

ISBT
TTID **R**esearch **Y**oung
Investigator **T**raining

I TRY IT
2016

COURSE SYLLABUS

There are 4 main objectives for the I TRY IT 2016 programme.

1. Over the next 6 months each I TRY IT participant will be expected to complete a research protocol for a study designed to be conducted in your country or where you work.
2. To learn how to provide and to receive constructive criticism of scientific research.
3. To help you to conduct the research project you designed as part of the programme and to analyze the data to answer your research question.
4. To learn essential aspects of communicating scientific results in abstracts and manuscripts.

The most challenging part is conducting the study and analyzing the data. However, these are easier if you begin with a solid foundation - the research protocol is that foundation.

Instructors:



Marion Vermeulen, BTech. Marion Vermeulen is the National Manager for Operations Testing at the South African National Blood services (SANBS). This entails management of the TTI screening (NAT and serology), Blood grouping serology, Virology Reference laboratory and the Biorepository at SANBS. She lectures on a part time basis at the university of Johannesburg. She is the Co-PI for SANBS for the SHIP EC study in South Africa and she is a co-investigator in the REDS III international program in South Africa. She is a member of the ISBT and the secretary of the Global blood safety working party and a member of the TTID working party.



Michael Schmidt, MD, Prof. Dr. Michael Schmidt is consultant in Transfusion Medicine, in Occupational Medicine and specialist in Quality Medicine. He is head of the blood donor screening department and the quality management department of the German Red Cross blood donor service Baden-Württemberg – Hesse. As a Professor in Transfusion Medicine he gives lectures at the Goethe University in Frankfurt in topics of blood safety and transfusion transmitted infectious diseases (TTID). He is member of the ISBT and member of the TTID working party.



Brian Custer, PhD, MPH Brian Custer is an Associate Director and Senior Investigator in Epidemiology and Health Policy Research at Blood Systems Research Institute in San Francisco. He is also an Adjunct Professor in the Department of Laboratory Medicine at the University of California San Francisco. He serves on the US Department of Health and Human Services, Advisory Committee on Blood and Tissue Safety and Availability. He conducts research on the epidemiology and health economics of the blood supply and transfusion medicine policy throughout the world, primarily focused on infectious diseases and donor health. Dr. Custer is the Principal Investigator for the REDS-III International program in Brazil and the Laboratory and Risk Factor Coordinating Center of the US Transfusion-Transmissible Infection Monitoring System.

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- **The ISBT Working Party on Transfusion Transmitted Infectious Diseases**

Lecture Format:

We are planning two approaches for the lectures. As participants and instructors are located all over the world, when possible we would like for you to participate during the live lectures online. Alternately, each lecture will be able to be downloaded via the ISBT Academy so that you can listen and view the content at times that works best for you or if your internet connection speed requires you to download the material.

We will be using GotoMeeting™ for course lectures. To participate, you will be invited to each lecture the meeting and then will have to join the lecture via the URL provided in each invitation.

We are going to use the ISBT Academy ePortal and TTID website to communicate with you. Lecture recordings will be posted on the ISBT Academy ePortal. Each of you will have a specific login and password to access the ePortal content.

Required Reading – We will provide copies of this book to you. **These will have to be sent to you directly around the time of the first course lecture.**

Designing Clinical Research, 4th Edition, 2013

by Stephen B Hulley, Steven R Cummings, Warren S Browner, Deborah G Grady, Thomas B Newman

Additional online reference material that accompanies the text book is available at:

<http://www.dcr-4.net/>

The lectures will focus on writing the protocol and results communication. The primary assignment for this course is the written protocol. Each homework assignment is part of or contributes directly to the overall protocol.

Protocol Outline

The protocol should not be more than 8 pages in length and will contain the following sections. We will use an expanded outline compared to that in the text book.

