Introduction

Biostatistics is a major sub-discipline of Statistics and encompasses statistical methods in the biological, pharmaceutical and health sciences. Statistics is fundamental to contemporary biomedical research and has played a crucial role in evaluating treatments for cancer and heart disease, measuring survival following heart and kidney transplants, and in monitoring and predicting major pandemics including HIV/AIDS and SARS. Statistics has also emerged in recent times as a key collaborating discipline in bioinformatics.

Expert advice from statisticians and epidemiologists is crucial for drug development, health-data collection and analysis, for informing government debate and for developing public health policies and strategies. Leading research institutes and pharmaceutical companies around the world are desperate for well-trained biostatisticians, and many major international university departments are devoted entirely to research and teaching in biostatistics - have a look at any issue of *Amstat News*, the bulletin of the American Statistical Association. At the present time, Australia is suffering from a chronic shortage of graduates in biostatistics: the 2002 October *Bulletin* reported that at a high-level meeting called to discuss the problem of finding statistical graduates, a pharmaceutical company representative claimed that his company’s US office was considering shelving plans for growth in Australia because it could not recruit the senior statisticians it needed here to run clinical trials.

Aims and objectives

This course aims to provide students with fundamental knowledge of the design and analysis of clinical trials and epidemiological studies, of statistical issues arising in biomedical research, and of important methods for the analysis of biostatistical data, including data from microarray experiments.

By the end of this course, students should be able to

- apply their biostatistical knowledge and tools to real-life problems in biomedical research;
- design and analyse clinical trials;
- design and analyse case-control, cohort and related studies;
- conduct 'low-level' statistical analysis of gene expression microarray data; and
- develop and carry out appropriate statistical analyses in R.
Units value: 2

Prerequisites and assumed knowledge

There is a prerequisite of either Mathematics I or Mathematics IM, and Statistical Practice I or equivalent course. It is also an advantage to have completed 4 units of the second year Statistics courses or equivalent. However, it is intended that Biostatistics III should be accessible to a broad range of students with differing mathematical and statistical backgrounds.

Staff

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Tutor: Mr Simon (Jono) Tuke, Room 206 in the main Mathematics Building.
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Lectures

The lectures will be held at 2.10 pm on Tuesdays in the Horace Lamb Lecture Theatre, and at 2.10 pm on Thursdays in the Kerr Grant Lecture Theatre.

We may occasionally use one of the lecture times for practical or tutorial work instead.

Sections of this course are new this year. Summary overheads will be discussed in the lectures and supplemented by working on the board, etc, so students should come along prepared to take their own notes. Scanned copies of the lecture slides and other supplementary material will be available from MyUni and my web page.

Consulting hours

My student consulting hour will be 11 am to 12 pm (noon) on Mondays.
Jono Tuke’s student consulting hours will be Wednesdays 1 pm to 2 pm, and Fridays 1pm to 2pm.

Tutorials and practicals

There will be an introductory computer practical in Week 2; this is intended to introduce students to the statistical and graphical package R. There will be further practicals in Weeks 3, 6, 9 and 12. All practicals will be held in the computing suite EM126.

Tutorials will be held at 2.10 pm on Fridays in various weeks. The first tutorial will be held on Friday in Week 4, and thereafter in Weeks 8 and 11.

We will be using the statistical package R in this course, which is a free-ware version of S-PLUS. Both are widely regarded as the most advanced statistical and programming
packages for the analysis of biostatistical data, and R is state-of-the-art in the analysis of microarray data and gene expression data.

Assignments

There will be 4 assignments including a short essay (which is Assignment 1) which will be due at the end of Week 2. There will be 3 further assignments due at the end of Weeks 5, 9 and 12 respectively.

Examination and assessment

There will be 4 assignments during the course (see above) and a final two-hour examination. The exam will be based on the work covered in the lectures, tutorials, practicals, assignments and other set work. The final mark will be calculated as follows. Let $e$ be the mark for the exam out of 100 and $a$ the mark for the best 3 assignments out of 20 then your final raw mark out of 100 will be:

$$\max\left\{ e, \frac{80}{100}e + a \right\}$$

So students have two chances of redemption in the assessment.

The Supplementary Examination will be held in December 2004. Students should refer to the School Policy on supplementary examinations available from the School website.

Course outline

Chapter 1: Introduction to epidemiology and clinical trials: What are they? The role of randomization.

Chapter 2: The design and analysis of clinical trials. Phase I to Phase IV trials. Key aspects of study design including the study protocol, the Data and Safety Monitoring Committee, class of trial, justification of randomization, including ethical considerations. Methods of randomization: unrestricted and restricted randomization, random permuted blocks, biased coin designs, stratification, minimization. Trial size: fixed, sequential and group sequential trials. More complex trial designs: factorial trials; crossover trials.


Applications: to drugs trials, heart disease, cancer, HIV/AIDS, acute myeloid leukaemia and angiogenesis.
References and recommended reading:

General

  
  *This book covers or touches on most of the topics we will be studying in clinical trials and epidemiology, and is recommended as the best general reference.*

  
  *The Encyclopedia contains some excellent articles on clinical trials and epidemiology that you may find useful background reading. I will give you copies of some articles from time to time as appropriate.*

  
  *This is a basic book written more for medical researchers who need statistics, but is very accessible and an easy read if you are looking for one!*

Clinical trials

  
  *An excellent general introduction to clinical trials.*

  
  *This is an older reference now, but is still an excellent introduction to the basics of clinical trials.*

  
  *I’ll be using this book for the section on crossover trials.*

  
  *This is a harder and more specialized book, but will be useful if you do end up designing clinical trials!*

Epidemiology

  
  *Probably the best books available on statistical epidemiology for statisticians.*
Microarray data analysis

  
  You should find the lectures notes on this topic sufficient, but Chapter 2 of the above book is an excellent introduction to the statistical issues facing statisticians today when dealing with the design and analysis of microarray experiments.

  
  This is not essential reading, but is an excellent and fun introduction to genetics for people who do not have a background in biology.

Statistical computing


  There is one copy of most of these books held on Reserve in the library, plus a second copy available for short or normal loan.

Handouts, preprints and other material for this course are available from MyUni at [http://www.myuni.adelaide.edu.au](http://www.myuni.adelaide.edu.au)

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Associate Professor Patty Solomon
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