Package ‘drugDemand’

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Title Drug Demand Forecasting
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Description Performs drug demand forecasting by modeling drug dispensing data while taking into account predicted enrollment and treatment discontinuation dates. The gap time between randomization and the first drug dispensing visit is modeled using interval-censored exponential, Weibull, log-logistic, or log-normal distributions (Anderson-Bergman (2017) <doi:10.18637/jss.v081.i12>). The number of skipped visits is modeled using Poisson, zero-inflated Poisson, or negative binomial distributions (Zeileis, Kleiber & Jackman (2008) <doi:10.18637/jss.v027.i08>). The gap time between two consecutive drug dispensing visits given the number of skipped visits is modeled using linear regression based on least squares or least absolute deviations (Birkes & Dodge (1993, ISBN:0-471-56881-3)). The number of dispensed doses is modeled using linear or linear mixed-effects models (McCulloch & Searle (2001, ISBN:0-471-19364-X)).

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| df1 | The subject-level enrollment and event data before enrollment completion. |

Description

A data frame with the following columns:

- **trialsdt** The trial start date.
- **usubjid** The unique subject ID.
- **randdt** The randomization date for each subject.
- **treatment** The treatment group.
- **treatment_description** Description of the treatment group.
- **time** The number of days elapsed since randomization.
- **event** The event indicator, with a value of 1 indicating the occurrence of an event, and 0 indicating no event.
- **dropout** The dropout indicator, where 1 corresponds to a dropout and 0 implies no dropout.
- **cutoffdt** The cutoff date. For drug demand forecasting, the event of interest is treatment discontinuation. The dropout variable is set to 0 for all patients in this context.
df2

Usage

df1

Format

An object of class tbl_df (inherits from tbl.data.frame) with 175 rows and 9 columns.

Description

A data frame with the following columns:

- trialsdt: The trial start date.
- usubjid: The unique subject ID.
- randdt: The randomization date for each subject.
- treatment: The treatment group.
- treatment_description: Description of the treatment group.
- time: The number of days elapsed since randomization.
- event: The event indicator, with a value of 1 indicating the occurrence of an event, and 0 indicating no event.
- dropout: The dropout indicator, where 1 corresponds to a dropout and 0 implies no dropout.
- cutoffdt: The cutoff date. For drug demand forecasting, the event of interest is treatment discontinuation. The dropout variable is set to 0 for all patients in this context.

Usage

df2

Format

An object of class tbl_df (inherits from tbl.data.frame) with 250 rows and 9 columns.
dosing_schedule_df  The dosing schedule data frame.

Description
A data frame with the following columns:
kit  The numeric code of the kit type.
target_days  Number of days per treatment cycle.
target_dose  Dose per treatment cycle.
max_cycles  Maximum number of treatment cycles.

Usage
dosing_schedule_df

Format
An object of class tbl_df (inherits from tbl, data.frame) with 4 rows and 4 columns.

f_cum_dose  Cumulative Dose

Description
Obtains the cumulative dose given treatment duration and dosing schedule.

Usage
f_cum_dose(x, w, d, N)

Arguments
x  Treatment duration.
w  Number of days per treatment cycle.
d  Dose per treatment cycle.
N  Maximum number of treatment cycles.

Value
The cumulative dose to dispense for the drug over a specified treatment duration.

Author(s)
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**f_dispensing_models**

**Examples**

```r
f_cum_dose(c(28, 70), 21, 2, 10000)
```

---

**f_dispensing_models  Drug Dispensing Model Fitting**

**Description**

Fits drug dispensing models to the observed drug dispensing data.

**Usage**

```r
f_dispensing_models(
  vf,
  dosing_schedule_df,
  model_k0,
  model_t0,
  model_t1,
  model_ki,
  model_ti,
  model_di,
  nreps,
  showplot = TRUE
)
```

**Arguments**

- `vf`  
  A data frame for subject-level drug dispensing data, including the following variables: drug, drug_name, kit, kit_name, usubjid, treatment, treatment_description, arrivalTime, time, event, dropout, day, dose, cum_dose, and row_id.

- `dosing_schedule_df`  
  A data frame providing dosing schedule information. It contains the following variables: kit, target_days, target_dose, and max_cycles.

- `model_k0`  
  The model for the number of skipped visits between randomization and the first drug dispensing visit. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".

- `model_t0`  
  The model for the gap time between randomization and the first drug dispensing visit when there is no visit skipping. Options include "constant", "exponential", "weibull", "log-logistic", and "log-normal".

- `model_t1`  
  The model for the gap time between randomization and the first drug dispensing visit when there is visit skipping. Options include "least squares", and "least absolute deviations".
f_dispensing_models

model_ki  The model for the number of skipped visits between two consecutive drug dispensing visits. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".

model_ti  The model for the gap time between two consecutive drug dispensing visits. Options include "least squares" and "least absolute deviations".

model_di  The model for the dispensed doses at drug dispensing visits. Options include "constant", "linear model", and "linear mixed-effects model".

nreps  The number of simulations for drawing posterior model parameters.

showplot  A Boolean variable that controls whether or not to show the model fit plot. It defaults to TRUE.

Value

A list with the following components:

• common_time_model: A Boolean variable that indicates whether a common time model is used for drug dispensing visits.
• k0_fit: The model fit for the number of skipped visits between randomization and the first drug dispensing visit.
• t0_fit: The model fit for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
• t1_fit: The model fit for the gap time between randomization and the first drug dispensing visit when there is visit skipping.
• ki_fit: The model fit for the number of skipped visits between two consecutive drug dispensing visits.
• ti_fit: The model fit for the gap time between two consecutive drug dispensing visits.
• di_fit: The model fit for the dispensed doses at drug dispensing visits.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

See Also

f_fit_t0, f_fit_ki, f_fit_ti, f_fit_di

Examples

library(dplyr)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)

dispensing_models <- f_dispensing_models(
    observed$vf, dosing_schedule_df,
    model_k0 = "zero-inflated poisson",
    model_t0 = "log-logistic",
    model_t1 = "least squares",
)
**f_dose_draw**

model_ki = "zero-inflated poisson",
model_ti = "least squares",
model_di = "linear mixed-effects model",
nreps = 200, showplot = FALSE)

dispensing_models$ki_fit$fit_plot

---

**f_dose_draw**  
**Drug Dispensing Data Simulation**

### Description

Simulates drug dispensing data after cutoff for both ongoing and new patients.

