OPTITXS.r

USER'S MANUAL

version 1.1 (April 2011)

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1. Installing and running the program

The program can be found at http://www.hsph.harvard.edu/faculty/spiegelman/optitxs.html. Save the program file to your computer by right-clicking on “R program” and then selecting “save target as” on the menu that appears.

Once inside R (see section 1.1 “Installing R” if you need to install R), load the program and it is functions by typing:

```
source(“optitxs.r”)
```

You may need to include the path. In Windows, you need to use double backslash (\\) or a slash (/) to specify the folders, e.g.

```
source(“c:\\My Documents\\longitudinal\\design\\optitxs.r”)
```

The program is now ready for running and it can be run in two different ways:

1. Interactively using a user interface that queries the user for all the information and parameters needed. The interactive use of the program is described in section 2.1.

2. In “batch” mode, where the user enters all needed parameters in an input file and the results are stored in an output file. This approach is useful when one wants to repeat the same calculation using different values of the parameters. Each row the input file represents a different set of parameters, and the calculations are performed for every row in the file. The “batch” use of the program is described in section 2.2.

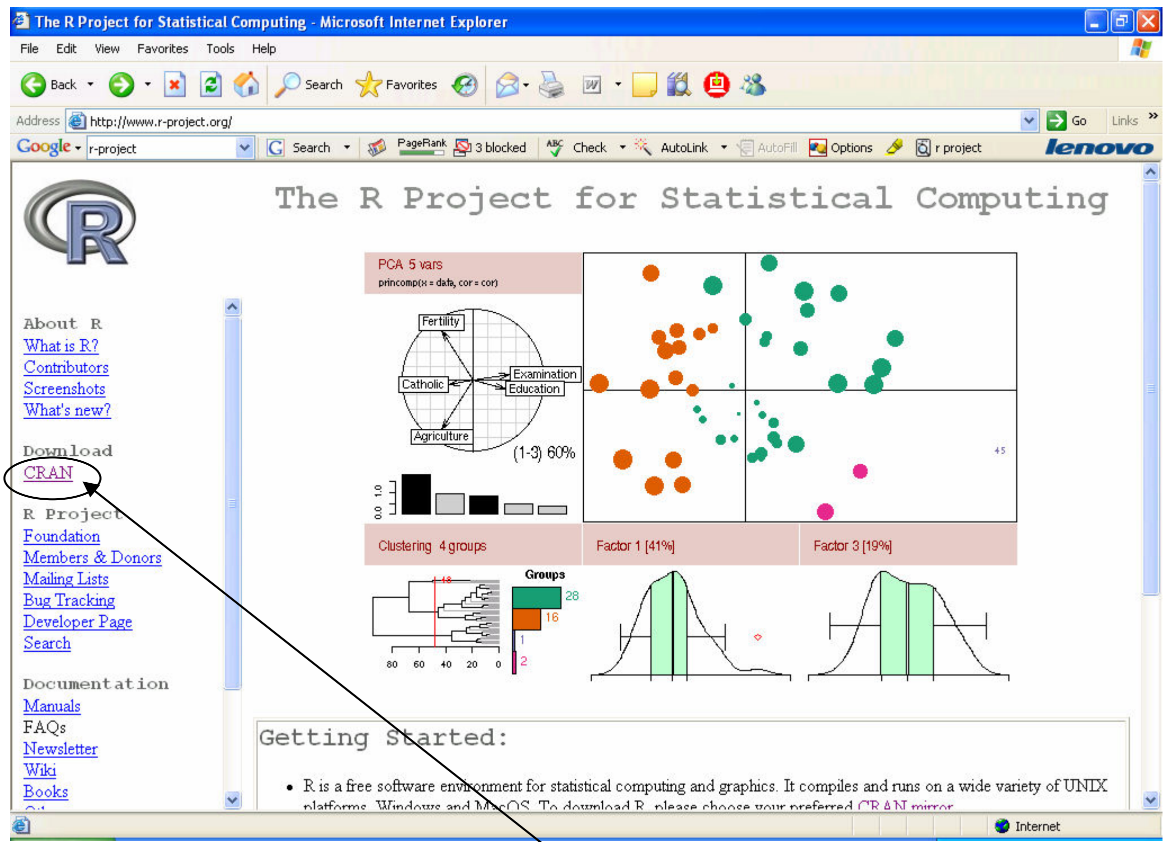
The program `optitxs` is based on the papers Basagaña and Spiegelman (2007), Basagaña and Spiegelman (2010), Basagaña, Liao and Speigelman (2010).

These papers are available at http://www.hsph.harvard.edu/faculty/spiegelman/optitxs.html.

1.2. Installing R

Example using Windows XP Professional, Internet Explorer 6, downloading version 2.3.1 or R (the most recent at the time this documents was created)

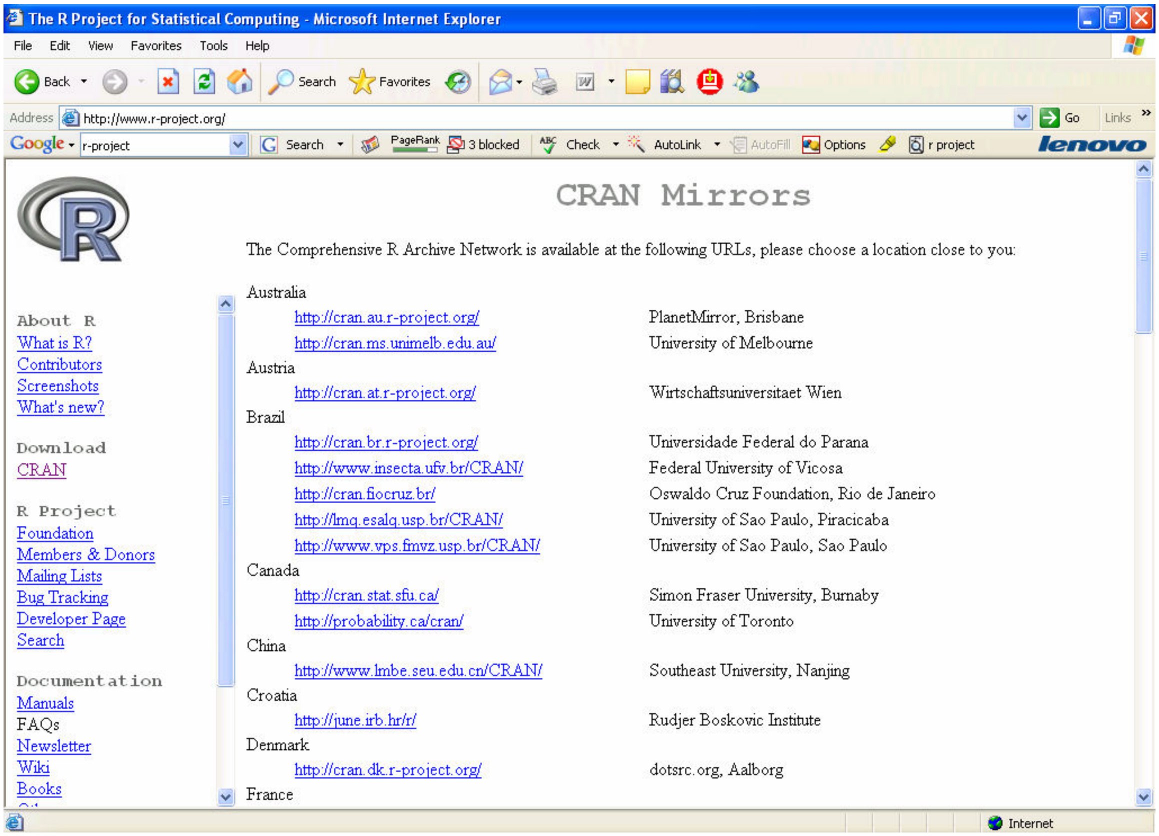
1) Go to www.r-project.com



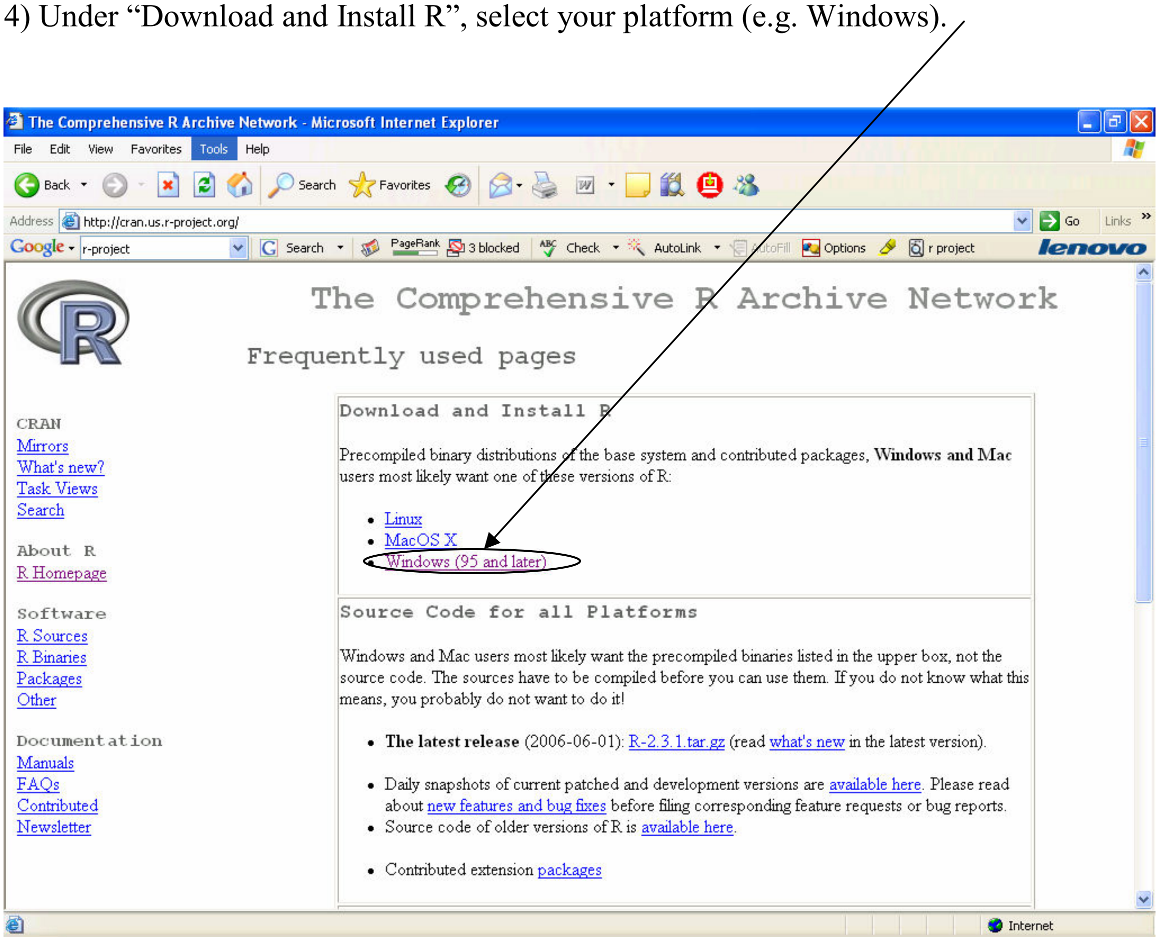
2) Click on the “CRAN” link under “Download”.

3) Select a location close to you from the list.

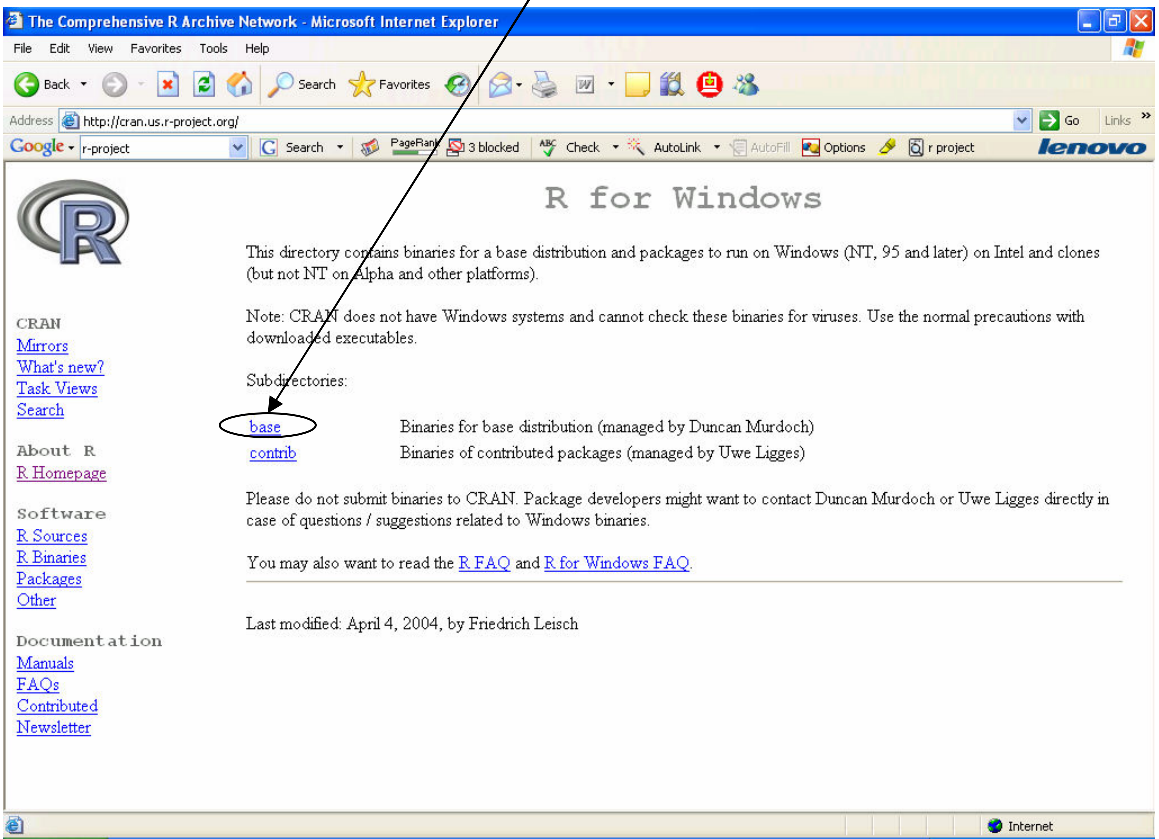
e.g. I selected http://cran.us.r-project.org/ , Pair Networks, Pittsburgh, PA, USA.



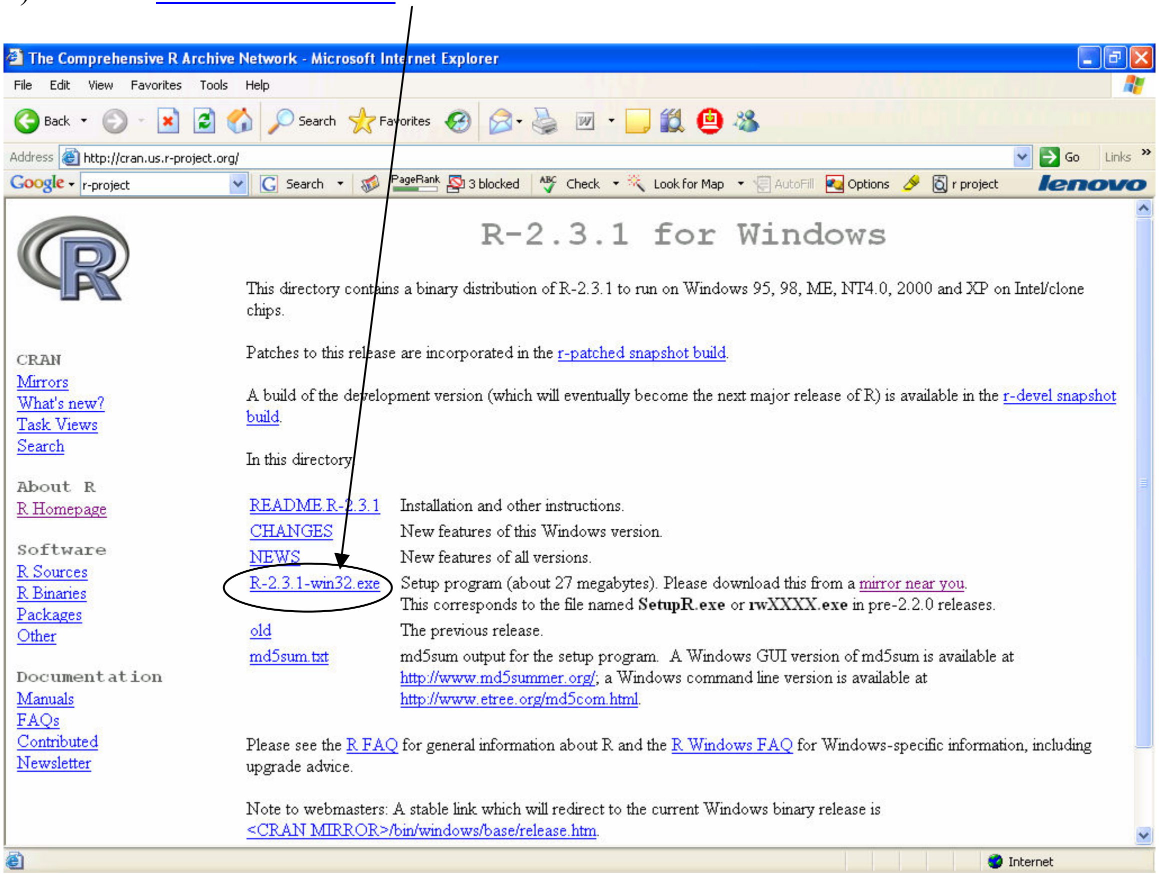
4) Under “Download and Install R”, select your platform (e.g. Windows).



