frame with all the patients in the given data and their life expectancies.

In functions double_cox_method1 and double_cox_method2, the definition of arguments to specify are:

data: Data set

dist: distribution of the time-to-failure ('Weibull' or 'Gompertz'):

cluster: The name of the covariate defining the random effect/frailty (equal to NULL for the fixed-effect model);

formula.shape: The object defining the fields for covariates influencing the shape;

cluster: The name of the covariate defining the random effect (is equal to NULL for the fixed-effect model);

formula.scale: The formula object defining the fields for time-to-failure (or time-of-start and time-to-failure) and for covariates influencing the scale proportional hazard terms;

age_of_diagnosis: Age of diagnosis for a condition/disease of interest

time_past_from_diagnosis: The time from diagnosis of a condition/disease of interest, i.e. how long ago this happened

working_directory: A working directory for temporary files to be saved.

Description of mylongevity_double_cox_method1

This method matches the attributes of inputted data with our results of life expectancies from the double Cox regression analysis on type 2 diabetes mellitus study. For a set of given attributes, this method produces a table with life expectancies.

In functions mylongevity_double_cox_method1, the definition of parameters to specify are:

data: data set of clients

indexes_of_variables: columns of interest in data

age_of_diagnosis: Age of diagnosis for a type 2 diabetes mellitus

time_past_from_diagnosis: The time past from diagnosis of a type 2 diabetes mellitus

Description of mylongevity_double_cox_method2

This method matches the attributes of inputted data with our results of life expectancies from the double Cox regression analysis on hormone replacement therapy study. For a set of given attributes, this method produces a table with relative life expectancies for cases compared to controls with the same attributes.

In functions mylongevity_double_cox_method2, the definition of parameters to specify are:

data: data set of clients

indexes_of_variables: columns of interest in data

age_of_diagnosis: Age of initiation of hormone replacement therapy

time_past_from_diagnosis: The time past from initiation of hormone replacement therapy

Description of mylongevity_double_cox_method3

This method matches the attributes of inputted data with our results of life expectancies from the double cox regression analysis on ischaemic stroke study. For a set of given attributes, this method produces a table with life expectancies.

In functions mylongevity_double_cox_method3, the definition of parameters to specify are:

data: data set of clients

indexes_of_variables: columns of interest in data

age_of_diagnosis: Age of diagnosis for ischaemic stroke

time_past_from_diagnosis: The time past from diagnosis of an ischaemic stroke

Description of mylongevity_double_cox_method4

This method matches the attributes of inputted data with our results of life expectancies from the double cox regression analysis on transient ischaemic stroke study. For a set of given attributes, this method produces a table with life expectancies.

In functions mylongevity_double_cox_method4, the definition of parameters to specify are:

data: data set of clients

age_of_diagnosis: Age of diagnosis for transient ischaemic stroke

time_past_from_diagnosis: The time past from diagnosis of a transient ischaemic stroke

Details and methodology for calculation of life expectancy using Double Cox regression

The life expectancies within these functions are calculated using formula

$$\text{Life expectancy} = \frac{\int_{\text{time}}^{\infty} S(t) dt}{S_{\text{total}}},$$

where the univariate survival function is given by

$$S(a, b, \beta_{\text{shape}}, \beta_{\text{scale}}, \sigma^2, u) = E \exp(-ZH(a, b, \beta_{\text{shape}}, \beta_{\text{scale}}, u)) = (1 + \sigma^2 H(a, b, \beta_{\text{shape}}, \beta_{\text{scale}}, u))^{-1/\sigma^2}$$

and parameters: time is the time past from diagnosis, u is the covariate vector, a and b are slope and shape parameters defining the hazard functions (Weibull or Gompertz), β_{shape} and β_{scale} are the Cox-regression parameters for shape and scale, respectively, and σ^2 is the variance of frailty.

When including the age as a continuous variable in the model, the formula for life expectancy slightly changes. In particular, the coefficient for scale becomes

$$\beta_{\text{scale}} = \beta_{\text{birth_cohort}} + \text{age}_{\text{at diagnosis}} \beta_{\text{at age of diagnosis}} + \beta_{\text{cases}}$$

and shape parameter becomes

$$\beta_{\text{shape}} = \beta_{\text{birth_cohort}}$$

In denominator, S_{total} will consist of three components

$$S_{\text{total}} = \exp(-(H_{\text{control}} + (H_{\text{case at time from diagnosis}} - H_{\text{case at diagnosis}})))$$

where

$$H_{\text{control}} = \exp(\beta_{\text{scale}} u) t / a^{b \exp(\beta_{\text{shape}} u)}$$

With t=0, a and b from the model output shape and scale parameters as

$$\beta_{\text{shape}} = \beta_{\text{birth_cohort}}$$

$$\beta_{\text{scale}} = \beta_{\text{birth_cohort}} + \text{age}_{\text{at diagnosis}} \beta_{\text{at age of diagnosis}}$$

The difference in hazards term for cases consist of $H_{case \ at \ time \ from \ diagnosis}$ and $H_{case \ at \ diagnosis}$ which are

$$H_{case \ at \ time \ from \ diagnosis} = \exp(\beta_{scale}u)t/a^{b\exp(\beta_{shape}u)}$$

With t the number of years from diagnosis and

$$\beta_{scale} = \beta_{birth_cohort}$$

$$\beta_{scale} = \beta_{birth_cohort} + age_{at \ diagnosis}\beta_{at \ age \ of \ diagnosis} + \beta_{cases}$$

And

$$H_{case \ at \ diagnosis} = \exp(\beta_{scale}u)t/a^{b\exp(\beta_{shape}u)}$$

With t=0 and

$$\beta_{shape} = \beta_{birth_cohort}$$

$$\beta_{scale} = \beta_{birth_cohort} + age_{at \ diagnosis}\beta_{at \ age \ of \ diagnosis} + \beta_{cases}$$

Structure of the data for double_cox_method1 and double_cox_method2

The data set includes the following fields:

- In the case without left truncation: Time-to-failure and censoring
- In the case with left truncation at the start time, time-of start, time-of-failure, and censoring. Censoring must be either 0 (no event) or 1 (event);
- Covariates (continuous or categorical) used in a study (can be empty set).

a and b are slope and shape parameters defining the hazard functions (Weibull or Gompertz, see details below), β_{shape} and β_{scale} are the Cox-regression parameters for shape and scale, respectively, and σ^2 is the variance of frailty

Main effects and interactions can be specified in scale and shape formulas inside formula.scale and formula.shape, respectively. It is not possible to include interaction effect without specifying main effects of the variables involved in this interaction. For a model with interactions without the main effects of variables involved in these interactions, these interactions must be reformatted as categorical variables with correct number of categories.