### Usage

```r
f_dose_draw(
 vf_ongoing,
 vf_new,
 common_time_model,
 k0_fit,
 t0_fit,
 t1_fit,
 ki_fit,
 ti_fit,
 di_fit,
 t0,
 t,
 ncores_max
)
```

### Arguments

**vf_ongoing**  
A data frame for the observed drug dispensing data for ongoing patients with drug dispensing records. It includes the following variables: draw, kit, kit_name, usubjid, day, dose, arrivalTime, treatment, treatment_description, time, and totalTime.

**vf_new**  
A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. It includes the following variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, and totalTime.

**common_time_model**  
A Boolean variable that indicates whether a common time model is used for drug dispensing visits.

**k0_fit**  
The model fit for the number of skipped visits between randomization and the first drug dispensing visit.
t0_fit  The model fit for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
t1_fit  The model fit for the gap time between randomization and the first drug dispensing visit when there is visit skipping.
ki_fit  The model fit for the number of skipped visits between two consecutive drug dispensing visits.
ti_fit  The model fit for the gap time between two consecutive drug dispensing visits.
di_fit  The model fit for the dispensed doses at drug dispensing visits.
t0    The cutoff date relative to the trial start date.
t    A vector of new time points for drug dispensing prediction.
ncores_max  The maximum number of cores to use for parallel computing. The actual number of cores used is the minimum of ncores_max and half of the detected number of cores.

Value
A list with two components:

- dosing_subject_new: A data frame containing observed and imputed subject-level dosing records for ongoing and new patients for the first iteration. It contains the following variables: draw, kit, kit_name, usubjid, day, dose, arrivalTime, treatment, treatment_description, time, and totalTime.
- dosing_summary_new: A data frame providing dosing summaries by drug, future time point, and simulation draw for ongoing and new patients. It contains the following variables: kit, kit_name, t, draw, and total_dose_b.

Author(s)
Kaifeng Lu, <kaifenglu@gmail.com>

See Also
f_fit_t0, f_fit_ki, f_fit_ti, f_fit_di

Examples

```r
set.seed(431)
library(dplyr)
pred <- eventPred::getPrediction(
  df = df2,
  to_predict = "event only",
  target_d = 250,
  event_model = "log-logistic",
  dropout_model = "none",
  pilevel = 0.95,
```
Drug Dispensing Data Simulation for One Iteration

Description

Simulates drug dispensing data for one iteration.
Usage

\[ f_{\text{dose\_draw\_1}} \]

```r
f_dose_draw_1(
  i,  
  common_time_model,  
  k0_fit,  
  t0_fit,  
  t1_fit,  
  ki_fit,  
  ti_fit,  
  di_fit,  
  vf_ongoing,  
  vf_ongoing1,  
  vf_new,  
  vf_new1,  
  vf_kit,  
  l,  
  t)
```

Arguments

- **i**: The iteration number.
- **common_time_model**: A Boolean variable that indicates whether a common time model is used for drug dispensing visits.
- **k0_fit**: The model fit for the number of skipped visits between randomization and the first drug dispensing visit.
- **t0_fit**: The model fit for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
- **t1_fit**: The model fit for the gap time between randomization and the first drug dispensing visit when there is visit skipping.
- **ki_fit**: The model fit for the number of skipped visits between two consecutive drug dispensing visits.
- **ti_fit**: The model fit for the gap time between two consecutive drug dispensing visits.
- **di_fit**: The model fit for the dispensed doses at drug dispensing visits.
- **vf_ongoing**: A data frame for the observed drug dispensing data for ongoing patients with drug dispensing records. It includes the following variables: draw, kit, kit_name, usubjid, day, dose, arrivalTime, treatment, treatment_description, time, and totalTime.
- **vf_ongoing1**: A data frame for the last observed drug dispensing date for ongoing patients with drug dispensing records. For the common time model, it includes the following variables: draw, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D. For separate time models, it includes the following variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D.
vf_new
A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. It includes the following variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, and totalTime.

vf_new1
A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. For the common time model, it includes the following variables: draw, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D. For separate time models, it includes the following variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D.

vf_kit
A data frame indicating the kit names for each subject by draw. It includes the following variables: draw, usubjid, kit, and kit_name.

l
Number of kit types.

t
A vector of new time points for drug dispensing prediction.

Value
A list of two components:

- dosing_subject_newi: A data frame for the drug dispensing data at the subject level by date for ongoing and new subjects for the given iteration. It contains the following variables: draw, kit, kit_name, usubjid, day, dose, arrivalTime, treatment, treatment_description, time, and totalTime.

- dosing_summary_newi: A data frame for the drug dispensing summary data by drug, time, and simulation draw for ongoing and new subjects for the given iteration. It includes the following variables: kit, kit_name, t, draw, and total_dose_b.