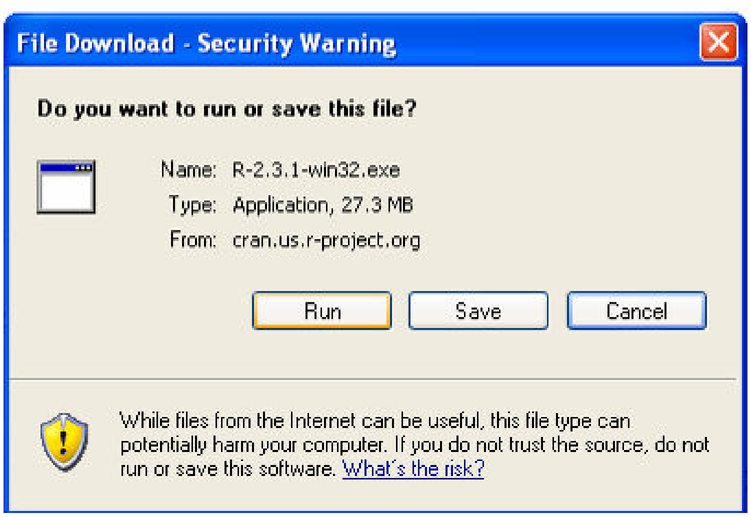
5) Under "Subdirectories", click on "base".



6) Click on R-2.3.1-win32.exe



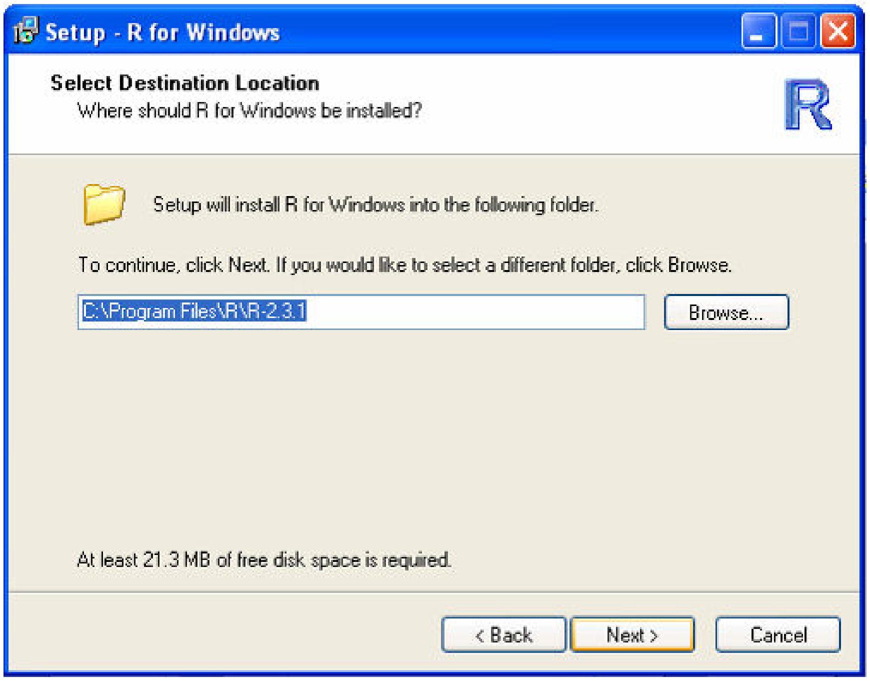
7) Click on "Run"



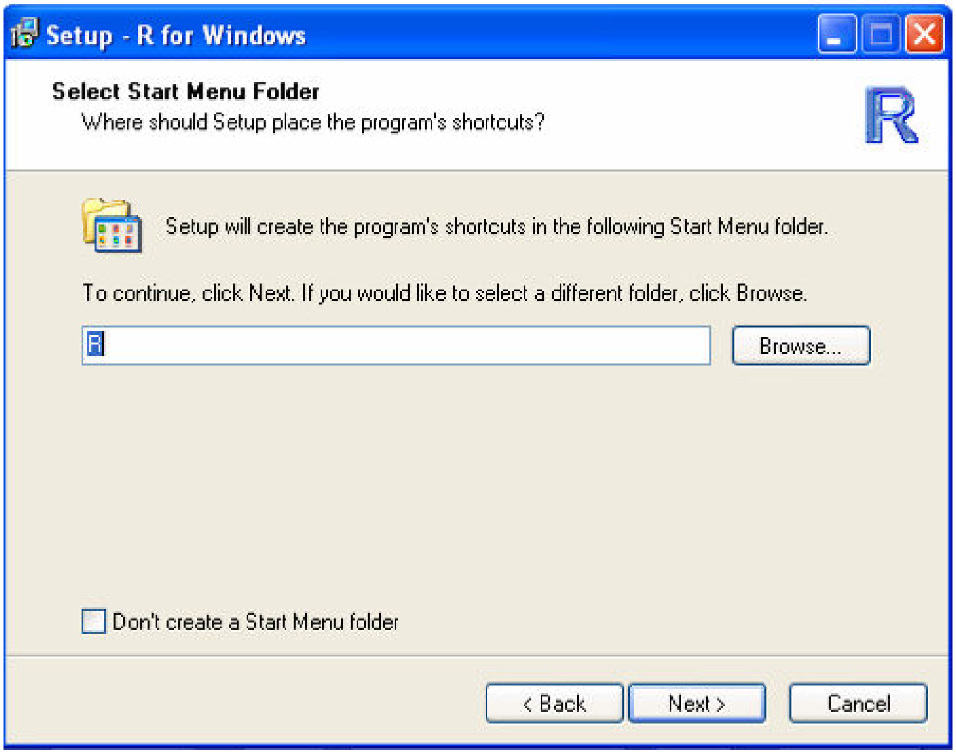
8) Click on “Run”

9) Select the language for installation.

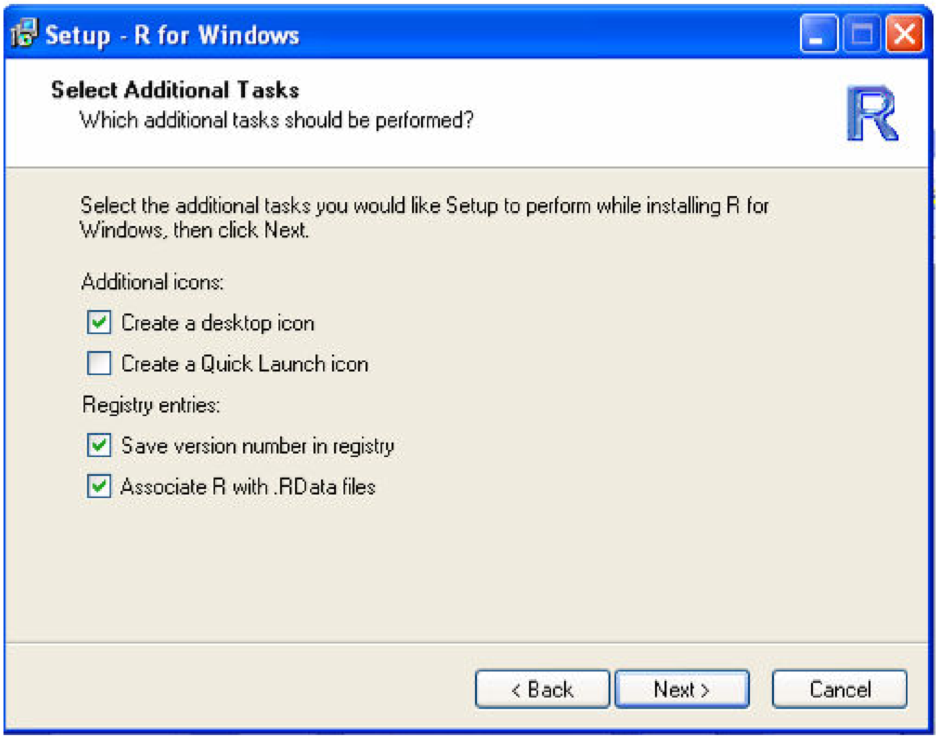
10) Select the folder where you want to install it.



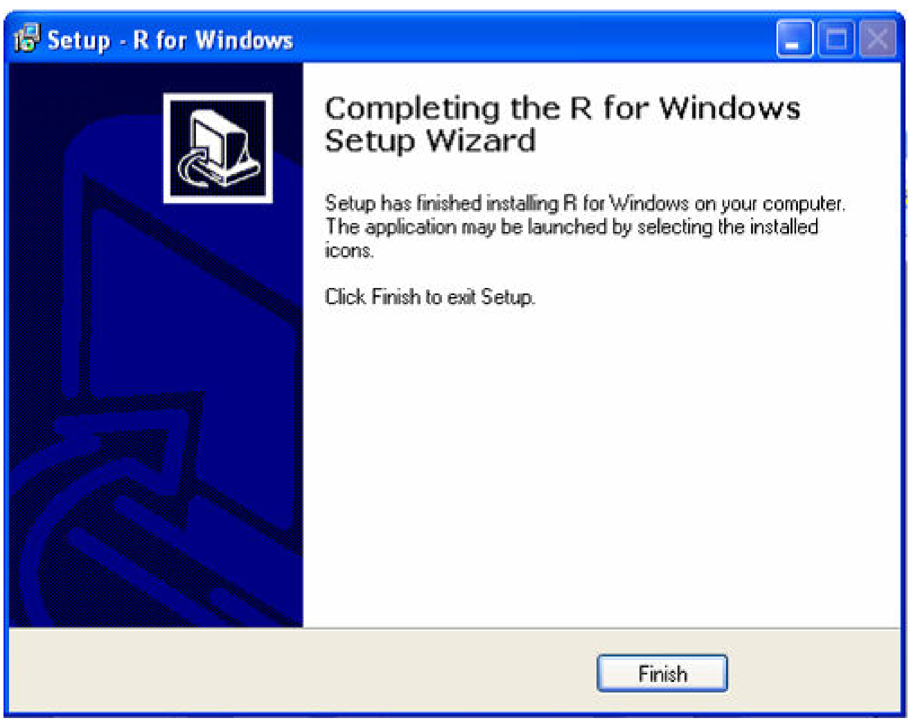
11) Select the name for the Shortcut in the Start Menu.



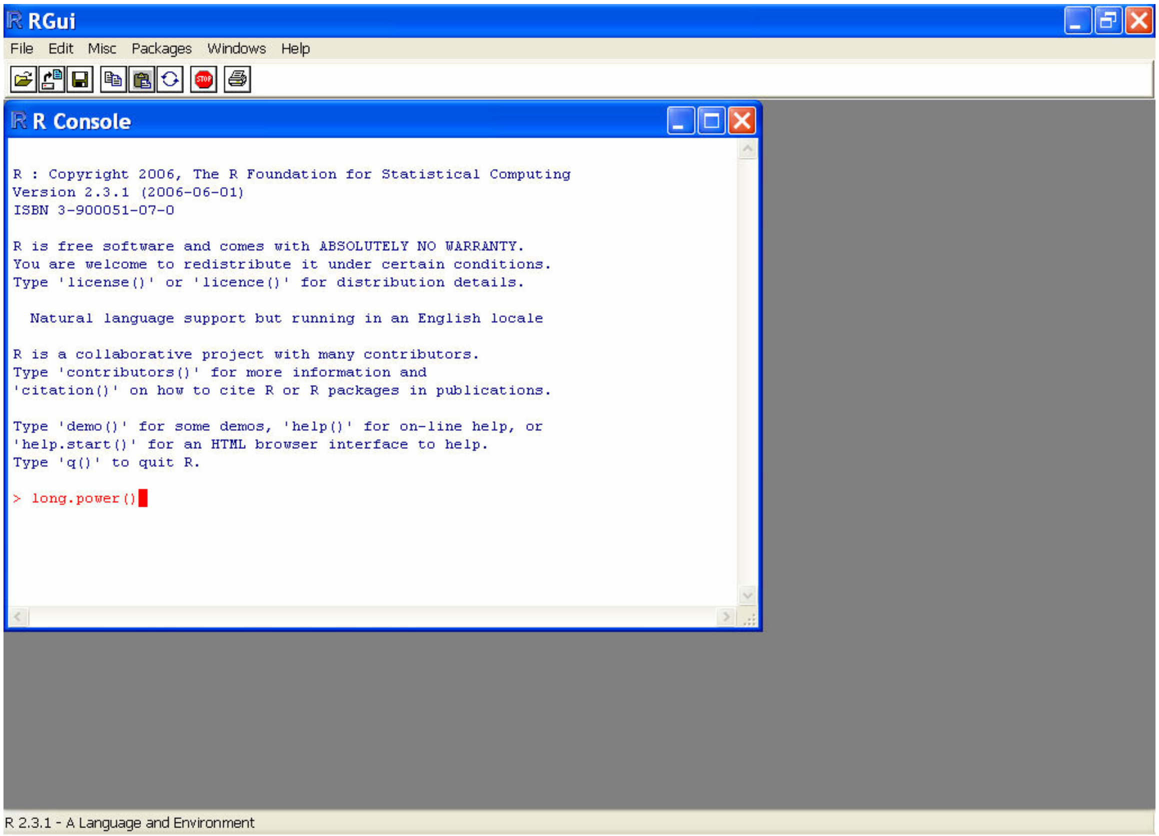
12) Select other installation options.



13) Click to “Finish”



14) R is installed. Click on the icon program to start it. This is the appearance of the program.



2. Program use

2.1. Interactive use of the program

After sourcing the program (see page 3), the program can be invoked by typing `optitxs()`. The user will then be asked to select one of the five following modules, and then the program will query the user on the necessary parameters.

```
> optitxs()

Do you want to:

 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power

Option:
```

The next section describes every query that can be encountered by running any of the five preceding modules. For each question, a default answer is provided between square brackets (see examples in section 2.1.2). If the user presses <Enter> without entering any value, then the default value for that question is used. When all parameters have been entered and the program has provided the requested quantity, the user can choose to continue using the program to perform more calculations. In that case, the default values for each question will be the values that the user entered in the previous iteration of the program. If, for example, the user wants to repeat the same calculation but just changing the value of ρ, he or she can press <Enter> in all the questions to accept the previous values and just change the response to the question asking the value of ρ. For the case where calculations for many values of the parameters are needed, some users may prefer to use the program in "batch" form, which is described in section 2.2.

2.1.1 Details about the queries of the program

The parameters that the user needs to provide are comprehensively discussed in Basagaña and Spiegelman (2007), with the additional parameters required for the case of time-varying exposure discussed in Basagaña & Spiegelman (2010) and Basagaña, Liao & Spiegelman (2010). A briefer discussion of the queries of the program with a description is given below:

- **General questions:**

```
Constant mean difference (CMD) or Linearly divergent difference (LDD)?
```

This refers to the assumed response profiles of the exposed and unexposed under the alternative hypothesis. CMD assumes that the difference between exposed and unexposed remains constant over time (regardless of the shape of the response over time within each group), i.e. it is considering response profiles that are parallel.
LDD assumes that the difference between exposed and unexposed that increases linearly with time (regardless of the shape of the response over time within each group). Basically, it assumes that there is an exposure by time interaction.
See figure 1 Basagaña and Spiegelman (2007) for more details.

```
Are you assuming the time between measurements (s) is fixed (1), or the
total duration of follow-up (tau) is fixed (2)?
```

This asks how the study duration is determined. If s is given, the frequency of measurement is fixed (e.g. patients visit the clinic every year, $s=1$); if τ is given, the follow-up period is fixed (e.g. the study will last $\tau=5$ years). This query is only asked when r is not fixed, i.e. when one wants to find r or the optimal combination (N,r).

- **Questions about study design quantities:**

```
Enter the total sample size (N):
```

N is the total number of participants in the study.

```
Enter the number of post-baseline measures (r):
```

It refers to the number of repeated measurements for each subject, ***excluding*** the baseline measure. In a study with $r = 6$, each subject has 7 measurements, one at baseline and 6 additional ones.

```
Enter the desired power (0<Pi<1):
```

This refers to the power that one aims to reach in the study.

```
Enter the time between repeated measures (s):
```

It refers to the time duration between measurements, in units of time used for all queries (e.g. months, years).

Enter the time of follow-up (tau):

It refers to the total length of follow-up, in the units of time used for all queries (e.g. months, years).

- **Questions about exposure and time distribution:**

Is the exposure time-invariant (1) or time-varying (2)?

The first option refers to the case where the exposure does not change over for any participant, while in the second option the exposure can vary over time for some or all participants.

Do you assume that the exposure prevalence is constant over time (1), that it changes linearly with time (2), or you want to enter the prevalence at each time point(3)

When the exposure is time-varying and the user wants to compute power, number of participants or minimum detectable effect, these three choices are allowed to describe the exposure prevalence at each time point. When the exposure is time-invariant or the user wants to compute the required number of repeated measures, or the optimal combination of participants and repeated measures, only a constant prevalence is allowed.
If the first option is chosen, the prevalence is assumed to be the same at each time point. In the second option, the prevalence is assumed to change linearly with time, and the user will need to enter the prevalence at baseline and at the end of follow-up. In the third option, the user will be required to enter the exposure prevalence at all time points.

Enter the exposure prevalence (pe) (0<pe<1):

It refers to the prevalence of exposure, when the exposure is time-invariant. If the prevalence is 10%, type 0.10

Enter the exposure prevalence at time *j* (0<pe*j* <1):

This question is asked for every time point when the user chose to enter all prevalences, or for the first and last time point if the prevalence was assumed to change linearly with time.