References

- Gitsels L.A., Kulinskaya E., Steel N. (2016) Survival Benefits of Statins for Primary Prevention: A Cohort Study. PLoS ONE 11(11): e0166847. doi:10.1371/journal.pone.0166847
- Gitsels L.A., Kulinskaya E., Steel N. (2017) Survival prospects after acute myocardial infarction in the United Kingdom: a matched cohort study 1987-2011. BMJ Open 7(1), DOI 10.1136/bmjopen-2016-013570
- Gitsels LA, Kulinskaya E. and Wright N. (2019) How Medical Advances and Health Interventions Will Shape Future Longevity, British Actuarial Journal, 24, e10,2019.
- Gitsels LA, Kulinskaya E Wright N (2019) How medical advances and health interventions will shape future longevity - Abstract of the Edinburgh Discussion. British Actuarial Journal, 24:e9.
doi:10.1017/S1357321718000326
- Begun A., Kulinskaya E. and MacGregor A. (2019) Risk-adjusted CUSUM control charts for shared frailty survival models with application to hip replacement outcomes: a study using the NJR dataset. *BMC Med Res Methodol* 19, 217 (2019). <https://doi.org/10.1186/s12874-019-0853-2>
- Kulinskaya E., Gitsels, LA., Bakbergenuly, I. and Wright, N.R. (2020a) Calculation of changes in individual and period life expectancy based on proportional hazards model of an intervention. *Insurance Mathematics and Economics*.
- Kulinskaya, E. , Gitsels, L.A., Bakbergenuly, I. and Wright, N.R. (2020b) Dynamic hazards modelling for predictive longevity risk assessment. *Insurance Mathematics and Economics* 2020 <https://doi.org/10.1016/j.insmatheco.2020.11.001>
- Gitsels, LA., Bakbergenuly, I., Steel N. and Kulinskaya E. (2021) "Do statins reduce mortality in older people? Findings from a longitudinal study using primary care records" *Family Medicine and Community Health* 2021;9:e000780. doi: 10.1136/fmch-2020-000780
Elena Kulinskaya, Ilyas Bakbergenuly and Lisanne Gitsels. A fine scale. The Actuary, May 2020, 24-27

Required packages

dplyr, survival, sqldf, MASS, stringr, ucminf, xtable

See Also

coxph, survfit, survreg

Examples

```
#example for mylongevity_method1
set.seed(1234)
n<-1000
age <-round(runif(n, min = 60, max = 85))
gender <- c(rep('M',times=n/2),rep('F',times=n/2))
townsend <- round(runif(n, min = 1, max = 5))
smokerCategory <- round(runif(n, min = 1, max = 3))
```

```

htn <- round(runif(n, min = 1, max = 3))
diabetesCategory <- round(runif(n, min = 0, max = 1))
hcl <- round(runif(n, min = 0, max = 1))
bmiCategory <- round(runif(n, min = 1, max = 3))
qRiskCategory <- round(runif(n, min = 0, max = 2))
statins <- round(runif(n, min = 0, max = 1))
data_of_clients <-
data.frame(age,gender,townsend,smokerCategory,htn,diabetesCategory,hcl,bmiCategory,qRiskCategory,statins)
indexes_for_columns <- c(1,2,3,4,5,6,7,8,9,10)
life_expectancy_table=mylongevity_method1(data=data_of_clients,indexes_of_variables=indexes_for_columns)

```

```

#dummy data example for mylongevity_method2
set.seed(1234)
n<-1000
gender <- c(rep('M',times=n/2),rep('F',times=n/2))
townsend <- round(runif(n, min = 1, max = 5))
smokerCategory <- round(runif(n, min = 1, max = 3))
HTN_diag_treat <- round(runif(n, min = 1, max = 3))
diabetes <- round(runif(n, min = 0, max = 1))
hypercholesterolaemia <- round(runif(n, min = 0, max = 1))
bmiCategory <- round(runif(n, min = 1, max = 3))
cvd_risk <- round(runif(n, min = 0, max = 2))
statins <- round(runif(n, min = 0, max = 1))
age <-61
a=-12.459132
b=0.11764571
list_of_variables<-c("statins","cvd_risk","diabetes","HTN_diag_treat","hypercholesterolaemia")
data<-data.frame(statins, cvd_risk, diabetes, HTN_diag_treat, hypercholesterolaemia)
indexes_of_variables <- c(1,2,3,4,5)
working_directory<-"E:/myproject/" #please edit this to your working directory
life_expectancy_table_method2<-
mylongevity_method2(data=data,indexes_of_variables=indexes_of_variables,list_of_variables,age,a,b,working_directory)

```

```

#dummy data example for mylongevity_method3
set.seed(1)
n<-10000
gender <- c(rep('M',times=n/2),rep('F',times=n/2))
townsend <- as.factor(round(runif(n, min = 1, max = 5)))
smokerCategory <- as.factor(round(runif(n, min = 1, max = 3)))
HTN_diag_treat <- as.factor(round(runif(n, min = 1, max = 3)))
diabetes <- as.factor(round(runif(n, min = 0, max = 1)))
hypercholesterolaemia <- as.factor(round(runif(n, min = 0, max = 1)))
bmiCategory <- as.factor(round(runif(n, min = 1, max = 3)))
cvd_risk <- as.factor(round(runif(n, min = 0, max = 2)))
statins <- as.factor(round(runif(n, min = 0, max = 1)))
aspirin<-as.factor(round(runif(n, min = 0, max = 1)))
Tstart<-rep(1,times=n)

```

```

Tstop<-abs(rnorm(n,mean=26,sd= 6))
death<-sample(c(0,1), replace=TRUE, size=n)
T_start_indicator <- "Tstart"
T_stop_indicator <- "Tstop"
status_indicator <- "death"
age <-70
a=-12.459132
b=0.11764571
indexes_of_variables<-c(1,2,3,4,5,6,7,8,9,10,11,12)
list_of_variables<-
c("statins","cvd_risk","diabetes","HTN_diag_treat","hypercholesterolaemia","bmiCategory","smoker
Category","townsend","aspirin")
data<-
data.frame(statins, cvd_risk, diabetes, HTN_diag_treat, hypercholesterolaemia, bmiCategory, smokerCa
tory, townsend, aspirin, Tstart, Tstop, death)
working_directory<-"E:/myproject/"
life_expectancy_table_method3<-
mylongevity_method3(data=data, indexes_of_variables=indexes_of_variables, list_of_variables, age, a
,b,
T_start_indicator, T_stop_indicator, status_indicator, working_directory)

#example for mylongevity_double_cox_method1
set.seed(1234)
n<-1000
atrial<-round(runif(n, min = 0, max = 1)) #indicator for atrial fibrillation (0 - absence of atrial
fibrillation or 1 - presence of atrial fibrillation)
birth_year<-round(runif(n, min = 0, max = 2)) #indicator for year of birth (0 - born in 1930-1939, 1 -
born in 1950-1960, 2 - born in 1940-1949)
bmi_regrp <-round(runif(n, min = 0, max = 2)) #indicator for body mass index (0 - Healthy, 1 -
Overweight, 2 - Obese)
diabetes<-round(runif(n, min = 0, max = 1)) #indicator of cases control group (0 - absence type 2
diabetes mellitus, 1 - presence type 2 diabetes mellitus)
hf<-round(runif(n, min = 0, max = 1)) #indicator for heart failure (0 - absence of heart failure, 1 -
presence of heart failure)
hyperchol<-round(runif(n, min = 0, max = 2)) #indicator for hypercholesterolemia (0 - absence of
hypercholesterolemia, 1 - presence of hypercholesterolemia)
hypert<-round(runif(n, min = 0, max = 2)) #indicator for hypertension (0 - absence of Hypertension, 1
- Treated Hypertension 2 - Untreated Hypertension)
miocardInfarct<-round(runif(n, min = 0, max = 1)) #indicator for myocardial infarction (0 - absence of
myocardial infarction, 1 - presence of myocardial infarction)
pvd<-round(runif(n, min = 0, max = 1)) #indicator for peripheral vascular disease (0 - absence of
peripheral vascular disease, 1 - presence of peripheral vascular disease)
sex<-round(runif(n, min = 0, max = 1)) #indicator for gender (0 - Female, 1 - Male)
smokes<-round(runif(n, min = 0, max = 2)) #indicator of smoking status (0 non-smoker, 1 - former
smoker, 2 - current smoker)
townsend<-round(runif(n, min = 0, max = 4)) #- deprivation index (0 - (Townsend 3), 1 - (Townsend
1) 2 - (Townsend 2) , 3 - (Townsend 4), 4 - (Townsend 5))

data<-
data.frame(atrial, birth_year, bmi_regrp, diabetes, hf, hyperchol, hypert, miocardInfarct, pvd, sex, smokes, t
ownsend)