Author(s)
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See Also
f_fit_t0, f_fit_ki, f_fit_ti, f_fit_di

Examples

```r
set.seed(431)
library(dplyr)

pred <- eventPred::getPrediction(
  df = df2,
  to_predict = "event only",
  target_d = 250,
  event_model = "log-logistic",
  dropout_model = "none",
  pilevel = 0.95,
```
f_dose_draw_1

nyears = 3,
nreps = 200,
showsummary = FALSE,
showplot = FALSE,
by_treatment = TRUE)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)

fit <- f_dispensing_models(
  observed$vf, dosing_schedule_df,
  model_k0 = "zero-inflated poisson",
  model_t0 = "log-logistic",
  model_t1 = "least squares",
  model_ki = "zero-inflated poisson",
  model_ti = "least squares",
  model_di = "linear mixed-effects model",
  nreps = 200, showplot = FALSE)

trialsdt = df2$trialsdt[1]
cutoffdt = df2$cutoffdt[1]
t0 = as.numeric(cutoffdt - trialsdt + 1)
nyears = 3
t1 = t0 + nyears*365
t = c(seq(t0, t1, 30), t1)
l = nrow(observed$kit_description_df)

vf_ongoing_new <- f_ongoing_new(
  pred$event_pred$newEvents,
  observed$kit_description_df,
  observed$treatment_by_drug_df,
  observed$vf)

vf_ongoing <- vf_ongoing_new$vf_ongoing
vf_new <- vf_ongoing_new$vf_ongoing

vf_kit <- vf_ongoing %>%
  select(-c("day", "dose")) %>%
  bind_rows(vf_new) %>%
  group_by(draw, usubjid, kit, kit_name) %>%
  slice(1) %>%
  select(c("draw", "usubjid", "kit", "kit_name"))

vf_ongoing1 <- vf_ongoing %>%
  group_by(draw, usubjid) %>%
  slice(n()) %>%
  mutate(V = day - 1,
         C = as.numeric(t0 - arrivalTime),
         D = pmin(time - 1, t1 - arrivalTime)) %>%
  select(-c("kit", "kit_name", "day", "dose"))

### new patients and ongoing patients with no dosing records ###

vf_new1 <- vf_new %>%
```r
f_dose_draw_t_1

group_by(draw, usubjid) %>%
slice(n()) %>%
mutate(V = 0,
       C = as.numeric(t0 - arrivalTime),
       D = pmin(time - 1, t1 - arrivalTime)) %>%
select(-c("kit", "kit_name"))

# first iteration to extract subject and summary data
list1 <- f_dose_draw_1(
  1, fit$common_time_model,
  fit$k0_fit, fit$t0_fit, fit$t1_fit,
  fit$ki_fit, fit$ti_fit, fit$di_fit,
  vf_ongoing, vf_ongoing1, vf_new, vf_new1,
  vf_kit, 1, t)

head(list1$dosing_subject_newi)
head(list1$dosing_summary_newi)
```

---

**f_dose_draw_t_1**  
*Drug Dispensing Visit Dates Simulation for One Iteration*

---

**Description**

Simulates drug dispensing visit dates for one iteration.

**Usage**

```r
f_dose_draw_t_1(
  i,
  k0_fit, 
  t0_fit, 
  t1_fit, 
  ki_fit, 
  ti_fit, 
  vf_ongoing, 
  vf_ongoing1, 
  vf_new, 
  vf_new1
)
```

**Arguments**

- **i**  
  The iteration number.
- **k0_fit**  
  The model fit for the number of skipped visits between randomization and the first drug dispensing visit.
- **t0_fit**  
  The model fit for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
The model fit for the gap time between randomization and the first drug dispensing visit when there is visit skipping.

The model fit for the number of skipped visits between two consecutive drug dispensing visits.

The model fit for the gap time between two consecutive drug dispensing visits.

A data frame for the last observed drug dispensing date for ongoing patients with drug dispensing records. For the common time model, it includes the following variables: `draw`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `totalTime`, `V`, `C`, and `D`. For separate time models, it includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `totalTime`, `V`, `C`, and `D`.

A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. For the common time model, it includes the following variables: `draw`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `totalTime`, `V`, `C`, and `D`. For separate time models, it includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `totalTime`, `V`, `C`, and `D`.

A data frame containing the simulated drug dispensing visit dates at the subject level for ongoing and new subjects. It includes the following variables: `usubjid`, `day`, `draw`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `totalTime`, and `status`.

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See Also

`f_fit_t0`, `f_fit_ki`, `f_fit_ti`

Examples

```r
set.seed(431)
library(dplyr)
pred <- eventPred::getPrediction(
df = df2,
to_predict =  "event only",
target_d = 250,
event_model =  "log-logistic",
dropout_model =  "none",
pilevel = 0.95,
nyears = 3,
nreps = 200,
showsummary = FALSE,
```
showplot = FALSE,
by_treatment = TRUE)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)

fit <- f_dispensing_models(
  observed$vf, dosing_schedule_df,
  model_k0 = "zero-inflated poisson",
  model_t0 = "log-logistic",
  model_t1 = "least squares",
  model_ki = "zero-inflated poisson",
  model_ti = "least squares",
  model_di = "linear mixed-effects model",
  nreps = 200, showplot = FALSE)

trialsdt = df2$trialsdt[1]
cutoffdt = df2$cutoffdt[1]
t0 = as.numeric(cutoffdt - trialsdt + 1)
nyears = 3
t1 = t0 + nyyears*365

vf_ongoing_new <- f_ongoing_new(
  pred$event_pred$newEvents,
  observed$kit_description_df,
  observed$treatment_by_drug_df,
  observed$vf)

vf_ongoing <- vf_ongoing_new$vf_ongoing
vf_new <- vf_ongoing_new$vf_new

vf_ongoing1 <- vf_ongoing %>%
group_by(draw, usubjid) %>%
slice(n()) %>%
mutate(V = day - 1,
  C = as.numeric(t0 - arrivalTime),
  D = pmin(time - 1, t1 - arrivalTime)) %>%
select(-c("kit", "kit_name", "day", "dose"))

### new patients and ongoing patients with no dosing records ###

vf_new1 <- vf_new %>%
group_by(draw, usubjid) %>%
slice(n()) %>%
mutable(V = 0,
  C = as.numeric(t0 - arrivalTime),
  D = pmin(time - 1, t1 - arrivalTime)) %>%
select(-c("kit", "kit_name"))

dosing_subject_new1 <- f_dose_draw_t_1(1, fit$k0_fit, fit$t0_fit, fit$t1_fit,
  fit$ki_fit, fit$ti_fit, vf_ongoing1, vf_new1)

head(dosing_subject_new1)
**f_dose_new_cpp**

**Dosing Date Imputation for New Patients**

**Description**

Imputes the dosing dates for new patients and ongoing patients with no dosing records.