Enter the intraclass correlation of exposure (min(rho.e)<rho.e<max(rho.e)):

The intraclass correlation of exposure can be regarded as a measure of within-subject variation of the exposure variable. When the exposure is time-invariant there is no variation within a subject, and $\rho_e = 1$. The lower the value of the intraclass correlation, the more the exposure variable changes within subjects. The upper and lower bounds that this parameter can take are provided, and they are a function of the number of repeated measures and the exposure prevalence. The intraclass correlation of exposure can also be regarded as measure of balance in the number of exposed periods per subject, $E_{i\bullet}$. When $E_{i\bullet}$ is balanced across subjects, then everyone is exposed for the same number of periods, for example as in a crossover study, and ρ_e takes its minimal value $-1/r$. Conversely, when the response is time-invariant, $p_{ej} = p_e \, \forall j$ and the imbalance is maximal since $E_{i\bullet}$ is either zero with probability $(1-p_e)$ or $r+1$ with probability p_e, and $\rho_e = 1$.

Enter the intraclass correlation of exposure (rho.e<=1) (lower bound is not checked since it depends on r)

It refers to the same quantity than the previous question. This question is asked when the user wants to calculate the required number of repeated measures or the optimal combination of participants and repeated measures. In this case, a lower bound for the intraclass correlation is not provided because it depends on the number of repeated measures, and this quantity is not fixed. It is not recommended to enter negative values or values that are very close to zero, since the lower bound can be exceeded for some values of *r*.

`Enter the variance of the time variable at baseline, V(t0) (enter 0 if all participants begin at the same time):`

This parameter is greater than zero when not all subjects enter the study at the same time. For example, when the time variable of interest is age and subjects enter the study at different ages, the user needs to provide an estimate of the variance of age at the start of follow-up.

`Enter the correlation between the time variable at baseline and exposure, rho_{e,t0}:`

This question is only asked if V(t0)>0. If the time variable of interest is age, this parameter refers to the correlation between age at entry and exposure. If the two exposure groups have a different mean age at entry, this parameter will be different than zero.

- **Questions about the effect:**

`Will you specify the alternative hypothesis on the absolute (beta coefficient) scale (1) or the relative (percent) scale (2)?`

"Beta coefficients" refer to the "betas" of the linear model, that is, the parameters are entered on the additive scale. For example, under CMD, you may want to be able to detect a difference of 0.25 units between exposed and unexposed. If that's the case, choose option (1), "coefficients".
Otherwise, you may express the effects in the percent scale, i.e. to detect a 10% difference between exposed and unexposed, choose option (2), "percent changes".

`Do you want the output as a coefficient (1) or as a percent change (2)?`

This is equivalent to the previous question, when you request the minimum detectable effect (i.e. when `long.effect()` is invoked). If you want to get the answer on the additive scale (coefficient or beta), choose (1). Otherwise, if you want the answer as a percentage, choose (2).

Percent change, CMD:

`Enter mean response at baseline among unexposed (mu00):`

The program queries for this quantity when the user uses percent changes (option 2 above), in the referent units of the dependent variable.

`Enter the percent difference between exposed and unexposed groups (p1) (e.g. enter .10 for a 10% difference):`

It refers to the percent difference between exposed and unexposed groups (p_1), where

$p_1 = \dfrac{E(Y_{ij} \mid k_i = 1) - E(Y_{ij} \mid k_i = 0)}{E(Y_{ij} \mid k_i = 0)}, i = 1,\ldots,N$, where Y_{ij} is the outcome of interest for the measurement taken at the jth time $(j = 0,\ldots,r)$ for the ith $(i = 1,\ldots,N)$ participant and $k_i = 0$

indicates the participant is not exposed and $k_i = 1$ the participant is exposed. Under CMD this ratio is the same for all *j*.

Percent change, LDD, fixed *s*:

Enter mean response at baseline among unexposed (mu00):

The program queries for this quantity when the user uses percent changes, in the referent units of the dependent variable.

Enter the percent change from baseline to time=s among unexposed (p2) (e.g. enter 0.10 for a 10% change):

When the frequency of measurement, s, is fixed, the program asks for the percent change from baseline to *s* time units (i.e. percent change from baseline to first post-baseline measurement) among unexposed.

$p_2 = \dfrac{E(Y_{is} \mid k_i = 0) - E(Y_{i0} \mid k_i = 0)}{E(Y_{i0} \mid k_i = 0)}$, $i = 1, \cdots, N(1 - p_e)$, where p_e is the prevalence of exposure.

Enter the percent baseline difference between exposed and unexposed groups (p1) (e.g. enter .10 for a 10% difference):

This is only queried for LDD if $p_2 = 0$, i.e. if the unexposed are assumed to experience no change in response over time. It refers to the percent difference between exposed and unexposed groups (p_1) at baseline (or at the mean initial time), where $p_1 = \dfrac{E(Y_{i0} \mid k_i = 1) - E(Y_{i0} \mid k_i = 0)}{E(Y_{i0} \mid k_i = 0)}$, $i = 1, \cdots, N$,

where Y_{ij} is the outcome of interest for the measurement taken at the jth time $(j = 0, \ldots, r)$ for the ith $(i = 1, \ldots, N)$ participant and $k = 0$ indicates the unexposed group and $k = 1$ the exposed group.

Enter the percent difference between the change from baseline to time=s in the exposed group and the unexposed group (p3) (e.g. enter 0.1 for a 10% difference):

When the frequency of measurement, *s*, is fixed, the program asks for the percent difference between the change from baseline (or from the mean initial time) to time s (the first repeated measurement) in the exposed group and the unexposed group (p_3), where

$$p_3 = \frac{E(Y_{is} - Y_{i0} \mid k_i = 1) - E(Y_{is} - Y_{i0} \mid k_i = 0)}{E(Y_{is} - Y_{i0} \mid k_i = 0)}, \; i = 1, \cdots, N.$$

Enter the percent change from baseline to time=s among the exposed (p3) (e.g. enter 0.10 for a 10% change):

When there is no effect of time among the unexposed, i.e. $p_2 = 0$, and the frequency of measurement, s, is fixed, p_3 is defined as the percent change from baseline (or from the mean initial time) to time s (the first repeated measurement) in the exposed group, $p_3 = \dfrac{E(Y_{is} \mid k_i = 1) - E(Y_{i0} \mid k_i = 1)}{E(Y_{i0} \mid k_i = 1)}$, $i = 1, \cdots, Np_e$

Percent change, LDD, fixed τ:

Enter mean response at baseline among unexposed (mu00):

The program queries for this quantity when the user uses percent changes, in the referent units of the dependent variable.

Enter the percent change from baseline to end of follow-up among unexposed (p2) (e.g. enter 0.10 for a 10% change):

When the follow-up period, τ, is fixed, the program asks for the percent change from baseline to the end of follow-up among unexposed.

$$p_2 = \frac{E\left(Y_{i\tau} \mid k_i = 0\right) - E\left(Y_{i0} \mid k_i = 0\right)}{E\left(Y_{i0} \mid k_i = 0\right)}, i = 1, \cdots, N(1 - p_e).$$

Enter the percent baseline difference between exposed and unexposed groups (p1) (e.g. enter .10 for a 10% difference):

This is only queried for LDD if $p_2 = 0$. It refers to the percent difference between exposed and unexposed groups (p_1) at baseline (or at the mean initial time), where

$p_1 = \frac{E\left(Y_{i0} \mid k_i = 1\right) - E\left(Y_{i0} \mid k_i = 0\right)}{E\left(Y_{i0} \mid k_i = 0\right)}$, $i = 1, \cdots, N$, where Y_{ij} is the outcome of interest for the measurement taken at the jth time $(j = 0, \ldots, r)$ for the ith $(i = 1, \ldots, n_k)$ participant and $k = 0$ indicates the unexposed group and $k = 1$ the exposed group.

Enter the percent difference between the change from baseline to end of follow-up in the exposed group and the unexposed group (p3) (e.g. enter 0.10 for a 10% difference):

When the follow-up period, τ, is fixed, the program asks for the percent difference between the change from baseline (or from the mean initial time) to the end of follow-up in the exposed group and the unexposed group (p_3), where $p_3 = \frac{E\left(Y_{i\tau} - Y_{i0} \mid k_i = 1\right) - E\left(Y_{i\tau} - Y_{i0} \mid k_i = 0\right)}{E\left(Y_{i\tau} - Y_{i0} \mid k_i = 0\right)}$, $i = 1, \cdots, N$.

Enter the percent change from baseline to end of follow-up among the exposed (p3) (e.g. enter 0.10 for a 10% change):

When there is no effect of time among the unexposed, i.e. $p_2 = 0$, and the follow-up period, τ, is fixed, p_3 is defined as the percent change from baseline (or from the mean initial time) to the end of follow-up (or to the mean final time) in the exposed group, $p_3 = \frac{E\left(Y_{i\tau} \mid k_i = 1\right) - E\left(Y_{i0} \mid k_i = 1\right)}{E\left(Y_{i0} \mid k_i = 1\right)}, i = 1, \cdots, Np_e$

Which model are you basing your calculations on:
(1) Model without time. No separation of between- and within-subject effects
(2) Model without time. Within-subject contrast only
(3) Model with time. No separation of between- and within-subject

effects
(4) Model with time. Within-subject contrast only
Model:

This question is asked when the exposure is time-varying and one will be testing a main effect of exposure (CMD hypothesis). The four models are described in Basagaña, Liao and Spiegelman (2010) and they are:

(1): $\mathbb{E}\left(Y_{ij} \mid \mathbf{X}_i\right)=\mathbb{E}\left(Y_{ij} \mid E_{ij}\right)=\beta_0+\beta_1 E_{ij}$

(2): $\mathbb{E}\left(Y_{i,j+1}-Y_{ij} \mid E_{i,j+1}, E_{ij}\right)=\beta_1^W\left(E_{i,j+1}-E_{ij}\right)$

(3): $\mathbb{E}\left(Y_{ij} \mid \mathbf{X}_i\right)=\mathbb{E}\left(Y_{ij} \mid E_{ij}, t_{ij}\right)=\beta_0+\beta_1 E_{ij}+\beta_2 t_{ij}$

(4): $\mathbb{E}\left(Y_{i,j+1}-Y_{i,j} \mid E_{i,j+1}, E_{ij}\right)=\beta_2^W+\beta_1^W\left(E_{i,j+1}-E_{ij}\right)$

Which model are you basing your calculations on:
(1) Cumulative exposure effect model. No separation of between- and within-subject effects
(2) Cumulative exposure effect model. Within-subject contrast only
(3) Acute exposure effect model. No separation of between- and within-subject effects
(4) Acute exposure effect model. Within-subject contrast only
Model:

This question is asked when the exposure is time-varying and one assumes the LDD hypothesis. The four models are described in Basagaña and Spiegelman (2010) and they are:

(1) $\mathbb{E}\left(Y_{ij} \mid \mathbf{X}_i\right)=\gamma_0+\gamma_t t_{ij}+\gamma_{e*} E_{ij}^*$

(2) $\mathbb{E}\left(Y_{ij}-Y_{i,j-1} \mid \mathbf{X}_i\right)=\gamma_t^W+\gamma_{e*}^W E_{ij}$

(3) $\mathbb{E}\left(Y_{ij} \mid \mathbf{X}_i\right)=\gamma_0+\gamma_t t_{ij}+\gamma_e E_{ij}+\gamma_{te}\left(E_{ij} \times t_{ij}\right)$

(4) $\mathbb{E}\left(Y_{i,j+1}-Y_{ij} \mid \mathbf{X}_i\right)=\gamma_t^W+\gamma_e^W\left(E_{i,j+1}-E_{ij}\right)+\gamma_{te}^W\left[\left(E_{i,j+1}-E_{ij}\right)t_{ij}+E_{i,j+1}\right]$

Absolute difference (beta coefficient), CMD:

Enter the difference between groups (beta2):

This question is asked when the exposure is time-invariant and the difference between exposed and unexposed is assumed to be constant over time (constant mean difference, CMD), beta2 is the difference between the exposed and unexposed in units of the response. Model: $\mathbb{E}\left(Y_{ij} \mid X_{ij}\right)=\beta_0+\beta_1 t_{ij}+\beta_2 k_i$

Enter the value of the coefficient of interest in your model, i.e. the difference between exposed and unexposed periods (beta):

This question is asked when the exposure is time-varying and one assumes the CMD hypothesis. For model (1) and (3), it refers to β_1, and for models (2) and (4) it refers to β_e^W.

Absolute difference (beta coefficient), LDD:

Enter the interaction coefficient (gamma3):

This question is asked when the exposure is time-invariant and it is assumed that there is an exposure by time interaction (linearly divergent differences, LDD), gamma3 is the value of the interaction term, that is, the difference in the slopes over time between exposed and unexposed, in units of response divided by units of time.

Model: $\mathbb{E}\left(Y_{ij} \mid X_{ij}\right) = \gamma_0 + \gamma_1 t_{ij} + \gamma_2 k_i + \gamma_3 \left(t_{ij} \times k_i\right)$

Enter the value of the coefficient of interest in your model, i.e. the difference in the rates of change of exposed and unexposed periods (gamma)

This question is asked when the exposure is time-varying and the LDD hypothesis is assumed. For model (1), it refers to γ_{e*}; for model (2), it refers to γ_e^W; for model (3), it refers to γ_{te}; and for model (4) it refers to γ_{te}^W.

- **Questions about the covariance:**

Which covariance matrix are you assuming: compound symmetry (1), damped exponential (2) or random slopes (3)?

Choose the assumed covariance structure for the residuals of the regression.

Compound Symmetry (CS)

Enter the variance of the response given the covariates (sigma2):

`sigma2` is the variance of the response given the covariates, which is assumed to be constant over time. This parameter is not equal to the marginal, cross-sectional variance. It can be approximated by the variance of the response among the unexposed at baseline, a quantity that may be available from the literature or pilot data, or if age is the time variable of interest, within a reasonably narrow age group. If only a marginal response variance is available over a range of ages and exposure levels, as will often be the case in epidemiology, the investigator can approximate the residual variance by multiplying it by the quantity $1-R^2$, where R^2 is the assumed proportion of the marginal variance of the response variable that is explained by the model to be fit when the study is conducted. Typically, in epidemiology, R^2 ranges from 0.10 to 0.30 or so.

Enter the correlation between two measures of the same subject (rho):

`rho` ($\rho \in [0,1)$) is the correlation between two measurements from the same subject. It is also called the reliability coefficient, or intraclass correlation coefficient, $\rho = \sigma_b^2 \big/ \left(\sigma_w^2 + \sigma_b^2\right)$, where σ_b^2 and σ_w^2 are the between- and within-subject residual variance, respectively, and $\sigma_w^2 + \sigma_b^2 = \sigma^2$.

Damped exponential (DEX)

Enter the variance of the response given the covariates (sigma2):

`sigma2` is the variance of the response given the covariates, which is assumed to be constant over time. This parameter is not equal to the marginal, cross-sectional variance. It can be approximated by the variance of the response among the unexposed at baseline, a quantity that may be available from the literature or pilot data, or if age is the time variable of interest, within a reasonably narrow age group. If only a marginal response variance is available over a range of ages and exposure levels, as will often be the case in epidemiology, the investigator can approximate the residual variance by multiplying it by the quantity $1-R^2$, where R^2 is the assumed proportion of the marginal variance of the response variable that is explained by the model to be fit when the study is conducted. Typically, in epidemiology, R^2 ranges from 0.10 to 0.30 or so.

Enter the correlation between two measures of the same subject separated by one unit (rho):

When damped exponential (DEX) covariance structure is assumed, rho is the correlation between two measures from the same subject separated by one unit of time, $\rho \in [0,1)$.

Enter the damping coefficient (theta):

When damped exponential (DEX) covariance structure is assumed, the parameter theta ($\theta \in [0,1]$) controls the degree of attenuation of the correlations over time. This covariance structure reduces to the compound symmetry when $\theta = 0$, and AR(1) covariance structure when $\theta = 1$.

If one wants to explore the resulting correlation matrix, the function `DEX.matrix(r,s,rho,theta)` can be used. This function has to be invoked from R, before or after invoking any of the long.power(), long.N(), long.r(), long.effect() or long.opt(), but not during its execution, i.e. it cannot be used when the user interface is printing the queries described in this section.
As an example, if one types `DEX.matrix(3,1,.8,.5)`, the following result is obtained:

```
      [,1]  [,2]  [,3]  [,4]
[1,] 1.000 0.800 0.729 0.679
[2,] 0.800 1.000 0.800 0.729
[3,] 0.729 0.800 1.000 0.800
[4,] 0.679 0.729 0.800 1.000
```

Random intercepts and slopes (RS)

Enter (1) for standard notation (variance of residuals and random effects) or (2) for "reliability" notation:

Under RS, the program allows two notations. The standard "mixed model" notation uses σ^2_{within}, the within-subject residual variance; $\sigma^2_{b_0}$, the variance of the random effect associated with the intercept, or the between-subjects variance at baseline or at mean initial time; $\sigma^2_{b_1}$ the variance of the random effect associated with time, and $\sigma_{b_0 b_1}$, the covariance between random effects. The reliability notation, which is more intuitive and may be preferable when pilot data is unavailable to provide estimates of the covariance parameters, uses $\sigma^2_{t_0}$, the residual variance at baseline or at mean initial time; ρ_{t_0}, the reliability coefficient at baseline or at mean initial time; $\rho_{b_l,s,\tilde{r}}$ or $\rho_{b_l,\tau,\tilde{r}}$, the slope reliability with $\tilde{r}$ repeated measures; and $\rho_{b_0 b_1}$, the correlation between random effects.