```

```

indexes_of_variables <- c(1,2,3,4,5,6,7,8,9,10,11,12)
age_of_diagnosis=60
time_past_from_diagnosis=1

life_expectancy_mylongevity_double_cox_method1<-mylongevity_double_cox_method1(data,
indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis)

#example for mylongevity_double_cox_method2
set.seed(1234)
n<1000
B_cohort<-round(runif(n, min = 0, max = 3)) # indicator for year of birth (0 - born in 1921-1930 , 1 -
born in 1931-1940, 2 - born in 1941-1950, 3 - born in 1951-1960)
BMIsome<-round(runif(n, min = 0, max = 5)) # indicator for interaction for body mass index and
smoking (0 - Healthy or Overweight and Non Smoker, 1 - healthy weight and current smoker, 2 -
healthy weight and ex smoker, 3, Obese and current smoker, 4 - Obese and ex-smoker, 5 - Obese
and non-smoker)
CHD<-round(runif(n, min = 0, max = 1)) # indicator for heart failure (0 - absence of coronary heart
disease , 1 - presence of coronary heart disease)
hrtcat<-round(runif(n, min = 0, max = 2)) # indicator for type of hormone replacement therapy (0 -
non users of hormone replacement therapy, 1 - Combined Oestrogen and Progesteron , 2 -
Oestrogen-only)
DMIIsmoke<-round(runif(n, min = 0, max = 5)) # interaction of diabetes and smoking variables (0 -
non diabetic and non smoker,1 - non diabetic and current smoker ,2 - non diabetic and ex-smoker,3
- diabetic and current smoker,4 - diabetic and ex smoker ,5 - diabetic and non-smoker)
opho<-round(runif(n, min = 1, max = 2)) # indicator of cases control group (0 - both uteras and
ovarian not removed, 1 - both uteras and ovarian removed, 2 - ovaries removed but not uteras)
hypertension<-round(runif(n, min = 0, max = 1)) # indicator for hypertension (0 - absence of
Hypertension, 1 - Treated Hypertension 2 - Untreated Hypertension)
deprivation <-round(runif(n, min = 0, max = 2))# deprivation index (0 - Low (Townsend 1 and
Townsend 2), 1 - High (Townsend 4 and Townsend 5), 2 - Medium (Townsend 3))

data<-data.frame(B_cohort,BMIsome,CHD,deprivation,DMIIsmoke,hrtcat,hypertension,opho)
indexes_of_variables <- c(1,2,3,4,5,6,7,8)
age_of_diagnosis=45
time_past_from_diagnosis=1

life_expectancy_mylongevity_double_cox_method2<-mylongevity_double_cox_method2(data,
indexes_of_variables, age_of_diagnosis, time_past_from_diagnosis)

#example for mylongevity_double_cox_method3
set.seed(1234)
n<1000
birth_cohort<-round(runif(n, min = 0, max = 3)) #: indicator for year of birth (0 - born in 1908-1920, 1
- born in 1921-1930, 2 - born in 1931-1940, 3 - born in 1941 - 1960)
IMD_Quintile<-round(runif(n, min = 1, max = 5)) #: deprivation index (1 (least deprived), 2, 3, 4, 5
(most deprived))
BMI_category<-round(runif(n, min = 0, max = 1)) #: categorical variable with numeric value for Body
Mass Index categories (0 - Healthy weight (BMI<25), 1 - Overweight (BMI>=25 and BMI<30) and
Obese (BMI>=30))
antiplatelet_drugs<-round(runif(n, min = 0, max = 1)) #: indicator for antiplatelet drugs (0 - no
antiplatelet drugs or 1 - no antiplatelet drugs)

```

```

COPD<-round(runif(n, min = 0, max = 1)) #: indicator for chronic obstructive pulmonary disease (0 - absence of chronic obstructive pulmonary disease or 1 - presence of chronic obstructive pulmonary disease)
heart_failure<-round(runif(n, min = 0, max = 1)) #: indicator for heart failure (0 - absence of heart failure or 1 - presence of heart failure)
myocardial_infarction<-round(runif(n, min = 0, max = 1)) #: indicator for myocardial infarction (0 - absence of myocardial infarction or 1 - presence of myocardial infarction)
PVD_PAD<-round(runif(n, min = 0, max = 1)) #: indicator for peripheral vascular disease (0 - absence of peripheral vascular disease or 1 - presence of peripheral vascular disease )
SMOKING<-round(runif(n, min = 0, max = 2)) #: indicator of smoking status (0 non-smoker, 1 - current smoker, 2 - former smoker)
anticoagulant_agents<-round(runif(n, min = 0, max = 1)) #: indicator for anticoagulant agents (0 - no anticoagulant agents, 1 - yes anticoagulant agents )
Diabetes_factor<-round(runif(n, min = 0, max = 2)) #: is a categorical variable with numeric value for diabetes status (0 - absence of diabetes or 1 - presence of diabetes and treated, 2 - absence of diabetes and untreated)
sex<-round(runif(n, min = 0, max = 1)) #: indicator for gender (0 - Female , 1 - Male)
groupscases<-round(runif(n, min = 0, max = 1)) #: indicator of cases control group (0 – group without ischemic stroke or 1 – group with ischemic stroke)
antihypertensive_agents<-round(runif(n, min = 0, max = 1))#: indicator for antihypertensive agents (0 - no antihypertensive agents, 1 - yes antihypertensive agents)

data<-data.frame(birth_cohort,IMD_Quintile,BMI_category, antiplatelet_drugs, COPD, heart_failure, myocardial_infarction,PVD_PAD,SMOKING,anticoagulant_agents,Diabetes_factor,sex,groupscases,antihypertensive_agents)
indexes_of_variables <- c(1,2,3,4,5,6,7,8,9,10,11,12,13,14)
age_of_diagnosis=65
time_past_from_diagnosis=1

life_expectancy_mylongevity_double_cox_method3<-mylongevity_double_cox_method3(data,
indexes_of_variables,age_of_diagnosis,time_past_from_diagnosis)

#example for mylongevity_double_cox_method4

set.seed(1234)
n<1000
birth_cohort<-round(runif(n, min = 0, max = 3)) #: indicator for year of birth (0 - born in 1908-1920, 1 - born in 1921-1930, 2 - born in 1931-1940, 3 - born in 1941 - 1960)
sex<-round(runif(n, min = 1, max = 2)) #: indicator for gender (0 - Female , 1 - Male)
IMD_Quintile<-round(runif(n, min = 1, max = 5)) #: deprivation index (1 (least deprived), 2, 3, 4, 5 (most deprived))
BMI_category<-round(runif(n, min = 0, max = 1)) #: categorical variable with numeric value for Body Mass Index categories (0 - Healthy weight ( $BMI < 25$ ), 1 - Overweight ( $BMI \geq 25$  and  $BMI < 30$ ) and Obese ( $BMI \geq 30$ ))
asthma<-round(runif(n, min = 0, max = 1)) #: indicator for asthma (0 - absence of asthma, 1 - presence of asthma)
COPD<-round(runif(n, min = 0, max = 1)) #: indicator for chronic obstructive pulmonary disease (0 - absence of chronic obstructive pulmonary disease, 1 - presence of chronic obstructive pulmonary disease)
CKD<-round(runif(n, min = 0, max = 1)) #: indicator for chronic kidney disease (0 - absence of chronic kidney disease , 1 - presence of chronic kidney disease)

