



Unit of Study Notes and Study Guide

Clinical Biostatistics [CLB]

Semester 1, 2017

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**Module 3 Diagnostic tests, Systematic Reviews and Meta-Analysis**

**Module 4 Clinical Trials**

# Study Guide

## 1. Introduction

This unit or course comprises four topics that are important for practising biostatisticians, especially those working in clinical settings or, more generally, evidence-based health care. Each topic is covered in a module designed to take 2 or 4 weeks to complete. Each module is more or less independent and comprises a study guide, readings, and exercises. There are 3 assignments, one covering modules 1 and 2, and the other two covering modules 3 and 4 respectively.

### ***Assumed knowledge***

The following BCA units are recommended pre-requisites (\*co-requisite).

MBB: Mathematical Background for Biostatistics

EPI: Epidemiology

PDT: Probability and Distribution Theory

DES: Design of Randomised Controlled Trials

PSI: Principles of Statistical Inference

\*LMR: Linear Models

## 2. Contacts

The coordinator and lecturer for this course Mark Jones whose contact details are:

School of Public Health, Public Health Building

University of Queensland

Herston Road, Herston QLD 4006

E-mail: [m.jones@sph.uq.edu.au](mailto:m.jones@sph.uq.edu.au)

Office phone: 07-3365 5116; Fax: 07-3365 5540

If you have difficulties contacting the coordinator or lecturer, or would like to discuss your BCA program in general, please contact the BCA Executive Office, Erica Jobling.

Medical Foundation Building

92 Parramatta Rd Camperdown NSW 2050 Australia

Email: [bca@ctc.usyd.edu.au](mailto:bca@ctc.usyd.edu.au)

Office phone: 02-9562 5076

### **3. Objectives**

The specific objectives of each module are as follows: on completion of the modules you should be able to:

#### **Module 1 – Statistical Process Control**

- Understand the concepts of Continuous Quality Improvement and their usage
- Distinguish between Special Causes and Common Causes of variation
- Detect Special Causes of variation using a Shewhart control chart
- Detect Common Causes of variation using a CUSUM control chart
- Detect Common Causes of variation using a EWMA chart

#### **Module 2 – Clinical Agreement**

- Explain the concepts of validity and reliability of measurements
- Explain the concepts of agreement and consistency between 2 or more measures how, for continuous measurements, these relate to simple correlation or regression
- Use appropriate graphical and analytical methods to assess agreement between 2 raters using continuous, nominal or ordinal category measurement using Bland-Altman methods and kappa statistics
- Use appropriate intra-class correlations for agreement and consistency involving more than 2 raters using continuous scale measurements

#### **Module 3 – Diagnostic Tests, Systematic Reviews and Meta-Analysis**

- Calculate measures of performance of a diagnostic test: sensitivity, specificity, and likelihood ratios.
- Translate the pre-test probability of disease for a particular patient into post-test, predictive values.
- Plot and interpret a ROC curve.
- Calculate the diagnostic odds ratio and explain its relationship to the ROC curve.
- Explain the rationale for doing systematic reviews, rather than narrative reviews.
- Describe the steps involved in undertaking a systematic review.
- Conduct a meta-analysis for various study types (including RCTs, observational studies and diagnostic tests) and various outcome variables.
- Estimate and interpret heterogeneity across studies.

## Module 4 – Clinical Trials

- Understand the advantages and disadvantages of using cross-over trials
- Be able to prepare appropriate graphical displays of cross-over trial data
- Be able to analyse 2x2 cross-over trials with a continuous response using both t-tests and analysis of variance
- Be able to produce point estimates and confidence intervals for the parameters of interest in a 2x2 cross-over trial with a continuous response
- Understand the underlying assumptions of these analyses and be able to perform appropriate model checks
- Be able to analyse 2x2 cross-over trials with binary outcomes
- Be able to estimate the sample size required for a 2x2 cross-over trial.
- Understand the difference between equivalence and efficacy designs
- Appreciate the impact of such designs on analysis principles, e.g. intention-to-treat, especially in the presence of non-compliance.
- Be able to work out the sample size needed in equivalence designs and understand the difference with a similar calculation in a standard efficacy trial
- Get some exposure to non-inferiority studies, their role and link with equivalence trials
- Be able to work out the sample size needed in non-inferiority studies
- Have an idea on internal validity of equivalence/non-inferiority studies

### 4. Method of Delivery & Communication

The unit materials will be posted to you, with your copy of this guide. The material is also available on the BCA eLearning site, along with the data sets for exercises and assignments.

We would like to encourage the use of the discussion board facilities on the eLearning site, in order to try and reduce the isolation of studying by distance. Firstly, you will see a ‘Student Introductions’ forum on the discussion board. You can add your own information to this forum, if you wish, so that others in the course can contact you. For example:

*Jonathan Bloggs*

[j.bloggs@ctc.edu.au](mailto:j.bloggs@ctc.edu.au)

*ph: 02-9999-9999*

*NHMRC Clinical Trials Centre, Sydney*

*Jonathan is a trainee biostatistician at the Clinical Trials Centre. He is currently working with trials of new medications for diabetes and heart disease.*

This is entirely optional. If you would like to be part of the forum, but without your contact details, that will be fine as well.

When you log in to the eLearning site, you will see under ‘Discussions’ various forum headings. We will include some general discussion points in each module to encourage discussion amongst the group, but would like you to discuss matters and help each other as much as you can. Some students in the past have said they haven’t used the discussion board as much as they would have liked, as they didn’t want to be seen to be colluding in the preparation of assignments. We encourage discussion about the course material, and assignments, as long as worked answers are not given. Based on feedback from previous students we are no longer allocating any marks for participation in discussions.