RS, standard notation

Enter the within-subject variance (sigma_within^2):

The within subject residual variance, σ^2_{within}, queried under RS when one uses the standard mixed model notation.

Enter the variance of the intercept random effect (sigma_{b0}^2):

The variance of the random effect associated with the intercept, $\sigma^2_{b_0}$, queried under RS when the standard mixed model notation is used.

Enter the variance of the random effect associated with time (sigma_{b1}^2):

The variance of the random effect associated with time, $\sigma^2_{b_1}$, queried under RS when the standard mixed model notation is used.

Enter the covariance of the random effects (sigma_{b0,b1}):

The covariance of the random effects of the intercept and time, $\sigma_{b_0 b_1}$, queried under RS when the standard mixed model notation is used.

If one wants to explore the resulting covariance and correlation matrix, the function `RS.matrix(r,s,sigma2w,sigma20,sigma21,sigma01)` can be used. This function has to be invoked from R, before or after invoking any of the long.power(), long.N(), long.r(), long.effect() or long.opt(), but not during its execution, i.e. it cannot be used when the user interface is printing the queries described in this section.
As an example, if one types `RS.matrix(4,1,.03,.27,0.01,-.005)`, the following result is obtained:

```
Covariance matrix:
      [,1]  [,2]  [,3]  [,4]  [,5]
[1,] 0.300 0.265 0.260 0.255 0.250
[2,] 0.265 0.300 0.275 0.280 0.285
[3,] 0.260 0.275 0.320 0.305 0.320
[4,] 0.255 0.280 0.305 0.360 0.355
[5,] 0.250 0.285 0.320 0.355 0.420

Correlation matrix:
          [,1]      [,2]      [,3]      [,4]      [,5]
[1,] 1.0000000 0.8833333 0.8391464 0.7759403 0.7042952
[2,] 0.8833333 1.0000000 0.8875587 0.8520129 0.8028965
[3,] 0.8391464 0.8875587 1.0000000 0.8986149 0.8728716
[4,] 0.7759403 0.8520129 0.8986149 1.0000000 0.9129615
[5,] 0.7042952 0.8028965 0.8728716 0.9129615 1.0000000
```

RS, reliability notation

Enter the variance of the response given the covariates at baseline (sigma2):

When random intercepts and slopes assumed (RS) is assumed, the variance of the response given the covariates changes with time. That is why the program asks about the variance of the response within exposures groups at baseline or at mean initial time. This parameter is not equal to the marginal, cross-sectional variance. It can be approximated by the variance of the response among the unexposed at baseline, a quantity that may be available from the literature or pilot data, or if age is the time variable of interest, within a reasonably narrow age group. If only a marginal response variance is available over a range of ages and exposure levels, as will often be the case in epidemiology, the investigator can approximate the residual variance by multiplying it by the quantity $1-R^2$, where R^2 is the assumed proportion of the marginal variance of the response variable that is explained by the model to be fit when the study is conducted. Typically, in epidemiology, R^2 ranges from 0.10 to 0.30 or so.

```
Enter the reliability coefficient at baseline (rho_t0):
```

When random intercepts and slopes (RS) is assumed, `rho_t0` ($\rho_{t_0} \in [0,1)$) is the reliability coefficient at baseline (or at mean initial time), i.e. the percentage of residual variance at baseline or at mean initial time that is due to between-subject variation.

```
Enter the trial value of the number of measurements at which the
 slope reliability will be provided (\tilde r>0 ):
```

When the number of repeated measures is not fixed, i.e. when r is one of the unknowns, $\tilde{r}$ is the trial value for the repeated measurements that was used to specify the slope reliability $\rho_{b_1,s,\tilde{r}}$ or $\rho_{b_1,\tau,\tilde{r}}$.

```
Enter the slope reliability for (\tilde r) repeated measurements
(0<rho[b1,s,\tilde r]<1 or 0<rho[b1,tau,\tilde r]<1):
```

When random intercepts and slopes (RS) is assumed and the reliability notation is used, $\rho_{b_1,s,\tilde{r}}$ or $\rho_{b_1,\tau,\tilde{r}}$ are the slope reliability with $\tilde{r}$ repeated measurments, i.e. the percentage of the variance of the slopes for time that is due to between-subject variation. This parameter belongs to the interval [0, 1), and when this parameter is 0, the resulting covariance matrix reduces to compound symmetry.

```
Enter the correlation between the random effects of slope and intercept
(-1<rho[b0,b1]<1):
```

When random intercepts and slopes are assumed, the correlation between the random effects associated with the intercept and the random effect associated with the slopes, $\rho_{b_0b_1}$, is needed. If it is assumed that participants have a range of values of time (e.g age) at the start of the study, it is assumed that the data are centered at the mean initial time.

If one wants to explore the resulting covariance and correlation matrix, the function `RS.matrix.reliab(r,s,sigma2,rho,rho.b1,rho01,r.tilde)` can be used, where rho is ρ_{t_0}, `rho.b1 is` $\rho_{b_1,s,\tilde{r}}$, and rho01 is $\rho_{b_0b_1}$. This function has to be invoked from R, before or after invoking any of the long.power(), long.N(), long.r(), long.effect() or long.opt(), but not during its execution, i.e. it cannot be used when the user interface is printing the queries described in this section. As an example, if one types `RS.matrix.reliab(4,1,.32,.8,0.5,-.2,5)`, the following result is obtained:

```
Covariance matrix:
          [,1]      [,2]      [,3]      [,4]      [,5]
[1,] 0.3200000 0.2498804 0.2437609 0.2376413 0.2315217
[2,] 0.2498804 0.3114180 0.2449556 0.2424931 0.2400307
[3,] 0.2437609 0.2449556 0.3101503 0.2473450 0.2485397
[4,] 0.2376413 0.2424931 0.2473450 0.3161969 0.2570487
[5,] 0.2315217 0.2400307 0.2485397 0.2570487 0.3295577

Correlation matrix:
```

```
          [,1]      [,2]      [,3]      [,4]      [,5]
[1,] 1.0000000 0.7915628 0.7737540 0.7470818 0.7129367
[2,] 0.7915628 1.0000000 0.7881872 0.7727675 0.7492543
[3,] 0.7737540 0.7881872 1.0000000 0.7898384 0.7773990
[4,] 0.7470818 0.7727675 0.7898384 1.0000000 0.7962894
[5,] 0.7129367 0.7492543 0.7773990 0.7962894 1.0000000
```

- **Questions about costs:**

`Do you want to maximize power subject to a given cost (1) or to minimize the total cost subject to a given power (2)?`

Used to determine which of the optimization problems to solve: maximize the power of the study without exceeding a certain cost or minimize the total cost of the study subject to the power of the study being equal or greater than a given power.

`Do you want to maximize power subject to a given cost (1) or to minimize the total cost subject to a given power (2)?`

Enter (1) to find the optimal (N, r) that maximizes the power of the study without exceeding a certain cost or budget, or (2) to find the optimal (N, r) that minimizes the total cost of the study subject to having at least the specified power.

`Enter the available budget (C>0):`

The total budget of the study, in monetary units.

`Enter the cost of the first observation of each subject (c1>0):`

The estimated cost of recruiting and interviewing the subject for the first time, in monetary units.

`Enter the ratio of costs between the first measure and the rest (kappa>=1)`

It is assumed that the first measurement will be more expensive than the rest, since the first measure includes the cost of recruiting the subject. `kappa` is the cost of the first measurement over the cost of the second (or any of the following) measurement. When `kappa` is 1, all observations have the same cost.

2.1.2. Examples of use

Example 1: power calculation.

In this example, we compute the power of a study with 133 subjects and 6 post-baseline repeated measures, assuming DEX covariance structure, to detect a 10% difference in slopes. It follows the example dataset used in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 1

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Enter the total sample size (N) [100]: 133

Enter the number of post-baseline measures (r) [1]: 6

Enter the time between repeated measures (s) [1]: 3

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<=pe<=1) [0.5]: 0.79

Enter the variance of the time variable at baseline, V(t0)
   (enter 0 if all participants begin at the same time) [0]: 100

Enter the correlation between the time variable at baseline and exposure,
rho_{e,t0}
   (enter 0 if all participants begin at the same time) [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Enter mean response at baseline among unexposed (mu00) [10]: 3.5

Enter the percent change from baseline to end of follow-up among unexposed (p2)
 (e.g. enter 0.10 for a 10% change) [0.1]: -.182

Enter the percent difference between the change from baseline to
 end of follow-up in the exposed group and the unexposed group (p3)
 (e.g. enter 0.10 for a 10% difference) [0.1]: .1
```

```
Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 2

Enter the residual variance of the response given the assumed model
 covariates (sigma2) [1]: .3179

Enter the correlation between two measures of the same subject separated
  by one unit (0<rho<1) [0.8]: .896

Enter the damping coefficient (theta) [0.5]: .18

Power =  0.1868039

Do you want to continue using the program (y/n) [y]? n

>
```

Example 2: Sample size calculation (*N*)

This is an example of a sample size calculation with 6 post-baseline measures, to provide a power no less than 0.9 (90%) to detect an interaction term (a difference between the slopes of the exposed and unexposed) of 15%. RS covariance structure is assumed. It follows the example dataset used in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 2

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Enter the number of post-baseline measures (r) [1]: 6

Enter the desired power (0<Pi<1) [0.8]: .9

Enter the time between repeated measures (s) [1]: 3

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<=pe<=1) [0.5]: .79

Enter the variance of the time variable at baseline, V(t0)
```

```
    (enter 0 if all participants begin at the same time) [0]: 100

Enter the correlation between the time variable at baseline and exposure,
 rho_{e,t0} [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Enter mean response at baseline among unexposed (mu00) [10]: 3.5

Enter the percent change from baseline to end of follow-up among unexposed (p2)
 (e.g. enter 0.10 for a 10% change) [0.1]: -.182

Enter the percent difference between the change from baseline to
 end of follow-up in the exposed group and the unexposed group (p3)
 (e.g. enter 0.10 for a 10% difference) [0.1]: .15

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 3

Enter (1) for standard notation (variance of residuals and random effects)
  or (2) for "reliability" notation [1]: 2

Enter the variance of the response given the assumed model covariates
 at baseline (sigma2) [1]: .34

Enter the reliability coefficient at baseline (0<rho_t0<1) [0.8]: .877

Enter the slope reliability for 6 repeated measurements
 (0<rho_{b1,s,\tilde r}<1  or 0<rho_{b1,tau,\tilde r}<1) [0.1]: .36

Enter the correlation between the random effects of slope
 and intercept (-1<rho[b0,b1]<1) [0]: -.32

Sample size =  563

Do you want to continue using the program (y/n) [y]? n

>
```

Example 3: Minimum detectable effect.

In this example, we find the minimum detectable effect (in units of the response) of a study with 133 subjects with 6 post-baseline measures, that assumes the difference is constant over time and the covariance structure is CS. It follows the example given in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
```

```
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 4

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Enter the total sample size (N) [100]: 133

Enter the number of post-baseline measures (r) [1]: 6

Enter the desired power (0<Pi<1) [0.8]: .9

Enter the time between repeated measures (s) [1]: 3

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<=pe<=1) [0.5]: .79

Enter the variance of the time variable at baseline, V(t0)
   (enter 0 if all participants begin at the same time) [0]: 100

Enter the correlation between the time variable at baseline and exposure,
 rho_{e,t0} [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 1

Do you want the output as a coefficient (1) or as a percent change (2) [1]? 1

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 1

Enter the residual variance of the response given the assumed model
 covariates (sigma2) [1]: .3214

Enter the correlation between two measures of the same subject
 (0<rho<1) [0.8]: .857

Minimum detectable beta1 = +/-  0.3664611

Do you want to continue using the program (y/n) [y]? n

>
```

Example 4: Finding the minimum number of repeated measurements for a fixed number of participants.

Here, we show how to find the number of repeated measures to detect a 10% difference in means (CMD) with power 0.9 (90%) and CS covariance structure, in a study with 133 subjects. It follows the example given in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 3

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Enter the total sample size (N) [100]: 133

Enter the desired power (0<Pi<1) [0.8]: .9

Are you assuming the time between measurements (s) is fixed (1), or
  the total duration of follow-up (tau) is fixed (2) [1]? 2

Enter the time of follow-up (tau) [1]: 18

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<pe<1) [0.5]: .79

Enter the variance of the time variable at baseline, V(t0)
   (enter 0 if all participants begin at the same time) [0]: 100

Enter the correlation between the time variable at baseline and exposure,
 rho_{e,t0} [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 1

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Enter mean response at baseline among unexposed (mu00) [10]: 3.5

Enter the percent difference between exposed and unexposed
 groups (p1) (e.g. enter .10 for a 10% difference) [0.1]: .1

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 1

Enter the residual variance of the response given the assumed model
 covariates (sigma2) [1]: .3214

Enter the correlation between two measures of the same subject
```

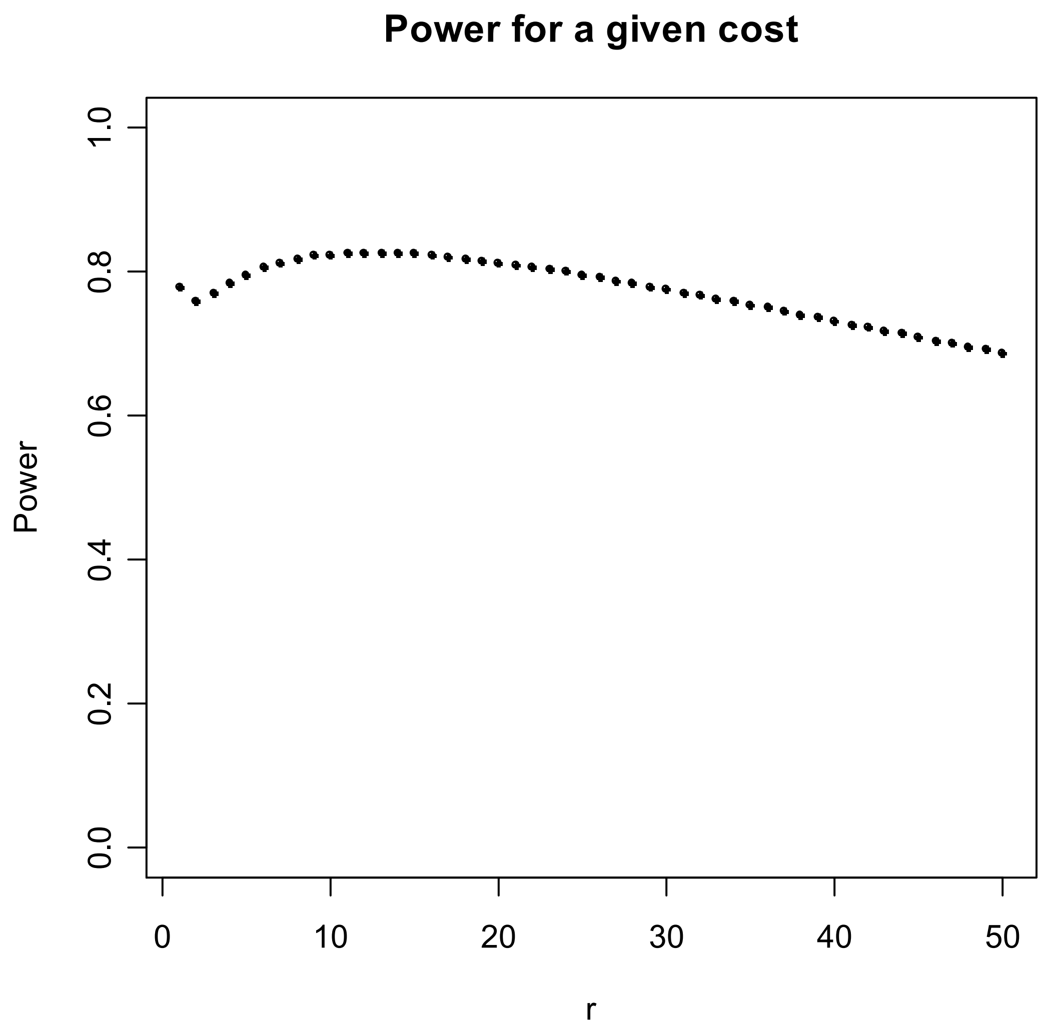
```
 (0<rho<1) [0.8]: .857

The maximum power (as r->infinity) that can be obtained in your study is
  0.8795273
You should take the largest number of measurements possible and use
  module long.power() to calculate the power achieved

Do you want to continue using the program (y/n) [y]? n

>
```

Example 5. Optimal combination of number of subjects and number of repeated measures to maximize power subject to a cost constraint.