Project title & your name

Research Question
study aims

Background and Significance (this must be limited to no more than 75% of 1 page)

Study Design
time frame and nature of controls (if relevant to your study)

Study Subjects
selection criteria, target and accessible populations
plans for sampling and for recruiting subjects

Measurements
predictor variables (intervention, if an experiment)
and potential confounding variables
outcome variables

Statistical Issues
hypotheses, sample size estimates, analytic approach

Quality Control and Data Management

Ethical Considerations

References (not included in the 8-page limit)

Appendices (not included in the 8-page limit)
Consent forms
Questionnaires and other data forms
Budget: personnel and other expenses

I TRY IT 2016 Program Content Outline

A. We will begin with a research question review and feasibility discussion, and assignment of a primary and secondary mentor to work directly with you. These activities will be completed through online meetings with each of you. For the initial meeting all 3 course instructors will participate. Thereafter, smaller group online meetings are planned.

Lecture Topics

1. Conceiving the Research Question and Study Hypothesis
2. Background & Significance Sections of a Protocol
 - Literature searches using Pubmed and other information warehouses
3. Basics of Measurement: Variable Types, Precision and Accuracy
4. Introduction to Statistics and Estimating Sample Size & Power
5. Overview of Study Designs
 - Observational Study Designs (case series, cohort, case-control)
 - Randomized Designs
6. Designing Studies of Medical Tests, including Sensitivity and Specificity
7. Data Validity, Cause and Effect, Issues of Bias
8. Research Ethics, Data Management, Quality Control, and “Big Data”

B. In person meeting in Dubai linked to the ISBT Congress – final revisions to your protocol, peer-review of protocols, and plans for setting the stage for conducting your study

Additional Topics to be covered late in the year

9. Data Analysis
10. Results Reporting, Creation of Tables and Figures, Results Section
11. Materials and Methods, Introduction Sections
12. How to Contextualize the Ideas - Discussion Section

Schedule of Lectures and Homework Due Dates

Lecture/Lecturer	Date	Topic	Homework Due
1 / Custer	10 May 2016 1500 UTC	Conceiving the research question and study hypothesis	17 May 2016 1500 UTC

Chapter 1: Getting Started: The Anatomy and Physiology of Clinical Research

Chapter 2: Conceiving the Research Question and Developing the Research Plan

Read Chapters 1 and 2 of DCR.

The first lecture will establish the basic overview of your research proposal. The draft proposal will undergo revisions as the course progresses.

Homework:

To be emailed to all courses lecturers within one week of the lecture:

“Research question”, revise your research question and write a one sentence version. Include any secondary research questions or aims you may have, but as much as possible try to focus on one central question or hypothesis to start.

Lecture/Lecturer	Date	Topic	Homework Due
2 / Schmidt	24 May 2016 1500 UTC	Background and significance section of a protocol	31 May 2016 1500 UTC

Chapter 3: Choosing the Study Subjects: Specification, Sampling and Recruitment

Read Chapter 3 of DCR

Homework:

To be emailed to all courses lecturers within one week of the lecture:

1. "Background and Significance", use PubMed to do internet literature search. Write a half page "Background and Significance" section into your protocol addressing your research question (about 5 to 10 key references are sufficient at this stage).
2. Add properly cited "References" section with the above citations. For our course we will use the Vancouver requirements for biomedical journals:
<http://www.biomedicaleditor.com/vancouver-style.html>

Lecture/Lecturer	Date	Topic	Homework Due
3 / Vermeulen	7 June 2016 1500 UTC	Basics of measurement: variable types, precision and accuracy	14 June 2016 1500 UTC

Chapter 4: Planning the Measurements: Precision, Accuracy and Validity

Read Chapter 4 of DCR.

Homework:

To be emailed to all courses lecturers within one week of the lecture:

A. This assignment is based on material in Chapter 4. Write a **less than one page** description of the “Measurements” section of your research protocol. This should include:

1. Lists of the main variables in your study:
 - Predictor variables
 - Outcome variables

2. Additional information on one important variable:
 - A description of the variable.
 - The rationale for measuring the variable.
 - A detailed description of how the variable will be measured (Use Appendix 4 in the book as a model).