**Usage**

```r
f_dose_new_cpp(
    usubjid,
    V, C, D,
    model_k0, theta_k0,
    model_t0, theta_t0,
    model_t1, theta_t1,
    model_k1, theta_k1,
    model_ti, theta_ti
)
```

**Arguments**

- **usubjid**: The unique subject ID.
- **V**: Initialized to 0 and corresponds to the randomization visit.
- **C**: The cutoff date relative to randomization.
- **D**: The discontinuation date relative to randomization.
- **model_k0**: The model for the number of skipped visits between randomization and the first drug dispensing visit. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".
- **theta_k0**: The model parameters for the number of skipped visits between randomization and the first drug dispensing visit.
- **model_t0**: The model for the gap time between randomization and the first drug dispensing visit when there is no visit skipping. Options include "constant", "exponential", "weibull", "log-logistic", and "log-normal".
- **theta_t0**: The model parameters for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
The model for the gap time between randomization and the first drug dispensing visit when there is visit skipping. Options include "least squares", and "least absolute deviations".

The model parameters for the gap time between randomization and the first drug dispensing visit when there is visit skipping.

The model for the number of skipped visits between two consecutive drug dispensing visits. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".

The model parameters for the number of skipped visits between two consecutive drug dispensing visits.

The model for the gap time between two consecutive drug dispensing visits. Options include "least squares" and "least absolute deviations".

The model parameters for the gap time between two consecutive drug dispensing visits.

A data frame with two variables:

- `usubjid`: The unique subject ID.
- `day`: The dosing visit date relative to randomization.

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Examples

```r
set.seed(529)
f_dose_new_cpp(
  usubjid = "Z001", V = 0, C = 87, D = 985,
  model_k0 = "zero-inflated poisson", theta_k0 = c(0.6, 1.1),
  model_t0 = "log-logistic", theta_t0 = c(-1.0, 0.7),
  model_t1 = "least squares", theta_t1 = c(21.5, 1.9),
  model_ki = "zero-inflated poisson", theta_ki = c(0.1, 0.4),
  model_ti = "least squares", theta_ti = c(21, 2.3))
```

**Observed Drug Dispensing Data Summary**

Provides an overview of the observed drug dispensing data, including the summary of cumulative dispensed doses, bar chart of the gap time between randomization and the first drug dispensing visit, the gap time between two consecutive drug dispensing visits, and the dispensed doses at drug dispensing visits by drug.
Usage

f_dose_observed(df = NULL, visitview = NULL, showplot = TRUE)

Arguments

- **df**: A data frame for subject-level enrollment and event data, including the following variables: `trialsdt`, `usubjid`, `randdt`, `treatment`, `treatment_description`, `time`, `event`, `dropout`, and `cutoffdt`.
- **visitview**: A data frame containing the observed drug dispensing data, including the following variables: `usubjid`, `visit`, `date`, `drug`, `drug_name`, `kit`, `kit_name`, `kit_number`, and `dispensed_quantity`.
- **showplot**: A Boolean variable that controls whether or not to show the drug dispensing model fit and drug demand prediction plots. It defaults to `TRUE`.

Value

A list with the following components:

- **trialsdt**: The trial start date.
- **cutoffdt**: The cutoff date.
- **vf**: A data frame for subject-level drug dispensing data, including the following variables: `drug`, `drug_name`, `kit`, `kit_name`, `usubjid`, `treatment`, `treatment_description`, `arrivalTime`, `time`, `event`, `dropout`, `day`, `dose`, `cum_dose`, and `row_id`.
- **treatment_by_drug_df**: A data frame indicating the treatments associated with each drug, including the following variables: `treatment` and `drug`.
- **kit_description_df**: A data frame indicating the drug and kit descriptions, including the following variables: `drug`, `drug_name`, `kit`, and `kit_name`.
- **dosing_summary_t**: A data frame for the cumulative doses dispensed by each observed time point. It contains the following variables: `kit`, `kit_name`, `t`, `n`, `lower`, `upper`, `mean`, and `var`, where `lower` and `upper` have missing values, `mean = n`, and `var = 0`.
- **dosing_summary_t0**: A data frame for the cumulative doses dispensed before the cutoff date. It contains the following variables: `kit`, `kit_name`, and `cum_dose_t0`.
- **cum_dispense_plot**: The step plot for the cumulative doses dispensed for each kit type.
- **bar_t0_plot**: The bar chart for the gap time between randomization and the first drug dispensing visit.
- **bar_ti_plot**: The bar chart for the gap time between two consecutive drug dispensing visits.
- **bar_di_plot**: The bar chart for the dispensed doses at drug dispensing visits.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

Examples

observed <- f_dose_observed(df = df2, visitview = visitview2)
Dosing Date Imputation for Ongoing Patients

Description
Imputes the dosing dates after cutoff for ongoing patients with dosing records.

Usage
f_dose_ongoing_cpp(usubjid, V, C, D, model_ki, theta_ki, model_ti, theta_ti)

Arguments
- **usubjid**: The unique subject ID.
- **V**: The last dosing visit date relative to randomization.
- **C**: The cutoff date relative to randomization.
- **D**: The discontinuation date relative to randomization.
- **model_ki**: The model for the number of skipped visits between two consecutive drug dispensing visits. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".
- **theta_ki**: The model parameters for the number of skipped visits between two consecutive drug dispensing visits.
- **model_ti**: The model for the gap time between two consecutive drug dispensing visits. Options include "least squares" and "least absolute deviations".
- **theta_ti**: The model parameters for the gap time between two consecutive drug dispensing visits.

