Study Guide

Design of Randomised Controlled Trials (DES)

Semester 2, 2016

Prepared by:
Murthy Mittinty and Thomas Sullivan
School of Public Health
The University of Adelaide

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This course, Design of Randomised Controlled Trials, was originally designed and written by Cate D’Este at The University of Newcastle, and by Val Gebski and Rachel O’Connell at The University of Sydney. Substantial modifications were made in 2007 and 2008 by Philip Ryan, Amy Salter, Gary Glonek, Lisa Yelland and Tom Sullivan at The University of Adelaide. Further modifications were made in 2015 by Amy Salter, Jennie Louise and Tom Sullivan at the University of Adelaide.

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ACADEMIC CO-ORDINATOR

Murthy N Mittinty

Senior Lecturer
School of Public Health
The University of Adelaide
Adelaide SA 5005

Phone: 08 8313 0961
Fax: 08 8223 4075
Email: Murthy.mittinty@adelaide.edu.au
ACADEMIC STAFF

Thomas Sullivan
Senior Statistician, Adelaide Health Technology Assessment
School of Public Health
The University of Adelaide
Adelaide SA 5005

Email: thomas.sullivan@adelaide.edu.au

Lyle Palmer
Professor
School of Public Health
The University of Adelaide
Adelaide SA 5005

Email: lyle.palmer@adelaide.edu.au
OTHER CONTACTS

If you have trouble contacting the academic coordinator/academic staff, or have any other queries, please contact:

**Erica Jobling**

Executive Officer  
Biostatistics Collaboration of Australia  
BCA c/o NHMRC Clinical Trials Centre  
Locked Bag 77  
Camperdown NSW 1450

Phone: 02 9562 5076  
Email: bca@ctc.usyd.edu.au
WELCOME LETTER

Dear Student,

Welcome to Design of Randomised Controlled Trials (DES). In this unit, we will present the more important issues that arise when designing randomised controlled trials. Much of the material presented is from published articles. This has the benefit of:

- Giving you some experience in obtaining information from ‘research’ papers, rather than simply from books, as novel ideas tend to be published in expository papers or reviews much faster than books or monographs.

- Introducing you to journals where such articles tend to appear.

- Providing interpretations of issues from the viewpoint of a number of different authors.

You should use the articles to help you understand the underlying concepts. You may find that some articles are more accessible than others. Use the papers as a reference source. If you come across other articles that you have also found useful, please let me know.

Please don’t hesitate to contact me if you are having problems with the course material.

Murthy Mittinty
July 2016
COURSE OVERVIEW

This subject will introduce randomised comparisons as a major tool used in medical research and the basis of providing evidence for improving clinical practice. This is a one semester course and will be offered in distance learning mode only.

Experimental designs play a critical role in the conduct of medical research. Underpinning evidence-based medicine are well-conducted randomised controlled trials, which form a basis for clinical practice. A solid introduction to principles of experimental design and issues related to randomised controlled trials is important to facilitate experiments having optimum statistical efficiency.

This course differs somewhat from many of the other BCA courses in the program in that it does not require much in the way of ‘hands on’ analysis or application of formulae (though there is some of this!). It mainly involves working through principles and concepts and applying these to real life situations and problems likely to be encountered in the design of trials. Generally the examples and assessment questions are based on actual studies. In many situations there is not necessarily a correct or incorrect answer. What is of importance is the appropriate discussion and consideration of relevant issues.

In keeping with the above philosophy, the course material is based around published articles and extracts from books. The use of eLearning is very important in this course and provides a guide to the course material. This is the forum used to generate discussion of the content and relevance of the articles provided, answer questions and ensure that students have a solid comprehension of the necessary concepts.

Major changes were made to DES in 2007 and 2008 and more recently in 2015 following a BCA curriculum review. Additional changes have been made in response to student feedback. Sections in the notes that generated a large amount of discussion have been updated, as have the reading materials and software programs made available.
COURSE OBJECTIVES

On completion of this unit, students should be able to:

1. Identify the benefits of randomisation as a mechanism for reducing bias, and implement a variety of randomisation schemes.

