# **Thesis Storyboard**

This document contains thoughts and ideas about the best way to combine the chapters in my thesis with an introduction and conclusion.

“Developments to established dose-finding methodologies for application in trials with complex and innovative design”

# **Introduction**

**Aims of the thesis**

Each chapter covers something different but they all fall under the umbrella of early-phase trials. Based on our title there are sort of two main themes that relate to statistical methodologies throughout the chapters:

* Extension
* Application

Each chapter involves, in some way extending some current methodology and demonstrating how it can be applied.

No idea how detailed to be with this section. If it’s made general as in we aim to explore different methodologies and how they can be extended the chapters are a bit random. Maybe we can specify the first half is on extending these designs and the second on developing visualisation tools.

**Introduction to Methodology**

* Detail early phase trials (phase I, phase II and adaptive phase I/II)
* Basics of Bayesian statistics
* Specific Methodology
  + CRM
  + Beta-Binomial

**Chapters in thesis**

* Add a brief summary of each chapter

# **ADePT-DDR**

The PO-TITE-CRM design is an extension created by WT, it solves the problem of having combinations of treatment and not knowing the order of doses.

We applied this in a setting that it was not originally designed for. (Combination treatment but one treatment is fixed. We still used it as the dosing schedule under investigation still led to the same issue). Our experiences applying a novel methodology and how it would compare to other approaches.

# **RtC-WT**

Extended an adaptive phase I/II design to explore the possibility of including a control arm.

# **TITE-DTPs**

Extended DTPs to work in the TITE setting. Explored the issues that arose with this.

Gave advice (guidance?) on how they could be applied / shouldn’t/ too difficult to apply

# **ETPs**

Not a direct extension but extended the concept behind DTPs to facilitate decision making in single-arm phase II trials

Developed code and an application to ensure these could easily be used in practice

**Introduction**

* Issues with decision making in early phase trials.
* Working with small sample sizes (by design or forced to ie rare diseases)
  + Lack appropriate level of evidence to make decisions. Compensate with:
    - Alternate trial designs: single arm
    - Bayesian methods
  + Look at the data more frequently
* As with DTPs it would be useful to map out the decisions that are made to help with the design/running of a trial like this

**Efficacy Transition Pathways**

* Give an example trial (Cindy mentioned she wanted this to illustrate something – to discuss)
  + Show how to construct an ETP (already had a lot of this written but can tailor it a specific example)
    - Create individual cells then combine them
  + Like with the TITE-DTP chapter show how we can change the ETP (discuss with cindy as this would be based on the examples she wanted to illustrate)
    - i.e clinician wants to change the decision rule
    - want to be more/less strict about stopping
    - change of prior evidence
    - change sample size / interim time-points
* Practical applications
  + Show how this has been practically implemented:
    - MonoGerm
    - Glo-BNHL
    - DETERMINE
* Example + Practical as motivation for the development of code/app
  + Small changes to the design have big impact on ETPs
  + Previous methods for creation were tedious
  + Reason DTPs are successful is because of pre-existing code dtpcrm/escalation

**Development of Web App for ETPs**

* Can keep this section as is for the most part
  + Can add video/plot like Kristian suggested
  + Link back to the example in the previous section to show how changing the sample size/decision criteria/priors is a click of a button
* Add more of a focus on the other features how they can be used for teaching etc.

# **Conclusion**