3. Propose and discuss strategies to reduce random and systematic error in your measurements (this section will be revised after lecture 7).

Lecture/Lecturer	Date	Topic	Homework Due
4 / Custer	21 June 2016 1500 UTC	Introduction to statistics and estimating sample size & power	28 June 2016 1500 UTC

Chapter 5: Getting Ready to Estimate Sample Size: Hypotheses and Underlying Principles
Chapter 6: Estimating Sample Size and Power: Applications and Examples

Read Chapters 5, 6 of DCR

Homework:

To be emailed to all courses lecturers within one week of the lecture:

In the “Statistical Issues” section of your protocol address the **sample size** of your study by doing either (A) or (B), below (option A is preferred for most studies and is more instructive, so do this if you can). Do not exceed **a half page**.

A. If your research question is primarily analytic (i.e., involves making a comparison between groups):

1. Specify your research hypothesis or hypotheses.
2. Develop a sample size estimate using one of the examples in chapter 6 as a model. This involves first deciding which statistical test you will use at the end of the study, then setting out the assumptions, and finally using one of the chapter 6 appendices to estimate the sample size. For example, if one of the variables can be considered continuous:
 - (a) select your statistical test (for a continuous variable this would be the t test)
 - (b) Develop null and alternative hypotheses
 - (c) specify:
 - effect size (and standardized effect size, if continuous outcome variable)
 - alpha (and number of tails)
 - beta
 - (c) turn to Chapter 6 Appendices 6A-6F (pp 73-82) and estimate sample size
3. Comment on and justify the following things:
 - (a) How you came up with your effect size and standard deviation. One of the best sources is prior publications of related work, so take this opportunity to become even more familiar with the relevant literature.
 - (b) Decisions about number of tails, size of alpha, amount of power, multiple hypotheses, etc. Imagine that you are writing this section for a grant application, and that you must convince a skeptical reviewer of the appropriateness of your plan.

4. Use the internet to verify your sample size calculation:

<http://www.epibiostat.ucsf.edu/dcr/> or <http://www.dcr-4.net/>

You will definitely want to bookmark this site as an entry to a treasure trove of interactive statistical tools.

- B. If your research question is primarily descriptive, you won't have a hypothesis but you still need to decide on a sample size. Follow the descriptive models in Examples 6.4 and 6.5 in the book, justifying any assumptions and judgments. Then follow the instructions in B3a, above, to enhance your knowledge of the literature, and in B4 on the Web.

Lecture/Lecturer	Date	Topic	Homework Due
5 / Vermeulen	5 July 2016 1500 UTC	Overview of study designs observational study designs (case series, cohort, case control) randomized designs	12 July 2016 1500 UTC

Chapter 7: Designing Cross-Sectional and Cohort Studies

Chapter 8: Designing Case-Control Studies

Chapter 10: Designing a Randomized Blinded Trial

Read Chapters 7, 8, and 10 of DCR

Homework:

Catch-up on any parts of your protocol that are not yet complete – No homework due because not all study designs have been covered. If your planned study design was described in today’s lecture it would be good to starting writing the “Study Design” section of your protocol

Lecture/Lecturer	Date	Topic	Homework Due
6 / Schmidt	19 July 2016 1500 UTC	Designing studies of medical tests, including sensitivity and specificity	26 July 2016 1500 UTC

Chapter 12: Designing Studies of Medical Tests

Chapter 13: Research Using Existing Data

Read Chapters 11, and 13 of DCR

Homework:

Refer to content and reading from lectures 5 and 6

To be emailed to all courses lecturers within one week of the lecture.

- A. Revise parts of your protocol so far: “Research Question”, “Background and Significance”, “Study Design”, and “References”.