Value
A data frame with two variables:
- **usubjid**: The unique subject ID.
- **day**: The dosing visit date relative to randomization.

Author(s)
Kaifeng Lu, <kaifenglu@gmail.com>

Examples
```r
set.seed(314)
f_dose_ongoing_cpp(
  usubjid = "A001", V = 297, C = 329, D = 569,
  model_ki = "zero-inflated poisson", theta_ki = c(0.4, 2.5),
  model_ti = "least squares", theta_ti = c(21, 2.3))
```
**f_dose_pp**

*Drug Demand Per Protocol*

**Description**

Obtains drug demand prediction based on protocol-assumed visit and dosing schedules.

**Usage**

```r
f_dose_pp(
    dosing_summary_t0,
    vf_ongoing,
    vf_new,
    dosing_schedule_df,
    t0,
    t,
    pilevel
)
```

**Arguments**

- **dosing_summary_t0**
  A data frame for the cumulative doses dispensed before the cutoff date. It contains the following variables: `kit`, `kit_name`, and `cum_dose_t0`.

- **vf_ongoing**
  A data frame for the observed drug dispensing data for ongoing patients with drug dispensing records. It includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `day`, `dose`, `arrivalTime`, `treatment`, `treatment_description`, `time`, and `totalTime`.

- **vf_new**
  A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. It includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, and `totalTime`.

- **dosing_schedule_df**
  A data frame providing dosing schedule information. It contains the following variables: `kit`, `target_days`, `target_dose`, and `max_cycles`.

- **t0**
  The cutoff date relative to the trial start date.

- **t**
  A vector of new time points for drug dispensing prediction.

- **pilevel**
  The prediction interval level.

**Value**

A data frame for dosing summary by drug and time point per protocol. It contains the following variables: `kit`, `kit_name`, `t`, `n`, `pilevel`, `lower`, `upper`, `mean`, and `var`.

**Author(s)**

Kaifeng Lu, <kaifenglu@gmail.com>
Examples

# Design stage drug demand forecasting per protocol.

```r
set.seed(312)
library(dplyr)
pred <- eventPred::getPrediction(
  df = NULL,
  to_predict = "enrollment and event",
  target_n = 250,
  target_d = 250,
  enroll_prior = list(
    model = "piecewise poisson",
    theta = c(-0.74, -1.18),
    vtheta = matrix(c(0.0087, 0, 0, 0.0082), 2, 2),
    accrualTime = c(0, 240)),
  event_prior = list(
    list(model = "log-logistic",
      theta = c(5.9, 0.02),
      vtheta = matrix(c(0.022, 0.004, 0.004, 0.012), 2, 2)),
    list(model = "log-logistic",
      theta = c(5.6, 0.02),
      vtheta = matrix(c(0.032, 0.003, 0.003, 0.012), 2, 2)),
    list(model = "log-logistic",
      theta = c(5.7, -0.3),
      vtheta = matrix(c(0.071, 0.013, 0.013, 0.054), 2, 2))),
  dropout_prior = NULL,
  pilevel = 0.95,
  nyears = 3,
  nreps = 200,
  showsummary = FALSE,
  showplot = FALSE,
  by_treatment = TRUE,
  ngroups = 3,
  alloc = c(2, 2, 1),
  treatment_label = c("Drug A + Drug B",
    "Drug C + Placebo",
    "Drug A + Placebo"))
```
t = c(seq(t0, t1, 30), t1)
pilevel = 0.95

dosing_pred_pp <- f_dose_pp(
    dosing_summary_t0, vf_ongoing_new$vf_ongoing, 
    vf_ongoing_new$vf_new, dosing_schedule_df, t0, t, pilevel)

head(dosing_pred_pp)

---

f_drug_demand

**Drug Demand Forecasting**

**Description**

Obtains drug demand forecasting via modeling and simulation.

**Usage**

```r
f_drug_demand(
    df = NULL, 
    newEvents = NULL, 
    visitview = NULL, 
    kit_description_df = NULL, 
    treatment_by_drug_df = NULL, 
    dosing_schedule_df = NULL, 
    model_k0 = "negative binomial", 
    model_t0 = "log-logistic", 
    model_t1 = "least squares", 
    model_ki = "negative binomial", 
    model_ti = "least absolute deviations", 
    model_di = "linear mixed-effects model", 
    pilevel = 0.95, 
    nyears = 1, 
    ncores_max = 10, 
    pred_pp_only = FALSE, 
    showplot = TRUE
)
```

**Arguments**

- **df**
  A data frame for subject-level enrollment and event data, including the following variables: trialsdt, usubjid, randdt, treatment, treatment_description, time, event, dropout, and cutoffdt.

- **newEvents**
  A data frame containing the imputed event data for both ongoing and new patients, typically obtained from the output of the getPrediction function of the eventPred package. It contains the following variables: draw, usubjid,
arrivalTime, treatment, treatment_description, time, event, dropout, and totalTime. It must be provided.

visitview
A data frame containing the observed drug dispensing data, including the following variables: usubjid, visit, date, drug, drug_name, kit, kit_name, kit_number, and dispensed_quantity.

kit_description_df
A data frame indicating the drug and kit descriptions, including the following variables: drug, drug_name, kit, and kit_name. It must be specified at the design stage. It will be replaced with the observed information at the analysis stage.

treatment_by_drug_df
A data frame indicating the treatments associated with each drug, including the following variables: treatment and drug. It must be specified at the design stage. It will be replaced with the observed information at the analysis stage.

dosing_schedule_df
A data frame providing dosing schedule information. It contains the following variables: kit, target_days, target_dose, and max_cycles. It must be provided.

model_k0
The model for the number of skipped visits between randomization and the first drug dispensing visit. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".

model_t0
The model for the gap time between randomization and the first drug dispensing visit when there is no visit skipping. Options include "constant", "exponential", "weibull", "log-logistic", and "log-normal".

