Package 'drugDemand'

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Type Package

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)).

License GPL (>= 2)

Imports Rcpp (>= 1.0.10), dplyr (>= 1.1.0), rlang (>= 1.1.0), purrr (>= 1.0.2), stringr (>= 1.4.0), plotly (>= 4.10.1), survival (>= 2.41-3), mvtnorm (>= 1.1-3), erify (>= 0.4.0), stats (>= 3.5.0), MASS (>= 7.3-54), nlme (>= 3.1-153), L1pack (>= 0.41-24), eventPred (>= 0.2.3), parallel (>= 4.1.2), foreach (>= 1.5.2), doParallel (>= 1.0.17), doRNG (>= 1.8.6)

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Author Kaifeng Lu [aut, cre] (<https://orcid.org/0000-0002-6160-7119>)

Maintainer Kaifeng Lu <kaifenglu@gmail.com>

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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.

df2	The subject-level enrollment and event data after enrollment comple-
	tion.

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

х	Treatment duration.
W	Number of days per treatment cycle.
d	Dose per treatment cycle.
Ν	Maximum number of treatment cycles.

Value

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

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

f_dispensing_models

Examples

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

```
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_schedul	.e_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".

model_ki	The model for the number of skipped visits between two consecutive drug dis- pensing 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

```
library(dplyr)
observed <- f_dose_observed(df2, visitview2, showplot = FALSE)</pre>
dispensing_models <- f_dispensing_models(</pre>
  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

```
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 dispens- ing visit when there is no visit skipping.
t1_fit	The model fit for the gap time between randomization and the first drug dispens- ing 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

```
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,</pre>
```

f_dose_draw_1

```
nyears = 3,
 nreps = 200,
 showsummary = FALSE,
 showplot = FALSE,
 by_treatment = TRUE)
observed <- f_dose_observed(df2, visitview2, showplot = FALSE)</pre>
fit <- f_dispensing_models(</pre>
 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$cutoffdt[1]
t0 = as.numeric(cutoffdt - trialsdt + 1)
nyears = 3
t1 = t0 + nyears * 365
t = c(seq(t0, t1, 30), t1)
vf_ongoing_new <- f_ongoing_new(</pre>
 pred$event_pred$newEvents,
 observed$kit_description_df,
 observed$treatment_by_drug_df,
 observed$vf)
dose_draw <- f_dose_draw(</pre>
 vf_ongoing_new$vf_ongoing,
 vf_ongoing_new$vf_new,
 fit$common_time_model,
 fit$k0_fit, fit$t0_fit, fit$t1_fit,
 fit$ki_fit, fit$ti_fit, fit$di_fit,
 t0, t, ncores_max = 2)
head(dose_draw$dosing_subject_new)
head(dose_draw$dosing_summary_new)
```

f_dose_draw_1

Drug Dispensing Data Simulation for One Iteration

Description

Simulates drug dispensing data for one iteration.

Usage

```
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,
 1,
 t
```

)

Arguments

i common_time_mod	The iteration number.
common_time_mod	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 dispens- ing visit when there is no visit skipping.
t1_fit	The model fit for the gap time between randomization and the first drug dispens- ing 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.

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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 fol- lowing 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.
1	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)

Kaifeng Lu, <kaifenglu@gmail.com>

See Also

f_fit_t0, f_fit_ki, f_fit_ti, f_fit_di

```
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,</pre>
```

```
nyears = 3,
  nreps = 200,
  showsummary = FALSE,
  showplot = FALSE,
  by_treatment = TRUE)
observed <- f_dose_observed(df2, visitview2, showplot = FALSE)</pre>
fit <- f_dispensing_models(</pre>
  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$cutoffdt[1]
t0 = as.numeric(cutoffdt - trialsdt + 1)
nyears = 3
t1 = t0 + nyears * 365
t = c(seq(t0, t1, 30), t1)
1 = nrow(observed$kit_description_df)
vf_ongoing_new <- f_ongoing_new(</pre>
  pred$event_pred$newEvents,
  observed$kit_description_df,
  observed$treatment_by_drug_df,
  observed$vf)
vf_ongoing <- vf_ongoing_new$vf_ongoing</pre>
vf_new <- vf_ongoing_new$vf_new</pre>
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 %>%

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f_dose_draw_t_1

f_dose_draw_t_1 Drug Dispensing Visit Dates Simulation for One Iteration

Description

Simulates drug dispensing visit dates for one iteration.

