Package 'SimRVPedigree'

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Type Package

Title Simulate Pedigrees Ascertained for a Rare Disease

Version 0.4.4

Description Routines to simulate and manipulate pedigrees ascertained to
contain multiple family members affected by a rare disease.
Christina Nieuwoudt, Samantha J Jones, Angela Brooks-Wilson,
and Jinko Graham (2018) <doi:10.1101/234153>.

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Author Christina Nieuwoudt [aut, cre],
Jinko Graham [aut]

Maintainer Christina Nieuwoudt <cnieuwou@sfu.ca>

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AgeSpecific_Hazards   *Age-specific hazard rate dataset*

Description

A dataset that contains age-specific hazard rates to **roughly mimic**: (1) the age-specific hazard rates for lymphoid cancer in the United States, (2) the age-specific hazard rates for death in the United States, and (3) the age-specific hazard rates for death for individuals, living in the United States, who have been diagnosed with a lymphoid cancer.

Usage

```
data(AgeSpecific_Hazards)
```

Format

A data frame with 100 rows and 3 variables:

pop_onset_hazard The age-specific population hazard rate for lymphoid cancer

unaffected_death_hazard The age-specific hazard rate for death in the **unaffected** population

affected_death_hazard The age-specific hazard rate for death in the **affected** population

Details

The AgeSpecific_Hazards dataset contains age-specific hazard rates which **roughly mimic**: (1) the age-specific hazard rates for lymphoid cancer onset in the United States, (2) the age-specific hazard rates for death in the United States, and (3) the age-specific hazard rates for death for individuals, living in the United States, who have been diagnosed with a lymphoid cancer. The age-specific hazard rates of lymphoid cancer onset and death in the affected population may be estimated by a program such as the Surveillance, Epidemiology, and End Results Program (SEER), and the age-specific hazard rates of death in the United States may be estimated from actuarial life tables provided by the Social Security Administration.

The three columns in the `AgeSpecific_Hazards` dataset provide age-specific hazard rates, in yearly increments, beginning at age 0 and ending with age 100. That is, the values in the first row describe the hazard rates for an individual whose age is contained in the interval [0, 1), while the values in the second row describe the hazard rates for an individual whose age is contained in the interval [1, 2), and so on.

References

The Surveillance, Epidemiology, and End Results (SEER) Program. https://seer.cancer.gov/

Bell, F. C., Miller, M. L. (2005). *Life Tables for the United States Social Security Area, 1900-2100*. Baltimore, Md.: Social Security Administration, Office of the Chief Actuary.

---

censor_ped	*Censor pedigree data*

Description

`censor_ped` censors a pedigree of any information that occurs after a specified year.

Usage

```
censor_ped(ped_file, censor_year = NULL)
```

Arguments

ped_file	An object of class ped. A pedigree generated by `sim_ped` or `sim_RVped`, or an object created by the function `new.ped`. See details.
censor_year	Numeric. The censor year. If not supplied, defaults to the year the pedigree was ascertained, i.e. the proband's onset year. See details.

Details

Upon supplying a pedigree and a censor year the `censor_ped` function will remove all individuals born after `censor_year` and censor all disease onset and death events after the `censor_year`.

Users who wish to use `censor_ped` for pedigrees not generated by `sim_ped` or `sim_RVped` must use `new.ped` to create an object of class ped. When creating the ped object please provide as much relevant date information as possible, i.e. years of birth, onset, and death. When present please specify a proband as described in `new.ped`.

By default, `censor_year` is set to the year that the pedigree is ascertained, i.e. the year the proband experienced disease onset. However, if `ped_file` does not contain the proband identification variable the user must supply a value for `censor_year`.

Value

The censored pedigree.

See Also

[new.ped](new.ped)

Examples

```
#Read in age-specific harard data and create hazard object.
data(AgeSpecific_Hazards)
haz_obj <- hazard(hazardDF = AgeSpecific_Hazards)

#Simulate a pedigree ascertained for multiple affecteds
set.seed(3)
RVped2015 <- sim_RVped(hazard_rates = haz_obj,
                       num_affected = 2,
                       ascertain_span = c(1900, 2015),
                       GRR = 30, carrier_prob = 0.002,
                       RVfounder = TRUE,
                       stop_year = 2015,
                       recall_probs = c(1),
                       founder_byears = c(1900, 1905),
                       FamID = 1)[[2]]

# Plot the 2015 pedigree
plot(RVped2015)
mtext(side = 3, line = 2, "Reference Year: 2015")

# Censor RVped2015 after 1960
RVped1960 <- censor_ped(ped_file = RVped2015, censor_year = 1960)

# Plot the 1960 pedigree
plot(RVped1960)
mtext(side = 3, line = 2, "Reference Year: 1960")
```

EgPeds   *Example pedigrees*

Description

A dataset containing five example pedigrees.

Usage

```
data(EgPeds)
```

Format

A data frame with 65 rows and 14 variables:

FamID Family identification number

ID Individual identification number

sex Gender identification variable: sex = 0 for males, and sex = 1 females.

dadID Identification number of father

momID Identification number of mother

affected Affection status: affected = TRUE if individual has developed lymphoid cancer, and FALSE otherwise.

DA1 Paternally inherited allele at the assumed disease locus: DA1 = 1 if rare variant is present, and 0 otherwise.

DA2 Maternally inherited allele at the assumed disease locus: DA2 = 1 if rare variant is present, and 0 otherwise.

birthYr Year of birth

onsetYr Year of disease onset, when applicable.

deathYr Year of death, when applicable.

RR The subject's relative-risk of disease

available Availability status, available = TRUE if the individual is unavailable, and FALSE 1 otherwise

Gen The subject's generation number relative to the founder who introduced the rare variant. That is, the founder who introduced the rare variant will have Gen = 1, his or her offspring will have Gen = 2, etc.

proband Proband identification variable, proband = TRUE if the individual is the proband, and FALSE otherwise.