model_t1
The model for the gap time between randomization and the first drug dispensing visit when there is visit skipping. Options include "least squares" and "least absolute deviations".

model_ki
The model for the number of skipped visits between two consecutive drug dispensing visits. Options include "constant", "poisson", "zero-inflated poisson", and "negative binomial".

model_ti
The model for the gap time between two consecutive drug dispensing visits. Options include "least squares" and "least absolute deviations".

model_di
The model for the dispensed doses at drug dispensing visits. Options include "constant", "linear model", and "linear mixed-effects model".

pilevel
The prediction interval level.

nyears
The number of years after the data cut for prediction.

ncores_max
The maximum number of cores to use for parallel computing. The actual number of cores used is the minimum of ncores_max and half of the detected number of cores.

pred_pp_only
A Boolean variable that controls whether or not to make protocol-based predictions only.

showplot
A Boolean variable that controls whether or not to show the drug dispensing model fit and drug demand prediction plots. It defaults to TRUE.
Value

For design-stage drug demand forecasting, a list with the following components:

- **kit_description_df**: A data frame indicating the drug and kit descriptions, including the following variables: drug, drug_name, kit, and kit_name.
- **treatment_by_drug_df**: A data frame indicating the treatments associated with each drug, including the following variables: treatment and drug.
- **dosing_schedule_df**: A data frame providing dosing schedule information. It contains the following variables: kit, target_days, target_dose, and max_cycles.
- **dosing_pred_df**: A data frame for dosing summary by kit type and time point per protocol. It includes the following variables: kit, kit_name, t, n, pilevel, lower, upper, mean, var, and parameter.
- **dosing_pred_plot**: A plot object for dosing prediction.

For analysis-stage drug demand forecasting, a list with the following components:

- **trialsdt**: The trial start date.
- **cutoffdt**: The cutoff date.
- **dosing_summary_t0**: A data frame for the cumulative doses dispensed before the cutoff date. It contains the following variables: kit, kit_name, and cum_dose_t0.
- **cum_dispense_plot**: The step plot for the cumulative doses dispensed for each kit type.
- **bar_t0_plot**: The bar chart for the time between randomization and the first drug dispensing visit.
- **bar_ti_plot**: The bar chart for the gap time between two consecutive drug dispensing visits.
- **bar_di_plot**: The bar chart for the doses dispensed at drug dispensing visits.
- **common_time_model**: A Boolean variable that indicates whether a common time model is used for drug dispensing visits.
- **k0_fit**: The model fit for the number of skipped visits between randomization and the first drug dispensing visit.
- **t0_fit**: The model fit for the gap time between randomization and the first drug dispensing visit when there is no visit skipping.
- **t1_fit**: The model fit for the gap time between randomization and the first drug dispensing visit when there is visit skipping.
- **ki_fit**: The model fit for the number of skipped visits between two consecutive drug dispensing visits.
- **ti_fit**: The model fit for the gap time between two consecutive drug dispensing visits.
- **di_fit**: The model fit for the dispensed doses at drug dispensing visits.
- **kit_description_df**: A data frame indicating the drug and kit descriptions, including the following variables: drug, drug_name, kit, and kit_name.
- **treatment_by_drug_df**: A data frame indicating the treatments associated with each drug, including the following variables: treatment and drug.
- **dosing_schedule_df**: A data frame providing dosing schedule information. It contains the following variables: kit, target_days, target_dose, and max_cycles.
f_drug_demand

• dosing_subject_df: A data frame for the observed and imputed subject-level dosing records for the first iteration. It includes the following variables: drug, drug_name, kit, kit_name, usubjid, treatment, treatment_description, arrivalTime, time, day, dose, cum_dose, row_id, subject_type, imputed, trialsdt, cutoffdt, randdt, adt, and date.

• dosing_pred_df: A data frame for dosing summary by kit type and time point. It includes the following variables: kit, kit_name, t, n, pilevel, lower, upper, mean, var, date, and parameter.

• dosing_pred_plot: A plot object for dosing prediction.

Author(s)
Kaifeng Lu, <kaifenglu@gmail.com>

See Also
f_fit_t0, f_fit_ki, f_fit_ti, f_fit_di

Examples

set.seed(529)

pred <- eventPred::getPrediction(
  df = df2,
  to_predict = "event only",
  target_d = 250,
  event_model = "log-logistic",
  dropout_model = "none",
  pilevel = 0.95,
  nyears = 1,
  nreps = 200,
  showplot = FALSE,
  by_treatment = TRUE)

drug_demand <- f_drug_demand(
  df = df2,
  newEvents = pred$event_pred$newEvents,
  visitview = visitview2,
  dosing_schedule_df = dosing_schedule_df,
  model_k0 = "zero-inflated poisson",
  model_t0 = "log-logistic",
  model_t1 = "least squares",
  model_ki = "zero-inflated poisson",
  model_ti = "least squares",
  model_di = "linear mixed-effects model",
  pilevel = 0.95,
  nyears = 1,
  ncores_max = 2,
  showplot = FALSE)
Model Fitting for Dispensed Doses

Description
Fits a linear mixed-effects model to the dispensed doses at drug dispensing visits.

Usage
f_fit_di(df, model, nreps, showplot = TRUE)

Arguments
- df: The subject-level dosing data, including usubjid, day, kit, and dose.
- model: The model used to analyze the dispensed doses, with options including "constant", "linear model", and "linear mixed-effects model".
- nreps: The number of simulations for drawing posterior model parameters.
- showplot: A Boolean variable that controls whether or not to show the fitted dose bar chart. It defaults to TRUE.

