



COURSE OUTLINE

Never Stand Still

Science

School of Mathematics and Statistics

MATH5906

DESIGN & ANALYSIS OF CLINICAL TRIALS

Semester 1, 2015

MATH5906 – Course Outline

Information about the course

Course Authority: Jake Olivier

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Consultation: To be advised.

Credit, Prerequisites, Exclusions:

This course counts for 6 Units of Credit (6UOC).

There are no prerequisites for this course.

There are no exclusions for this course.

Lectures: There will be one 3 hour lecture per week: Wednesday 5-8pm. Most classes will be in RC-3085, but some (to be advised) will be held in the computer labs.

Tutorials: There are no separate tutorials.

UNSW Moodle: Further information and course material will be provided via UNSW Moodle.

Course aims

The aim of this course is to introduce the main statistical concepts, methods and models used in the design and analysis of clinical trials.

Relation to other mathematics and statistics courses

This course is an elective course for the Master of Statistics program and a core course for the Master of Biostatistics program. Whilst there are no formal prerequisites for the course, it does make use of techniques based on statistical theory such as maximum likelihood estimation and hypothesis testing, and some familiarity with these ideas is assumed. In this sense, the course is related to MATH5905: Statistical Inference, which covers the theory behind some of the techniques we will apply. The main aim of a clinical trial is to assess whether there is a treatment effect on the primary outcome, a variable which might be continuous, binary, categorical, or a survival time, for example. Hence, the course is related to MATH5806: Applied Regression Analysis, MATH5945: Categorical Data Analysis, and MATH5916:

Survival Analysis. Long-term clinical trials also typically collect repeated measurements of variables over time, so this course is related to MATH5885: Longitudinal Data Analysis. The course also has links with MATH5826: Statistical Methods in Epidemiology, which covers techniques applicable to observational, rather than experimental, studies.

Student Learning Outcomes

By the end of this course, you should be able to:

- Explain the key features of randomized controlled clinical trials and what distinguishes them from other types of studies
- Explain bias and how it might affect clinical trials
- Explain the importance of randomization and the different methods of random allocation used in clinical trials, and prepare randomization schemes based on these methods
- Explain how sample sizes can be calculated for different types of outcomes in clinical trials, and implement these calculations
- Explain the intention-to-treat principle and why it is widely used in clinical trials
- Explain why and how clinical trials are monitored, and implement monitoring schemes
- Explain the issues related to subgroup analyses and perform a subgroup analysis
- Explain the issues related to multiple comparisons and how adjustments should be made for them
- List the different types of clinical trials, such as parallel group, crossover, and equivalence trials, explain their key features and the distinctions between them, and analyse data from these trials
- Perform appropriate analyses of data from clinical trials, using the computer language R, and interpret R output
- Solve theoretical problems related to the design and analysis of clinical trials

Relation to graduate attributes

Computing skills developed in this course will improve *information literacy* (Science Graduate Attribute 6).

Assignments, problems, and lab exercises will develop *research, inquiry and analytical thinking abilities* (Science Graduate Attribute 1).

Teaching strategies underpinning the course

To support the learning outcomes, the course will use the following teaching strategies:

- Lectures, explaining the necessary statistical concepts and theory applicable to clinical trials
- Computer labs, providing essential practice in applying the techniques explained in lectures
- Independent study of the course notes and readings, to reflect more deeply on ideas introduced in lectures
- Problems and assignments, giving you an opportunity to independently solve theoretical problems, analyse datasets using statistical software, reflect on aspects of the course, and evaluate your understanding
- Assessment in this course will use problem-solving tasks of a similar form to those in practice problems and computer labs, to encourage the development of the core analytical and computing skills underpinning this course.

Rationale for learning and teaching strategies

We believe that effective learning is best supported by a climate of inquiry, in which students are actively engaged in the learning process. Hence, this course is structured with a strong emphasis on problem-solving tasks in computer labs and in assessment tasks, and students are expected to devote the majority of their class and study time to the solving of such tasks.

Assessment

Assessment in this course will consist of two assignments (10% each), a presentation and report (20%), and a final examination (60%). UNSW assesses students under

a standards based assessment policy. For how this policy is applied in the School of Mathematics and Statistics see

<http://www.maths.unsw.edu.au/currentstudents/assessment-policies>

Knowledge and abilities assessed: All assessment tasks will assess the learning outcomes outlined above, specifically, the ability to explain the concepts and theory underlying statistical techniques for clinical trials, to apply the techniques in analysing real datasets and critically interpret the results of analyses, and to solve theoretical problems related to the statistical aspects of clinical trials.

Assessment criteria: The main criteria for marking assessment tasks involving explanation of theory and solution of theoretical problems will be clear and logical presentation of correct solutions. In the case of assessment tasks involving the application of techniques to the analysis of real datasets, the main criteria will be selection and justification of appropriate analysis methods; clear, logical, and well-documented computer code; well-organised output giving evidence of successful implementation; correct interpretation of results; and clear, complete, and fully justified conclusions.

