

The University of Birmingham
Registry - Academic Services

DOCTORAL REPORT FORM
PART ONE: INDEPENDENT REPORT ON THESIS
(A JOINT REPORT IS NOT ACCEPTABLE)

Independent Report normally 500 words which should address the following.

- a) Was the nature and purpose of the research made clear and was this substantially achieved?
- b) To what extent does the thesis demonstrate that the candidate has an adequate understanding of the subject and knowledge of the literature? Is there coverage of recent and relevant literature in the field of study which shows critical appraisal and an original synthesis?
- c) Has the candidate chosen the appropriate methodology for the study? Is the methodology then used effectively? Are the findings interpreted in a valid way?
- d) What evidence is there of independent critical and analytical skills, and the ability to evaluate evidence?
- e) Is there an understanding of the theoretical field associated with the study? Is the linkage and balance between practical investigation and theory satisfactory?
- f) Are the arguments put forward in an appropriate and coherent form?
- g) To what extent does the thesis show evidence of originality and make a contribution to knowledge? Does it contain matter suitable for publication in whole or in part in a learned journal or the equivalent?
- h) What is your view of the overall quality of the research described in the thesis?
- i) Is the synopsis an adequate summary of the work presented?
- j) Is the thesis clearly written and presented? Is the style and structure of the thesis satisfactory?

This thesis covers the area of early-phase dose-finding trials and phase II oncology trials using Bayesian methods. The thesis presents several areas of research that broadly fall into two main areas: complexities of incorporating time-to-event outcomes into dose-finding trials and representing how a complex trial may unfold using ideas from 'dose transition pathways'.

Chapter 1 provides an introduction to phase I and II trials and how more complex approaches could be useful but are typically rarely used. It then overviews the rest of the thesis.

Chapter 2 provides an overview of the ADEPT-DDR trial and how the PO-TITE-CRM was implemented. Some simulation study results are provided to show how the design performs and how other approaches might have performed. Here, and throughout, the simulation studies are performed and presented in a clear way.

Chapter 3 considers phase I/II designs that assess both futility and efficacy. An extension to a previous phase I/II design is proposed that allows incorporating a control arm. The properties of this are evaluated with a simulation study, and compared to some simpler approaches that might be used. Overall I thought this was a good set of work. My most major comment was that a case study motivated the original design work and this would have been interesting to frame the results.

Chapter 4 considers the issue of dose transition pathways in the context of time-to-event designs, e.g. TITE-CRMs. DTPs are a useful tool for presenting possible dose recommendations based on what unfolds in the current and future cohorts. However for time-to-event, there is a lot of dependence on the amount of follow-up time which can vary a lot between patients, so the number of DTPs explodes. This chapter provides some useful investigation on this and concludes that it is feasible to look at a current cohort of size 3.

Chapter 5 considers how one can use ideas from dose transition pathways in the visualisation of efficacy stopping rules in phase II single-arm trials. Although in my opinion the transition pathway concept is not

quite so useful as it is in dose-finding, being able to visualise different possible outcomes of interims is useful. A R shiny app is presented which is good to see.

Chapter 6 summarises the work of the thesis well. I would have liked to have seen some more potential future work that was motivated by the thesis, but this is something that can be asked in the viva.

Overall, the thesis presents some useful work that has potential to improve early-phase oncology trials. I would say that there is potential for three published papers worth of material. The thesis was generally written in a clear manner and there were only a limited number of typos I found.

Please return this part BEFORE the Oral, (keeping a copy for yourself) to Research Student Administration Team via e-mail to pgrstudentrecords@contacts.bham.ac.uk.

Date Of Oral (please insert)	21/06/2024
An oral examination is compulsory for a doctoral thesis	

Examiner	Name (Block Capitals)	Signature (if sending by e-mail insert "by e-mail")	Date
External	James Wason	By email	16/06/2024

DOCTORAL REPORT FORM
PART TWO: JOINT REPORT ON THE ORAL EXAMINATION

A joint report (approximately 200 words), should be completed immediately after the oral examination and returned, with Parts 3 and 4, to Research Student Administration via pgrstudentrecords@contacts.bham.ac.uk.

Date of Oral (please insert)	21-06-2024
An oral examination is compulsory for a doctoral thesis	

We (James Wason and Pavel Mozgunov) examined Amit Patel on 21st June 2024 with Simon Gates as the internal independent chair. The viva lasted approximately 2.5 hours.

We were both very impressed by Amit's performance in the viva. We asked a lot of broad and specific questions and he answered them very well and showed a good level of independent thinking and broad experience of implementing advanced clinical trial designs. We have recommended some minor revisions are made (the details are provided below) and given his new job, would recommend that he is given three months to make this revisions rather than the standard one month.