Value
A list with three components:
- fit: A list of results from the model fit that includes
  - model: The specific model used in the analysis.
  - mud: The estimated mean dose.
  - vmud: The estimated variance of mud.
  - sigmab: The estimated between-subject standard deviation.
  - sigmae: The estimated within-subject residual standard deviation.
  - aic: The Akaike Information Criterion value.
  - bic: The Bayesian Information Criterion value.
- fit_plot: A fitted dose bar chart.
- theta: Posterior draws of model parameters.
  - fixed: Posterior draws of fixed model parameters: mud, sigmab, and sigmae.
  - random: Posterior draws of subject random effects.
  - usubjid: The unique subject ID associated with the subject random effects.

Author(s)
Kaifeng Lu, <kaifenglu@gmail.com>
Examples

```r
library(dplyr)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)
vf <- observed$vf

vf1 <- vf %>% filter(kit == 3)
di_fit <- f_fit_di(vf1, model = "linear mixed-effects model", nreps = 200)
```

---

### f_fit_ki

**Model Fitting for Number of Skipped Visits**

#### Description

Fits a count model to the number of skipped visits between two consecutive drug dispensing visits.

#### Usage

```r
f_fit_ki(df, model, nreps, showplot = TRUE)
```

#### Arguments

- `df`: The subject-level dosing data, including `skipped` to indicate the number of skipped visits.
- `model`: The count model used to analyze the number of skipped visits, with options including "constant", "poisson", "zero-inflated poisson", and "negative binomial".
- `nreps`: The number of simulations for drawing posterior model parameter values.
- `showplot`: A Boolean variable that controls whether or not to show the fitted count bar chart. It defaults to `TRUE`.

#### Value

A list with three components:

- `fit`: A list of results from the model fit that includes
  - `model`: The specific model used in the analysis.
  - `theta`: The estimated model parameters.
  - `vtheta`: The estimated covariance matrix of `theta`.
  - `aic`: The Akaike Information Criterion value.
  - `bic`: The Bayesian Information Criterion value.
- `fit_plot`: A fitted count bar chart.
- `theta`: Posterior draws of model parameters.
Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

Examples

```r
clean(f)

data <- f_dose_observed(df2, visitview2, showplot = FALSE)
do <- observed$vf

do <- do %>% left_join(dosing_schedule_df, by = "kit")

df_t0 <- do %>%
  mutate(time = lead(day) - day,
         skipped = pmax(floor((time - target_days/2)/target_days), 0),
         ki = skipped + 1)

df_t0 <- df_t0 %>% filter(row_id < n())

ki_fit <- f_fit_ki(df_t0, model = "zero-inflated poisson", nreps = 200)
```

---

**f_fit_t0**  
*Model Fitting for Dispensing Delay After Randomization*

**Description**

Fits a specified time-to-event model to the gap time between randomization and the first drug dispensing visit when there is no visit skipping.

**Usage**

```r
f_fit_t0(df, model, nreps, showplot = TRUE)
```

**Arguments**

- **df**  
The subject-level dosing data, including the following variables:
  - **time**: The number of days between randomization and the first drug dispensing visit (first drug dispensing visit date - randomization date + 1).
  - **left**: Equals time - 1, used to indicate the left endpoint of an interval for interval censoring.
  - **right**: Equals time, used to indicate the right endpoint of an interval for interval censoring.

- **model**  
The event model used to analyze the gap time between randomization and the first drug dispensing visit when there is no visit skipping, with options including "constant", "exponential", "weibull", "log-logistic", and "log-normal".

- **nreps**  
The number of simulations for drawing posterior model parameter values.

- **showplot**  
A Boolean variable that controls whether or not to show the fitted time-to-event bar chart. It defaults to **TRUE**.
**Value**

A list with three components:

- **fit**: A list of results from the model fit that includes
  - **model**: The specific model used in the analysis.
  - **theta**: The estimated model parameters.
  - **vtheta**: The estimated covariance matrix of **theta**.
  - **aic**: The Akaike Information Criterion value.
  - **bic**: The Bayesian Information Criterion value.
- **fit_plot**: A fitted time-to-event bar chart.
- **theta**: Posterior draws of model parameters.

**Author(s)**

Kaifeng Lu, <kaifenglu@gmail.com>

**Examples**

```r
library(dplyr)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)

vf <- observed$vf

vf <- vf %>% left_join(dosing_schedule_df, by = "kit")

# time from randomization to the first drug dispensing visit
df_k0 <- vf %>%
  filter(row_id == 1) %>%
  mutate(time = day,
         skipped = floor((time - target_days/2)/target_days) + 1)

# no skipping
df_t0 <- df_k0 %>%
  filter(skipped == 0) %>%
  mutate(left = time - 1, right = time)

t0_fit <- f_fit_t0(df_t0, model = "log-logistic", nreps = 200)
```

---

**f_fit_ti**

Model Fitting for Gap Times

**Description**

Fits a linear regression model to the gap time between two consecutive drug dispensing visits.
Usage

\texttt{f\_fit\_ti(df, model, nreps, showplot = TRUE)}

Arguments

\textbf{df} \hspace{2cm} The subject-level dosing data, including the following variables:
- \textit{time}: The gap time to the next drug dispensing visit.
- \textit{skipped}: The number of skipped visits.
- \textit{k1}: The covariate for the linear regression. It equals \textit{skipped} for the gap time between randomization and the first drug dispensing visit and \textit{skipped} + 1 for the gap time between two consecutive drug dispensing visits.

\textbf{model} \hspace{2cm} The model used to analyze the gap time. Options include "least squares" and "least absolute deviations".

\textbf{nreps} \hspace{2cm} The number of simulations for drawing posterior model parameter values.

\textbf{showplot} \hspace{2cm} A Boolean variable that controls whether or not to show the fitted gap time bar chart. It defaults to \texttt{TRUE}.

Value

A list with three components:
- \textit{fit}: A list of results from the model fit that includes
  - \textit{model}: The specific model used in the analysis.
  - \textit{beta}: The estimated regression coefficient for the covariate.
  - \textit{vbeta}: The estimated variance of \textit{beta}.
  - \textit{sigma}: The estimated residual standard deviation.
  - \textit{df}: The residual degrees-of-freedom.
  - \textit{aic}: The Akaike Information Criterion value.
  - \textit{bic}: The Bayesian Information Criterion value.
- \textit{fit\_plot}: A fitted gap time bar chart.
- \textit{theta}: Posterior draws of model parameters.