---

find_mrca *Find the most recent common ancestor of two pedigree members*

Description

Find the most recent common ancestor of two pedigree members

Usage

```
find_mrca(ped, ID1, ID2)
```

Arguments

ped	A ped object
ID1	The ID of the first relative
ID2	The ID of the second relative

Value

The ID of the common ancestor

Examples

```
library(SimRVPedigree)
data(AgeSpecific_Hazards)


set.seed(5)
ex_ped <- sim_ped(hazard_rates = hazard(hazardDF = AgeSpecific_Hazards),
                  GRR = 10, FamID = 1,
                  founder_byears = c(1800, 1900),
                  stop_year = 2020)

plot(ex_ped)

# Find most recent common ancestor of individuals with IDs 19 and 21
find_mrca(ped = ex_ped, ID1 = 19, ID2 = 21)

# Note that someone can be their own most recent common ancestor.
# In the following example, since the individual with ID 8 is the grandmother
# of the individual with ID 21, the find_mrca function returns 8.
find_mrca(ped = ex_ped, ID1 = 8, ID2 = 21)

# For unrelated individuals, the find_mcra function returns NA
find_mrca(ped = ex_ped, ID1 = 8, ID2 = 15)
find_mrca(ped = ex_ped, ID1 = 5, ID2 = 4)
```

---

hazard   *Create an object of class hazard.*

Description

Create a hazard object, required input for [sim_RVped](#), [sim_ped](#), and [sim_life](#) functions.

Usage

```
hazard(hazardDF, partition = NULL, subtype_ID = NULL)
```

Arguments

hazardDF	Data.frame. A data.frame contianing the age-specific hazard rate(s) of *disease* in the population of interest, the age-specific hazard rate for *death* in the **unaffected** population, and the age-specific hazard rate for *death* in the **affected** population. See details.
partition	Numeric vector. The partition of ages, in years, over which to apply the age-specific hazard rates in hazardDF. If not supplied, defaults to a partition that starts at 0 and increases in yearly increments. See details.
subtype_ID	List. If specifying a disease with multiple subtypes, a list of character subtype IDs. By default, subtype_ID = NULL, i.e. no subtypes to simulate.

Details

Users are permitted to specify harzard objects for two scenarios: (1) for a disease without subtypes or (2) for a disease with multiple subtypes.

When simulating a disease *without subtypes*, hazardDF must contain 3 columns that meet the following criteria:

column 1: age-specific hazard rates of *disease* for the population of interest

column 2: age-specific hazard rates of *death* for the **unaffected** population. If the disease of interest is sufficiently rare, so that death by the disease is rare, the user may choose to use the population, age-specific, hazard rates of death instead.

column 3: age-specific hazard rates of *death* for the **affected** population.

When simulating a disease *with n disease subtypes*, hazardDF must contain n + 2 columns that meet the following criteria:

column 1: age-specific hazard rates of *disease* for the first subtype of interest

column 2: age-specific hazard rates of *disease* for the second subtype of interest

...

column n: age-specific hazard rates of *disease* for the nth subtype of interest

column n + 1: age-specific hazard rates of *death* for the **unaffected** population. If the disease of interest is sufficiently rare, so that death by the disease is rare, the user may choose to use the population, age-specific, hazard rates of death instead.

column n + 2: age-specific hazard rates of *death* for an individual affectd by any of the n subtypes.

Users must provide partition in years; e.g. a hazard rate for a baby between 6 months and 1 year of age should have lower bound 0.5 years and an upper bound 1 year. Additionally, partition must apply to all of the age-specific hazard rates in hazardDF.

Value

An object of class hazard.

Examples

```
# Specifying the hazard rates for a disease
# with only one subtype (or grouped subtypes).
data(AgeSpecific_Hazards)

head(AgeSpecific_Hazards)
nrow(AgeSpecific_Hazards)

my_HR <- hazard(hazardDF = AgeSpecific_Hazards)
class(my_HR)
head(my_HR[[1]])

#NOTE: since partition was not supplied, the partition has been assummed to
# start at 0 and increase in yearly increments.
my_HR[[2]]
```

```
my_HR


# Specifying the hazard rates for a with teo disease subtypes
data(SubtypeHazards)

head(SubtypeHazards)
nrow(SubtypeHazards)

my_SHR <- hazard(hazardDF = SubtypeHazards,
                 subtype_ID = c("Hodgkin Lymphoma", "Non-Hodgkin Lymphoma"))
class(my_SHR)
head(my_SHR[[1]])
my_SHR
```

---

new.ped   *Create an object of class ped.*

Description

Create an object of class ped, from a data.frame, required input for reassign_gen, censor_ped, and trim_ped functions.

Usage

```
new.ped(ped_file)
```

Arguments

ped_file   Data.frame. A pedigree, see details.

Details

The data frame supplied to new.ped, ped_file, *must* contain the following variables:

name	type	description
FamID	numeric	family identification number
ID	numeric	individual identification number
dadID	numeric	identification number of father
momID	numeric	identification number of mother
sex	numeric	gender identification; if male sex = 0, if female sex = 1
affected	logical	disease-affection status:
		affected = TRUE if affected by disease, and FALSE otherwise,

Optionally, `ped_file` *may* contain any of the following variables:

name	type	description
available	logical	availibility status;
		`available` = TRUE if available, and FALSE otherwise.
DA1	numeric	paternally inherited allele at the assumed disease locus:
		DA1 = 1 if rare variant is present, and 0 otherwise
DA2	numeric	maternally inherited allele at the assumed disease locus:
		DA2 = 1 if rare variant is present, and 0 otherwise
birthYr	numeric	the individual's birth year
onsetYr	numeric	the individual's year of disease onset, when applicable, otherwise NA
deathYr	numeric	the individual's year of death, when applicable, otherwise NA
RR	numeric	the individual's relative-risk of disease
Gen	numeric	the individual's generation number relative to the eldest founder.
		For the eldest founder Gen = 1, for his or her offspring Gen = 2, etc.
proband	logical	proband identifier:
		`proband` = TRUE if individual is the proband, and FALSE otherwise.
subtype	character	the individual's disease subtype, when applicable, otherwise NA

We note that some of the optional fields above may be required for various ped functions

Value

An object of class ped.

Examples

```
data(EgPeds)
head(EgPeds)

ped1 = new.ped(EgPeds[EgPeds$FamID == 1, ])
head(ped1, n = 3)
class(ped1)
summary(ped1)

AllPeds = new.ped(EgPeds)
head(AllPeds)
class(AllPeds)
summary(AllPeds)
```

---

ped2pedigree   *Create a kinship2 pedigree structure from an object of class ped*

Description

Create a kinship2 pedigree structure from an object of class ped

Usage

```
ped2pedigree(x)
```

Arguments

x   A ped object.

Value

A pedigree object. See [pedigree](#) for details.