```

```

myocardial_infarction<-round(runif(n, min = 0, max = 1)) #: indicator for myocardial infarction (0 - absence of myocardial infarction, 1 - presence of myocardial infarction)
PVD_PAD<-round(runif(n, min = 0, max = 1)) #: indicator for peripheral vascular disease (0 - absence of peripheral vascular disease, 1 - presence of peripheral vascular disease)
SMOKING<-round(runif(n, min = 0, max = 2)) #: indicator of smoking status (0 non-smoker, 1 - current smoker, 2 - former smoker)
alcohol_cat<-round(runif(n, min = 0, max = 1)) #: indicator for alcohol intake variable (0 – non - drinker, 1 - drinker)
atrial_fibrillation<-round(runif(n, min = 0, max = 1)) #: indicator for atrial fibrillation (0 - absence of atrial fibrillation, 1 - presence of atrial fibrillation)
Diabetes_factor<-round(runif(n, min = 0, max = 2)) #: indicator for diabetes (0 – absence of diabetes or 1 - presence of diabetes and treated, 2 - absence of diabetes and untreated)
anticoagulant_agents<-round(runif(n, min = 0, max = 1)) #: indicator for anticoagulant agents (0 - no anticoagulant agents, 1 - yes anticoagulant agents)
groupscases<-round(runif(n, min = 0, max = 1)) #: indicator of cases control group (0 - without transient ischemic attack, 1 - with transient ischemic attack)
antihypertensive_agents<-round(runif(n, min = 0, max = 1)) #: indicator for antihypertensive agents (0 - no antihypertensive agents, 1 - yes antihypertensive agents)
APL<-round(runif(n, min = 0, max = 1)) #: indicator for antiplatelet therapy (0 - no antiplatelet therapy, 1 - yes antiplatelet therapy)
heart_failure<-round(runif(n, min = 0, max = 1)) #: indicator for heart failure (0 - absence of heart failure or 1 - presence of heart failure)

```

```

data<-
data.frame(birth_cohort,sex,IMD_Quintile,BMI_category,asthma,COPD,CKD,myocardial_infarction,P
VD_PAD,SMOKING,alcohol_cat,atrial_fibrillation,Diabetes_factor,anticoagulant_agents,groupscases,
antihypertensive_agents,APL,heart_failure)
indexes_of_variables <- c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18)
age_of_diagnosis=65
time_past_from_diagnosis=1

res4<-mylongevity_double_cox_method4(data, indexes_of_variables, age_of_diagnosis,
time_past_from_diagnosis)

```

```

#####
#####example for double_cox_longevity1 and double_cox_longevity2#####
#####
set.seed(1)
###working example for double cox regression model
n<-10000
clinic<-as.factor(round(runif(n, min = 1, max = 1000)))###suppose we have 200 clinic
gender <- c(rep('M',times=n/2),rep('F',times=n/2))
townsend <- as.factor(round(runif(n, min = 1, max = 5)))
smokerCategory <- as.factor(round(runif(n, min = 1, max = 3)))
HTN_diag_treat <- as.factor(round(runif(n, min = 1, max = 3)))
diabetes <- as.factor(round(runif(n, min = 0, max = 1)))
hypercholesterolaemia <- as.factor(round(runif(n, min = 0, max = 1)))
bmiCategory <- as.factor(round(runif(n, min = 1, max = 3)))
age_cat<- as.factor(round(runif(n, min = 1, max = 3)))
birth_cohort<- as.factor(round(runif(n, min = 0, max = 3)))

```

```

cvd_risk <- as.factor(round(runif(n, min = 0, max = 2)))
statins <- as.factor(round(runif(n, min = 0, max = 1)))
aspirin<-as.factor(round(runif(n, min = 0, max = 1)))
age_c<-rnorm(n,mean=70, sd=10)
Tstart<-rep(60,times=n)
Tstop<-abs(rnorm(n,mean=70, sd= 6))
death<-sample(c(0,1), replace=TRUE, size=n)
T_start_indicator <- "Tstart"
T_stop_indicator <- "Tstop"
status_indicator <- "death"
working_directory<-"E:/myproject/"
data<-
data.frame(clinic,statins,age_c,birth_cohort, cvd_risk,diabetes,HTN_diag_treat,hypercholesterolaemia,bmiCategory,age_cat,smokerCategory,townsend,aspirin,Tstart,Tstop,death)
data<-data[data$Tstop>data$Tstart,] #removing all the observations where Tstop happened before T start

age_of_diagnosis<-60 ##age at diagnosis
time_past_from_diagnosis<-5 ## time from diagnosis
name_for_age_factor=NULL
cluster="clinic"
dist="Weibull"

formula.scale=as.formula("survival::Surv(Tstart,Tstop,death)~birth_cohort+age_c+HTN_diag_treat+smokerCategory")
formula.shape=as.formula("survival::Surv(Tstart,Tstop, death) ~birth_cohort")

life_expectancy_double_cox_longevity1<-
double_cox_longevity1(data,dist,cluster,formula.shape,formula.scale,age_of_diagnosis,time_past_from_diagnosis,working_directory,name_for_age_factor=NULL)

life_expectancy_double_cox_longevity2<-
double_cox_longevity2(data,dist,cluster,formula.shape,formula.scale,age_of_diagnosis,time_past_from_diagnosis,working_directory,name_for_age_factor="age_c")

```

Appendix

1. Parameters with 95% confidence intervals from landmark analysis model used in functions mylongevity_method1 and mylongevity_method2

The years are counted from age 60 to 85 every 6 month.

