User Manual for LateOnset_MI
Version 3.0.0
April 6, 2015

LateOnset_MI can be used to monitor *toxicity* or/and *efficacy* that are potentially late-onset for phase II trials. When toxicity and efficacy are not late-onset, it becomes the method proposed by Thall and Simon (Biometrics, 1994, 337-349), which monitors the event based on posterior probabilities. The program also provides the option to monitor *disease progression* because in some trials, the efficacy endpoint cannot be evaluated in real time, and what can be evaluated in real time is disease progression (i.e., no efficacy).

The program requires 6 external, user-specified files, in order to operate.

These files are:

Input Data Files (3 files)
data_toxicity.txt
data_efficacy.txt
data_diseaseProgression.txt

Configuration Files (3 files)
TrialConfig_Toxicity.config
TrialConfig_Efficacy.config
TrialConfig_DiseaseProgression.config

Output File:
Summary.txt

All six of these files must be located in the same directory as the executable code. Different trials should have their own local copies of the executable and the above files. The configuration files should be set based upon the Protocol document. The three files should be kept up to date based upon the latest information regarding the patients enrolled in the trial. Templates of these files are provided in the software package.

Steps to use the software to conduct a trial

1). Modify the corresponding configuration file to reflect the actual settings of the trial. For example, if we want o monitor toxicity, we modify the file "**TrialConfig_Toxicity.config**"

EXAMPLE

TrialConfig_Toxicity.config

```
TrialType          =    toxicity          # This is the outcome being collected. Can be toxicity, efficacy or diseaseProgression

RateBound          =    0.5               # This is an upper bound of toxicity rate (when dealing with toxicity)
                                          # and a lower bound for efficacy/disease progression rates when dealing
                                          # with efficacy or disease progression.
                                          # Stopping rule for toxicity Pr(toxicity rate > upper bound) > CutoffProbability
                                          # Stopping rule for efficacy Pr(efficacy rate < lower bound) > CutoffProbability
                                          # Stopping rule for disease progression Pr(disease progression rate > 1-lower bound) >
                                          # CutoffProbability

CutoffProbability  =    0.95              # Probability bound for terminating a trial

MaxEvaluationWindow =   6                 # Duration of assessment window. For example, if the assessment window is 3.5 months,
                                          # please enter 3.5. Note: the unit of duration should be the same with the event time
                                          # entered in the data.txt file.

InputDataFileName  =    data_Toxicity.txt # Filename where the patient relevant data is stored
```

2) Update data files so that they are the latest. The go/no-go decision recommended by the program is based upon the data being the latest possible. For example, when we monitor toxicity, we only need to update the toxicity data file "**data_toxicity.txt**".

EXAMPLE

data_toxicity.txt

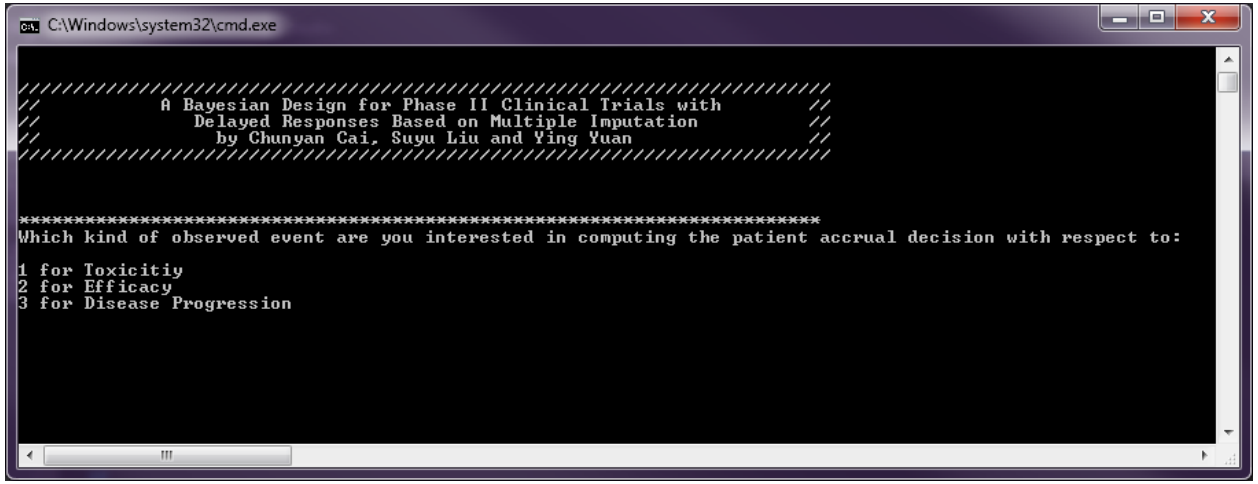
PTID	toxicity_event	time_to_event	follow-up
0	0	0	6
1	1	5.64	6
2	1	3.2	6
3	0	0	6
4	1	4.7	6
5	1	5.4	6
6	1	3.9	6
7	0	0	6
8	0	0	6
9	1	5.2	6
10	0	0	6
11	0	0	6
12	0	0	6
13	1	5.3	6
14	1	4	6
15	0	0	5
16	0	0	4
17	0	0	3
18	0	0	2
19	0	0	1

Comments: "PTID" is patient id
"toxicity_event" is an indicator variable: 1=event, 0=censored
"time_to_event" is time to the event (i.e., toxicity)
"follow-up" to record the total time patient has been followed.

3) After all files have been properly updated, start the executable “LateOnsetMI.ext”. Choose the appropriate event to be monitored, and code will run. Upon program completion, the results are appended to a file called “Summary.txt”, located in the current (calling) directory. If anything in the configuration is wrong (except inappropriately entered values in data tables) the code will terminate before running the computations. It will state errors (informative) indicating changes needing to be made to files.

EXAMPLE

Command-line UI: Enter 1, 2 or 3 and that’s all.



An output example in “Summary.txt”

Thu Sep 17 14:11:38 2015
Number of patients entered=20
Maximum Follow up time = 6
Upper bound of toxicity rate= 0.5
Trial will be terminated if Pr(toxicity rate>0.5)>0.95

Please check the following data whether they are the same as you entered.

****

patient ID 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Toxicity 0 1 1 0 1 1 1 0 0 1 0 0 0 1 1 0 0 0 0 0

Time to event 0 5.64 3.2 0 4.7 5.4 3.9 0 0 5.2 0 0 0 5.3 4 0 0 0 0 0

Follow-up time 6 6 6 6 6 6 6 6 6 6 6 6 6 6 5 4 3 2 1

****

RESULTS: Pr(Toxicity rate >0.5)=0.523959

Compared with cut-off 0.95, it is LOWER than the cut-off, therefore we suggest to CONTINUE the trial.

****
********** Decision *******
********** CONTINUE the trial *******
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----------The End----------