Introduction to Clinical Trials [MCLM11002]

Course Planner 2013/14

The following planner provides you with a weekly overview of the course with key dates and deadlines. As this is a fully online course that is being undertaken alongside work and other commitments, each week is scheduled to run from Monday to Sunday, and assignment deadlines are usually set for midnight on Sundays. This is to provide you with extra choice and flexibility in when to study, and does not indicate any expectation that course participants should necessarily need to work on weekends or during the holidays.

Please note:

Times will always be reported in GMT (Greenwich Mean Time)

Virtual office hours (VOH) are held online every Tuesday from 6-7 pm until announced otherwise. The time may be adjusted to accommodate time zones more fairly. The VOH will be facilitated by one member of the course teaching team.

Each **new week's** announcement and learning material will become available noontime (GMT) on a Monday of that week.

Help & contact information

- Technical problems (Moodle, email, library resources, MyEd services)

  IS Helpline: IS.Helpline@ed.ac.uk or +44(131) 651-5151

- Online course materials, assignments, tasks, due dates etc.

  (Not just for) problems forum available in Moodle

- Personal issues and problems (from Sept. 16th)

  MSc CT personal tutors (PT): helpmscct@ed.ac.uk

- University of Edinburgh IT services status & alerts page

  http://www.ed.ac.uk/schools-departments/information-services/services/status-alerts

Foundation module

Week 1 Mon Sept 16th to Sun Sept 22nd 2013

This week has been set aside to give you an opportunity to review relevant course information and to familiarise yourself with the institutional Virtual Learning Environment (VLE), Moodle. A number of induction activities have been created which you are expected to complete in order to highlight potential software and/or hardware problems with enough time for them to be resolved before formal study commences in week 3. Furthermore, the Introductory discussion gives everyone the chance to become acquainted with one another whilst becoming comfortable with asynchronous (time-delayed) online communication, our main mode of communication and collaboration.

Your first tasks after logging into the course

- Listen to Prof. Stuart Ralston's audio welcome (requires speakers)
- Read relevant information related to the organisation of the course including the coursework and materials found in the folders
    - Course guide
    - Assignment specifications
    - Planner

Lesson I Technology toolkit & Lesson II Library skills tutorial

Your main tasks for Lesson I will be to help build our online class community by joining the Introduction discussion, contribute to the Welcome wiki and to practice the use of the online technologies that feature on the course. In Lesson II you will work through a library tutorial designed to introduce you to the University's e-resources and how to effectively select, evaluate, manage and use the volume of published medical literature. The accompanying online discussion questions will also hopefully raise critical awareness for some of the barriers to evidence based medicine informed by clinical trials.

By the end of this week you should have a clearer idea of what to expect from the course, made a friend or two and be more familiar with many of the key online tools and library e-resources that we will be using in the upcoming weeks.

Your tasks

- Complete induction activities
- Join 'Introductions & more' discussion

- Post a photo and a bit about yourself on the Welcome wiki
- Work through Library skills tutorial including Library discussion
- Double check access to UoE library e-resources
- Post any problems in the (Not just for) problems forum in Moodle promptly

Key dates

- Join Virtual office hours (VOH) this week only:
  - Tues Sept 17th 6 - 7 pm (technology focus)
  - Wed Sept 18th 8 - 9 pm (administrative focus)
  - Thur Sept 19th 6 - 7 pm (literacy focus)

  [URL and joining instructions made available in week 1]

Foundation module

Week 2 Mon Sept. 23rd to Sun Sept. 29th

Lesson III: Basic medical statistics in practice

This week gives latecomers the opportunity to complete the week 1 induction tasks while working through a practice-orientated medical statistics tutorial designed to introduce basic statistics terminology and techniques relevant to clinical trial design and analysis. The tutorial is informed by a current published clinical trial which introduces many of the key terms, concepts and approaches inherent to trial design and data reporting and analysis. Multiple choice questions offer the opportunity to check and consolidate basic understanding and computational skills. The lesson introduces critical appraisal skills in evidence-based medicine and gives students the guided opportunity to review a published clinical trials study for its methodology, data, results and relevance.

Key terms

- The randomised controlled trial
- Data handling
- Sampling and estimation
- Hypothesis testing
- Basic techniques for analysing data
- Critical appraisal

Your tasks

- Join the 'Introductions & more' discussion if you haven't done so yet

- Work through Lessons I-IV of statistics tutorial
- Post problems in the (Not just for) problems forum

Key dates

- Join Virtual office hours (VOH) this week only:
  - Tues Sept 24th 6 - 7 pm (general enquiries)
  - Thurs Sept 26th 8 - 10 pm (statistics tutorial focus)

Unit 1 Introduction to clinical trials

Week 3 Mon Sept 30th to Sun Oct 6th

This week marks the start of Unit 1 and of your formal studies. The course material has been split into four taught Units designed to introduce you to the key concepts of design, management, analysis and reporting of clinical trials. Care has been taken to draw from authentic clinical practice wherever possible and case studies help bring definitions and regulations to life. Unit 1 is the shortest Unit beginning with the origins of clinical trials and their intended purpose. The Unit 1 discussion questions probe deeper into the rationale for conducting clinical trials whilst identifying key characteristics of good trial design and raising awareness for the flaws.