Examiner	Name (Block Capitals)	Signature (if sending by e-mail insert "by e-mail")	Date
External	JAMES WASON	By email	21-06-2024
	PAVEL MOZGUNOV	By email	23-06-2024

DOCTORAL REPORT FORM
PART THREE: FINAL RECOMMENDATION

- For definitions of minor and major corrections and revise and resubmit and their time limits, please refer to the Examiners Guidance Notes.
- Where a recommendation is minor or major corrections or revisions to the thesis, examiners must complete Part Four of the report.
- Where examiners agree, a joint Part Three report should be completed.
- Where examiners are unable to agree on a final recommendation, please refer to the Examiners Guidance notes. In this situation each examiner should complete a separate final recommendation form.

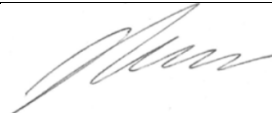
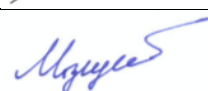
The whole examination process should be completed by 20 June 2024.

I/We recommend:

Tick One Option

1.	That the degree for which the thesis was submitted be awarded	<input type="checkbox"/>
2.	<p>That the degree for which the thesis was submitted was submitted be awarded subject to minor corrections being carried out to the satisfaction of insert name of external examiner nominated to check the corrected thesis</p> <p>Complete a list of corrections on Part 4.</p> <p>The normal timeframe for completion of minor corrections is one month. Please state here if the examiners wish to give the candidate a longer period. Three months</p> <p>An electronic copy of the corrected thesis will be emailed to the external examiner for checking.</p> <p>If you prefer to check a paper bound copy please tick here <input type="checkbox"/></p>	<input checked="" type="checkbox"/>
3.	<p>That the degree for which the thesis was submitted be awarded subject to major corrections being carried out to the satisfaction of both examiners.</p> <p>Complete a list of corrections on Part 4.</p> <p>The normal timeframe for completion of major corrections is six months. Please state here if the examiners wish to give the candidate a longer period. Click here to enter text.</p> <p>An electronic copy of the corrected thesis will be emailed to both examiners.</p> <p>If you prefer to check a paper bound copy please tick here <input type="checkbox"/></p>	<input type="checkbox"/>
4.	<p>That the thesis be revised and resubmitted for the degree for which it was submitted.</p> <p>Complete a list of corrections on Part 4.</p> <p>A further oral will be held following resubmission.</p> <p>The normal timeframe for revision and resubmission is one year. Please state here if the examiners wish to give the candidate a longer period. Click here to enter text.</p>	<input type="checkbox"/>

5.	<p>That the degree should not be awarded, but: (Please tick <u>one</u> of the following options)</p>	
	<p>a) Award an appropriate Masters degree. (The candidate shall have the right of appeal.)</p> <p>Enter programme title of Masters degree here: Click here to enter text.</p>	<input type="checkbox"/>
	<p>b) Award an appropriate Masters degree (MPhil, MA/MSc by Research, MRes (only applicable where 60 credits of taught modules have been completed), subject to Minor/Major* corrections (*please delete as appropriate).</p> <p>Enter title of Master's degree here: Click here to enter text.</p> <p>Complete a list of corrections on Part 4 of the report form.</p> <p>The normal timeframe for completion of minor corrections is one month and for major corrections six months. Please state here if the examiners wish to give the candidate a longer period. Click here to enter text.</p> <p>An electronic copy of the corrected thesis will be emailed to one examiner for minor and both examiners for major corrections.</p> <p>If you prefer to check a paper bound copy please confirm here <input type="checkbox"/></p> <p>The candidate shall have the right of appeal.</p>	<input type="checkbox"/>
	<p>c) That the thesis be revised and resubmitted for an appropriate Master's degree (MPhil, MA/MSc by Research, MRes (only applicable where 60 credits for taught modules have been completed).</p> <p>Enter title of Masters degree here: Click here to enter text.</p> <p>Complete a list of corrections on Part 4.</p> <p>The normal timeframe for revision and resubmission is one year. Please state here if the examiners wish to give the candidate a longer period. Click here to enter text.</p> <p>The candidate shall have the right of appeal.</p>	<input type="checkbox"/>
6.	<p>That the thesis be rejected, without opportunity for resubmission and a degree not awarded.</p> <p>The candidate shall have the right of appeal.</p>	<input type="checkbox"/>

Examiner	Name (Block Capitals)	Signature	Date
External 1	JAMES WASON		21-06-2024
External 2	PAVEL MOZGUNOV		23-06-2024

DOCTORAL REPORT FORM
PART FOUR: LIST OF CORRECTIONS/REVISIONS

This part must be completed in all cases where the recommendation is minor or major corrections or revise and resubmit the thesis.

To remove any ambiguity examiners should be explicit in the guidance given with regard to corrections.

Corrections have been noted on the body of the thesis	YES	NO
If yes, has the thesis been returned to candidate	YES	NO

Our suggested revisions are:

Throughout: make Open source code available for each relevant chapter.