References

Terry M Therneau and Jason Sinnwell (2015). **kinship2: Pedigree Functions.** *R package version 1.6.4.* https://CRAN.R-project.org/package=kinship2

---

plot.ped	*Plot pedigree*

Description

Plot pedigree

Usage

```
## S3 method for class 'ped'
plot(x, ref_year = NULL, gen_lab = FALSE,
  plot_legend = TRUE, location = "topleft", radius = 0.2,
  density = c(-1, 35, 55), angle = c(90, 65, 40), gen_stretch = 2,
  cex = 1, adj = 1, line = 2, mar = c(5.1, 4.1, 4.1, 2.1), ...)
```

Arguments

x   An object of class ped.

ref_year   When provided, the reference year for age labels. Users may supply a (numeric)
                    year which will create age labels at the specified year. Alternatively, users may
                    set ref_year = "ascYR", which will create age lables for the year the pedigree
                    was ascertained, when ascertained. By default, ref_year = NULL and no age
                    labels are created.

gen_lab   Logical. Should generation labels be printed in the margin. By default, FALSE.

plot_legend   Logical. Should legend for symbol shading be plotted. By default, TRUE.

location   The location for the pedigree legend, as in [pedigree.legend](#). Options in-
                    clude: "topleft", "topright", "bottomright", or "bottomleft". By de-
                    fault, location = "topleft".

radius   The radius size for the pedigree legend, as in [pedigree.legend](#). By default,
                    radius = 0.2.

density	The density of shading in plotted symbols, as in `plot.pedigree`. By default, `density = c(-1,35,55)`.
angle	The angle of shading in plotted symbols, as in `plot.pedigree`. By default, `angle = c(90,65,40)`.
gen_stretch	Numeric. Used to stretch the spacing between generation lables. By default, `gen_stretch = 2`. Increase for more space between labels, decrease for less space.
cex	The text size. By default, `cex = 1`.
adj	When `ref_year` is supplied, used to adjust position of reference year, as in `mtext`. By default, `adj = 1`.
line	When `ref_year` is supplied, used to adjust position of reference year, as in `mtext`. By default, `line = 2`.
mar	The sizes for plot margins, as in `par`.
...	Extra options that feed to `plot.pedigree`, or `plot`.

References

Terry M Therneau and Jason Sinnwell (2015). **kinship2: Pedigree Functions.** *R package version 1.6.4.* https://CRAN.R-project.org/package=kinship2

See Also

`plot.pedigree`, `pedigree.legend`, `plot`, `par`

Examples

```
#Read in age-specific harard data and create hazard object.
data(AgeSpecific_Hazards)
haz_obj <- hazard(hazardDF = AgeSpecific_Hazards)

#Simulate a pedigree ascertained for multiple affecteds
set.seed(2)
RVped2015 <- sim_RVped(hazard_rates = haz_obj,
                       num_affected = 2,
                       ascertain_span = c(1900, 2015),
                       GRR = 30, carrier_prob = 0.002,
                       RVfounder = TRUE,
                       stop_year = 2015,
                       recall_probs = c(1),
                       founder_byears = c(1900, 1905),
                       FamID = 1)[[2]]


summary(RVped2015)

#plot pedigree without age labels
plot(RVped2015)

#plot pedigree with age labels, set the
#reference year to be the ascertainment year
```

```
plot(RVped2015, ref_year = "ascYr")

#plot pedigree with age lablels at specified reference years.
plot(RVped2015, ref_year = 2015, cex = 0.75, symbolsize = 0.95)
plot(RVped2015, ref_year = 2005, cex= 0.75, symbolsize = 1.25)
plot(RVped2015, ref_year = 1995, cex= 0.75, symbolsize = 1.25)
plot(RVped2015, ref_year = 1985, cex= 0.75, symbolsize = 1.25)

# plot pedigree generation labels
plot(RVped2015, ref_year = 2015,
     gen_lab = TRUE,
     cex = 0.75, symbolsize = 0.95)

# use gen_stretch to place extra space between generation labels
# NOTE: by default, gen_stretch = 2; increase for extra space.
plot(RVped2015, ref_year = 2015,
     gen_lab = TRUE, gen_stretch = 3,
     cex = 0.75, symbolsize = 0.95)
```

---

reassign_gen   *Reassign generation number based on affected status*

Description

The `reassign_gen` function assigns generation numbers among affected family members so that
generation 1 represents the most recent generation that a putative disease variant shared identical by
descent (IBD), as defined in Thompson (2000), by affected members could have been introduced
into the pedigree.

Usage

```
reassign_gen(ped_file)
```

Arguments

ped_file   An object of class ped. A pedigree generated by `sim_ped` or `sim_RVped`, or an
                  object created by the function `new.ped`. See details.

Details

`reassign_gen` *cannot be applied to pedigrees that contain loops or inbreeding.*

The `reassign_gen` function accepts a pedigree and reassigns generation numbers among disease-
affected relatives so that generation 1 represents the generation of the most recent common ancestor
of all disease-affected relatives. We note that the individual in generation 1 could themselves be
disease-affected, i.e. an individual can be considered their own ancestor.

For example, consider a family with 2 affected members. If the disease-affected relatives are a par-
ent and a child, the affected parent would be assigned generation 1, and the affected child generation

2. However, if the disease-affected relatives are a pair of siblings, each is be assigned generation 2 since a common parent of the two is assumed to be a carrier of a latent susceptibility variant. Similarly, if the disease-affected relatives are a pair of cousins, is assigned generation 3, since a common grandparent is the most recent common ancestor from whom they could have inherited a shared variant associated with the disease.

Users who wish to assign generation number based on affection status in pedigrees that have not been simulated with the SimRVpedigree package must create a ped object using `new.ped`.

Value

A ped object containing only affected members, obligate carriers, and founders with generation numbers reassigned among disease-affected relatives based on their most recent common ancestor, as described in details.

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018). *Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives.* Source Code for Biology and Medicine, 13:2.

Thompson, E. (2000). *Statistical Inference from Genetic Data on Pedigrees.* NSF-CBMS Regional Conference Series in Probability and Statistics, 6, I-169.