“Study Design”, describe your study design in a paragraph, amplifying on terms such as cross-sectional and randomized clinical trial by giving more information on timing of visits, measurements, treatments, etc. Discuss briefly why this design is best for your study. A schematic diagram with a horizontal time sequence is sometimes useful. This can usually be described in a paragraph, amplifying on terms such as cross-sectional and randomized blinded trial by giving more information on timing of visits, measurements, treatments, etc.

Write a **one page outline** of the protocol for your study. Your one page outline should include the research question, and it should concisely present relevant information on significance, design **(see Outline format on page 5 of this syllabus)**. This type of brief outline is useful for organizing your thoughts about a possible study and for presenting ideas to colleagues. Does your study meet the “FINER” criteria?

Lecture/Lecturer	Date	Topic	Homework Due
7 / Custer	9 Aug 2016 1500 UTC	Data validity, cause and effect, issues of bias	16 Aug 2016 1500 UTC

Chapter 9: Enhancing Causal Inference in Observational Studies

Read Chapters 9 and 15 in DCR.

Homework:

To be emailed to all courses lecturers within one week of the lecture:

A. Do either #1 or #2 of the following tasks designed to enhance causal inference:

1. If you are working on an observational study, in less than a page make a list of the variables that may be confounders in your study.
 - a. Develop at least two specific plans for coping with these confounders
 - b. Discuss which is best, and comment on the process of drawing causal inference from your study.

2. If you are working on an experiment, in less than a page:
 - a. Make a decision about whether or not to include each of the following strategies, specify how it will be done, and justify your decision:
 - randomized?
 - blinded?
 - run-in design?
 - factorial design?
 - stratified blocked randomization?
 - b. If you are planning to do a randomized blinded trial, describe the nitty-gritty of how you will carry out a tamper proof randomization, and how you maximize the success of the efforts at blinding.

Lecture/Lecturer	Date	Topic	Homework Due
8 / Schmidt	23 Aug 2016 1500 UTC	Research ethics, data management, quality control and big data	30 Aug 2016 1500 UTC

Chapter 14: Addressing Ethical Issues

Chapter 16: Data Management and Quality Control

Read Chapters 14, 16 in DCR.

Homework:

To be emailed to all courses lecturers within one week of the lecture.

Do EITHER A or B

Do C, D, and E

A. If you are conducting a survey or medical record data abstraction:

Find an existing questionnaire and/or data collection form that you might use in your study; this may include your donor intake forms. You can do this by asking your mentor for one, by discovering one in a published report, or by making a phone call to a scientist who is known to you only through her published work. Has the instrument been “validated”, and if so, what was the nature of the validation? Modify the existing questionnaire or data form to your study question, or write a new one. Comment on specific approaches to pretesting and validation.

B. If you are collecting other kinds of data or using existing data:

Create a spreadsheet of data or variables you will obtain in your research project. Consider and discuss whether your project will involve previously collected data or data from one or more sources that will have to be combined together.

C. Create a plan (in one paragraph) for pretesting your study. This may include several phases to address the issues of recruiting subjects and making measurements, including questionnaires. Be specific about such things as where the subjects for the pretest will come from, how many of them there will be (and how you picked this N) and what you will do with responses.

D. In **one paragraph**, discuss the ethical issues in your study, and any design options you are considering as a result (See examples). In **one page**, draft a consent form for your study, if necessary summarizing what would be presented in a longer version.

E. Continue the task of modifying and assembling all the pieces of your protocol that you have been working on, so that you end up with a reasonably complete draft of your 6-page protocol (see suggested format on the next page). Here are some optional other sections that you could add if appropriate and desired:

- Budget, resources, equipment, physical facilities (be brief)
- Statistical issues. Amplify on your sample size calculation by thinking through plans for analysis and interpretation.
- Timetable, organizational chart

As time and interest permits before meeting in person read the remaining Chapters in DCR. These chapters can be helpful for other parts of your protocol.