Years	Statin			QRISK>40 or CVD			QRISK<20		
	logHR	L	U	logHR	L	U	logHR	L	U
0	-0.091	-0.273	0.092	0.095	-0.035	0.224	-0.062	-0.145	0.021
0.5	-0.109	-0.268	0.050	0.113	-0.001	0.228	-0.067	-0.141	0.007
1	-0.127	-0.265	0.011	0.131	0.030	0.233	-0.072	-0.137	-0.006
1.5	-0.144	-0.264	-0.024	0.149	0.058	0.240	-0.077	-0.135	-0.018
2	-0.159	-0.264	-0.055	0.166	0.085	0.247	-0.081	-0.133	-0.029
2.5	-0.174	-0.266	-0.083	0.182	0.109	0.256	-0.085	-0.132	-0.038
3	-0.188	-0.269	-0.108	0.198	0.132	0.265	-0.089	-0.132	-0.047
3.5	-0.202	-0.274	-0.129	0.213	0.152	0.275	-0.093	-0.133	-0.053
4	-0.214	-0.280	-0.148	0.228	0.171	0.285	-0.096	-0.134	-0.059
4.5	-0.226	-0.287	-0.165	0.242	0.188	0.296	-0.099	-0.135	-0.064
5	-0.237	-0.295	-0.179	0.255	0.203	0.307	-0.102	-0.137	-0.067
5.5	-0.247	-0.302	-0.192	0.268	0.218	0.317	-0.104	-0.138	-0.070
6	-0.257	-0.310	-0.204	0.280	0.231	0.328	-0.106	-0.139	-0.072
6.5	-0.266	-0.318	-0.215	0.291	0.244	0.338	-0.107	-0.140	-0.073
7	-0.275	-0.325	-0.225	0.301	0.255	0.347	-0.107	-0.140	-0.074
7.5	-0.283	-0.332	-0.234	0.311	0.266	0.355	-0.107	-0.140	-0.074
8	-0.291	-0.339	-0.243	0.320	0.276	0.363	-0.106	-0.139	-0.074
8.5	-0.298	-0.345	-0.251	0.328	0.286	0.370	-0.105	-0.137	-0.073
9	-0.305	-0.351	-0.259	0.335	0.294	0.377	-0.103	-0.134	-0.071
9.5	-0.312	-0.357	-0.266	0.342	0.302	0.382	-0.100	-0.131	-0.069
10	-0.318	-0.363	-0.272	0.348	0.308	0.387	-0.097	-0.127	-0.066
10.5	-0.324	-0.369	-0.278	0.353	0.314	0.392	-0.092	-0.122	-0.062
11	-0.329	-0.375	-0.283	0.357	0.319	0.395	-0.087	-0.117	-0.057
11.5	-0.335	-0.381	-0.288	0.360	0.323	0.398	-0.081	-0.111	-0.051
12	-0.340	-0.387	-0.293	0.363	0.325	0.401	-0.074	-0.105	-0.042
12.5	-0.345	-0.393	-0.297	0.365	0.327	0.402	-0.066	-0.099	-0.032
13	-0.351	-0.400	-0.301	0.365	0.327	0.404	-0.057	-0.093	-0.020
13.5	-0.356	-0.406	-0.305	0.365	0.326	0.404	-0.047	-0.088	-0.005
14	-0.361	-0.412	-0.309	0.364	0.325	0.404	-0.036	-0.083	0.011

14.5	-0.366	-0.419	-0.313	0.362	0.322	0.403	-0.024	-0.078	0.031
15	-0.371	-0.426	-0.316	0.359	0.318	0.401	-0.010	-0.073	0.052
15.5	-0.376	-0.434	-0.318	0.355	0.313	0.398	0.004	-0.068	0.076
16	-0.382	-0.443	-0.321	0.350	0.307	0.394	0.020	-0.063	0.103
16.5	-0.387	-0.453	-0.322	0.345	0.299	0.390	0.037	-0.058	0.132
17	-0.393	-0.465	-0.321	0.338	0.291	0.384	0.055	-0.054	0.163
17.5	-0.399	-0.479	-0.320	0.330	0.282	0.378	0.074	-0.049	0.197
18	-0.406	-0.495	-0.316	0.321	0.272	0.371	0.095	-0.044	0.234
18.5	-0.412	-0.514	-0.311	0.311	0.260	0.363	0.117	-0.039	0.273
19	-0.420	-0.536	-0.303	0.300	0.247	0.354	0.141	-0.034	0.315
19.5	-0.427	-0.560	-0.294	0.288	0.232	0.345	0.166	-0.029	0.360
20	-0.435	-0.588	-0.282	0.275	0.215	0.335	0.192	-0.024	0.408
20.5	-0.444	-0.619	-0.268	0.261	0.196	0.326	0.220	-0.019	0.459
21	-0.453	-0.654	-0.251	0.246	0.175	0.317	0.250	-0.014	0.514
21.5	-0.462	-0.692	-0.232	0.229	0.151	0.307	0.281	-0.009	0.571
22	-0.472	-0.734	-0.211	0.212	0.125	0.298	0.314	-0.005	0.632
22.5	-0.483	-0.780	-0.187	0.193	0.096	0.290	0.348	0.000	0.696
23	-0.495	-0.829	-0.160	0.173	0.065	0.281	0.384	0.005	0.763
23.5	-0.507	-0.883	-0.131	0.152	0.030	0.274	0.422	0.009	0.835
24	-0.520	-0.941	-0.098	0.130	-0.007	0.267	0.461	0.013	0.910
24.5	-0.534	-1.004	-0.063	0.106	-0.047	0.260	0.503	0.017	0.988
25	-0.548	-1.071	-0.026	0.082	-0.091	0.254	0.546	0.021	1.071

Years	Overweight			Obese			Diabetes		
	logHR	L	U	logHR	L	U	logHR	L	U
0	-0.045	-0.083	-0.006	0.098	0.047	0.149	0.604	0.525	0.684
0.5	-0.044	-0.082	-0.006	0.097	0.047	0.147	0.588	0.515	0.660
1	-0.044	-0.082	-0.006	0.095	0.046	0.144	0.571	0.504	0.638
1.5	-0.045	-0.083	-0.006	0.093	0.044	0.142	0.555	0.492	0.618
2	-0.046	-0.084	-0.007	0.091	0.042	0.140	0.540	0.480	0.599
2.5	-0.047	-0.086	-0.008	0.088	0.039	0.137	0.525	0.468	0.582
3	-0.049	-0.088	-0.010	0.085	0.036	0.134	0.510	0.455	0.565
3.5	-0.051	-0.091	-0.012	0.082	0.033	0.131	0.496	0.443	0.550
4	-0.054	-0.094	-0.015	0.079	0.030	0.127	0.483	0.431	0.535
4.5	-0.057	-0.097	-0.018	0.075	0.026	0.123	0.469	0.418	0.520
5	-0.061	-0.100	-0.021	0.071	0.023	0.119	0.457	0.407	0.507
5.5	-0.064	-0.104	-0.025	0.067	0.019	0.114	0.444	0.395	0.494
6	-0.068	-0.107	-0.030	0.062	0.015	0.109	0.433	0.384	0.481
6.5	-0.073	-0.111	-0.034	0.057	0.011	0.104	0.421	0.373	0.469
7	-0.077	-0.115	-0.039	0.053	0.006	0.099	0.410	0.363	0.457
7.5	-0.082	-0.119	-0.044	0.047	0.002	0.093	0.399	0.353	0.445
8	-0.086	-0.124	-0.049	0.042	-0.003	0.088	0.389	0.343	0.434
8.5	-0.091	-0.128	-0.054	0.037	-0.008	0.082	0.379	0.334	0.423
9	-0.096	-0.133	-0.059	0.031	-0.014	0.076	0.369	0.325	0.413
9.5	-0.101	-0.137	-0.064	0.026	-0.019	0.070	0.360	0.316	0.403