See Also

`new.ped`

Examples

```
# Read in example pedigrees
data(EgPeds)
class(EgPeds)

# Create ped object
Bpeds <- new.ped(EgPeds)
summary(Bpeds)

# Reassign generation numbers in the first four pedigrees in EgPeds
Apeds <- lapply(seq_len(5), function(x){
                reassign_gen(Bpeds[Bpeds$FamID == x, ])})
Apeds <- do.call(rbind, Apeds)

# Compare pedigrees before and after reassigning
# generation number based on affected status
par(mfrow = c(1, 2))
for (k in 1:5) {
  plot(subset(Bpeds, FamID == k), gen_lab = TRUE, plot_legend = FALSE)
  mtext(paste0("Ped", k, ": before generation reassignment", sep = ""),
        side = 3, line = 1.5)

  plot(subset(Apeds, FamID == k), gen_lab = TRUE, plot_legend = FALSE)
  mtext(paste0("Ped", k, ": after generation reassignment", sep = ""),
```

```
        side = 3, line = 1.5)
}
par(mfrow = c(1, 1))
```

SimRVPedigree   *Simulate pedigrees ascertained for disease status*

Description

The `SimRVPedigree` package provides methods to simulate and manipulate pedigrees ascertained
to contain multiple relatives affected by a rare disease.

Details

Family-based studies to identify genetic susceptibility factors associated with rare diseases are re-
gaining traction. The resurgence in popularity is due to the fact that family-based studies have
more power to detect rare variants, require smaller sample sizes, and can more accurately detect
sequencing errors than case-control studies, Wijsman (2012). However, identifying a suitable num-
ber of families for analysis can require years of continued collaboration between researchers and
clinicians. As a result, collecting new data to replicate findings or evaluate methodology is im-
practical. The `SimRVPedigree` package aims to address this problem by providing a platform to
randomly simulate families ascertained to contain multiple relatives affected by a rare disease. The
distinguishing feature of the `SimRVPedigree` package is that it aims to mimic the process of family
development, while allowing users to incorporate multiple facets of family ascertainment.

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018).
Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives. Source Code for Biol-
ogy and Medicine, 13:2.

Ellen M. Wijsman (2012). *The role of large pedigrees in an era of high-throughput sequencing.*
Human Genetetics, 131, 1555-1563

---

sim_life   *Simulate all life events*

Description

Primarily intended as an internal function, `sim_life` simulates all life events for an individual
starting at birth, age 0, and ending with death or the end of the study.

Usage

```
sim_life(hazard_rates, GRR, carrier_prob, RV_status, YOB, stop_year,
  NB_params = c(2, 4/7), fert = 1)
```

Arguments

hazard_rates   An object of class hazard, created by [hazard](#).

GRR   Numeric. The genetic relative-risk of disease, i.e. the relative-risk of disease for individuals who carry at least one copy of the causal variant. Note: When simulating diseases with multiple subtypes GRR must contain one entry for each simulated subtype. See details.

carrier_prob   Numeric. The carrier probability for all causal variants with relative-risk of disease GRR. By default, carrier_prob = 0.002

RV_status   Numeric. RV_status = TRUE if the individual is a carrier of a rare variant that increases disease suseptibility, and FALSE otherwise.

YOB   A positive number. The indivdiual's year of birth.

stop_year   Numeric. The last year of study. If not supplied, defaults to the current year.

NB_params   Numeric vector of length 2. The size and probability parameters of the negative binomial distribution used to model the number of children per household. By default, NB_params = c(2,4/7), due to the investigation of Kojima and Kelleher (1962).

fert   Numeric. A constant used to rescale the fertility rate after disease-onset. By default, fert = 1.

Details

Starting at birth, age 0, sim_life generates waiting times to reproduction, onset, and death. The event with the shortest waiting time is chosen as the next life event, and the individual's age is updated by the waiting time of the winning event. Conditioned on the individual's new age, this process is applied recursively, until death or until the end of the study is reached.

We make the following assumptions regarding the simulation of waiting times:

1. We assume that, given an individual's current age, their time to disease onset is the waiting time in a non-homogeneous Poisson process with an age-specific hazard rate that follows a proportional hazards model. In this model, individuals who have NOT inherited the rare variant experience disease onset according to the baseline (or population) hazard rate of disease. On the other hand, individuals who have inherited the rare variant are assumed to have an increased risk of disease onset relative to those who have inherited it. The user is expected to supply the baseline hazard rate of disease, as well as the relative-risk of disease for genetic cases. Additionally, we impose the restriction that individuals may only experience disease onset once, and remain affected from that point on.

2. We assume that, given an individual's current age, their time to death is the waiting time in a non-homogeneous Poisson process with age-specific hazard rate determined by their affection status. We assume that disease-affected individuals experience death according to the age-specific hazard rate for death in the *affected* population. On the other hand, we assume that *unaffected* individuals experience death according to the age-specific hazard rate for death in the *unaffected* population. If the disease of interest is sufficiently rare, the user may choose to substitute the *population* age-specific hazard rate for death for the aforementioned age-specific hazard rate for death in the *unaffected* population. The user is expected to supply age-specific hazard rates of death for both the *affected* and *unaffected* populations.

3. We assume that, given an individual's current age, their time to reproduction is the waiting time in a homogeneous Poisson process. That is, we assume that individuals reproduce at uniform rate during their reproductive years. For example, one's reproductive years may span from age 20 to age 35 years. To mimic observed age-specific fertility data, the birth range for an individual is simulated as follows: first we sample the lower bound uniformly from ages 16 to 27, next we sample the range of the birth span uniformly from 10 to 18 years and add this value to the lower bound to determine the upper bound of the birth range. We do not allow for offspring to be produced outside of an individual's simulated reproductive birth span.

The events simulated by `sim_life` are labelled as follows:

- "Start" the individual's year of birth.
- "Child" a reproductive event, i.e. creation of offspring
- "Onset" disease onset event,
- "Death" death event

Value

an object of class `event`. An object of class `event` is a list that contains the following items.

life_events	A named numeric vector of life events, see details.
repro_events	A vector of reproduction years, that is the year(s) that the individual produces offspring. When the individual does not reproduce `repro_events = NULL`.
onset_event	Numeric. When applicable the year of disease-onset. When onset does not occur `onset_event = NA`
death_event	Numeric. When applicable the year of death. When death is censored `death_event = NA`
subtype	Character. When applicable, the disease subtype.
censor_year	Numeric. When applicable the last year that data was observed. Note: after death `censor_year = NA`

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018). *Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives*. Source Code for Biology and Medicine, 13:2.

Ken-Ichi Kojima, Therese M. Kelleher. (1962), *Survival of Mutant Genes*. The American Naturalist 96, 329-346.