2. Demonstrate knowledge of the principles behind the common experimental designs.

3. Describe the efficiency advantages of crossover designs, and be able to design and interpret the two-period crossover study.

4. Demonstrate an understanding of the principles underlying Phase I, II, III and IV studies, as well as an appreciation of the scientific basis underlying issues in clinical studies including intention-to-treat, blinding, interim analyses, subgroup analyses and the handling of missing data.

5. Appreciate the importance of sample size in clinical studies, and perform sample size calculations for a variety of trial designs with different outcomes.
COURSE CONTENT

The subject will consist of five modules. These will cover the topics of:

- Module 1: Randomisation
- Module 2: Design of RCTs
- Module 3: Sample Size
- Module 4: Phase I and Phase II Studies - Interim Analysis and Early Stopping
- Module 5: Analysis and Reporting of RCTs

Modules 1, 2 and 3 will require approximately 2 weeks of study each. Modules 4 and 5 will require approximately 3 weeks of study. This will leave 1 week for revision, or to cover other issues which may arise during the course.

Material will be accessed through the text book, which is required reading. Additional material will be provided as required. Notes will be provided for each module which will include the relevant text references, copies of additional readings, notes and exercises. Written material will be supplemented by discussion on eLearning.

In addition, students will be provided with a copy of *win_*_sam* and *PS*, software programs for calculation of sample size. These can be downloaded from eLearning. Note these programs only run on Windows.

TEXT BOOK

The text book for this subject is:


It will be necessary for you to have access to this book, as some of the course material is contained in the text book. You may be able to access a copy through your place of employment or a local library.

Note: Students enrolled in the University of Sydney have access to an electronic version of the text book through the University of Sydney library.
METHOD OF DELIVERY

Students will be provided with five modules, as outlined in the previous section. These modules, excluding readings, will also be made available on eLearning. The sample size programs and course assessments will be available on eLearning and will not be provided to students on an individual basis. Important announcements will also be placed on eLearning, so students should regularly monitor eLearning.

Communication should generally be via eLearning (unless of a personal/confidential nature) as responses to questions and discussion of issues is of benefit to all students. eLearning is an integral component of the DES course as it hopefully reduces the isolation which can occur in distance learning. Students can post questions, ideas, suggestions and discussion on eLearning. The tutors will monitor and respond to all communication, however, students are also encouraged to respond and take part in these communications.

STAFF ROLES

There are three staff involved in delivering the course. As the academic co-ordinator, Murthy Mittinty will be primarily responsible for the course. However, all staff will contribute to the discussion on eLearning and respond to content-related questions.

CONTACTING STAFF

You can use the general DES email address (BCA_DES@adelaide.edu.au) to contact all staff involved in delivering this course.

Alternatively, you can contact Murthy Mittinty directly in relation to requests for extensions or other personal matters. Email is the preferred method of contact and a copy of all emails should be sent to Thomas Sullivan (email addresses are stated earlier in this Study Guide).

To facilitate timely responses to your enquiries, please include BCA – DES and the module in question, or general enquiry, in the subject field of all emails. For example, you may send an email with one of the following subject lines: ‘BCA – DES Module 1 enquiry’ or ‘BCA – DES general enquiry’.
ASSESSMENT

The assessment for this unit will involve three written assignments.

Assignment 1 will cover Modules 1 and 2 and will be worth 30%.

Assignment 2 will cover Modules 3 and 4 and will be worth 30%.

Assignment 3 will cover Module 5, as well as Modules 1-4, and will be worth 40%.

All assignments will be posted on eLearning three weeks prior to the submission date. Model solutions/guides will be posted on eLearning after the submission date.