Key terms

- Definition of clinical trials
- History of clinical trials
- Rationale for clinical trials
- Funding

Your tasks

- Work through the Unit 1 assigned readings and online lessons
- Join the Unit 1 Thought discussion (open until end of week 4)
- Review the assignment specifications for Individual projects I & II
- Final check for availability to core e-resources notify tutors of any problems
- Take the Unit 1 self-test
- (Not just for) problems forum welcomes your questions

Key dates

- Monday Sept 30th Unit 1 announcement, lesson, discussion and readings made available
- Sun October 6th for survey response to choice of online expert guest

lecture date in November [the expert guest is Dr. David Crook from Brighton, UK]. The options are:

- Mon Nov 18th 8 -10 pm
- Wed Nov 20th 3 – 5 pm
- Fri Nov 22nd 8 – 10 am

Unit 2 Types of clinical trials

Week 4 Mon Oct 7th to Sun Oct 13th

Unit 2 opens with a video recording of your course leader, Prof. Stuart Ralston describing the PRISM Trial, a pragmatic randomised controlled trial, which ended in 2012. What is the difference between a pragmatic trial and a clinical trial performed by a pharmaceutical company to gain marketing authorisation? What is the significance of the randomised controlled (RCT) trial? How can the different sources for bias within trials be identified and how can bias be prevented? This and many other questions set the scene for the lessons to follow in which the different types of classifications of clinical trials are outlined. Selected trial types are brought to life by video stories from expert clinicians who share the 'good, the bad and the ugly' in their recent and ongoing clinical trials. The Unit 2 Thought discussion asks students to identify and compare trial designs and their respective outcomes which will begin to inform the Individual project assignments

Key terms

- Phase I-IV clinical trials
- Randomised double blind, comparative clinical trials
- Bioequivalence trials
- Randomised crossover trials
- N-of-one trials
- Pragmatic trials
- Prospective randomised open label, blinded endpoint
- Adaptive trials
- Zelen trial design
- Cohort multiple randomised trials
- Cluster randomised trials
- Endpoints

Your tasks

- Work through the Unit 2 assigned readings and online lessons
- Join Unit 2 Thought discussion
- Contribute to Unit 1 Thought discussion

- Complete and submit Individual project I
- Take the Unit 2 self-test
- (Not just for) problems forum

Key dates

- Monday Oct 7th Unit 2 announcement, lesson, discussion and readings made available
- Sunday Oct 13th
    - Submission due date for Individual project I to the Turnitin assignment dropbox in Moodle
    - Close Unit 1 Thought discussion

Revision week-no formal lessons

Monday Oct 14th to Sunday Oct. 20th

Your tasks

There are no new taught lessons or VOH this week.

Unit 2 Types of clinical trials (cont'd)

Week 5 Mon Oct 21st to Sun Oct. 27th

- Continuation of Unit 2 Thought discussion
- Group membership confirmation
- Group members to contact one another
- (Not just for) problems forum

Week 6 - Mon Oct 28th to Sun Nov 3rd

- Group case study project starts this week-get in touch with your group members now!
- Release of Group project case study resource base
- Group project start-up online tutorials (facilitated by group tutor)
- Continuation and close of Unit 2 Thought discussion
- Take the Unit 2 self-test
- (Not just for) problems forum

Key dates

- Sun Nov. 3rd by the end of week 6 the group chairperson should post the group's learning contract to the group's discussion board

for the tutor, along with a brief update of initial progress

Unit 3 Statistics and clinical trial design

Week 7 - Mon Nov 4th to Sun Nov 10th

Our attention in Unit 3 turns to some basic statistical issues around clinical trial design. After the basic medical statistics tutorial in the Foundation module we pick up here first with setting up remote access to and use of the software packages Minitab and SPSS for descriptive statistics. We then turn our focus to particular issues in statistical trial design such as sample size, which has in the past often been shown to be too small. How large then does our sample size need to be in order to make sure the difference in interventions is not due to chance? Why does a small *p* value not always indicate a large effect? These and other questions around clustering, randomisation and blinding are addressed in Unit 3 in collaborative problem-based activities and discussions for students to engage with.