Examples

```
data(AgeSpecific_Hazards)
my_HR <- hazard(hazardDF = AgeSpecific_Hazards)

# The following commands simulate all life events for an individual who
# has NOT inherited a causal variant, born in 1900.  From the output, this
# individual has two children, one in 1921 and another in 1923, and then
# dies in 1987.
```

```
set.seed(135)
sim_life(hazard_rates = my_HR, GRR = 10,
         carrier_prob = 0.002,
         RV_status = FALSE,
         YOB = 1900, stop_year = 2000)

# Using the same random seed, notice how life events can vary for
# someone who has inherited the causal variant, which carries a
# relative-risk of 10. From the output, this individual also has
# two children, but then experiences disease onset in 1974,
# and dies in 1976.
set.seed(135)
sim_life(hazard_rates = my_HR, GRR = 10,
              carrier_prob = 0.002,
              RV_status = TRUE,
              YOB = 1900, stop_year = 2000)

# The following commands simulate life events for an individual who
# has inherited a causal rare variant, with relative risk 100 for
# the subtype "HL" and no increased relative risk for the subtype"NHL".
set.seed(1)
sim_life(hazard_rates = hazard(SubtypeHazards,
                                 subtype_ID = c("HL", "NHL")),
         GRR = c(100, 1),
         carrier_prob = 0.002,
         RV_status = TRUE,
         YOB = 1900, stop_year = 2000)
```

---

sim_ped   *Simulate a pedigree*

Description

Please note the distinction between sim_ped and sim_RVped. Pedigrees simulated using sim_ped
do not account for study design. To simulate a pedigree ascertained to contain multiple family
members affected by a disease please use sim_RVped.

Usage

```
sim_ped(hazard_rates, GRR, FamID, founder_byears, stop_year = NULL,
  carrier_prob = 0.002, RVfounder = FALSE, NB_params = c(2, 4/7),
  fert = 1)
```

Arguments

hazard_rates   An object of class hazard, created by hazard.

GRR   Numeric. The genetic relative-risk of disease, i.e. the relative-risk of disease
                    for individuals who carry at least one copy of the causal variant. Note: When
                    simulating diseases with multiple subtypes GRR must contain one entry for each
                    simulated subtype. See details.

FamID   Numeric. The family ID to assign to the simulated pedigree.

founder_byears   Numeric vector of length 2. The span of years from which to simulate, uni-
                    formly, the birth year for the founder who introduced the rare variant to the
                    pedigree.

stop_year   Numeric. The last year of study. If not supplied, defaults to the current year.

carrier_prob   Numeric. The carrier probability for all causal variants with relative-risk of
                    disease GRR. By default, carrier_prob = 0.002

RVfounder   Logical. Indicates if all pedigrees segregate the rare, causal variant. By default,
                    RVfounder = FALSE See details.

NB_params   Numeric vector of length 2. The size and probability parameters of the negative
                    binomial distribution used to model the number of children per household. By
                    default, NB_params = c(2,4/7), due to the investigation of Kojima and Kelleher
                    (1962).

fert   Numeric. A constant used to rescale the fertility rate after disease-onset. By
                    default, fert = 1.

Details

To introduce the rare variant to the pedigree, We allow users to choose from one of the following
two assumptions:

1. Assume that the variant is rare enough that a single copy has been introduced by one founder,
   and begin the simulation of the pedigree with this founder, as in Bureau (2014).

2. Simulate the starting founder's rare-variant status with probability equal to the carrier proba-
   bility of the rare variant in the population. We note that under this setting pedigrees may not
   segregate the rare variant.

The sim_ped function starts simulating the pedigree by generating the birth year for the starting
founder, uniformly between the years specified by founder_byears. Next, all life events are sim-
ulated for the founder via [sim_life](#). Possible life events include: reproduction, disease onset, and
death. We only allow disease onset to occur once, i.e. no remission. Computationally, this implies
that after disease onset, the waiting time to death is always simulated using the age-specific mortal-
ity rates for the *affected* population. Life events for individuals who have inherited the rare variant
are simulated such that their relative-risk of disease is GRR, according to a proportional hazards
model. The relative-risk of disease onset for individuals who have not inherited the causal variant
is assumed to be 1. Any life events that occur after stop_year are censored.

When segregating in the pedigree, the rare variant is transmitted from parent to offspring accord-
ing to Mendel's laws. The process of simulating life events is repeated for any offspring that are
produced before stop_year.

Value

The simulated pedigree.

See Also

sim_RVped, sim_life

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018). *Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives*. Source Code for Biology and Medicine, 13:2.

Ken-Ichi Kojima, Therese M. Kelleher. (1962), *Survival of Mutant Genes*. The American Naturalist 96, 329-346.

Alexandre Bureau, Samuel G. Younkin, Margaret M. Parker, Joan E. Bailey-Wilson, Mary L. Marazita, Jeffrey C. Murray, Elisabeth Mangold, Hasan Albacha-Hejazi, Terri H. Beaty, and Ingo Ruczinski (2014). *Inferring rare disease risk variants based on exact probabilities of sharing by multiple affected relatives.* Bioinformatics; Vol. 30, No. 15, pp. 2189-2196.

Examples

```
data(AgeSpecific_Hazards)

# Simulate a random pedigree
set.seed(5)
ex_ped <- sim_ped(hazard_rates = hazard(hazardDF = AgeSpecific_Hazards),
                  GRR = 10,
                  FamID = 1,
                  founder_byears = c(1900, 1910),
                  stop_year = 2015)

# View the simulated pedigree
ex_ped

# Plot the pedigree
plot(ex_ped, location = "topleft")

# Plot the pedigree, this time with age labels for
# all descendents of the starting founder (ID 1)
plot(ex_ped, ref_year = 2015,
     cex= 0.75, symbolsize = 1.25,
     location = "topleft")


# Simulate a random pedigree. This time set RVfounder to TRUE so that
# the eldest introduces a causal rare variant with probability 1.
set.seed(5)
ex_ped <- sim_ped(hazard_rates = hazard(hazardDF = AgeSpecific_Hazards),
                  RVfounder = TRUE,
                  GRR = 10,
                  FamID = 1,
                  founder_byears = c(1900, 1910),
                  stop_year = 2015)
```

```
# Plot the pedigree with age labels
plot(ex_ped, ref_year = 2015,
     cex= 0.75, symbolsize = 1.25,
     location = "topleft")
```

---

sim_RVped   *Simulate a pedigree ascertained to contain multiple disease-affected*
                                relatives

Description

sim_RVped simulates a pedigree ascertained to contain multiple affected members, selects a proband,
and trims the pedigree to contain only those individuals that are recalled by the proband.

