This paper introduces a new R-package, crmPack, for dose-finding clinical trials. It allows some flexibility for the planning of the clinical study and it can be easily extend to new designs thanks to the S4 classes and methods.

The structure of the article is particularly clear and organized. Each section is well written and well developed, including a diversity of interesting figures. The R package Implements model-based and algorithm-based designs, ranging from '3+3' to modified CRM based on dose limiting toxicity endpoints to dual-endpoint designs taking into account a biomarker/efficacy outcome.

Major comments

- It seems that the proposed CRM design is a modified version of the CRM. However this is not clearly written and it causes confusion, since placebo groups cannot be used in the classic version of the CRM (for example as implemented in the dfcrm package). The package name is also misleading.
- The new R-package is proposing the implementation of existing methods (3+3 design, CRM, etc), similar to the already existing softwares (e.g. crm in Stata, dfcrm and bcrm in R, etc). The crmPack has no big novel statistical designs (except of the dual-endpoint designs and the placebo group for healthy studies) as we would expect to see in a new R-package for dose-escalation designs. For example, all the mentioned commercial packages (ESCALATE in East, df in ADDPLAN and FACTS) can offer extensions for the 3+3 design and/or implement various versions of the CRM. Similarly, the Stata package crm and the R packages dfcrm and bcrm can implement CRM models and offer a wide range of different dose escalation designs. Why would the user need to learn/use this new R-package? What is the advantage in using this package and not the other ones? Why this version cannot be an extension of dfcrm package?
- There is no novelty in the structure or on the flexibility of the package, except the class structure, which is still similar to the other packages, in order to intrigue the user to use this new package instead of using the already existing packages.
- Since the crmPack is using a modified CRM and the article is already mentioning some existing solutions, it could also include other packages that are using modified CRM dose finding designs. For example the R-package ordcrm using likelihood-Based Continual Reassessment Method (CRM) dose finding designs has not been mentioned. Another R-package, dfpk, implements bayesian dose finding designs (including a modified model of CRM design) using pharmacokinetics for phase I clinical trials. Other existing packages should be mentioned, besides the classical ones (dfcrm, bcrm, etc.), in order to provide the reader with a better overview of what already exists and what is missing in the programming domain of these designs.
- Looking at the different examples, only one of the available models is used (i.e. LogisticLogNormal), but the article suggests that the package includes many different models without giving details about each model neither where to search for more information on this matter. It might be better to be clearer on where to find more documentation (i.e. in the R documentation on CRAN). Also it will be more understandable if the article could include a figure with the model class structures including the GeneralModel & the ModelPseudo classes.
- Figure 1 (page 3) is not so clear. It's a little confusing and it does not give the first clear idea of the package's framework. It might be better to split it in two figures.