10	-0.105	-0.142	-0.069	0.020	-0.025	0.065	0.351	0.307	0.394
10.5	-0.110	-0.147	-0.073	0.014	-0.031	0.059	0.342	0.299	0.385
11	-0.115	-0.152	-0.078	0.008	-0.038	0.053	0.334	0.290	0.377
11.5	-0.120	-0.157	-0.082	0.002	-0.045	0.048	0.325	0.282	0.369
12	-0.124	-0.162	-0.086	-0.005	-0.052	0.042	0.318	0.273	0.362
12.5	-0.128	-0.167	-0.089	-0.011	-0.059	0.037	0.310	0.265	0.355
13	-0.132	-0.172	-0.093	-0.017	-0.066	0.031	0.303	0.257	0.348
13.5	-0.136	-0.176	-0.096	-0.024	-0.074	0.026	0.296	0.249	0.342
14	-0.140	-0.181	-0.098	-0.030	-0.081	0.021	0.289	0.242	0.336
14.5	-0.143	-0.185	-0.101	-0.037	-0.089	0.015	0.282	0.234	0.331
15	-0.146	-0.189	-0.103	-0.043	-0.097	0.010	0.276	0.227	0.325
15.5	-0.148	-0.193	-0.104	-0.050	-0.104	0.005	0.270	0.219	0.321
16	-0.150	-0.196	-0.105	-0.056	-0.112	0.000	0.264	0.212	0.316
16.5	-0.152	-0.199	-0.105	-0.062	-0.121	-0.004	0.258	0.205	0.312
17	-0.153	-0.202	-0.104	-0.069	-0.129	-0.009	0.253	0.198	0.308
17.5	-0.154	-0.205	-0.103	-0.075	-0.138	-0.013	0.247	0.190	0.304
18	-0.154	-0.207	-0.101	-0.081	-0.147	-0.016	0.242	0.183	0.301
18.5	-0.154	-0.209	-0.098	-0.088	-0.156	-0.019	0.237	0.175	0.299
19	-0.152	-0.211	-0.093	-0.094	-0.167	-0.021	0.232	0.167	0.297
19.5	-0.151	-0.214	-0.088	-0.100	-0.178	-0.022	0.227	0.158	0.296
20	-0.148	-0.216	-0.081	-0.106	-0.189	-0.022	0.222	0.149	0.296
20.5	-0.145	-0.218	-0.072	-0.111	-0.202	-0.021	0.218	0.138	0.297
21	-0.141	-0.221	-0.062	-0.117	-0.216	-0.018	0.213	0.127	0.299
21.5	-0.137	-0.223	-0.050	-0.122	-0.230	-0.015	0.209	0.115	0.303
22	-0.131	-0.226	-0.037	-0.128	-0.246	-0.009	0.204	0.101	0.307
22.5	-0.125	-0.229	-0.022	-0.133	-0.263	-0.003	0.200	0.087	0.314
23	-0.118	-0.232	-0.004	-0.138	-0.281	0.005	0.196	0.071	0.321
23.5	-0.110	-0.235	0.015	-0.143	-0.300	0.015	0.192	0.053	0.330
24	-0.101	-0.238	0.036	-0.147	-0.320	0.026	0.188	0.034	0.341
24.5	-0.091	-0.242	0.060	-0.152	-0.342	0.039	0.183	0.014	0.353
25	-0.080	-0.245	0.085	-0.156	-0.365	0.054	0.179	-0.008	0.366

Years	Hypercholesterolemia			Ex-Smoker			Current Smoker		
	logHR	L	U	logHR	L	U	logHR	L	U
0	-0.226	-0.298	-0.155	0.387	0.331	0.444	0.891	0.853	0.929
0.5	-0.221	-0.288	-0.153	0.385	0.334	0.437	0.885	0.850	0.921
1	-0.216	-0.280	-0.151	0.384	0.336	0.432	0.880	0.846	0.914
1.5	-0.210	-0.272	-0.148	0.382	0.337	0.428	0.875	0.841	0.909
2	-0.205	-0.265	-0.145	0.381	0.338	0.424	0.871	0.837	0.904
2.5	-0.200	-0.259	-0.141	0.380	0.338	0.422	0.867	0.833	0.901
3	-0.195	-0.252	-0.137	0.379	0.338	0.420	0.863	0.828	0.897
3.5	-0.190	-0.247	-0.133	0.378	0.339	0.418	0.859	0.825	0.894
4	-0.185	-0.241	-0.129	0.378	0.339	0.417	0.856	0.821	0.891

4.5	-0.180	-0.235	-0.125	0.377	0.339	0.416	0.853	0.817	0.888
5	-0.175	-0.230	-0.121	0.377	0.339	0.415	0.850	0.814	0.886
5.5	-0.171	-0.224	-0.117	0.377	0.339	0.414	0.847	0.811	0.883
6	-0.166	-0.219	-0.113	0.376	0.340	0.413	0.844	0.808	0.880
6.5	-0.161	-0.213	-0.109	0.376	0.340	0.412	0.841	0.805	0.877
7	-0.157	-0.208	-0.105	0.376	0.340	0.411	0.838	0.802	0.874
7.5	-0.152	-0.203	-0.102	0.376	0.340	0.411	0.835	0.799	0.872
8	-0.148	-0.197	-0.098	0.375	0.341	0.410	0.832	0.796	0.869
8.5	-0.143	-0.192	-0.094	0.375	0.341	0.409	0.829	0.792	0.866
9	-0.139	-0.187	-0.090	0.375	0.341	0.409	0.825	0.788	0.862
9.5	-0.134	-0.183	-0.086	0.374	0.340	0.408	0.822	0.784	0.859
10	-0.130	-0.178	-0.082	0.374	0.340	0.407	0.817	0.779	0.855
10.5	-0.126	-0.174	-0.078	0.373	0.339	0.407	0.813	0.774	0.852
11	-0.121	-0.170	-0.073	0.372	0.338	0.406	0.808	0.768	0.848
11.5	-0.117	-0.166	-0.069	0.371	0.337	0.405	0.803	0.762	0.843
12	-0.113	-0.162	-0.064	0.370	0.335	0.404	0.797	0.755	0.838
12.5	-0.109	-0.158	-0.060	0.368	0.333	0.404	0.790	0.748	0.833
13	-0.105	-0.155	-0.055	0.367	0.331	0.403	0.783	0.740	0.827
13.5	-0.101	-0.151	-0.050	0.365	0.328	0.401	0.776	0.731	0.820
14	-0.096	-0.148	-0.045	0.362	0.325	0.400	0.767	0.721	0.813
14.5	-0.092	-0.145	-0.040	0.360	0.322	0.398	0.758	0.710	0.806
15	-0.088	-0.142	-0.035	0.357	0.318	0.397	0.748	0.699	0.798
15.5	-0.084	-0.139	-0.029	0.354	0.314	0.394	0.737	0.686	0.789
16	-0.080	-0.136	-0.024	0.351	0.309	0.392	0.726	0.672	0.779
16.5	-0.076	-0.134	-0.018	0.347	0.304	0.389	0.713	0.657	0.769
17	-0.072	-0.132	-0.013	0.343	0.299	0.386	0.700	0.641	0.759
17.5	-0.068	-0.130	-0.006	0.338	0.292	0.383	0.685	0.623	0.748
18	-0.064	-0.128	0.000	0.333	0.285	0.380	0.670	0.603	0.737
18.5	-0.060	-0.128	0.007	0.327	0.278	0.377	0.653	0.581	0.726
19	-0.056	-0.127	0.015	0.321	0.269	0.373	0.636	0.557	0.714
19.5	-0.052	-0.128	0.024	0.315	0.259	0.370	0.617	0.531	0.703
20	-0.048	-0.130	0.034	0.308	0.248	0.367	0.597	0.502	0.691
20.5	-0.044	-0.132	0.044	0.300	0.236	0.365	0.575	0.471	0.679
21	-0.040	-0.136	0.056	0.292	0.222	0.362	0.552	0.438	0.666
21.5	-0.036	-0.141	0.069	0.283	0.206	0.360	0.528	0.402	0.654
22	-0.032	-0.147	0.083	0.274	0.190	0.358	0.503	0.363	0.642
22.5	-0.028	-0.154	0.098	0.264	0.171	0.357	0.476	0.322	0.629
23	-0.024	-0.163	0.115	0.253	0.151	0.356	0.447	0.278	0.616
23.5	-0.020	-0.173	0.133	0.242	0.129	0.356	0.417	0.230	0.604
24	-0.016	-0.184	0.153	0.230	0.105	0.356	0.385	0.180	0.591
24.5	-0.012	-0.197	0.174	0.218	0.079	0.357	0.352	0.126	0.577
25	-0.007	-0.211	0.196	0.205	0.051	0.358	0.317	0.070	0.564