Usage

```
sim_RVped(hazard_rates, GRR, num_affected, ascertain_span, FamID,
  founder_byears, stop_year = NULL, recall_probs = NULL,
  carrier_prob = 0.002, RVfounder = FALSE, NB_params = c(2, 4/7),
  fert = 1, first_diagnosis = NULL, sub_criteria = NULL)
```

Arguments

hazard_rates	An object of class hazard, created by [hazard]().
GRR	Numeric. The genetic relative-risk of disease, i.e. the relative-risk of disease for individuals who carry at least one copy of the causal variant. Note: When simulating diseases with multiple subtypes GRR must contain one entry for each simulated subtype. See details.
num_affected	Numeric vector. The minimum number of disease-affected relatives required for ascertainment.
ascertain_span	Numeric vector of length 2. The year span of the ascertainment period. This period represents the range of years during which the proband developed disease and the family would have been ascertained for multiple affected relatives.
FamID	Numeric. The family ID to assign to the simulated pedigree.
founder_byears	Numeric vector of length 2. The span of years from which to simulate, uniformly, the birth year for the founder who introduced the rare variant to the pedigree.
stop_year	Numeric. The last year of study. If not supplied, defaults to the current year.
recall_probs	Numeric. The proband's recall probabilities for relatives, see details. If not supplied, the default value of four times kinship coefficient between the proband and the relative is used.
carrier_prob	Numeric. The carrier probability for all causal variants with relative-risk of disease GRR. By default, carrier_prob = 0.002

RVfounder   Logical. Indicates if all pedigrees segregate the rare, causal variant. By default, RVfounder = FALSE See details.

NB_params   Numeric vector of length 2. The size and probability parameters of the negative binomial distribution used to model the number of children per household. By default, NB_params = c(2,4/7), due to the investigation of Kojima and Kelleher (1962).

fert   Numeric. A constant used to rescale the fertility rate after disease-onset. By default, fert = 1.

first_diagnosis
                   Numeric. The first year that reliable diagnoses can be obtained regarding disease-affection status. By default, first_diagnosis = NULL so that all diagnoses are considered reliable. See details.

sub_criteria   List. Additional subtype criteria required for ascertainment. The first item in sub_criteria is expected to be a character string indicating a subtype label and the second is a numeric entry indicating the minimum number of relatives affected by the identified subtype for ascertainment. By default, sub_criteria = NULL so that no additional criteria is applied. See details.

Details

When RV_founder = TRUE, all simulated pedigrees will segregate a genetic susceptibility variant. In this scenario, we assume that the variant is rare enough that it has been introduced by one founder, and we begin the simulation of the pedigree with this founder. Alternatively, when RV_founder = FALSE we simulate the starting founder's causal variant status with probability carrier_prob. When RV_founder = FALSE pedigrees may not segregate the genetic susceptibility variant. The default selection is RV_founder = FALSE. Additionally, we note that sim_RVpedigree is intended for rare causal variants; users will recieve a warning if carrier_prob > 0.002.

We note that when GRR = 1, pedigrees do not segregate the causal variant regardless of the setting selected for RVfounder. When the causal variant is introduced to the pedigree we transmit it from parent to offspring according to Mendel's laws.

When simulating diseases with multiple subtypes GRR is a numeric list indicating the genetic-relative risk for each subtype specified in the [hazard](#) object supplied to hazard_rates. For example, for a disease with two disease subtypes, if we set GRR = c(20,1) individuals who inherit the causal variant are 20 times more likely than non-carriers to develop the first subtype and as likely as non-carriers to develop the second subtype.

We begin simulating the pedigree by generating the year of birth, uniformly, between the years specified in founder_byears for the starting founder. Next, we simulate this founder's life events using the [sim_life](#) function, and censor any events that occur after the study stop_year. Possible life events include: reproduction, disease onset, and death. We continue simulating life events for any offspring, censoring events which occur after the study stop year, until the simulation process terminates. We do not simulate life events for marry-ins, i.e. individuals who mate with either the starting founder or offspring of the starting founder.

We do not model disease remission. Rather, we impose the restriction that individuals may only experience disease onset once, and remain affected from that point on. If disease onset occurs then we apply the hazard rate for death in the affected population.

sim_RVped will only return ascertained pedigrees with at least num_affected affected individuals. That is, if a simulated pedigree does not contain at least num_affected affected individuals

sim_RVped will discard the pedigree and simulate another until the condition is met. We note that even for num_affected = 2, sim_RVped can be computationally expensive. To simulate a pedigree with no proband, and without a minimum number of affected members use sim_ped instead of sim_RVped.

When simulating diseases with multiple subtypes, users may wish to apply additional ascertainment criteria using the sub_criteria argument. When supplied, this argument allows users to impose numeric subtype-specific ascertainmet criteria. For example, if and sub_criteria = list("HL",1) then at least 1 of the num_affected disease-affected relatives must be affected by subtype "HL" for the pedigree to be asceratained. We note that the first entry of sub_criteria, i.e. the subtype label, must match the one of subtype labels in the hazards object supplied to hazard_rates. See examples.

Upon simulating a pedigree with num_affected individuals, sim_RVped chooses a proband from the set of available candidates. Candidates for proband selection must have the following qualities:

1. experienced disease onset between the years specified by ascertain_span,

2. if less than num_affected - 1 individuals experienced disease onset prior to the lower bound of ascertain_span, a proband is chosen from the affected individuals, such that there were at least num_affected affected individuals when the pedigree was ascertained through the proband.

We allow users to specify the first year that reliable diagnoses can be made using the argument first_diagnosis. All subjects who experience disease onset prior to this year are not considered when ascertaining the pedigree for a specific number of disease-affected relatives. By default, first_diagnosis = NULL so that all affected relatives, recalled by the proband, are considered when ascertaining the pedigree.

After the proband is selected, the pedigree is trimmed based on the proband's recall probability of his or her relatives. This option is included to model the possibility that a proband either cannot provide a complete family history or that they explicitly request that certain family members not be contacted. If recall_probs is missing, the default values of four times the kinship coefficient, as defined by Thompson, between the proband and his or her relatives are assumed. This has the effect of retaining all first degree relatives with probability 1, retaining all second degree relatives with probability 0.5, retaining all third degree relatives with probability 0.25, etc. Alternatively, the user may specify a list of length l, such that the first $l - 1$ items represent the respective recall probabilities for relatives of degree $1, 2, ..., l - 1$ and the lth item represents the recall probability of a relative of degree l or greater. For example, if recall_probs = c(1,0.75,0.5), then all first degree relatives (i.e. parents, siblings, and offspring) are retained with probability 1, all second degree relatives (i.e. grandparents, grandchildren, aunts, uncles, nieces and nephews) are retained with probability 0.75, and all other relatives are retained with probability 0.5. To simulate fully ascertained pedigrees, simply specify recall_probs = c(1).