Chapter 2:

- Add literature review (update applications of partial ordering CRM use)
- add a toy example to illustrate how the compared methods work in practice.

Chapter 3:

- Add paper (Mozgunov, P., Jaki, T. and Paoletti, X., 2019. Randomized dose-escalation designs for drug combination cancer trials with immunotherapy. *Journal of Biopharmaceutical Statistics*, 29(2), pp.359-377.) and add a toy example to illustrate how the compared methods work in practice (at discretion of candidate add model to simulations or toy example)

Chapter 4:

- Compare how DTPs change with weight – compare couple of weight function
- Revise informal language (see marked up PDF from Pavel)

Chapter 5:

- Add how operating characteristics change when ETPs change
- Revise informal language (see marked up PDF from Pavel)

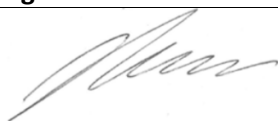

Chapter 6:

- add future work

Typos/minor (from James)

- Page 3: *Often times* - > *Oftentimes*
- Page 14 “*non actually*” -> *none actually*
- Page 24 “*DLT’s*” - > *DLTs (this appears multiple times)*
- *Page 83 – I didn’t follow where the 1:5.06 came from, why not 1:5? – make clearer
- Page 57: “*multiple working models mean the*” -> *means*
- Page 77 “*high probabilities of selecting the OBD 76%-80%*” – better with brackets or hyphens to divide OBD and 76%
- Page 115 “*DTPs main use*” -> “*DTP’s main use*” or “*The main use of DTPs*”

Further minor points from Pavel are highlighted in the attached pdf. The question are highlighted in the yellow highlight text, and the sentences/phrases requiring rewording are strikethrough.

Examiner	Name (Block Capitals)	Signature	Date
External 1	JAMES WASON		21-06-2024
External 2	PAVEL MOZGUNOV		23-06-2024

Completed Parts 2, 3 and 4 should be returned together to Research Student Administration Team via email to pgstudentrecords@contacts.bham.ac.uk.

Candidate's Name: A Patel	Student ID: 2227725	Date Thesis Submitted: 08/03/2024
School/Department: Inst of Cancer / Genomic Sci		
Permitted Word Length: 50000		Actual Word Length: 47897

PART FIVE: EXTERNAL EXAMINERS' COMMENT ON ACADEMIC STANDARDS AND PROCEDURES

External examiners **are invited** to complete this form on the quality and standards of research degrees and administrative arrangements for the examination of research degrees at the University of Birmingham. Please indicate **YES, NO** or **Not Applicable** and provide brief comments where appropriate to the questions listed below. If necessary, please continue on a separate sheet, which should be signed and dated.

In your opinion:

- i. Are the descriptor levels for research degree programmes (Regulation 6.1.3 <https://intranet.birmingham.ac.uk/as/registry/legislation/regulations.aspx>) set out on Page 2 of the Examiners Guidance notes of the appropriate standard and do they provide clear and sufficient guidance?

Yes
Comments:

- ii. Are the arrangements for Research Degree Programmes with Taught Elements clear and comprehensive (Regulation 6.1.4 available at: <https://intranet.birmingham.ac.uk/as/registry/legislation/regulations.aspx>)

Yes
Comments:

- iii. Are the requirements for the degree (Regulation 7.4.1 <https://intranet.birmingham.ac.uk/as/registry/legislation/regulations.aspx>) available on page 3 of the Examiners Guidance notes of the appropriate standard?

Yes
Comments:

- iv. Are the assessment requirements (Regulation 7.4. available at: <https://intranet.birmingham.ac.uk/as/registry/legislation/regulations.aspx>) appropriate and satisfactory?

Yes
Comments:

Candidate's Name: A Patel	Student ID: 2227725	Date Thesis Submitted: 08/03/2024
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- v. Are the recommendations available to examiners appropriate and satisfactory for each award? (See page 6 of the Examiners Guidance notes).

Yes
Comments:

- vi. Were the arrangements and procedures for all stages of the examination satisfactory?

Yes
Comments:

- vii. Were you satisfied that you understood your role in the oral examination and that you were able to perform that role?

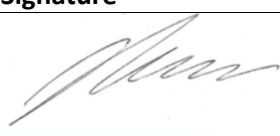

Yes
Comments:

- viii. Did the information provided to you offer you clear guidance on your role and on the recommendations you could make?

Yes
Comments:

- ix. Do you have any further comments on the quality and standard of the University's research awards, processes or any other issues of wider concern about this candidate's research thesis or supervision which you would like to raise?

Yes
Comments:

	Name (Block Capitals)	Signature	Date
External Examiner	JAMES WASON		21-06-2024
	PAVEL MOZGUNOV		23-06-2024

Candidate's Name: A Patel	Student ID: 2227725	Date Thesis Submitted: 08/03/2024
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***Please return to Research Student Administration Team via e-mail to
pgrstudentrecords@contacts.bham.ac.uk.***