Years	Treated Hypertension			Untreated Hypertension		
	logHR	L	U	logHR	L	U
0	0.224	0.173	0.275	0.057	0.016	0.097
0.5	0.213	0.166	0.260	0.058	0.020	0.096
1	0.203	0.159	0.247	0.059	0.022	0.096
1.5	0.193	0.152	0.234	0.059	0.023	0.096
2	0.183	0.144	0.223	0.060	0.023	0.096
2.5	0.174	0.136	0.212	0.060	0.023	0.096
3	0.164	0.127	0.202	0.059	0.023	0.096
3.5	0.155	0.119	0.192	0.059	0.022	0.096
4	0.146	0.110	0.182	0.058	0.021	0.096
4.5	0.137	0.102	0.173	0.058	0.020	0.096
5	0.129	0.093	0.164	0.057	0.019	0.095
5.5	0.120	0.085	0.156	0.056	0.018	0.095
6	0.112	0.077	0.147	0.056	0.017	0.094
6.5	0.104	0.069	0.138	0.055	0.016	0.094
7	0.096	0.062	0.130	0.055	0.016	0.093
7.5	0.088	0.054	0.122	0.054	0.015	0.093
8	0.080	0.046	0.113	0.054	0.015	0.093
8.5	0.072	0.039	0.105	0.054	0.014	0.094
9	0.064	0.031	0.097	0.054	0.014	0.095
9.5	0.056	0.023	0.090	0.055	0.014	0.096
10	0.049	0.015	0.082	0.056	0.014	0.098
10.5	0.041	0.008	0.075	0.057	0.015	0.100
11	0.033	0.000	0.067	0.059	0.015	0.103
11.5	0.026	-0.008	0.060	0.061	0.016	0.106
12	0.018	-0.017	0.053	0.064	0.018	0.110
12.5	0.011	-0.025	0.046	0.067	0.020	0.115
13	0.003	-0.033	0.039	0.071	0.022	0.120
13.5	-0.005	-0.042	0.032	0.076	0.025	0.126
14	-0.013	-0.051	0.026	0.081	0.029	0.133
14.5	-0.020	-0.060	0.019	0.087	0.033	0.140
15	-0.028	-0.069	0.012	0.093	0.038	0.148
15.5	-0.036	-0.078	0.005	0.101	0.044	0.158
16	-0.044	-0.087	-0.002	0.109	0.050	0.168
16.5	-0.053	-0.097	-0.009	0.118	0.058	0.179
17	-0.061	-0.107	-0.015	0.128	0.065	0.191
17.5	-0.070	-0.117	-0.022	0.139	0.074	0.204
18	-0.078	-0.128	-0.029	0.151	0.083	0.219
18.5	-0.087	-0.139	-0.035	0.164	0.092	0.235
19	-0.096	-0.151	-0.041	0.178	0.102	0.254
19.5	-0.105	-0.164	-0.046	0.193	0.112	0.274
20	-0.114	-0.178	-0.051	0.209	0.123	0.296
20.5	-0.124	-0.193	-0.055	0.227	0.133	0.320

21	-0.134	-0.209	-0.058	0.246	0.144	0.347
21.5	-0.144	-0.226	-0.061	0.266	0.155	0.377
22	-0.154	-0.245	-0.063	0.287	0.165	0.408
22.5	-0.165	-0.265	-0.065	0.309	0.176	0.443
23	-0.175	-0.286	-0.065	0.333	0.187	0.480
23.5	-0.187	-0.308	-0.065	0.359	0.197	0.520
24	-0.198	-0.332	-0.063	0.386	0.208	0.563
24.5	-0.210	-0.358	-0.061	0.414	0.219	0.609
25	-0.222	-0.385	-0.058	0.444	0.230	0.659

2. Type 2 Diabetes results used in mylongevity_double_cox_method1. Gompertz distribution is used for baseline hazards.

Definition of parameter	Parameter	Estimates	CI	p-value
1000a	Scale	1.202	1.09-1.325	0
100b	Shape	10.301	9.717-10.92	0
born in 1950+	Shape	0.937	0.854-1.027	0.1653
born in 1940-1949	Shape	0.828	0.782-0.878	0
Atrial fibrillation - Present	Shape	1.333	1.252-1.419	0
Treated Hypertension	Shape	1.295	1.221-1.373	0
Untreated Hypertension	Shape	0.893	0.821-0.972	0.0095
born in 1950+	Scale	1.754	1.614-1.905	0
born in 1940-1949	Scale	1.454	1.379-1.533	0
Cases group	Scale	1.417	1.356-1.481	0
(Age -50) as continuous	Scale	1.095	1.092-1.099	0
Gender - Males	Scale	1.399	1.365-1.434	0
Former Smoker	Scale	1.615	1.526-1.71	0
Current Smoker	Scale	2.868	2.736-3.006	0
Townsend Score 1	Scale	0.841	0.81 - 0.872	0
Townsend Score 2	Scale	0.917	0.885 - 0.95	0
Townsend Score 4	Scale	1.061	1.024-1.101	0.0012
Townsend Score 5	Scale	1.181	1.134-1.231	0
Atrial fibrillation - Present	Scale	0.736	0.683-0.794	0
Heart failure - Present	Scale	1.145	1.097-1.195	0
Treated hypercholesterolemia	Scale	0.908	0.878-0.939	0
Untreated hypercholesterolemia	Scale	1.222	1.154-1.293	0
Treated Hypertension	Scale	0.744	0.707-0.783	0
Untreated Hypertension	Scale	1.411	1.335-1.491	0
Myocardial infarction - Present	Scale	1.322	1.264-1.382	0
Peripheral vascular disease - Present	Scale	1.052	1.017-1.089	0.0034
Body Mass Index – Overweight (25<=BMI<30)	Scale	0.998	0.953-1.046	0.9357
Body Mass Index - Obese (BMI>30)	Scale	1.168	1.109-1.23	0
Interaction of Cases and Myocardial infarction	Scale	0.749	0.699-0.803	0

Interaction of Cases and Former Smoker	Scale	0.759	0.711-0.809	0
Interaction of Cases and Current Smoker	Scale	0.423	0.394-0.454	0
Interaction of Former Smoker and BMI Overweight	Scale	0.881	0.82 - 0.947	7.00E-04
Interaction of Current Smoker and BMI Overweight	Scale	0.83	0.777-0.885	0
Interaction of Former Smoker and BMI Obese	Scale	0.849	0.784-0.918	1.00E-04
Interaction of Current Smoker and BMI Obese	Scale	0.832	0.771-0.898	0
Variance (sigma2)		0.15	0.13 - 0.172	0

Baseline is born in 1930-1939, absence of atrial fibrillation, absence of hypertension, Female group, non-smoker, Townsend deprivation score 3, absence of heart failure, absence of hypercholesterolemia, absence of hypertension, absence of myocardial infarction, absence of peripheral vascular disease, Normal Body Mass Index (BMI<25)

3. Hormone replacement therapy results mylongevity_double_cox_method2. Weibull distribution is used for baseline hazards.