Here, we show how to find the optimal combination (*N*, *r*) that maximizes power, subject to the cost being less than 100,000 monetary units. The cost of the first measure is 80 monetary units and the ratio of costs of the first measurement versus the rest is 20. We assume RS covariance structure and LDD, and want to detect a 10% difference in the slopes of the exposed compared to the unexposed. It follows the example given in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 5

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Do you want to maximize power subject to a given cost (1) or to
  minimize the total cost subject to a given power (2)[1]? 1

Are you assuming the time between measurements (s) is fixed (1), or
  the total duration of follow-up (tau) is fixed (2) [1]? 2

Enter the time of follow-up (tau) [1]: 18

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<=pe<=1) [0.5]: .79

Enter the variance of the time variable at baseline, V(t0)
   (enter 0 if all participants begin at the same time) [0]: 100
```

```
Enter the correlation between the time variable at baseline and exposure,
 rho_{e,t0} [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Enter mean response at baseline among unexposed (mu00) [10]: 3.5

Enter the percent change from baseline to end of follow-up among unexposed (p2)
 (e.g. enter 0.10 for a 10% change) [0.1]: -.182

Enter the percent difference between the change from baseline to
 end of follow-up in the exposed group and the unexposed group (p3)
 (e.g. enter 0.10 for a 10% difference) [0.1]: .1

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 3

Enter (1) for standard notation (variance of residuals and random effects)
  or (2) for "reliability" notation [1]: 2

Enter the variance of the response given the assumed model covariates
 at baseline (sigma2) [1]: .34

Enter the reliability coefficient at baseline (0<rho_t0<1) [0.8]: .877

Enter the trial value of the number of measurements at which the
        slope reliability will be provided (\tilde r>0 ) [5]: 6

Enter the slope reliability for 6 repeated measurements
 (0<rho_{b1,s,\tilde r}<1  or 0<rho_{b1,tau,\tilde r}<1) [0.1]: .364

Enter the correlation between the random effects of slope
 and intercept (-1<rho[b0,b1]<1) [0]: -.32

Enter the available budget (C>0) [1000]: 100000

Enter the cost of the first observation of each subject (c1>0) [80]: 80

Enter the ratio of costs between the first measure and the rest (kappa) [2]: 20

Power optimization problem (max power for a given cost):
   Optimal r= 12 , Optimal N= 781 , Power= 0.83 ,Cost= 99968

Slope reliability at r= 12 :  0.4818737
```




```
Do you want to continue using the program (y/n) [y]? n
```

Data: df.show

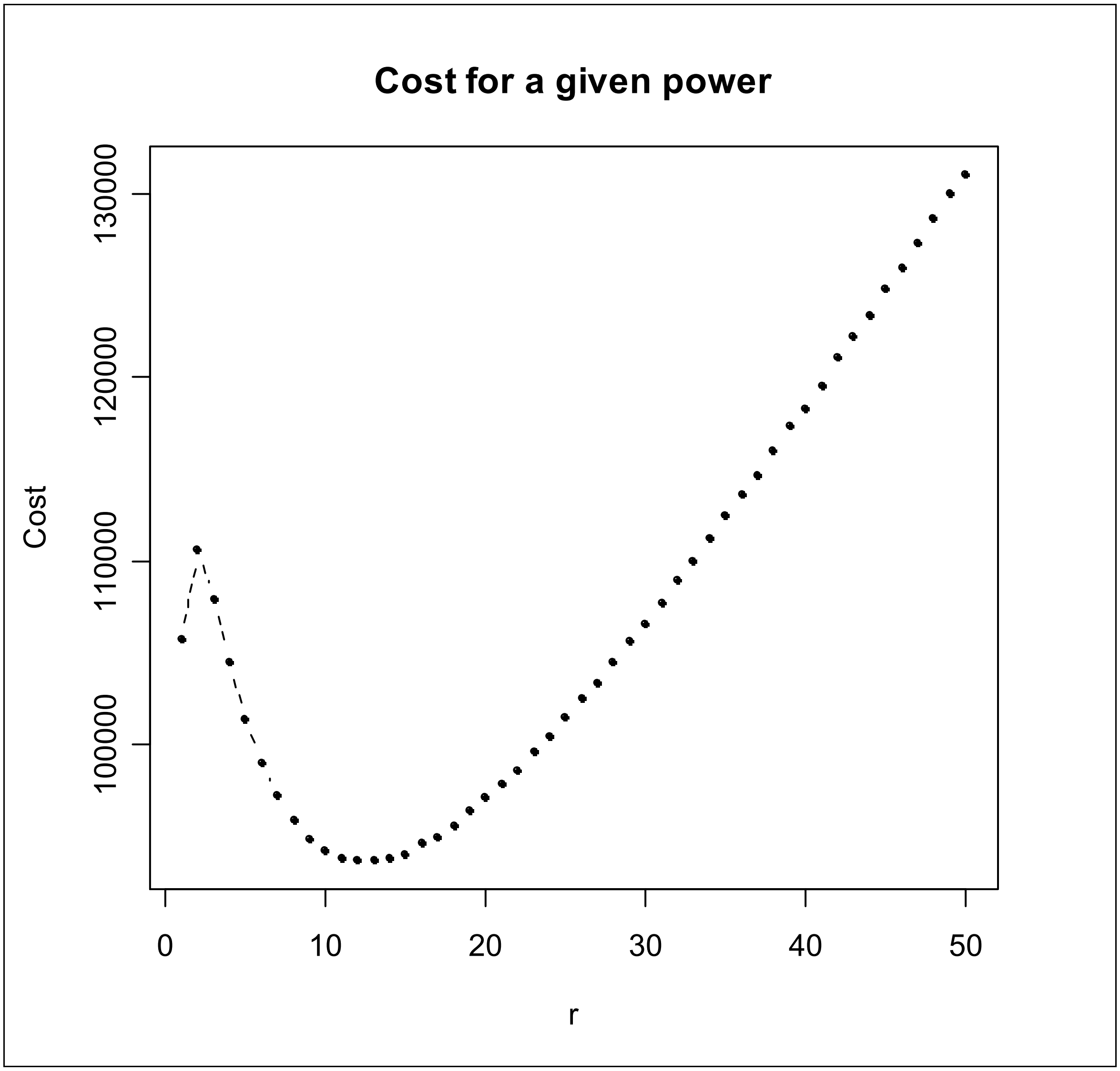
	N	r	Power	Cost
1	1190	1	0.78	99960
2	1136	2	0.76	99968
3	1086	3	0.77	99912
4	1041	4	0.78	99936
5	1000	5	0.79	1e+05
6	961	6	0.8	99944
7	925	7	0.81	99900
8	892	8	0.82	99904
9	862	9	0.82	99992
10	833	10	0.82	99960
11	806	11	0.82	99944
12	781	12	0.83	99968
13	757	13	0.82	99924
14	735	14	0.82	99960
15	714	15	0.82	99960
16	694	16	0.82	99936
17	675	17	0.82	99900
18	657	18	0.82	99864
19	641	19	0.81	99996
20	625	20	0.81	1e+05
21	609	21	0.81	99876
22	595	22	0.81	99960
23	581	23	0.8	99932
24	568	24	0.8	99968

Example 6. Optimal combination of number of subjects and number of repeated measures to minimize the total cost of the study subject to achieving a fixed power.

Here the optimal combination (N, r) which minimizes cost, subject to the power of the study being at least 80%, the cost of the first measure being 80 monetary units and the ratio of costs of the first measurement versus the rest being 20, is determined. We assume RS covariance structure and LDD, and want to detect a 10% difference in the interaction term. It is based on the dataset used in Basagaña and Spiegelman (2007).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 5

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Do you want to maximize power subject to a given cost (1) or to
  minimize the total cost subject to a given power (2)[1]? 2

Enter the desired power (0<Pi<1) [0.8]: .8
```

```
Are you assuming the time between measurements (s) is fixed (1), or
  the total duration of follow-up (tau) is fixed (2) [1]? 2

Enter the time of follow-up (tau) [1]: 18

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Enter the exposure prevalence (pe) (0<=pe<=1) [0.5]: .79

Enter the variance of the time variable at baseline, V(t0)
   (enter 0 if all participants begin at the same time) [0]: 100

Enter the correlation between the time variable at baseline and exposure,
 rho_{e,t0} [0]: 0

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Enter mean response at baseline among unexposed (mu00) [10]: 3.5

Enter the percent change from baseline to end of follow-up among unexposed (p2)
 (e.g. enter 0.10 for a 10% change) [0.1]: -.182

Enter the percent difference between the change from baseline to
 end of follow-up in the exposed group and the unexposed group (p3)
 (e.g. enter 0.10 for a 10% difference) [0.1]: .1

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 3

Enter (1) for standard notation (variance of residuals and random effects)
  or (2) for "reliability" notation [1]: 2

Enter the variance of the response given the assumed model covariates
 at baseline (sigma2) [1]: .34

Enter the reliability coefficient at baseline (0<rho_t0<1) [0.8]: .877

Enter the trial value of the number of measurements at which the
        slope reliability will be provided (\tilde r>0 ) [5]: 6

Enter the slope reliability for 6 repeated measurements
 (0<rho_{b1,s,\tilde r}<1  or 0<rho_{b1,tau,\tilde r}<1) [0.1]: .364

Enter the correlation between the random effects of slope
 and intercept (-1<rho[b0,b1]<1) [0]: -.32

Enter the cost of the first observation of each subject (c1>0) [80]: 80

Enter the ratio of costs between the first measure and the rest (kappa) [2]: 20

Cost optimization problem (min cost for a given power):
   Optimal r= 12 , Optimal N= 732 , Power= 0.8 ,Cost= 93696

Slope reliability at r= 12 :  0.4818737
```


Cost for a given power
Cost
130000
120000
110000
100000
0
10
20
30
40
50
r

Data: df.show

	N	r	Power	Cost
1	1259	1	0.8	105756
2	1257	2	0.8	110616
3	1173	3	0.8	107916
4	1088	4	0.8	104448
5	1014	5	0.8	101400
6	952	6	0.8	99008
7	900	7	0.8	97200
8	856	8	0.8	95872
9	818	9	0.8	94888
10	785	10	0.8	94200
11	757	11	0.8	93868
12	732	12	0.8	93696
13	710	13	0.8	93720
14	690	14	0.8	93840
15	672	15	0.8	94080
16	657	16	0.8	94608
17	642	17	0.8	95016
18	629	18	0.8	95608
19	618	19	0.8	96408
20	607	20	0.8	97120
21	597	21	0.8	97908
22	587	22	0.8	98616
23	579	23	0.8	99588
24	571	24	0.8	100496
25	564	25	0.8	101520
26	557	26	0.8	102488

```
Do you want to continue using the program (y/n) [y]? n
```

Example 7. Power calculation, time varying-exposure.

Here, we compute the power of a study with 31 partitiparticipants and 14 post-baseline measures, assuming CS covariance structure of the response, to detect a 10 L/min decrease in PEF associated with vaccuuming. We assume CMD and a model without time and we want to estimate the within-subject effect of exposure, so we assume the model $\mathbb{E}\left(Y_{i,j+1} - Y_{ij} \mid E_{i,j+1}, E_{ij}\right) = \beta_e^W \left(E_{i,j+1} - E_{ij}\right)$. This example is based on the dataset on respiratory function and cleaning tasks/product used in Basagaña, Liao and Spiegelman (2010).

```
> optitxs()
Do you want to:
  (1) Compute POWER for fixed sample size and number of repeated measures
  (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
  (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
  (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
  (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 1

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.
```

```
* Press <Esc> to quit

Enter the total sample size (N) [100]: 31

Enter the number of post-baseline measures (r) [1]: 14

Enter the time between repeated measures (s) [1]: 1

Is the exposure time-invariant (1) or time-varying (2) [1]? 2

Do you assume that the exposure prevalence is constant over time (1),
 that it changes linearly with time (2), or you want to enter the prevalence at
 each time point(3) [1]? 1

Enter the mean exposure prevalence (0<pe<1) [0.5]: .37

Enter the intraclass correlation of exposure (-0.066<rho.e<1) [0.5]: .13

Constant mean difference (1) or Linearly divergent difference (2) [1]: 1

Which model are you basing your calculations on:
(1) Model without time. No separation of between- and within-subject effects
(2) Model without time. Within-subject contrast only
(3) Model with time. No separation of between- and within-subject effects
(4) Model with time. Within-subject contrast only
Model [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 1

Enter the value of the coefficient of interest in your model, i.e. the
 difference between exposed and unexposed periods (beta) [0.1]: 10

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 1

Enter the residual variance of the response given the assumed model
 covariates (sigma2) [1]: 4570

Enter the correlation between two measures of the same subject
 (0<rho<1) [0.8]: .88

Power =  0.9796308


Do you want to continue using the program (y/n) [y]? n
```

Example 8. Sample size calculation, time varying-exposure.

Here, we compute the required sample size for a study with 31 partitipants and 14 post-baseline measures to detect a 5 L/min decrease in PEF associated with the use of air-freshener sprays with 90% power, assuming DEX covariance structure of the response, We assume LDD and a cumulative exposure effect, and we want to estimate the within-subject effect of exposure, so we assume the model $\mathbb{E}\left(Y_{ij}-Y_{i,j-1}\mid \mathbf{X}_i\right)=\gamma_t^W+\gamma_e^W E_{ij}$. This example is based on the dataset on respiratory function and cleaning tasks/product used in Basagaña, Liao and Spiegelman (2010).

```
> optitxs()
Do you want to:
 (1) Compute POWER for fixed sample size and number of repeated measures
 (2) Compute the required NUMBER OF PARTICIPANTS to achieve a pre-specified
      power for a fixed number of repeated measures
 (3) Compute the required NUMBER OF REPEATED MEASURES to achieve a
      pre-specified power for a fixed number of participants
 (4) Compute the MINIMUM DETECTABLE EFFECT that one can achieve with a
      specified power and for a fixed number of participants and repeated
      measures
 (5) Compute the OPTIMAL COMBINATION of number of subjects and number of
      repeated measures in terms of maximizing the power to detect a difference
      for a fixed budget or in terms of minimizing cost subject to fixed power
Option: 2

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Enter the number of post-baseline measures (r) [1]: 14

Enter the desired power (0<Pi<1) [0.8]: .9

Enter the time between repeated measures (s) [1]: 1

Is the exposure time-invariant (1) or time-varying (2) [1]? 2

Do you assume that the exposure prevalence is constant over time (1),
 that it changes linearly with time (2), or you want to enter the prevalence at
 each time point(3) [1]? 2

Enter the exposure prevalence at time 0 (0<pe0<1) [0.5]: .35

Enter the exposure prevalence at time 14 (0<pe14<1) [0.5]: .45

Enter the intraclass correlation of exposure (-0.071<rho.e<0.808) [0.5]: .13

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Which model are you basing your calculations on:
(1) Cumulative exposure effect model. No separation of between- and
     within-subject effects
(2) Cumulative exposure effect model. Within-subject contrast only
(3) Acute exposure effect model. No separation of between- and
     within-subject effects
(4) Acute exposure effect model. Within-subject contrast only
Model [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 1

Enter the interaction coefficient (gamma3) [0.1]: 5

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 2
```

```
Enter the residual variance of the response given the assumed model
 covariates (sigma2) [1]: 4570

Enter the correlation between two measures of the same subject separated
  by one time unit (0<rho<1) [0.8]: .88

Enter the damping coefficient (theta) [0.5]: .12

Sample size =  28

Do you want to continue using the program (y/n) [y]? n
```

2.1.3. Decide a plausible value for the intraclass correlation of exposure ρ_e

If $\boldsymbol{\Sigma}_E$ is the covariance matrix of exposure, we define the intraclass correlation of exposure as

$$\rho_e = \frac{\mathbf{1}'\boldsymbol{\Sigma}_E\mathbf{1} - \mathrm{tr}(\boldsymbol{\Sigma}_E)}{r\ \mathrm{tr}(\boldsymbol{\Sigma}_E)}.$$

See Basagaña, Liao and Spiegelman (2010) for more details.

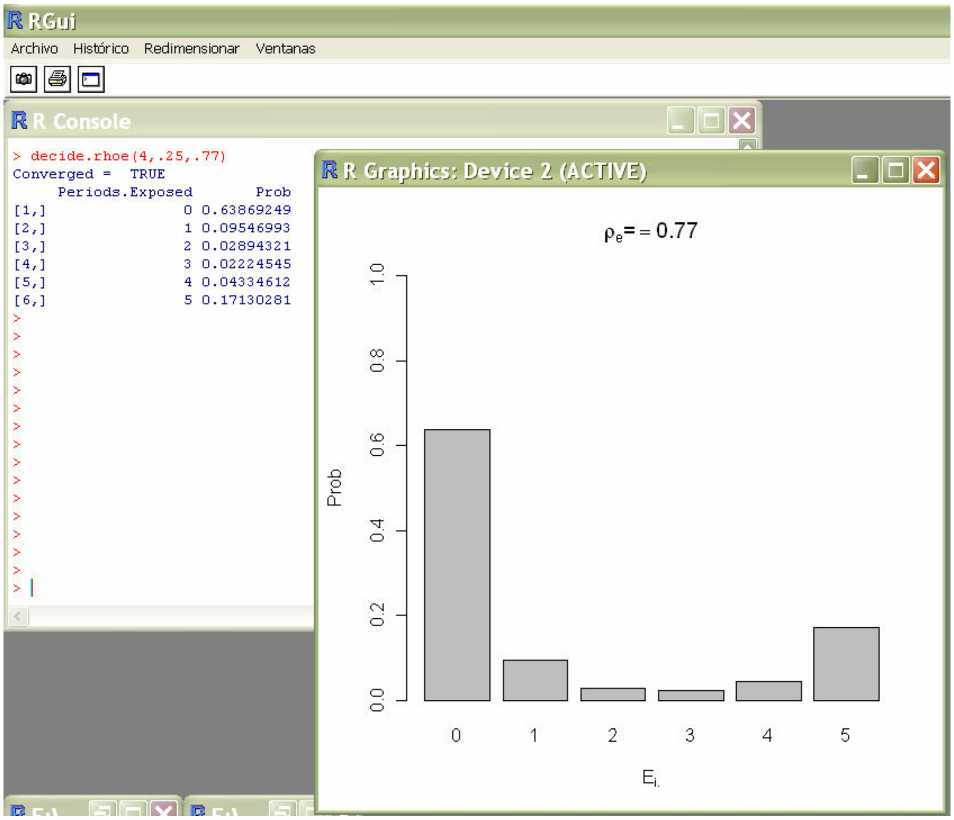
The intraclass correlation of exposure can be regarded as a measure of within-subject variation of exposure. When ρ_e takes its maximum, $\rho_e = 1$, there is no within-subject variation of exposure, that is participants are either exposed or unexposed for the whole period (time-invariant exposure). Conversely, when it takes its minimum, $-1/r$, the within-subject variation of exposure is maximal.