Please send your assignments to us using the eLearning assessment icon. This will enable you to receive an automated acknowledgement of receipt. Assignments will be sent, and marks posted using the eLearning assessment tool.

We encourage you to maintain regular contact with the coordinator and get in touch with him or her if you have any problems.

## **5. Unit Materials**

The course consists of four modules. Each module has some brief notes to guide your reading and study. The modules usually begin with an overview paper, generally written from a more clinical perspective, in order to orient you to the significance of the topic, and to put it in context of real-world clinical problems. The rest of the readings in each module then give more statistical depth to the topic. An exception to this format is the module on clinical trials where the notes are self-contained. We have chosen to present this course using mainly journal articles, rather than a textbook. Firstly, there is no textbook that covers all the topics. Secondly, reading journal articles and extracting the relevant information to the problem at hand is part of the real-world experience of a practising biostatistician. It is not an easy skill to develop! We suggest you practise summarising what you did learn, and what you could not decipher from each article. Then go to the discussion board and see if you can work it out with your fellow students. Materials are changed from year to year in response to student feedback and the availability of new, better materials.

Each week we will upload a short video to go with the material for that week. The videos are power-point presentations with slides and an audio track that will hopefully enhance the written material. Each module includes exercises, for which outline solutions will be posted on the eLearning site for CLB.

## **6. Software**

For this course you will need access to software that can perform the various analyses required for the exercises and assignments. *Stata* is recommended, although other students have successfully completed this course using *R* or *SAS*. *Excel* is quite useful for several modules. *Stata* commands given are in some modules. Data sets for the course are provided on the CLB eLearning site.

## 7. Textbooks

There is no recommended textbook for this course. Readings are provided for each module instead.

## 8. References

The main readings from journal papers and textbooks are provided with each module. Additional resource materials are provided on the CLB eLearning site.

## 9. Assessment

The assessment is based entirely on the assignments. There is no examination. Details of assignments are given in the modules. They are in the form of written reports. They must follow a logical form, be in correct English and contain relevant, well labelled tables and figures (but raw computer output is not acceptable). We suggest you consider writing your assignments in a similar fashion to a journal article, with clearly defined aims, methods, results and conclusions. The following two documents available on the BCA website as resources for current students may be helpful:

Guide for Reporting Statistical Results  
Referencing Style Guide

They are available at [www.bca.edu.au/currentstudents.html](http://www.bca.edu.au/currentstudents.html)

The dates for submitting the assignments are listed below (see Timetable). For the first 2 modules there is an assignment worth 30% (15% for each module). There is an assignment worth 35% for each of modules 3 and 4. All assessment must be submitted to pass the course.

Before commencing the course, you should read the BCA assessment guide (Appendix), and the information about the plagiarism policy of your home university.

**Assessment deadlines are important.**

***Extensions or late submissions policy***

Requests for an extension an assignment must be made in advance of the due date. Requests should be made directly to the module coordinator by email. The module coordinator will reply with the decision as to whether an extension has been granted and the new due date. Please be aware that requests for extensions of greater than 3 days may need to be directed through your home university.

Extensions can cause delays in feedback for other students who submitted on time. Also due to prerequisites, late results may preclude you from studying subsequent units. Different universities have different result submission deadlines. BCA results have to be transmitted between universities, which shortens the available time.



## 10. Timetable

Week	Dates	Module	Co-ordinator	Due date for Assignment and end date for discussion of the Module
1	March 6 - 12	1	Mark Jones	
2	March 13 - 19	1		
3	March 20 - 26	2		
4	March 27-April 2	2		
5	April 3 - 9	3		
	April 10 - 23	Semester break & public holidays		
6	April 24 - 30	3		April 24 for Modules 1-2
7	May 1 - 7	3		
8	May 8 - 14	3		
9	May 15 - 21	4		May 15 for Module 3
10	May 22 -28	4		
11	May 29-June 4	4		
12	June 5 - 11	4		
				June 12 for Module 4

## 11. Complaints policy

Please see the BCA complaints policy in the Assessment Guide and in online assessment submission pages.

## 12. Summary of recent changes to materials and/or procedures

In 2012 there was an external review of the BCA curriculum which recommended several changes including no longer offering a unit on Advanced Clinical Trials. The most important parts of that unit were to be moved to DES and CLB, with DES and PSI becoming pre-requisites for CLB. The full implementation of these recommendations has taken time, with universities' approvals needed and then the changes to DES had to be made before the changes to CLB could be introduced.

This is the second offering of the revised version of CLB. To accommodate the new Module 4 on Clinical Trials we have reduced and re-arranged the other modules. This has been achieved by removing concepts and methods that are less commonly used in biostatistical practice and eliminating many of the readings. Additionally, in response to student feedback, we have reduced the number of assignments from 4 to 3.

Feedback is always welcomed to improve the units. As part of the BCA commitment to continuous quality improvement your feedback about this revised unit is especially important.

# Appendix – BCA Assessment Guide

Can be downloaded from:

[http://www.bca.edu.au/linked%20docs/Student%20resources/BCA\\_assessment\\_guide\\_student.pdf](http://www.bca.edu.au/linked%20docs/Student%20resources/BCA_assessment_guide_student.pdf)

Please note that any previous instructions for the 'own work' declarations are now redundant as assignments will be submitted via Turnitin.