Definition of parameter	Parameter	Estimates	Lower bound	Upper bound
a	Scale	79.896	71.27	89.566
b	Shape	3.256	3.026	3.504
Born in 1931 - 1940	Shape	0.884	0.817	0.957
Born in 1941 - 1950	Shape	0.79	0.729	0.857
Born in 1951 - 1960	Shape	0.713	0.644	0.79
Age as continuous	Scale	1.107	1.099	1.116
Born in 1931 - 1940	Scale	0.569	0.415	0.78
Born in 1941 - 1950	Scale	0.38	0.282	0.514
Born in 1951 - 1960	Scale	0.266	0.178	0.397
Oestrogen + progesterone	Scale	0.932	0.883	0.985
Oestrogen	Scale	1.077	0.955	1.214
Townsend 4 - 5	Scale	1.462	1.377	1.553
Townsend 3	Scale	1.222	1.144	1.305
Hypertension Present	Scale	1.453	1.379	1.53
Coronary heart disease	Scale	1.605	1.433	1.797
Removed uterus and ovaries	Scale	0.767	0.681	0.864
Removed ovaries without hysterectomy	Scale	0.872	0.8	0.95
Interaction of BMI Overweight & Current Smoker	Scale	2.129	1.992	2.275
Interaction of BMI Overweight & Ex-Smoker	Scale	1.425	1.305	1.557
Interaction of BMI Obese & Current Smoker	Scale	2.198	2.034	2.375
Interaction of BMI Obese & Ex-smoker	Scale	1.636	1.49	1.796
Interaction of BMI Obese & Non-smoker	Scale	1.31	1.213	1.415
Interaction of Type 2 diabetes & Current Smoker	Scale	1.442	1.353	1.536
Interaction of Type 2 diabetes & Ex-Smoker	Scale	1.078	0.995	1.168
Interaction of Type 2 diabetes & Current Smoker	Scale	3.282	2.845	3.786
Interaction of Type 2 diabetes & Ex-Smoker	Scale	2.146	1.785	2.579
Interaction of Type 2 diabetes & Non-Smoker	Scale	3.104	2.722	3.538
Variance (sigma2)		0.098	0.076	0.127

Baseline is born in 1921-1930, no hormone replacement therapy, deprivation 1-2 classed as Low, absence of hypertension, absence of coronary heart disease, presence of both uterus and ovaries

4. Ischemic stroke results mylongevity_double_cox_method3. Weibull distribution is used for baseline hazards.

Definition of parameter	Parameter	Estimates	Lower	Upper	p-value
a	Scale	338.339	266.075	430.23	0
b	Shape	2.254	2.157	2.355	0
Born in 1921-1930	Shape	0.903	0.86	0.949	0
Born in 1931-1940	Shape	0.885	0.837	0.935	0
Born in 1941-1960	Shape	0.782	0.723	0.845	0
Antiplatelet drugs	Shape	0.866	0.835	0.898	0
Born in 1921-1930	Scale	0.476	0.341	0.664	0
Born in 1931-1940	Scale	0.351	0.242	0.509	0
Born in 1941-1960	Scale	0.162	0.1	0.262	0
IMD Quintile 2	Scale	0.951	0.871	1.037	0.253
IMD Quintile 3	Scale	0.96	0.879	1.047	0.3549
IMD Quintile 4	Scale	0.825	0.754	0.903	0
IMD Quintile 5	Scale	0.827	0.752	0.909	1.00E-04
BMI (Overweight + Obese)	Scale	0.797	0.756	0.84	0
Antiplatelet drugs	Scale	0.409	0.318	0.528	0
Chronic obstructive pulmonary disease	Scale	1.884	1.715	2.07	0
Heart failure Present	Scale	1.639	1.489	1.803	0
Myocardial infarction Present	Scale	1.238	1.14	1.344	0
Peripheral Artery Disease/Peripheral Vascular Disease	Scale	1.14	1.073	1.212	0
Current smoker	Scale	1.941	1.8	2.093	0
Ex-smoker	Scale	1.27	1.198	1.345	0
Anticoagulant agents Present	Scale	1.313	1.198	1.439	0
Treated Diabetes	Scale	1.78	1.655	1.914	0
Untreated Diabetes	Scale	1.329	1.169	1.511	0
Gender - Males	Scale	1.343	1.272	1.417	0
Cases group	Scale	2.345	2.14	2.569	0
Antihypertensive drugs	Scale	1.483	1.374	1.601	0
Age as continuous	Scale	1.084	1.078	1.09	0
Interaction of cases& antihypertensive drugs	Scale	0.803	0.72	0.896	1.00E-04
Variance (Sigma2)		0.059	0.042	0.083	0

5. Transient ischemic stroke results mylongevity_double_cox_method4. Weibull distribution is used for baseline hazards.

Definition of parameter	Parameter	Estimates	CI	P-values
a	Scale	225.137	179.407 - 282.524	0
b	Shape	2.412	2.313 - 2.514	0
Born in 1921-1930	Shape	0.934	0.891 - 0.979	0.0044
Born in 1931-1940	Shape	0.864	0.817 - 0.914	0
Born in 1941-1960	Shape	0.772	0.703 - 0.848	0
Heart-failure - Present	Shape	0.936	0.92 - 0.952	0
Antiplatelet therapy	Shape	0.894	0.861 - 0.928	0
Born in 1921-1930	Scale	0.524	0.389 - 0.705	0
Born in 1931-1940	Scale	0.274	0.197 - 0.382	0
Born in 1941-1960	Scale	0.12	0.072 - 0.201	0
Females	Scale	0.673	0.637 - 0.712	0
IMD Quintile 2	Scale	0.852	0.778 - 0.932	5.00E-04
IMD Quintile 3	Scale	0.833	0.762 - 0.911	1.00E-04
IMD Quintile 4	Scale	0.755	0.689 - 0.827	0
IMD Quintile 5	Scale	0.719	0.652 - 0.793	0
BMI (Overweight & Obese)	Scale	0.825	0.782 - 0.87	0
Asthma - Present	Scale	1.241	1.139 - 1.353	0
Chronic obstructive pulmonary disease	Scale	1.696	1.516 - 1.898	0
Chronic Kidney Disease	Scale	1.183	0.997 - 1.405	0.0545
Myocardial infarction	Scale	1.311	1.203 - 1.429	0
Peripheral Artery Disease/Vascular Disease	Scale	1.201	1.127 - 1.279	0
Current smoker	Scale	1.995	1.85 - 2.151	0
Ex-smoker	Scale	1.3	1.224 - 1.381	0
Alcohol intake - Yes	Scale	0.902	0.85 - 0.958	7.00E-04
Atrial fibrillation - Present	Scale	1.213	1.089 - 1.352	4.00E-04
Treated Diabetes	Scale	1.777	1.634 - 1.932	0
Untreated Diabetes	Scale	1.269	1.094 - 1.472	0.0016
Anticoagulant agents	Scale	1.395	1.244 - 1.564	0
Cases-group	Scale	1.641	1.515 - 1.777	0
Antihypertensive agents	Scale	1.328	1.25 - 1.41	0
Antiplatelet therapy	Scale	0.561	0.439 - 0.718	0
Age as continuous	Scale	1.085	1.078 - 1.092	0
Interaction of cases & Antiplatelet Therapy	Scale	0.803	0.712 - 0.905	3.00E-04
Variance (sigma2)		0.066	0.046 - 0.093	0