Usage

```
f_dose_draw_t_1(
    i,
    k0_fit,
    t0_fit,
    t1_fit,
    ki_fit,
    ti_fit,
    vf_ongoing1,
    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 dispens- ing visit when there is no visit skipping.

t1_fit	The model fit for the gap time between randomization and the first drug dispens- ing 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.
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 fol- lowing variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D.
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 fol- lowing variables: draw, kit, kit_name, usubjid, arrivalTime, treatment, treatment_description, time, totalTime, V, C, and D.

Value

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.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

See Also

f_fit_t0, f_fit_ki, f_fit_ti

```
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,</pre>
```

```
showplot = FALSE,
 by_treatment = TRUE)
observed <- f_dose_observed(df2, visitview2, showplot = FALSE)</pre>
fit <- f_dispensing_models(</pre>
 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$cutoffdt[1]
t0 = as.numeric(cutoffdt - trialsdt + 1)
nyears = 3
t1 = t0 + nyears * 365
vf_ongoing_new <- f_ongoing_new(</pre>
 pred$event_pred$newEvents,
 observed$kit_description_df,
 observed$treatment_by_drug_df,
 observed$vf)
vf_ongoing <- vf_ongoing_new$vf_ongoing</pre>
vf_new <- vf_ongoing_new$vf_new</pre>
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()) %>%
 mutate(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(</pre>
  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

```
f_dose_new_cpp(
    usubjid,
    V,
    C,
    D,
    model_k0,
    theta_k0,
    model_t0,
    theta_t0,
    model_t1,
    theta_t1,
    model_ki,
    theta_ki,
    model_ti,
    theta_ti
```

)

Arguments

usubjid	The unique subject ID.
V	Initialized to 0 and corresponds to the randomization visit.
С	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.

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".
theta_t1	The model parameters for the gap time between randomization and the first drug dispensing visit when there is visit skipping.
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

```
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))
```

f_dose_observed Observed Drug Dispensing Data Summary

Description

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 fol- lowing 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>

```
observed <- f_dose_observed(df = df2, visitview = visitview2)</pre>
```

f_dose_ongoing_cpp 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.
С	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 dis- pensing 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>

```
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

Description

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

Usage

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

Arguments

t0		
A data frame for the cumulative doses dispensed before the cutoff date. It con- tains the following variables: kit, kit_name, and cum_dose_t0.		
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.		
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.		
The cutoff date relative to the trial start date.		
A vector of new time points for drug dispensing prediction.		
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>

f_dose_pp

```
# Design stage drug demand forecasting per protocol.
set.seed(312)
library(dplyr)
pred <- eventPred::getPrediction(</pre>
  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, -0.2),
         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"))
dosing_summary_t0 = kit_description_df %>%
  mutate(cum_dose_t0 = 0) %>%
  select(-c("drug", "drug_name"))
vf_ongoing_new <- f_ongoing_new(</pre>
  pred$event_pred$newEvents, kit_description_df,
  treatment_by_drug_df, NULL)
t0 = 1
nyears = 3
t1 = t0 + nyears * 365
```

```
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)</pre>
```

f_drug_demand

Drug Demand Forecasting

Description

Obtains drug demand forecasting via modeling and simulation.

Usage

```
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 pa- tients, typically obtained from the output of the getPrediction function of the eventPred package. It contains the following variables: draw, usubjid,

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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.

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.

- 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

```
set.seed(529)
```

```
pred <- eventPred::getPrediction(</pre>
 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(</pre>
 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)
```

drug_demand\$dosing_pred_plot

f_fit_di

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 "con- stant", "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>

f_fit_ki

Examples

```
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)</pre>
```

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

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 in- cluding "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

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

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.

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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

library(dplyr)

```
observed <- f_dose_observed(df2, visitview2, showplot = FALSE)
vf <- observed$vf</pre>
```

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

```
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)</pre>
```

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

f_fit_ti(df, model, nreps, showplot = TRUE)

Arguments

df	The subject-level dosing data, including the following variables:
	• time: The gap time to the next drug dispensing visit.
	 skipped: The number of skipped visits.
	 k1: The covariate for the linear regression. It equals skipped for the gap time between randomization and the first drug dispensing visit and skipped + 1 for the gap time between two consecutive drug dispensing visits.
model	The model used to analyze the gap time. Options include "least squares" and "least absolute deviations".
nreps	The number of simulations for drawing posterior model parameter values.
showplot	A Boolean variable that controls whether or not to show the fitted gap time 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.
 - beta: The estimated regression coefficient for the covariate.
 - vbeta: The estimated variance of beta.
 - sigma: The estimated residual standard deviation.
 - df: The residual degrees-of-freedom.
 - aic: The Akaike Information Criterion value.
 - bic: The Bayesian Information Criterion value.
- fit_plot: A fitted gap time bar chart.
- theta: Posterior draws of model parameters.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

```
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 %>%
```

f_ongoing_new

f_ongoing_new

Observed Dosing for Ongoing and New Subjects

Description

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

Usage

```
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 pa-
	tients, typically obtained from the output of the getPrediction function of
	the eventPred package. It contains the following variables: draw, usubjid,
	<pre>arrivalTime, treatment, treatment_description, time, event, dropout,</pre>
	and totalTime.
kit_description	u_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.
<pre>treatment_by_dr</pre>	rug_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.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

Examples

```
set.seed(2000)
pred <- eventPred::getPrediction(</pre>
  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)</pre>
vf_ongoing_new <- f_ongoing_new(</pre>
  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.

rdirichlet

Usage

kit_description_df

Format

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

rdirichlet

Random Number Generator for the Dirichlet Distribution

Description

Generates cell probabilities from the Dirichlet distribution.

Usage

rdirichlet(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

rdirichlet(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 comple-
	tion.

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.

visitview2

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

visitview2

Format

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

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