Author(s)

Kaifeng Lu, \texttt{<kaifenglu@gmail.com>}

Examples

\begin{verbatim}
library(dplyr)

observed <- f_dose_observed(df2, visitview2, showplot = FALSE)
vf <- observed$vf

vf <- vf %>% left_join(dosing_schedule_df, by = "kit")

df_ti <- vf %>%
\end{verbatim}
f_ongoing_new

```r
mutate(time = lead(day) - day,
        skipped = pmax(floor((time - target_days/2)/target_days), 0),
        k1 = skipped + 1) %>%
filter(row_id < n())
```

ti_fit <- f_fit_ti(df_ti, model = "least squares", nreps = 200)

---

**f_ongoing_new**  
**Observed Dosing for Ongoing and New Subjects**

**Description**

Prepares the dosing data sets to impute for ongoing and new subjects.

**Usage**

```r
f_ongoing_new(newEvents, kit_description_df, treatment_by_drug_df, vf)
```

**Arguments**

- `newEvents`: A data frame containing the imputed event data for both ongoing and new patients, typically obtained from the output of the `getPrediction` function of the `eventPred` package. It contains the following variables: `draw`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, `event`, `dropout`, and `totalTime`.

- `kit_description_df`: A data frame indicating the drug and kit descriptions, including the following variables: `drug`, `drug_name`, `kit`, and `kit_name`. It must be specified at the design stage. It will be replaced with the observed information at the analysis stage.

- `treatment_by_drug_df`: A data frame indicating the treatments associated with each drug, including the following variables: `treatment` and `drug`.

- `vf`: A data frame for subject-level drug dispensing data, including the following variables: `drug`, `drug_name`, `kit`, `kit_name`, `usubjid`, `treatment`, `treatment_description`, `arrivalTime`, `time`, `event`, `dropout`, `day`, `dose`, `cum_dose`, and `row_id`.

**Value**

A list with the following components:

- `vf_ongoing`: A data frame for the observed drug dispensing data for ongoing patients with drug dispensing records. It includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `day`, `dose`, `arrivalTime`, `treatment`, `treatment_description`, `time`, and `totalTime`.

- `vf_new`: A data frame for the randomization date for new patients and ongoing patients with no drug dispensing records. It includes the following variables: `draw`, `kit`, `kit_name`, `usubjid`, `arrivalTime`, `treatment`, `treatment_description`, `time`, and `totalTime`.
Examples

```r
set.seed(2000)

pred <- eventPred::getPrediction(
  df = df2,
  to_predict = "event only",
  target_d = 250,
  event_model = "log-logistic",
  dropout_model = "none",
  pilevel = 0.95,
  nyears = 1,
  nreps = 200,
  showplot = FALSE,
  by_treatment = TRUE)

observed <- f_dose_observed(df = df2, visitview = visitview2)

vf_ongoing_new <- f_ongoing_new(
  pred$event_pred$newEvents,
  observed$kit_description_df,
  observed$treatment_by_drug_df,
  observed$vf)

head(vf_ongoing_new$vf_ongoing)
head(vf_ongoing_new$vf_new)
```

---

**kit_description_df**

*The kit description data frame.*

**Description**

A data frame with the following columns:

- **drug** The numeric code of the drug.
- **drug_name** The name of the drug.
- **kit** The numeric code of the kit type.
- **kit_name** The name of the kit type.
- **p_kit** The prior probability of different kit types within a drug.
rdichlet

Usage

kit_description_df

Format

An object of class tbl_df (inherits from tbl, data.frame) with 4 rows and 5 columns.

rdichlet Random Number Generator for the Dirichlet Distribution

Description

Generates cell probabilities from the Dirichlet distribution.

Usage

rdichlet(n = 1, alpha)

Arguments

n The number of observations.
alpha The shape parameters of the Dirichlet distribution.

Value

A matrix of n rows and k columns, where n is the number of observations and k is the number of cells.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

Examples

rdichlet(2, c(50, 20, 30))
treatment_by_drug_df  The data frame indicating the treatments associated with each drug.

Description
A data frame with the following columns:
treatment  The numeric code of the treatment group.
drug  The numeric code of the drug.

Usage
treatment_by_drug_df

Format
An object of class tbl_df (inherits from tbl.data.frame) with 6 rows and 2 columns.

visitview1  The observed subject drug dispensing data before enrollment completion.

Description
A data frame with the following columns:
usubjid  The unique subject ID.
visit  The drug dispensing visit, e.g., "Cycle 1 Day 1".
date  The date of the drug dispensing visit.
drug  The numeric code of the drug.
drug_name  The name of the drug.
kit  The numeric code of the kit type.
kit_name  The name of the kit type.
kit_number  The kit number for drug dispensing.
dispensed_quantity  The number of kits dispensed at the visit.

Usage
visitview1

Format
An object of class tbl_df (inherits from tbl.data.frame) with 2290 rows and 9 columns.
The observed subject drug dispensing data after enrollment completion.

**Description**

A data frame with the following columns:

- **usubjid**: The unique subject ID.
- **visit**: The drug dispensing visit, e.g., "Cycle 1 Day 1".
- **date**: The date of the drug dispensing visit.
- **drug**: The numeric code of the drug.
- **drug_name**: The name of the drug.
- **kit**: The numeric code of the kit type.
- **kit_name**: The name of the kit type.
- **kit_number**: The kit number for drug dispensing.
- **dispensed_quantity**: The number of kits dispensed at the visit.

**Usage**

```r
visitview2
```

**Format**

An object of class `tbl_df` (inherits from `tbl.data.frame`) with 5006 rows and 9 columns.
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