I TRY IT Programme attendance before and after the ISBT Congress in Dubai is required

We will meet in Dubai. The Dubai ISBT meeting is scheduled for 3 – 8 September, 2016. We will meet before the Congress to review course content we have covered and to provide final assistance with your protocol, and will meet after the Congress for further lectures on writing scientific papers, peer review, and course evaluations.

During the 2-day meeting before the Congress, you will finalize your protocol (first day) and provide it to another I TRY IT participant (second day). Each I TRY IT participant will review another participant's protocol (peer review) and provide a formal evaluation of the protocol during the in person meeting following the Congress. The meeting following the congress will focus on scientific results communication and peer review. This will be 1 to 1 and ½ days in length.

PEER REVIEW

You will be asked to do a peer review of one of your colleague's protocol. Keep your comments to about 15 minutes. In making your comments, remember that most people are sensitive about criticism, but that everyone wants advice and help. Here is a suggested format for providing feedback:

A. Start the critique by summarizing the study plan in a few sentences. This shows that you understood the big picture. And remember that you need to tell everyone else in the room what the study is about since they have not read it. For example:

This is a (design) study to examine the research question _____ . They will enroll a study population _____. The data analysis will see if there is an association between (predictor variable) and (outcome variable) in (population).

B. Next, give 2 or 3 particular strengths of the protocol. Uplifting and positive comments are the most comfortable format for criticism and will make the researcher more receptive to constructive criticism in other areas.

D. Then pick 2-3 major issues to discuss (limit the number so that you can give proper emphasis). Suggest solutions for any problems you note. **Try to stimulate discussion by the whole group.**

E. For minor comments and suggestions, provide written comments on a copy of the protocol and give to the author at the end.

Study Communication – Submitting Abstracts and Publishing Manuscripts in Refereed Journals

These topics will be covered later in the year. Specific dates have not yet been defined for these topics because we will assess how the course is proceeding and discuss the best approaches for how and when to cover these topics. I TRY IT 2015 participants will also be invited to these lectures.

Lecture	Date	Topic	Homework Due
9.		Data Analysis	

Lecture	Date	Topic	Homework Due
10		Results Reporting, Creation of Tables and Figures, Results Section	

Lecture	Date	Topic	Homework Due
11		Materials and Methods, Introduction Sections	

Lecture	Date	Topic	Homework Due
12		How to Contextualize the Ideas - Discussion Section	

Description

With the increasing amount of blood safety research studies conducted there is a need to communicate the main findings and use them for policy making process and design of further intervention, blood safety and surveillance studies.

This part of the course aims to build skills of participants in scientific writing for peer reviewed journals. The aim is to allow medical professionals and researchers to convert the results of research projects into manuscripts, which can be submitted for publication to peer-reviewed journals.

The content is structured to lead participants through the whole process of manuscript writing, from conception to final presentation of the results. Participants will gain experience of peer review on their own writing, and also facilitate peer review and feedback on papers prepared by other participants.

Learning objectives

Participants will learn how to make the writing process efficient, from developing the manuscript outline and writing up the results section to searching for the most appropriate title and

submitting the manuscript. These skills will help you when it comes time to report the results of your study.

Key topics in this part of the programme are:

- Broad and basic considerations for publishing research in refereed journals
- Preparing specific sections of a manuscript
- Presenting the data – tables, figures, text
- How to clearly conceptualize the ideas
- Discussing the importance of the findings
- Describing the limitations
- Importance of the abstract
- Choosing a title that captures attention
- Authorship
- Preparing the references
- Common reasons for failure to publish
- Communicating with journal editors when submitting a manuscript

Homework after the course:

- Complete primary analysis as much as possible
- Summarize your data in tables and figures
- Submit abstracts to ISBT congresses and manuscript to journals

Suggested Textbook

If sufficient funds are available we will provide this book to you as part of the course.

Publishing and Presenting Clinical Research, 3rd Edition, 2012
By Warren S Browner