The parameter ρ_e has other useful interpretations. When the exposure prevalence is constant over time and the exposure has compound symmetry covariance, the intraclass correlation coefficient is equal to the common correlation. The intraclass correlation of exposure can also be regarded as a measure of imbalance in the number of exposed periods per subject, $E_{i\cdot}$. When $E_{i\cdot}$ is equal across subjects, then everyone is exposed for the same number of periods as, for example, in uniform crossover studies. Then, $\rho_e = -1/r$. Conversely, when the exposure is time invariant, the imbalance is maximal since $E_{i\cdot}$ is either zero with probability $(1 - p_e)$ or $r + 1$ with probability p_e, and $\rho_e = 1$.

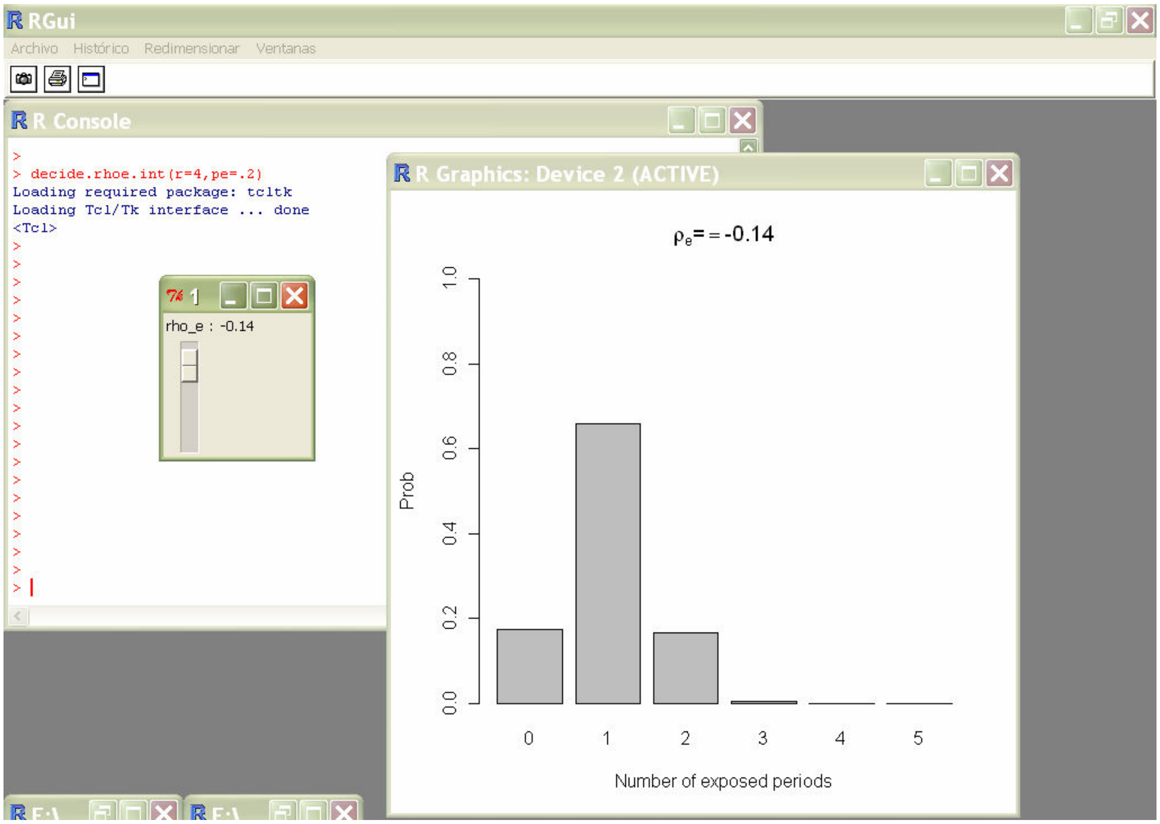
In observational studies, intermediate values between $\rho_e = -1/r$ (same number of exposed periods for all participants) and $\rho_e = 1$ (time-invariant exposure) will often be observed, and when pilot data are not available, the investigator can assess the sensitivity of the study design over a range of plausible values for ρ_e. To help the investigator assess what values of ρ_e are appropriate for his or her exposure, our program can compute the distribution of $E_{i\cdot}$ once r and $\overline{p}_e$ are fixed and a CS covariance of exposure is assumed. The investigator is more likely to know if the distribution of the number of exposed periods makes sense for their population than to assess directly values of ρ_e.

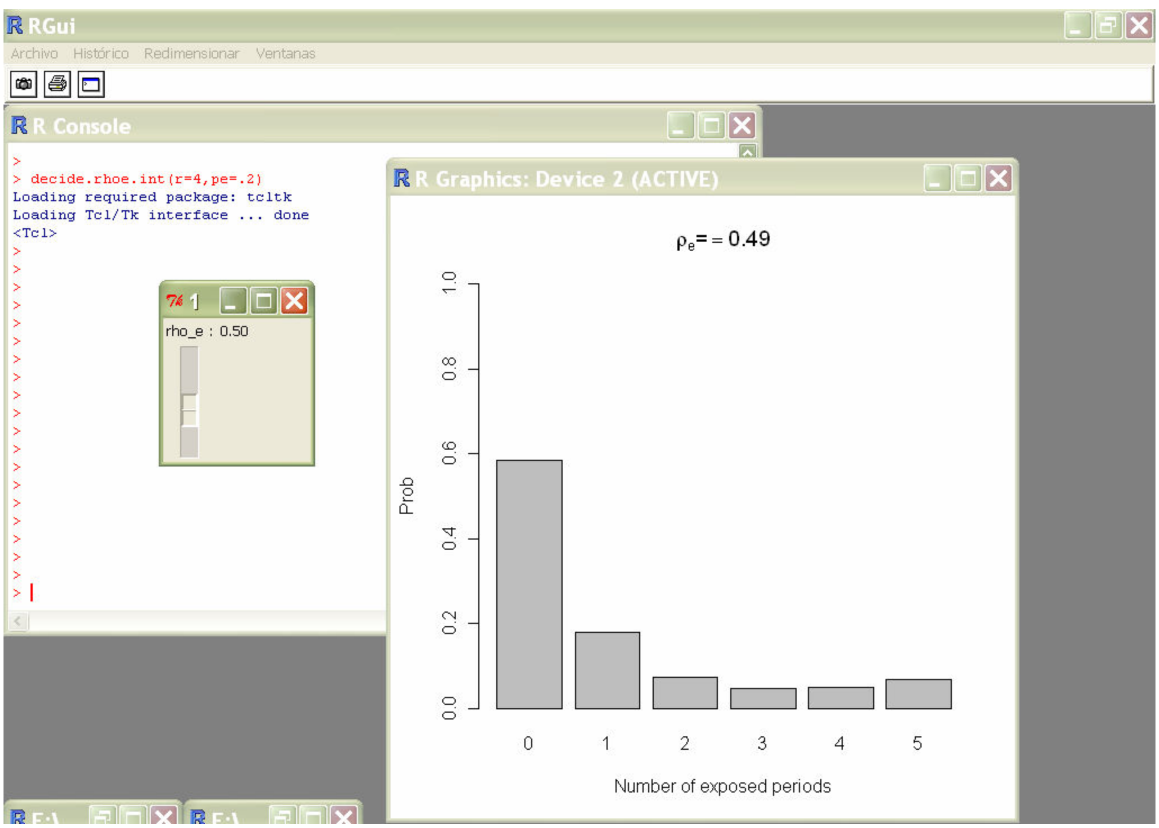
There are two functions in optitxs() that serve this purpose:
`decide.rhoe(r,pe,rhoe)` and `decide.rhoe.int(r,pe)`.

In the first one, the user enters the value of r, the number of post-baseline repeated measures, p_e, the (average) prevalence of exposure, and a value of ρ_e, and the program returns a table and a graph of the corresponding distribution of the number of exposed periods.



The second function, only requires a value for *r* and for p_e. Then the user can move a slide bar to change the values of ρ_e and graphically see the effects it produces on the distribution of the number of exposed periods.


RGui
Archivo Histórico Redimensionar Ventanas
R Console
> decide.rhoe.int(r=4,pe=.2)
Loading required package: tcltk
Loading Tcl/Tk interface ... done
<Tcl>
rho_e : -0.14
R Graphics: Device 2 (ACTIVE)
ρe= = -0.14
Prob
Number of exposed periods


RGui
Archivo Histórico Redimensionar Ventanas
R Console
> decide.rhoe.int(r=4,pe=.2)
Loading required package: tcltk
Loading Tcl/Tk interface ... done
<Tcl>
rho_e : 0.50
R Graphics: Device 2 (ACTIVE)
ρe= = 0.49
Prob
Number of exposed periods

2.2. Batch use of the program

In "batch" mode, the user enters all needed parameters in an input file and the results are stored in an output file. This approach is useful when one wants to repeat the same calculation using different values of the parameters. Each row of the input file represents a different set of parameters, and the calculations are performed for every row in the file. Since our program can be used to compute several quantities, and since it fits several different cases (e.g. CMD/LDD hypothesis, time-invariant or time-varying exposure) and it allows different notations (e.g. coefficients vs. percent changes, traditional vs. reliability notation), a lot of different cases requiring different input parameters arise. In the next section, the different possible cases are represented using flow charts, and they point to the function that needs to be invoked for each particular case, and what parameters need to be entered in the input file. However, one can also invoke the function `long.function()`, which will ask the user to answer some questions and then it will provide the name of the function to use and what parameters the input file must contain. Next section provides an example of use.

The output file will contain the following:

- For functions returning the power of the study: the power of the study, π.
- For functions returning the samples size: the required sample size, *N*.
- For functions returning the minimum detectable effect: the minimum detectable effect, either in form of a coefficient or in percent form, depending on what the user specified.
- For functions returning the required number of repeated measurements: the required number of repeated measurements, *r*. In addition, the following codes can be obtained:
    - -999: The required power is greater than limit of the power as *r* goes to infinity for this particular case.
    - -888: The required power cannot be reached with fewer than `max.r` post-baseline measures.
- For functions returning the optimal combination of number of participants and number of repeated measurements subject to a cost or a power constraint, each row contains four values: *N*, *r*, power (π), and the total cost of the study.

2.2.1. Description of all possible input parameters

Papers	Name in R	Description
N	`N`	Number of participants
r	`r`	Number of post-baseline measurements
	`max.r`	Maximum value of r that will be considered when finding the required number of repeated measures or the optimal combination of participants and repeated measures
Π	`Pi`	Power
	`fixed`	1 indicates s is fixed, 2 indicates τ is fixed
	`s.or.tau`	if fixed=1, enter the value of s, if fixed=2, enter the value of τ
p_e	`pe`	Prevalence of exposure
p_{e0}	`pe0`	Exposure prevalence at baseline
p_{er}	`per`	Exposure prevalence at the end of follow-up
ρ_e	`rho.e`	Intraclass correlation of exposure
$V(t_0)$	`vt0`	Variance of time at entry
ρ_{e,t_0}	`rho.exp.t0`	Correlation between exposure and time at entry
	`model.cmd`	Models for CMD and time-varying exposure: 1 = Model without time. No separation of between- and within-subject effects 2 = Model without time. Within-subject contrast only 3 = Model with time. No separation of between- and within-subject effects 4 = Model with time. Within-subject contrast only
	`model.ldd`	Models for LDD and time-varying exposure: 1 = Cumulative exposure effect model. No separation of between- and within-subject effects 2 = Cumulative exposure effect model. Within-subject contrast only 3 = Acute exposure effect model. No separation of between- and within-subject effects 4 = Acute exposure effect model. Within-subject contrast only
β_2, β_1, or β_e^W	`beta`	Coefficient of interest under CMD
γ_3, γ_{e*}, γ_e^W, γ_{te}, or γ_{te}^W	`gamma`	Coefficient of interest under LDD
μ_{00}	`mu00`	Expected value of the response at baseline among unexposed
p_1	`p1`	Percent difference between exposed and unexposed at baseline

p_2	`p2`	Percent change from baseline to time = s (if fixed=1) or to time = τ (if fixed=2)
p_3	`p3`	Percent difference between the change from baseline to time = s (if fixed=1) or to time = τ (if fixed=2) in the exposed and unexposed
σ^2	`sigma2`	Residual variance of the response
$\sigma_{t_0}^2$	`sigma2`	Residual variance of the response at baseline under RS
ρ	`rho`	Intraclass correlation of the response
θ	`theta`	Damping parameter under DEX
ρ_{t_0}	`rho`	Intraclass correlation of the response at baseline under RS
$\rho_{b_1,s,\tilde{r}}$, $\rho_{b_1,\tau,\tilde{r}}$	`rho.b1`	Slope reliability under RS
ρ_{b_0,b_1}	`rho01`	Correlation between intercept and slope random effects
$\tilde{r}$	`r.tilde`	Trial value of r at which the slope reliability will be provided
σ_{within}^2	`sigma2w`	Within-subject variance of the response under RS
$\sigma_{b_0}^2$	`sigma20`	Variance of the random effect associated with the intercept
$\sigma_{b_1}^2$	`sigma21`	Variance of the random effect associated with time
$\sigma_{b_0 b_1}$	`sigma01`	Covariance between intercept and slope random effects
α	`alpha`	Type I error
C	`budget`	Available butget for the study
c_1	`c1`	Cost of the first observation of each participant
κ	`k`	Ratio of costs between the first measure and the rest

2.2.2. Example of use:

```
> long.function()

* By just pressing <Enter> after each question, the default value, shown
  between square brackets, will be entered.

* Press <Esc> to quit

Do you want to compute:
(1) Power (Pi)
(2) Number of participants (N)
(3) Minimum detectable effect
(4) Number of repeated measurements (r)
(5) Optimal (N,r) to maximize power subject to a cost constraint
(6) Optimal (N,r) to minimize cost subject to a power constraint
Option [1]: 6

Is the exposure time-invariant (1) or time-varying (2) [1]? 1

Constant mean difference (1) or Linearly divergent difference (2) [1]: 2

Will you specify the alternative hypothesis on the absolute (beta coefficient)
 scale (1) or the relative (percent) scale (2) [1]? 2

Which covariance matrix are you assuming: compound symmetry (1),
 damped exponential (2) or random slopes (3) [1]? 3

Enter (1) for standard notation (variance of residuals and random effects)
  or (2) for "reliability" notation [1]: 2

Function: opt.cost.LDD.p.RS.reliab(infile,outfile)
The input file should contain the following columns:
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho rho.b1 rho01
r.tilde c1 k max.r alpha

Do you want to continue using the program (y/n) [y]? n
```

Now, we can invoke the function `opt.cost.LDD.p.RS.reliab`, and do the calculations for serveral values of the parameters:

```
> opt.cost.LDD.p.RS.reliab("c:\\optitxs\\inExample.txt","c:\\optitxs\\
outExample.txt")
```

The input file `inExample.txt` contained the following:

```
0.8 2 18 .79 100 0 3.5 .1 -.182 .1 .34 .877 .364 -.32 6 80 5 50 .05
0.8 2 18 .79 100 0 3.5 .1 -.182 .1 .34 .877 .5 -.32 6 80 5 50 .05
0.8 2 18 .79 100 0 3.5 .1 -.182 .1 .34 .877 .8 -.32 6 80 5 50 .05
0.8 2 18 .79 100 0 3.5 .1 -.182 .1 .34 .877 .364 -.32 6 80 10 50 .05
0.8 2 18 .79 100 0 3.5 .1 -.182 .1 .34 .877 .364 -.32 6 80 20 50 .05
```

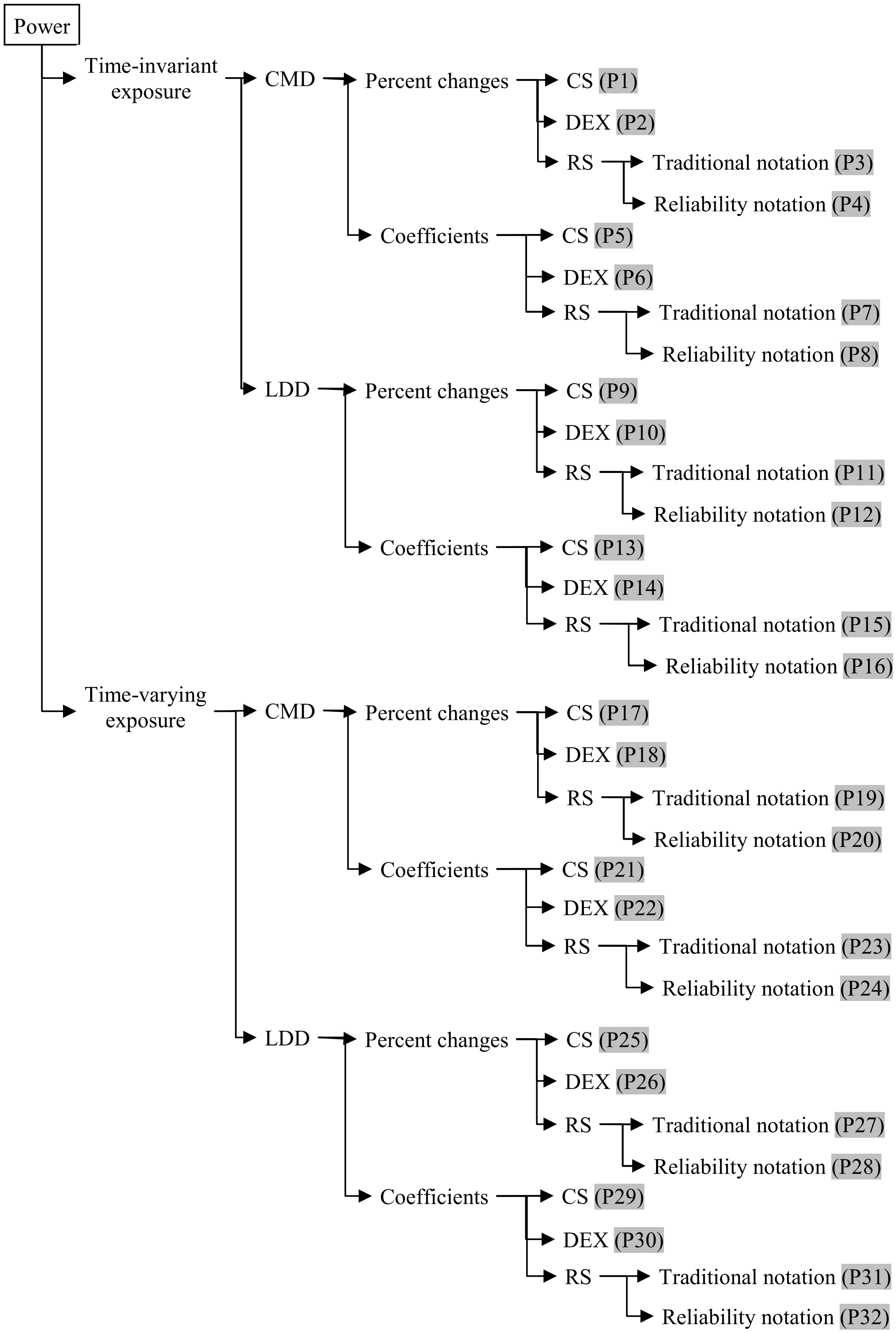
This example is inspired on example 7 of this document. The first three rows are identical, the only difference being the value of `rho.b1`. The last two rows try different values of the cost ratio, `k`. **The file should not contain the column names**. Each row indicates a different set of parameters, so one should not press "enter" until all parameters for that row have been entered. **Columns have to be space-separated.** It is advisable to press "enter" after the last line has been entered.

