

MRC Biostatistics Unit



UNIVERSITY OF CAMBRIDGE

Improving implementation of Adaptive Multi-Arm Multi-Stage Trials: The MAMS R Package

Nikita Mozgunov, Dominique-Laurent Couturier, Michael Grayling, Dominic Magirr, Philip Pallmann, Thomas Jaki

About MAMS Package

Trial Design

In the MAMS package, each experimental treatment is compared with a common control.

$$H_0 : \mu_k \leq \mu_0$$

$$H_1 : \mu_k > \mu_0$$

Development

Version 0.1 (25/04/2012): Initial release

…

Version 1.0 (19/07/2016): Altered mams function to improve consistency for different allocation ratios

…

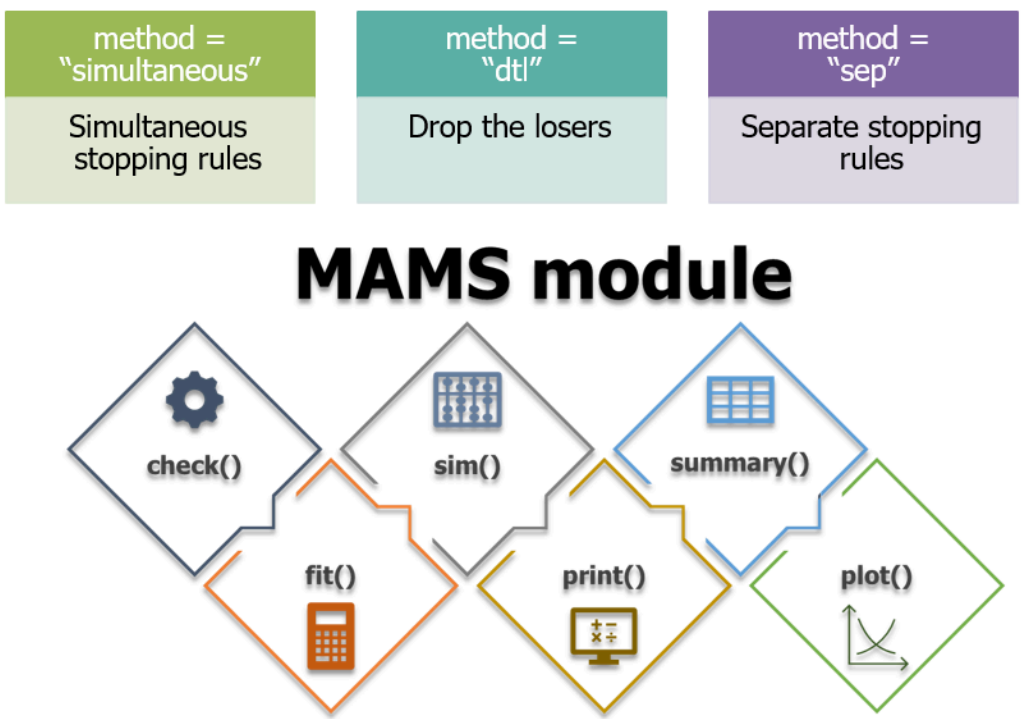
Version 2.0.0 (14/01/2022): Parallelisation framework included for several functions; recoded parts of the functions in C

…

Version 3.0.0 (30/09/2024): New major release

Modular Design Approach

- Implemented three key methods:
  - **Simultaneous stopping rules**
  - **Drop-the-losers design**
  - **Separate stopping rules**
- New methods can be integrated seamlessly
- Expands applicability to various MAMS trial designs



Input parameters

Design	Function call	Description
Investigation of 4 experimental treatments in 2 stages with normal endpoints.	K = 4	Number of experimental treatments
	J = 2	Number of stages
One-sided familywise error rate of 0.05 and desired power of 0.9.	alpha = 0.05	One-sided familywise error rate
	power = 0.9	Desired power
Allocation ratios: r = 1:2 for experimental treatments, r0 = 1:2 for control.	r = 1:2	Vector of allocation ratios
	r0 = 1:2	Vector ratio on control
Effect size parameters	p = 0.75	Interesting treatment effect on probability scale
	p0 = 0.5	Uninteresting treatment effect on probability scale
	delta = NULL	Interesting treatment effect on traditional scale
	delta0 = NULL	Uninteresting treatment effect on traditional scale
	sd = NULL	Standard deviation
Fixed lower boundary with shape "obf" for upper boundary.	ushape = obf	Shape of upper boundary
	lshape = fixed	Shape of lower boundary
	ufix = NULL	Fixed upper boundary
	lfix = 0	Fixed lower boundary
Sample Size and Computational Settings	nstart = 1	Starting point for sample size
	nstop = NULL	Stopping point for sample size
	sample.size = TRUE	Find sample size
	Q = 20	Number of quadrature points
Simulations using 50,000 iterations, considering H0 = True.	nsim = 50000	Number of simulations
	H0 = TRUE	Consider case with all effect sizes set to 0

Example Application

Installing package ...

```
1   library(MAMS)
2
3   mams_1 <- mams(method = "dtl", K = c(4,2,1), J=3, power = .9, alpha = .05,
4                  r = c(1,2,3), r0 = c(1,2,3), delta = 0.954, delta0 = 0, sd = 1,
5                  ushape = "obf", lshape = "fixed", nsim = 50000)
```

MAMS



Designing multi-arm multi stage studies

This package allows to design multi-arm multi-stage (MAMS) studies with asymptotically normal endpoints and known variance. It considers normal, binary, ordinal and time-to-event endpoints in which either the single best treatment or all promising treatments are continued at the interim analyses.

Installation

You can install the latest released version from CRAN from within R:

```
install.packages("MAMS")
```

Details

Currently implemented functions are:

- **`mams()`** : a function allowing to design multi-arm multi-stage studies with normal endpoints,
- **`new.bounds()`** : a function allowing to update the lower and upper boundaries of a multi-arm multi-stage study, typically initally defined by `mams()` , based on observed sample

Links

View on CRAN

License

GPL-2

Citation

Citing MAMS

Developers

Thomas Jaki
Author, maintainer

Dominique-Laurent Couturier
Author

Dominic Magirr
Author

Nikita Mozgunov
Author

Philip Pallmann
Author

Dev status

CRAN 3.0.0

Conclusion

- **Enhanced Methodologies:**
  New advanced methods have been implemented to improve the design and simulation of adaptive multi-arm multi-stage trials.
- **Increased Flexibility:**
  The MAMS package now supports a wider range of stopping rules (simultaneous, drop-the-losers, separate) and can easily adapt to different trial scenarios.
- **Backward Compatibility:**
  Despite new features, the package remains compatible with existing MAMS designs, ensuring a smooth transition for current users.
- **Future-Proofing Adaptive Trials:**
  These improvements contribute to more reliable decision-making and streamlined implementation of adaptive clinical trials.

MRC Biostatistics Unit

UNIVERSITY OF CAMBRIDGE

Q&A