Key terms

- Sample size
- Power
- Missing data
- Clustering
- Randomisation
- Blinding

Your tasks

- Group project activities and online tutorials
- Manage remote access to SPSS and/or Minitab
- Work through the Unit 3 assigned readings and online lessons
- Join Unit 3 Thought discussion
- Have you begun your Individual project II??
- (Not just for) problems forum

Key date(s)

- Monday Nov 4th Unit 3 Announcement, lesson, discussion board and recommended readings made available
- Sunday Nov 10th group learning contract feedback/sign off by tutor

Week 8 - Mon Nov 11th to Sun Nov 17th

Your tasks

- Continuation of Unit 3 Thought discussion
- Group project activities and online meetings
- Take the Unit 3 self-test
- (Not just a) problems forum

Key date(s)

Unit 4. Professional conduct of clinical trials

In our last taught Unit we engage with the guidelines, regulations and processes inherent to the clinical trial design, conduct and reporting. We begin with the 13 Principles of Good Clinical Practice (GCP). These are national and international regulatory requirements that the clinical researcher must be aware of and must plan for. Further challenges such as data handling, recruitment and informed consent are highlighted in case study scenarios and brought to life in interviews with experienced trialists. The last topic-related Thought discussion raises awareness in particular for past and present ethical conduct in trials while picking up from the Foundation module to re-emphasise the role of meta-analysis in evidence based medicine. Instances of poor trial design, conduct and reporting in the literature have been highlighted throughout the course and continue to inform the debate around the manner in which to best improve the robustness and quality of clinical trials and hence their results for health care practice.

Week 9 - Mon Nov 18th to Sun Nov 24th

Key terms

- Good clinical practice (GCP)
- Regulatory requirements
- Ethical & regulatory approval
- Local
- Contractual agreements
- Amendments
- Members of the trial team
- Consent
- Data collection
- Data handling and storage
- Recruitment
- Monitoring
- Data cleaning
- Statistical analysis

- Reporting
- Closing a trial
- Meta-analysis
- Pharmacovigilance

Your tasks

- Work through the Unit 4 assigned readings and online lessons
- Join Unit 4 Thought discussion
- Continuation and close of Unit 3 Thought discussion
- Group project activities and online tutorials
- (Not just for) problems forum

Key date(s):

- Monday Nov 18th Unit 4 readings, lessons and Thought discussion become available
- Sunday Nov 24th Unit 3 Thought discussion closes
- Date still to be confirmed in a class poll for online expert guest lecture by Dr. David Crook from Brighton, UK.

Week 10 - Mon Nov 25th to Sun Dec 1st

- Continuation of Unit 4 discussion
- Take the Unit 4 self-test
- (Not just for) problems forum

Key date(s):

- Sun Dec 1st submit choice of 5 strongest contributions to Units 1-4 Thought discussion to portfolio tool, PebblePad, in Moodle.

Unit 5.

Our activities in this Unit will all be geared towards supporting the work you will be doing within the context of the Group project and second Individual project. There will be no new discussions. Our online communication time will instead be used for continuing the Unit 4 Thought discussions, collaborative working within your groups, and for finalising your Individual project II.

Week 11 - Mon Dec 2nd to Sun December 8th

- Continuation and end of Unit 4 Thought discussion
- Final group project activities and online tutorials

- (Not just for) problems forum

Key date(s):

- Sun Dec 8th submission of group report as instructed in Moodle

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Week 12 - Mon Dec 9th to Sun Dec 15th

Key date(s):

- Sun December 15th Individual project II to be submitted to the Turnitin assignment dropbox

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END OF SEMESTER I (SEMESTER II BEGIN 13th JAN 2014)

Appendix

I. Overview of course assignments

Due date	Assignment	Topic	Submission in Moodle	Learning outcomes	Weighting
Sun Oct 13th	Individual project I	Published clinical trial report appraisal (800 W)	Turnitin dropbox	1 & 3	15%
Sun Nov. 3rd	Group learning contracts	Group member roles & tasks are assigned and agreed including milestones	Group wiki	NA	Must be submitted before case study resource base is released
Sun Dec 1st	Choice of 4-6 best discussion posts from at least 2 Thought discussions	The final mark is a weighted average of self-assessment & tutor mark (1000-1200 W)	PebblePad	2 & 4	20%
Sun Dec 8th	Group project report & reflective element about group work experience	Phase III trial design (informed by a current open Phase II trial) (1500 + 500 W)	Group wiki	1, 3, 4 & 5	25% + 10%
Sun Dec 15th	Individual project II	Clinical trial design for study of new drug intervention (1200 W)	Turnitin dropbox	1, 6 & 7	30%

II Course Learning outcomes

1. Critically assess the factors that contribute to suitable trial design for a research question including selection of appropriate endpoints, choice of sample size, data analysis, presentation of results and implementation in routine clinical practice.
2. Engage and contribute to current and emerging debate around clinical trial transparency, registration and disclosure
3. Contribute to the design, authoring and evaluation of a clinical trials protocol
4. Critically discuss the challenges of clinical trial delivery including study design, trial set up, recruitment, follow up and data collection
5. Apply the principles of data analysis, dissemination of results and implementation of key findings
6. Critically appraise the methods by which procedural and epidemiological data underpin the development of clinical trials
7. Identify and apply the principles of Good Clinical Practice (GCP) ensuring safety of participants and integrity of data in relation to clinical trials.