The output file for this example contains the following:

```
1259 1 0.8 120864
1527 1 0.8 146592
3411 1 0.8 327456
1259 1 0.8 110792
732 12 0.8 93696
```

2.2.3. Cases and their corresponding functions and input parameters

2.2.3.1. Functions that return the power of the study



P1. `power.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho alpha
```

P2. `power.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho theta
alpha
```

P3. `power.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2w sigma20
sigma21 sigma01 alpha
```

P4. `power.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho rho.b1
rho01 r.tilde alpha
```

P5. `power.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho alpha
```

P6. `power.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho theta alpha
```

P7. `power.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2w sigma20 sigma21
sigma01 alpha
```

P8. `power.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho rho.b1 rho01
r.tilde alpha
```

P9. `power.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
alpha
```

P10. `power.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
theta alpha
```

P11. `power.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

P12. `power.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

P13. `power.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho alpha
```

P14. `power.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho theta
alpha
```

P15. `power.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2w sigma20
sigma21 sigma01 alpha
```

P16. `power.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho rho.b1
rho01 r.tilde alpha
```

P17. `power.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
alpha
```

P18. `power.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
theta alpha
```

P19. `power.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2w
sigma20 sigma21 sigma01 alpha
```

P20. `power.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

P21. `power.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho alpha
```

P22. `power.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho theta
alpha
```

P23. `power.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd beta sigma2w sigma20
sigma21 sigma01 alpha
```

P24. `power.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho rho.b1
rho01 r.tilde alpha
```

P25. `power.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho alpha
```

P26. `power.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho theta alpha
```

P27. `power.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

P28. `power.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho rho.b1 rho01 r.tilde alpha
```

P29. `power.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
alpha
```

P30. `power.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
theta alpha
```

P31. `power.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

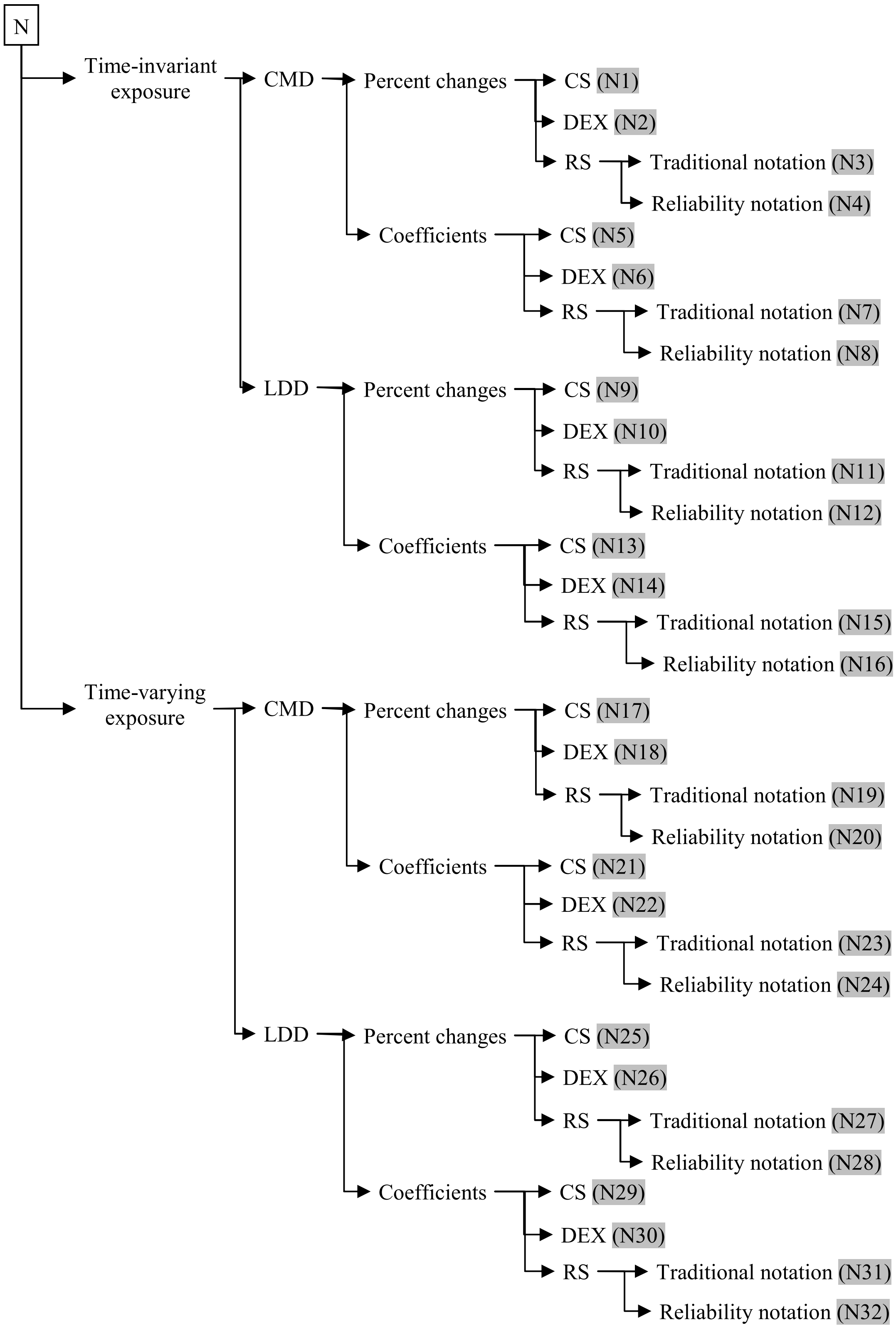
```
N r fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2w sigma20
sigma21 sigma01 alpha
```

P32. `power.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

2.2.3.2. Functions that return the required sample size



N1. `N.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho alpha`

N2. `N.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho theta alpha`

N3. `N.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2w sigma20 sigma21 sigma01 alpha`

N4. `N.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho rho.b1 rho01 r.tilde alpha`

N5. `N.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho alpha`

N6. `N.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho theta alpha`

N7. `N.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2w sigma20 sigma21 sigma01 alpha`

N8. `N.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

`r Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho rho.b1 rho01 r.tilde alpha`

N9. `N.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
alpha
```

N10. `N.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
theta alpha
```

N11. `N.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

N12. `N.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

N13. `N.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho alpha
```

N14. `N.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho theta
alpha
```

N15. `N.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2w sigma20
sigma21 sigma01 alpha
```

N16. `N.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho rho.b1
rho01 r.tilde alpha
```

N17. `N.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
alpha
```

N18. `N.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
theta alpha
```

N19. `N.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2w
sigma20 sigma21 sigma01 alpha
```

N20. `N.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 p1 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

N21. `N.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho alpha
```

N22. `N.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho theta
alpha
```

N23. `N.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd beta sigma2w sigma20
sigma21 sigma01 alpha
```

N24. `N.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.cmd beta sigma2 rho
rho.b1 rho01 r.tilde alpha
```

N25. `N.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho alpha
```

N26. `N.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho theta alpha
```

N27. `N.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

N28. `N.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 p3 sigma2
rho rho.b1 rho01 r.tilde alpha
```

N29. `N.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
alpha
```

N30. `N.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
theta alpha
```

N31. `N.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

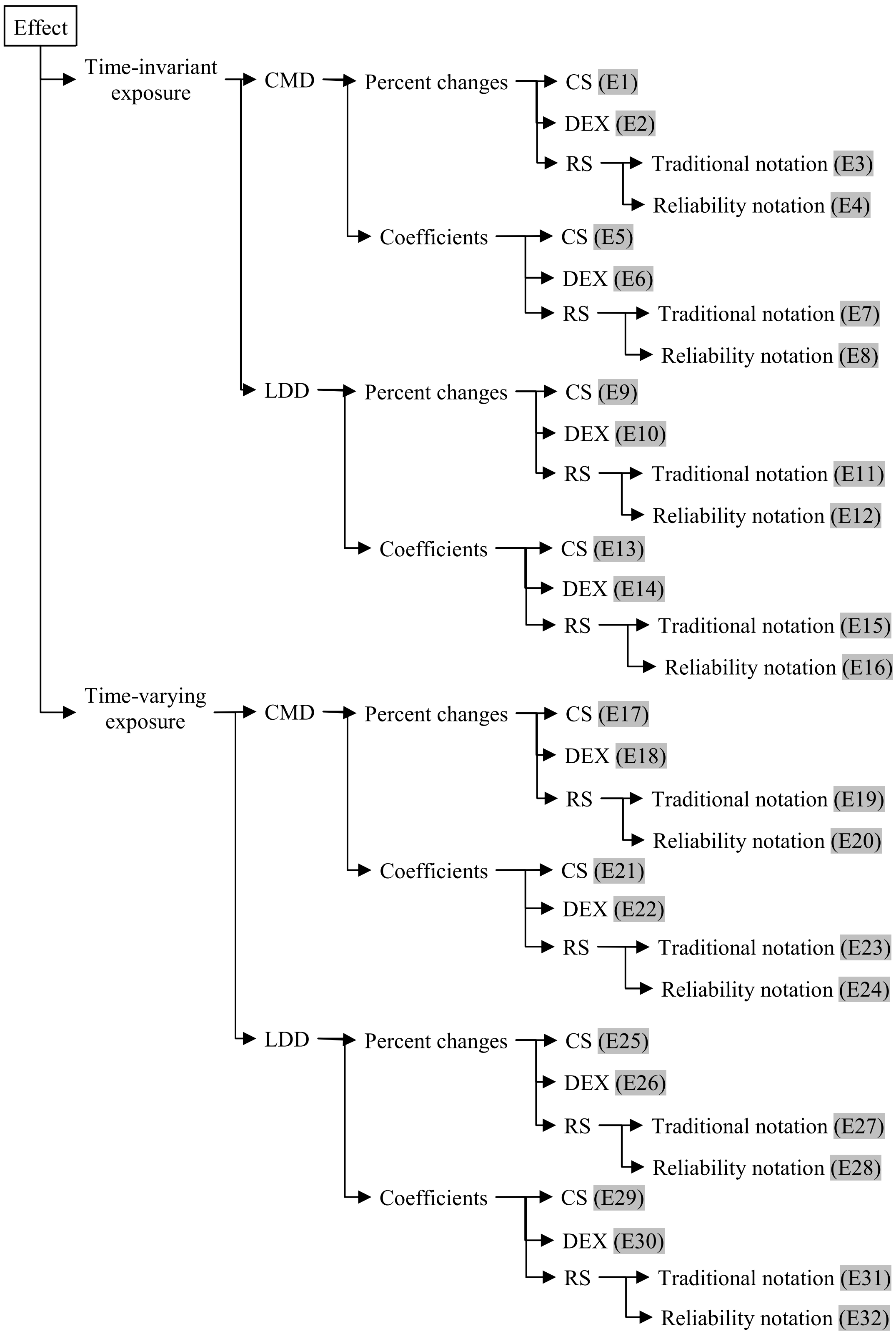
```
r Pi fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2w
sigma20 sigma21 sigma01 alpha
```

N32. `N.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
r Pi fixed s.or.tau pe0 per rho.e model.ldd gamma3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

2.2.3.3. Functions that return the minimum detectable effect



E1. `effect.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 sigma2 rho alpha
```

E2. `effect.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 sigma2 rho theta
alpha
```

E3. `effect.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 sigma2w sigma20
sigma21 sigma01 alpha
```

E4. `effect.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 sigma2 rho rho.b1
rho01 r.tilde alpha
```

E5. `effect.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho alpha
```

E6. `effect.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho theta alpha
```

E7. `effect.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2w sigma20 sigma21
sigma01 alpha
```

E8. `effect.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho rho.b1 rho01
r.tilde alpha
```

E9. `effect.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 sigma2 rho
alpha
```

E10. `effect.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 sigma2 rho
theta alpha
```

E11. `effect.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 sigma2w
sigma20 sigma21 sigma01 alpha
```

E12. `effect.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

E13. `effect.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho alpha
```

E14. `effect.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho theta alpha
```

E15. `effect.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2w sigma20 sigma21
sigma01 alpha
```

E16. `effect.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe vt0 rho.exp.t0 sigma2 rho rho.b1 rho01
r.tilde alpha
```

E17. `effect.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 sigma2 rho
alpha
```

E18. `effect.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 sigma2 rho
theta alpha
```

E19. `effect.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 sigma2w
sigma20 sigma21 sigma01 alpha
```

E20. `effect.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd mu00 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

E21. `effect.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd sigma2 rho alpha
```

E22. `effect.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd sigma2 rho theta
alpha
```

E23. `effect.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd sigma2w sigma20
sigma21 sigma01 alpha
```

E24. `effect.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.cmd sigma2 rho rho.b1
rho01 r.tilde alpha
```

E25. `effect.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 sigma2
rho alpha
```

E26. `effect.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 sigma2
rho theta alpha
```

E27. `effect.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 sigma2w
sigma20 sigma21 sigma01 alpha
```

E28. `effect.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd mu00 p1 p2 sigma2
rho rho.b1 rho01 r.tilde alpha
```

E29. `effect.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd sigma2 rho alpha
```

E30. `effect.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd sigma2 rho theta
alpha
```

E31. `effect.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

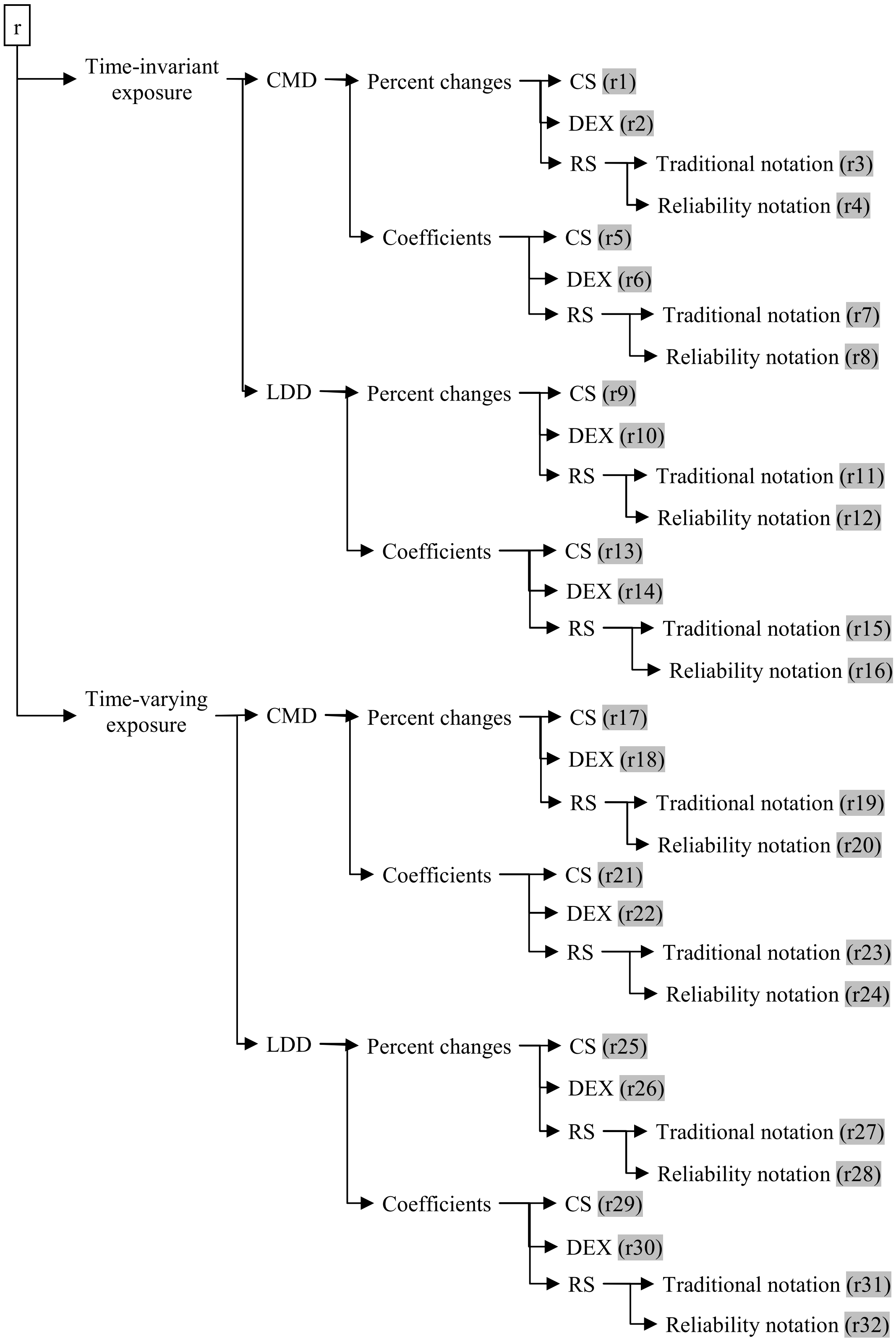
```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd sigma2w sigma20
sigma21 sigma01 alpha
```