Assignments

Rationale: Assignments will give students an opportunity to practice solving theoretical problems related to clinical trials, and to apply statistical methods for clinical trials in analysing real datasets and interpreting the results of those analyses.

Assignments must be YOUR OWN WORK, or severe penalties will be incurred.

You should consult the University web page on plagiarism

www.lc.unsw.edu.au/plagiarism

Schedule and weighting:

| Task | Date Avail. | Date Due | Form of Submission | Weighting |
|--------|----------------------|---------------------------|--------------------|-----------|
| Asst 1 | Wed 18 Mar Week 3 | 5pm Wed 1 April Week 5 | Written | 10% |
| Asst 2 | Wed 6 May Week 9 | 5pm Wed 20 May Week 11 | Written | 10% |

Assignments must be submitted by 5pm (at the start of class). In general, late assignments will NOT be accepted without good documented reasons (such as illness or misadventure).

Presentation

Duration and schedule: a 15 minute presentation during the lecture in week 11, together with a written report.

Rationale: The presentation and report will give students the opportunity to research a particular area related to the statistical aspects of clinical trials in more detail.

Weighting: 20% of your final mark.

Further details about the presentation and report will be given in class.

Examination

Duration: Two hours.

Rationale: The final examination will assess student mastery of the material covered in the lectures.

Weighting: 60% of your final mark.

Further details about the final examination will be given in class closer to the time.

Additional resources and support

Lecture notes

Lecture notes (including computer lab exercises and practice problems) will be distributed in class.

Textbooks

You will need access to a copy of the textbook:

Matthews, John N.S. (2006). *Introduction to Randomized Controlled Clinical Trials, Second Edition*. Boca Raton, FL: Chapman & Hall/CRC.

This book is available from the UNSW bookshop at a cost of approximately \$80.

References: Other references will be suggested in class.

UNSW Moodle

All course materials (excluding photocopied handouts) will be available on UNSW Moodle. You should check regularly for new materials.

Computer laboratories

Computer laboratories (RC-M020 and RC-G012) are open 9-5 Monday-Friday on teaching days. RC-M020 has extended teaching hours (usually 8:30-9pm Monday-

Friday, and 9-5 Monday-Friday on non-teaching weeks).

Library information

The library website is <http://www.library.unsw.edu.au/>.

Course Evaluation and Development

The School of Mathematics and Statistics evaluates each course each time it is run. We carefully consider the student responses and their implications for course development. It is common practice to discuss informally with students how the course and their mastery of it are progressing.

Administrative matters

Help and Information

See <http://www.maths.unsw.edu.au/currentstudents/help-students-postgraduate> and <http://www.maths.unsw.edu.au/currentstudents/student-services>.

School Rules and Regulations

Fuller details of the general rules regarding attendance, release of marks, special consideration etc are available via the School of Mathematics and Statistics Web page at <http://www.maths.unsw.edu.au/currentstudents/assessment-policies>, and at <https://student.unsw.edu.au/policy>.

Plagiarism and academic honesty

Plagiarism is the presentation of the thoughts or work of another as one's own. Issues you must be aware of regarding plagiarism and the university's policies on academic honesty and plagiarism can be found at <https://student.unsw.edu.au/plagiarism> and <https://student.unsw.edu.au/conduct>.

Occupational Health and Safety

UNSW Occupational Health and Safety policies and expectations can be found at <http://www.ohs.unsw.edu.au>.

Equity and Diversity

Student equity and diversity issues should be directed to the Student Equity Officers (Disability) in the Student Equity and Diversity Unit (phone 9385 4734). Further information for students with disabilities is available at <http://www.studentequity.unsw.edu.au/>.

Course schedule

An approximate schedule for the course is given below.

| Date of class | Topic | Computer lab | Assessment |
|--------------------|--|----------------|--------------------------------|
| Week 1 4 March | Definitions, background and history. Bias. | | |
| Week 2 11 March | Overview of a real trial. Sample size considerations | Computer lab 1 | |
| Week 3 18 March | Sample size calculations. Introduction to randomization | | Assignment 1 distributed |
| Week 4 25 March | Randomization methods. Assessment, blinding, and placebos | Computer lab 2 | |
| Week 5 1 April | Baseline measurements, analysis of covariance | | Assignment 1 due 5pm* |
| MID-SESSION BREAK | | | |
| Week 6 15 April | Trial monitoring and group sequential trials | | |
| Week 7 22 April | Subgroup analysis | Computer lab 3 | |
| Week 8 29 April | Multiple comparisons | | |
| Week 9 6 May | Intention-to-treat, protocols | | Assignment 2 distributed |
| Week 10 13 May | Crossover trials | Computer lab 4 | |
| Week 11 20 May | Presentations | | Assignment 2, reports due 5pm* |
| Week 12 27 May | Equivalence trials | | |
| Week 13 3 June | No lecture | | |

* At the **START** of the lecture