Individual feedback on assignments will be provided to each student. Students will also be provided with summary statistics on the results for the entire class so that they can judge their relative performance for each assignment.

Students are expected to monitor eLearning for the posting of assignments, solutions and feedback. Email notifications and other channels of communication will not be used.

Examples and exercises are contained in each module to enable students to ascertain their level of understanding of various topics. These will not form part of the assessment for this course.

The Course Timetable below shows the due dates for the assignments and a guide to the pace at which students should progress through the course material.
COURSE TIMETABLE

Semester 2, 2016 will commence on Monday July 25.

<table>
<thead>
<tr>
<th>Week</th>
<th>Week Commencing</th>
<th>Module</th>
<th>Topic</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25 July 2016</td>
<td>Module 1</td>
<td>Randomisation</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 August 2016</td>
<td>Module 1</td>
<td>Randomisation</td>
<td>Assignment # 1 – Available 2 August</td>
</tr>
<tr>
<td>3</td>
<td>8 August 2016</td>
<td>Module 2</td>
<td>Design of RCTs</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15 August 2016</td>
<td>Module 2</td>
<td>Design of RCTs</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>22 August 2016</td>
<td>Module 3</td>
<td>Sample Size</td>
<td>Assignment #1 - Due 24 August</td>
</tr>
<tr>
<td>6</td>
<td>29 August 2016</td>
<td>Module 3</td>
<td>Sample Size</td>
<td></td>
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<tr>
<td>7</td>
<td>5 September 2016</td>
<td>Module 4</td>
<td>Phase I and Phase II Studies</td>
<td></td>
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<tr>
<td>8</td>
<td>12 September 2016</td>
<td>Module 4</td>
<td>Phase I and Phase II Studies</td>
<td>Assignment # 2 – Available 13 September</td>
</tr>
<tr>
<td>9</td>
<td>19 September 2016</td>
<td>Module 4</td>
<td>Phase I and Phase II Studies</td>
<td></td>
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<td></td>
<td>26 September 2016</td>
<td></td>
<td>Mid Semester Break 1 week only</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3 October 2016</td>
<td>Module 5</td>
<td>Analysis and Reporting of RCTs / Multiple Comparisons</td>
<td>Assignment #2 - Due 5 October</td>
</tr>
<tr>
<td></td>
<td>Note: Monday is a public holiday in some states.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>11</td>
<td>10 October 2016</td>
<td>Module 5</td>
<td>Analysis and Reporting of RCTs</td>
<td>Assignment # 3 – Available 11 October</td>
</tr>
<tr>
<td>12</td>
<td>17 October 2016</td>
<td>Module 5</td>
<td>Analysis and Reporting of RCTs</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>24 October 2016</td>
<td></td>
<td>Revision</td>
<td>Assignment #3 - Due 2 November</td>
</tr>
<tr>
<td>14</td>
<td>31 October 2016</td>
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</tbody>
</table>
EXTENSIONS

For various reasons, you may sometimes experience difficulties in getting your assignments submitted on the due date. Requests for an extension for an assignment must be made in advance of the due date for that assignment. The normal grounds for an extension being granted are bereavement, personal illness or illness in a family member requiring you to exercise a significant carer role.

These requests must be made directly to Murthy Mittinty by email (with a cc to Thomas Sullivan). Murthy will note the date and time of the request and reply to the request by email with the decision as to whether an extension has been granted and, if so, stating the length of the extension.

Length of extension: Extensions granted by Unit Coordinators will normally be no longer than three days.

PENALTIES FOR LATE SUBMISSION

Assignments should be submitted no later than midnight EST on the due date. Submissions after this time will be penalised at a rate of 5% of the earned mark per day, up to a maximum of 50%. Submissions after the solutions have been posted on eLearning will not be awarded any marks.