E32. `effect.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N r Pi fixed s.or.tau pe0 per rho.e model.ldd sigma2 rho rho.b1
rho01 r.tilde alpha
```

2.2.3.4. Functions that return the required number of repeated measures



r1. `r.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho alpha
```

r2. `r.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho theta
alpha
```

r3. `r.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2w sigma20
sigma21 sigma01 alpha
```

r4. `r.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho rho.b1
rho01 r.tilde alpha
```

r5. `r.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho alpha
```

r6. `r.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho theta alpha
```

r7. `r.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2w sigma20
sigma21 sigma01 alpha
```

r8. `r.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho rho.b1
rho01 r.tilde alpha
```

r9. `r.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
alpha
```

r10. `r.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
theta alpha
```

r11. `r.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

r12. `r.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

r13. `r.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho alpha
```

r14. `r.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho theta
alpha
```

r15. `r.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2w sigma20
sigma21 sigma01 alpha
```

r16. `r.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho rho.b1
rho01 r.tilde alpha
```

r17. `r.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho alpha
```

r18. `r.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho theta
alpha
```

r19. `r.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2w sigma20
sigma21 sigma01 alpha
```

r20. `r.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho rho.b1
rho01 r.tilde alpha
```

r21. `r.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho alpha
```

r22. `r.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho theta
alpha
```

r23. `r.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd beta sigma2w sigma20
sigma21 sigma01 alpha
```

r24. `r.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho rho.b1
rho01 r.tilde alpha
```

r25. `r.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho
alpha
```

r26. `r.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho
theta alpha
```

r27. `r.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 alpha
```

r28. `r.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde alpha
```

r29. `r.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho alpha
```

r30. `r.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho theta
alpha
```

r31. `r.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

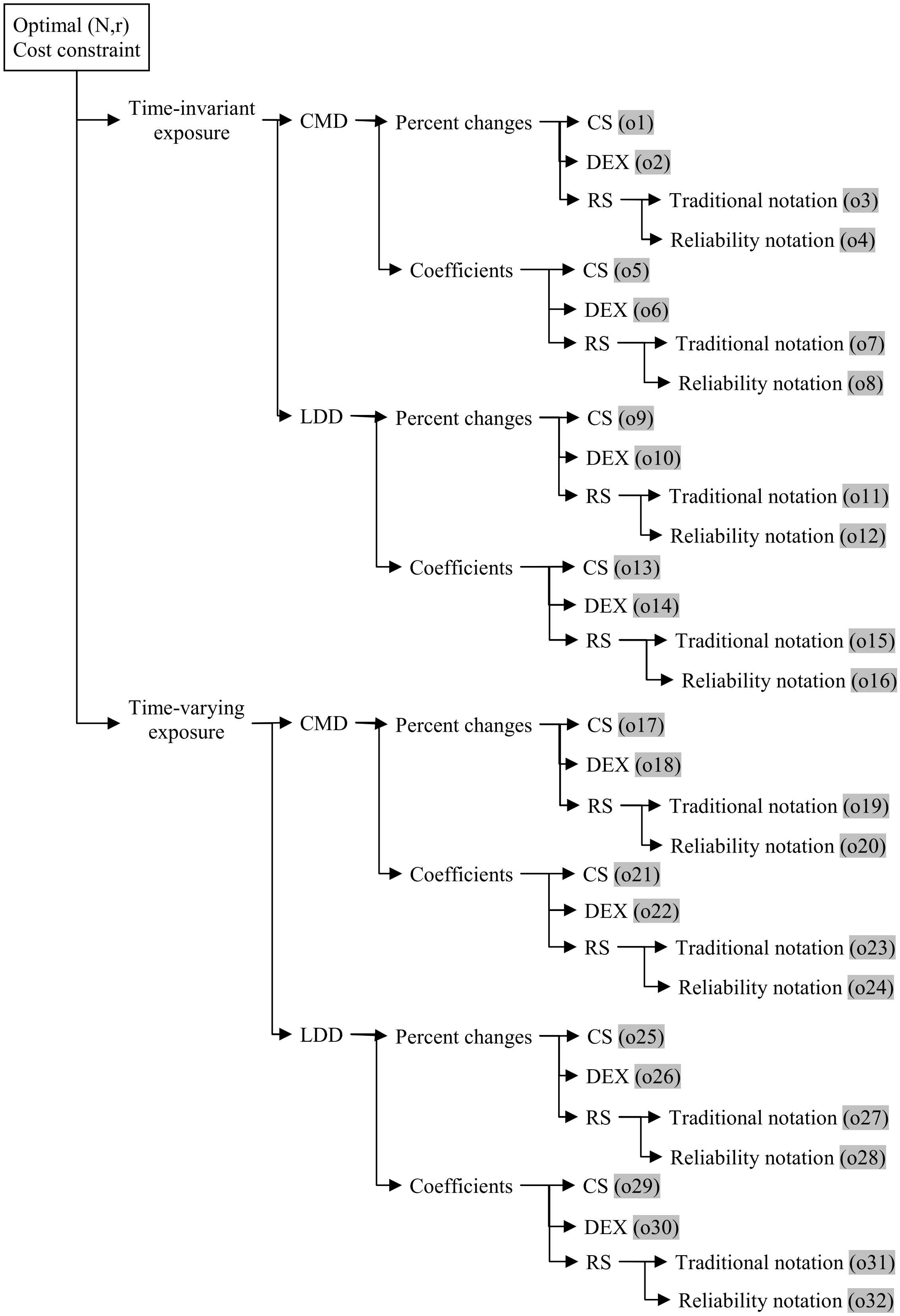
```
N Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2w sigma20
sigma21 sigma01 alpha
```

r32. `r.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
N Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho rho.b1
rho01 r.tilde alpha
```

2.2.3.5. Functions that return the optimal combination (*N*, *r*) under a cost constraint



o1. `opt.power.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho budget c1 k
max.r alpha
```

o2. `opt.power.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho theta budget
c1 k max.r alpha
```

o3. `opt.power.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o4. `opt.power.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

o5. `opt.power.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho budget c1 k
max.r alpha
```

o6. `opt.power.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho theta budget c1
k max.r alpha
```

o7. `opt.power.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o8. `opt.power.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

o9. `opt.power.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho budget
c1 k max.r alpha
```

o10. `opt.power.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho theta
budget c1 k max.r alpha
```

o11. `opt.power.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2w sigma20
sigma21 sigma01 budget c1 k max.r alpha
```

o12. `opt.power.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho rho.b1
rho01 r.tilde budget c1 k max.r alpha
```

o13. `opt.power.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho budget c1 k
max.r alpha
```

o14. `opt.power.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho theta budget
c1 k max.r alpha
```

o15. `opt.power.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o16. `opt.power.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

o17. `opt.power.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho budget c1 k
max.r alpha
```

o18. `opt.power.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho theta budget
c1 k max.r alpha
```

o19. `opt.power.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o20. `opt.power.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

o21. `opt.power.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd beta sigma2 rho budget c1 k
max.r alpha
```

o22. `opt.power.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd beta sigma2 rho theta budget c1
k max.r alpha
```

o23. `opt.power.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd beta sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o24. `opt.power.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.cmd beta sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

o25. `opt.power.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho budget
c1 k max.r alpha
```

o26. `opt.power.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho theta
budget c1 k max.r alpha
```

o27. `opt.power.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2w sigma20
sigma21 sigma01 budget c1 k max.r alpha
```

o28. `opt.power.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho rho.b1
rho01 r.tilde budget c1 k max.r alpha
```

o29. `opt.power.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho budget c1 k
max.r alpha
```

o30. `opt.power.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho theta budget
c1 k max.r alpha
```

o31. `opt.power.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

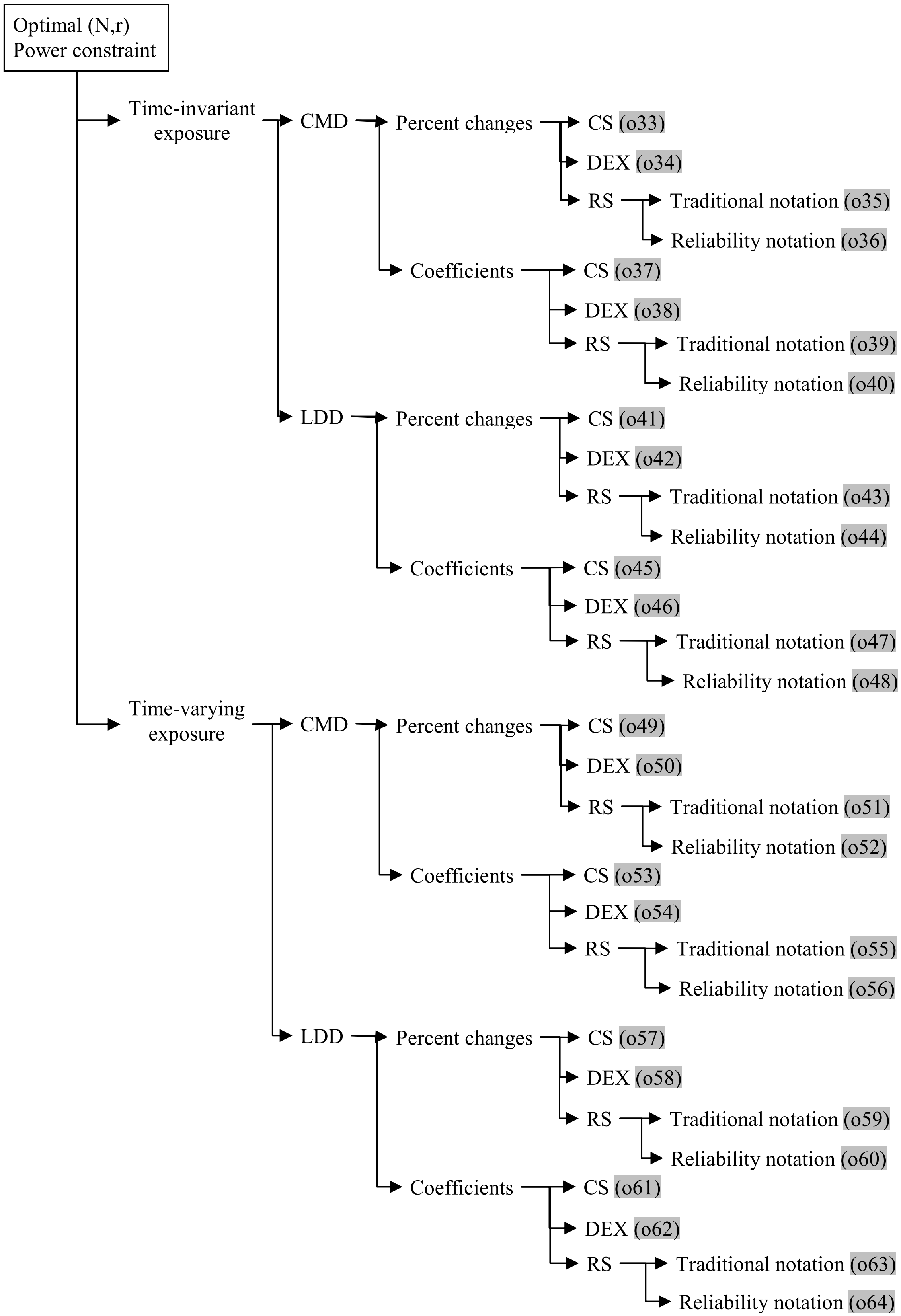
```
fixed s.or.tau pe rho.e model.ldd gamma3 sigma2w sigma20 sigma21
sigma01 budget c1 k max.r alpha
```

o32. `opt.power.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho rho.b1 rho01
r.tilde budget c1 k max.r alpha
```

2.2.3.6. Functions that return the optimal combination (*N*, *r*) under a power constraint



o33. `opt.cost.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho c1 k max.r
alpha
```

o34. `opt.cost.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho theta c1 k
max.r alpha
```

o35. `opt.cost.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2w sigma20
sigma21 sigma01 c1 k max.r alpha
```

o36. `opt.cost.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 sigma2 rho rho.b1
rho01 r.tilde c1 k max.r alpha
```

o37. `opt.cost.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho c1 k max.r
alpha
```

o38. `opt.cost.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho theta c1 k
max.r alpha
```

o39. `opt.cost.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2w sigma20 sigma21
sigma01 c1 k max.r alpha
```

o40. `opt.cost.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 beta sigma2 rho rho.b1 rho01
r.tilde c1 k max.r alpha
```

o41. `opt.cost.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho c1 k
max.r alpha
```

o42. `opt.cost.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
theta c1 k max.r alpha
```

o43. `opt.cost.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2w sigma20
sigma21 sigma01 c1 k max.r alpha
```

o44. `opt.cost.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde c1 k max.r alpha
```

o45. `opt.cost.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho c1 k max.r
alpha
```

o46. `opt.cost.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho theta c1 k
max.r alpha
```

o47. `opt.cost.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2w sigma20
sigma21 sigma01 c1 k max.r alpha
```

o48. `opt.cost.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe vt0 rho.exp.t0 gamma3 sigma2 rho rho.b1
rho01 r.tilde c1 k max.r alpha
```

o49. `opt.cost.tv.CMD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho c1 k
max.r alpha
```

o50. `opt.cost.tv.CMD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho theta c1
k max.r alpha
```

o51. `opt.cost.tv.CMD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2w sigma20
sigma21 sigma01 c1 k max.r alpha
```

o52. `opt.cost.tv.CMD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd mu00 p1 sigma2 rho rho.b1
rho01 r.tilde c1 k max.r alpha
```

o53. `opt.cost.tv.CMD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho c1 k max.r
alpha
```

o54. `opt.cost.tv.CMD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho theta c1 k
max.r alpha
```

o55. `opt.cost.tv.CMD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd beta sigma2w sigma20 sigma21
sigma01 c1 k max.r alpha
```

o56. `opt.cost.tv.CMD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.cmd beta sigma2 rho rho.b1 rho01
r.tilde c1 k max.r alpha
```

o57. `opt.cost.tv.LDD.p.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho c1
k max.r alpha
```

o58. `opt.cost.tv.LDD.p.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho
theta c1 k max.r alpha
```

o59. `opt.cost.tv.LDD.p.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2w
sigma20 sigma21 sigma01 c1 k max.r alpha
```

o60. `opt.cost.tv.LDD.p.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd mu00 p1 p2 p3 sigma2 rho
rho.b1 rho01 r.tilde c1 k max.r alpha
```

o61. `opt.cost.tv.LDD.coef.CS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho c1 k max.r
alpha
```

o62. `opt.cost.tv.LDD.coef.DEX(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho theta c1 k
max.r alpha
```

o63. `opt.cost.tv.LDD.coef.RS(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2w sigma20
sigma21 sigma01 c1 k max.r alpha
```

o64. `opt.cost.tv.LDD.coef.RS.reliab(infile,outfile)`

The input file should contain the following columns:

```
Pi fixed s.or.tau pe rho.e model.ldd gamma3 sigma2 rho rho.b1
rho01 r.tilde c1 k max.r alpha
```

Changes from previous version

- A general menu has been introduced. Now the program is called as `optitxs()`, instead of having five different calls, one for each module.
- The functions `decide.rhoe()` and `decide.rhoe.int()` have been incorporated to help decide a value for ρ_e.
- The phrasing of the question for p_1 under CMD has been changed.
- Corrected a bug on power calculation when N=0.
- For the optimal combination part, in addition to the plot, now the program shows a spreadsheet with all combinations of (N,r), their power, and their costs.

References

Basagaña X. Spiegelman D. (2007) The design of observational longitudinal studies.

Basagaña X, Spiegelman D. Power and sample size calculations for longitudinal studies comparing rates of change with a time-varying exposure. Stat Med 2010; 29 (2): 181-92.

Basagaña X, Liao X, Spiegelman D. Power and sample size calculations for longitudinal studies estimating a main effect of a time-varying exposure. Stat Methods Med Res 2010 [Epub ahead of print]