In the event that a trimmed pedigree fails the num_affected condition, sim_RVped will discard that pedigree and simulate another until the condition is met. For this reason, the values specified for recall_probs affect computation time.

Value

A list containing the following data frames:

full_ped   The full pedigree, prior to proband selection and trimming.

ascertained_ped

> The ascertained pedigree, with proband selected and trimmed according to proband recall probability. See details.

See Also

[sim_ped](), [trim_ped](), [sim_life]()

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018). *Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives.* Source Code for Biology and Medicine, 13:2.

Ken-Ichi Kojima, Therese M. Kelleher. (1962), *Survival of Mutant Genes.* The American Naturalist 96, 329-346.

Thompson, E. (2000). *Statistical Inference from Genetic Data on Pedigrees.* NSF-CBMS Regional Conference Series in Probability and Statistics, 6, I-169.

Examples

```
#Read in age-specific hazards
data(AgeSpecific_Hazards)

#Simulate pedigree ascertained for multiple affected individuals
set.seed(2)
ex_RVped <- sim_RVped(hazard_rates = hazard(hazardDF = AgeSpecific_Hazards),
                      GRR = 20,
                      RVfounder = TRUE,
                      FamID = 1,
                      founder_byears = c(1900, 1905),
                      ascertain_span = c(1995, 2015),
                      num_affected = 2,
                      stop_year = 2017,
                      recall_probs = c(1, 1, 0))

# Observe: ex_RVped is a list containing two ped objects
summary(ex_RVped)

# The first is the original pedigree prior
# to proband selection and trimming
plot(ex_RVped[[1]])

# The second is the ascertained pedigree which
# has been trimmed based on proband recall
plot(ex_RVped[[2]])
summary(ex_RVped[[2]])


# NOTE: by default, RVfounder = FALSE.
# Under this setting pedigrees segregate a causal
# variant with probability equal to carrier_prob.
```

```
#------------------------------------------------#
# Simulate Pedigrees with Multiple Disease Subtypes #
#------------------------------------------------#
# Simulating pedigrees with multiple subtypes
# Import subtype-specific hazards rates for
# Hodgkin's lymphoma and non-Hodgkin's lymphoma
data(SubtypeHazards)
head(SubtypeHazards)

my_hazards <- hazard(SubtypeHazards,
                     subtype_ID = c("HL", "NHL"))


# Simulate pedigree ascertained for at least two individuals
# affected by either Hodgkin's lymphoma or non-Hodgkin's lymphoma.
# Set GRR = c(20, 1) so that individuals who carry a causal variant
# are 20 times more likely than non-carriers to develop "HL" but have
# same risk as non-carriers to develop "NHL".
set.seed(45)
ex_RVped <- sim_RVped(hazard_rates = my_hazards,
                      GRR = c(20, 1),
                      RVfounder = TRUE,
                      FamID = 1,
                      founder_byears = c(1900, 1905),
                      ascertain_span = c(1995, 2015),
                      num_affected = 2,
                      stop_year = 2017,
                      recall_probs = c(1, 1, 0))

plot(ex_RVped[[2]], cex = 0.6)

# Note that we can modify the ascertainment criteria so that
# at least 1 of the two disease-affected relatives are affected by
# the "HL" subtype by supplying c("HL", 1) to the sub_criteria
# argument.
set.seed(69)
ex_RVped <- sim_RVped(hazard_rates = my_hazards,
                      GRR = c(20, 1),
                      RVfounder = TRUE,
                      FamID = 1,
                      founder_byears = c(1900, 1905),
                      ascertain_span = c(1995, 2015),
                      num_affected = 2,
                      stop_year = 2017,
                      recall_probs = c(1, 1, 0),
                      sub_criteria = list("HL", 1))

plot(ex_RVped[[2]], cex = 0.6)
```

SubtypeHazards *Age-specific hazard rate dataset with subtypes*

Description

A dataset that contains the following age-specific hazard rates: (1) the age-specific hazard rates for Hodgkin Lymphoma and Non-Hodgkin Lymphoma in the United States, (2) the age-specific hazard rates for death in the United States, and (3) the age-specific hazard rates for death for individuals, living in the United States, who have been diagnosed with either Hodgkin Lymphoma and Non-Hodgkin Lymphoma.

Usage

```
data(SubtypeHazards)
```

Format

A data frame with 100 rows and 4 variables:

pop_HL_hazard The population, age-specific hazard rate for Hodgkin Lymphoma

pop_NHL_hazard The population, age-specific hazard rate for Non-Hodgkin Lymphoma

unaffected_death_hazard The age-specific hazard rate for death in the **unaffected** population

affected_death_hazard The age-specific hazard rate for death in the **affected** population

Details

The SubtypeHazards dataset contains the following age-specific hazard rates which **roughly mimic**: (1) the age-specific hazard rates for Hodgkin Lymphoma and Non-Hodgkin Lymphoma in the United States, (2) the age-specific hazard rates for death in the United States, and (3) the age-specific hazard rates for death for individuals, living in the United States, who have been diagnosed with either Hodgkin Lymphoma and Non-Hodgkin Lymphoma. The age-specific hazard rates of disease onset and death in the affected populations were estimated by the Surveillance, Epidemiology, and End Results Program (SEER) SEER*Stat Software, and the age-specific hazard rates of death in the United States were estimated from actuarial life tables provided by the Social Security Administration.

The four columns in the SubtypeHazards dataset provide age-specific hazard rates, in yearly increments, beginning at age 0 and ending with age 100. That is, the values in the first row describe the hazard rates for an individual whose age is contained in the interval [0, 1), while the values in the second row describe the hazard rates for an individual whose age is contained in the interval [1, 2), and so on.

References

The Surveillance, Epidemiology, and End Results (SEER) Program. https://seer.cancer.gov/

Bell, F. C., Miller, M. L. (2005). *Life Tables for the United States Social Security Area, 1900-2100.* Baltimore, Md.: Social Security Administration, Office of the Chief Actuary.

---

summary.ped *Summarize a sample of pedigrees*

Description

Summarize a sample of pedigrees

Usage

```
## S3 method for class 'ped'
summary(object, ...)
```

Arguments

object	An object of class ped.
...	additional arguments passed to other methods.