For example, if your mark for an assignment is 40/50 but you submit it two days late, 10% of your mark will be deducted so your final mark will be 36/50.
The online learning package used by the BCA is called eLearning. The BCA eLearning site will be accessed through the University of Sydney server. The BCA online facilities are, however, independent of the policies and procedures of this university. You will have access to online help at the University of Sydney ITS and eLearning Helpdesks. A guide to getting started in eLearning is posted in the Student Resources section on the BCA website.

Online learning will be one of the tools used to provide access to materials and solutions to exercises, and as a communication tool. Students are encouraged to post content-related questions in the Discussion facility in eLearning.

**eLEARNING HELPDESK**

For further assistance with eLearning, you can contact the eLearning Helpdesk at http://sydney.edu.au/elearning/student/help/emailUs.php

**Please note:**

If you have queries about the subject matter for DES, you should contact the academic coordinator, Murthy Mittinty.

If you are experiencing difficulties getting help, please contact the BCA coordinating office on 02 9562 5076, or email Erica.Jobling@ctc.usyd.edu.au.
ASSIGNMENT SUBMISSION

You will need to submit assignments using the “Turnitin” tool in eLearning. Assignments must be word-processed and submitted in PDF format. No special software will be required for converting a word document into a PDF document. If you are using word 2008 and later versions you can save your word document as a PDF file using “File-- save as”.

Identifying details (DES assignment and number, and your name) must be inserted in the header or footer box so that they appear on every page. If your submission is hand written, please write these details on every page. You must also include the page number and the total number of pages on each page of your assignment (e.g. Page 1 of 10).

For more details on submitting your assignment using “Turnitin” refer to pages 2-4 in the BCA Assessment guide.

In the unlikely event that the system is unavailable, you can email your assignment to the unit coordinator with a scanned copy of the cover sheet to the submission email.
BCA Assessment Guide - DES

You should read through the BCA Assessment Guide - DES for further information on the following topics:

- Guidelines for written work
- Guidelines for submission of assignments and exams
- BCA policies and procedures
- Assignment must be submitted using “Turnitin”.
APPENDIX 1: DES 2016 ASSIGNMENT COVER SHEET
Attention: Thomas Sullivan

If you are submitting your assignment via email, scan the signed cover sheet and submit it with your assignment, or fax the signed cover sheet only (do not fax your assignment). If you are sending a hard copy of your assignment, include the signed cover sheet with your submission and send by Express Post. If you are submitting using eLearning, you do not need to complete this cover sheet.

Email: BCA_DES@adelaide.edu.au
Fax: 08 8223 4075
Post: Attn: Thomas Sullivan
Level 7, 178 North Terrace, Terrace Towers
School of Public Health
Mail Drop DX650 511
The University of Adelaide
Adelaide SA 5005

DES 2016: assignment no. _____

Academic coordinator: Murthy Mittinty

I certify that:

1. I have read the policy on plagiarism associated with the University in which I am enrolled;
2. I understand that failure to comply with the student plagiarism policy and procedures of the University in which I am enrolled may lead to the University commencing proceedings against me for student misconduct, in accordance with the By-Laws of the University;
3. this Work is substantially my own work, and to the extent that any part of this Work is not my own, I have indicated that it is not by acknowledging the source of that part or those parts of the Work;
4. this Work or substantial parts of it have not previously been submitted for academic credit in any formal course of study; and
5. the Work is not the result of collaboration with others.

And, I agree that:

1. the assessor of this Work may, for the purpose of assessing this Work, reproduce this Work and provide a copy of this Work to another BCA unit coordinator or member of the BCA Board of Assessment.

NAME ____________________________
SIGNED __________________________
DATE ____________________________

See ‘BCA Assessment Guide - DES’ (Appendix 1 of the DES 2016 Study Guide) for a complete list of submission guidelines and bca.edu.au/linked docs/Student resources/BCA_assessment_guide_student.pdf for BCA assessment policies and procedures. The guide contains a list of Home University websites outlining university policies, procedures and advice regarding plagiarism, submitting assignments using turnitin.