Details

The summary.ped function returns two data frames. The first is called family_info, and contains the following fields for each family supplied.

variable	description
FamID	family identification number
totalRelatives	total number of relatives
numAffected	total number of disease-affected individuals
aveOnsetAge	average onset age among the disease-affected relatives
aveIBD	average of the pairwise IBD probabilities among the disease-affected relatives
ascertainYear	the year the pedigree was ascertained
segRV	logical Indicates whether or not pedigree segregates a causal variant. If the pedigree segregates the variant segRV = TRUE.
p_subtypeLabel	NOTE: this is only listed when pedigrees contain relatives affected by multiple subtypes. the proportion of disease-affected relatives in the family with the specified subtype. Here "subtypeLabel" is determined by subtype ID specifed by the user when creating the [hazard] object.

The second item returned by summary.ped is called affected_info, and contains the following fields for each disease-affected relative supplied.

variable	description
FamID	family identification number
ID	individual identification number
birthYr	the individual's birth year, when applicable, otherwise NA
onsetYr	the individual's year of disease onset, when applicable, otherwise NA
deathYr	the individual's year of death, when applicable, otherwise NA
proband	a proband identifier: proband = TRUE if the individual is the proband, and FALSE otherwise.

RVstatus   the individual's causal RV status; set to 1 if individual is a carrier, and 0 otherwise.

subtype   NOTE: this is only listed when pedigree was simulated for diseases with multiple subtypes. The individual's disease subtype.

Value

family_info   A data frame containing family specific variables for each pedigree supplied. See details.

affected_info   A data frame containing information for the affected individuals in each pedigree supplied. See details.

Examples

```
#Read in age-specific harard data and create hazard object.
data(AgeSpecific_Hazards)
haz_obj <- hazard(hazardDF = AgeSpecific_Hazards)

#Simulate a pedigree ascertained for multiple affecteds
set.seed(6)
RVped2015 <- sim_RVped(hazard_rates = haz_obj,
                       num_affected = 2,
                       ascertain_span = c(1900, 2015),
                       GRR = 30, carrier_prob = 0.002,
                       RVfounder = TRUE,
                       stop_year = 2015,
                       recall_probs = c(1),
                       founder_byears = c(1900, 1925),
                       FamID = 1)[[2]]

# Plot the pedigree with age labels at the year 2015
plot(RVped2015, ref_year = 2015)

# View summary information for the pedigree
summary(RVped2015)



# Import the EgPeds dataset and create ped object
data(EgPeds)
study_peds <- new.ped(EgPeds)

# View summary information for study_peds
summary(study_peds)
```

---

    trim_ped   *Trim pedigree based on proband recall*

Description

Primarily intended as an internal function, `trim_ped` chooses a proband and trims relatives based on the proband's probability of recalling his or her relatives.

Usage

```
trim_ped(ped_file, recall_probs = NULL)
```

Arguments

ped_file   An object of class ped. A pedigree generated by `sim_ped` or `sim_RVped`, or an object created by the function `new.ped`. See details.

recall_probs   Numeric. The proband's recall probabilities for relatives, see details. If not supplied, the default value of four times kinship coefficient between the proband and the relative is used.

Details

By default `recall_probs` is four times the kinship coefficient, as defined by Thompson (see references), between the proband and the probands relative, which results in a recall probability of $2^{-(n-1)}$ for a relative of degree n. Alternatively, the user may specify a list of recall probabilities of length $l > 0$, in which case the first *l-1* items in `recall_probs` are the respective proband recall probabilities for relatives of degree *1, 2, ..., l-1*, and the *l*th item in `recall_probs` is the proband's recall probability for all relatives of degree *l or greater*. For example if `recall_probs = c(1)` all relatives will be recalled by the proband with probability 1.

Occasionally, a trimmed family member must be retained to ensure that the pedigree can be plotted. When this occurs, family members who share a non-zero kinship coefficient with the proband are censored of all pertinent information, and will always have the following qualities:

1. availability status = 0

2. affected status = NA

3. birth year = NA

4. onset year = NA

5. death year = NA

6. RR = NA

Users who wish to use `trim_ped` for pedigrees not generated by `sim_ped` or `sim_RVped` must use `new.ped` to create an object of class ped. The ped object *must* contain the following variables for each pedigree member:

name	type	description
FamID	numeric	family identification number
ID	numeric	individual identification number
dadID	numeric	identification number of father
momID	numeric	identification number of mother
sex	numeric	gender identification; if male sex = 0, if female sex = 1
affected	logical	disease-affection status:

proband	logical	a proband identifier: proband = TRUE if the individual is the proband, and FALSE otherwise.
		affected = TRUE if affected by disease , and FALSE otherwise,
birthYr	numeric	the individual's birth year.
onsetYr	numeric	the individual's disease onset year, when applicable.
deathYr	numeric	the individual's death year, when applicable.
RR	numeric	the individual's relative risk of disease.
available	logical	availibility status;
		available = TRUE if available, and FALSE otherwise.

Value

ped_trim The trimmed pedigree.

References

Nieuwoudt, Christina and Jones, Samantha J and Brooks-Wilson, Angela and Graham, Jinko (2018). *Simulating Pedigrees Ascertained for Multiple Disease-Affected Relatives.* Source Code for Biology and Medicine, 13:2.

Thompson, E. (2000). *Statistical Inference from Genetic Data on Pedigrees.* NSF-CBMS Regional Conference Series in Probability and Statistics, 6, I-169.

See Also

[sim_RVped](), [sim_ped](), [new.ped]()

Examples

```
#Read in example pedigree to trim
data(EgPeds)
egPeds <- new.ped(EgPeds)

#plot example_ped using kinship2
plot(subset(egPeds, FamID == 1), location = "topright", cex = 0.85)
mtext("Original Pedigree", side = 3, line = 2)


## Trim pedigree examples
# Illustrate the effect of various settings for recall_probs
Recall_Probabilities <- list(c(1),
                             c(1, 0.5),
                             c(1, 0.25, 0.1))


for (k in 1:length(Recall_Probabilities)) {
   set.seed(2)
   #trim pedigree
   TrimPed <- trim_ped(ped_file = subset(egPeds, FamID == 1),
                       recall_probs = Recall_Probabilities[[k]])

   plot(TrimPed, location = "topright", cex = 0.85)
```

```
    mtext(paste0("recall_probs = (", sep = "",
                 paste(Recall_Probabilities[[k]], collapse = ", "), ')' ),
                 side = 3, line = 2 )
}
```

Index