Exploring Immunology

Thursday 5th & Thursday 12th November 2020, 10am-12.15pm
Via Zoom – link will be sent prior to session
Facilitators: Dr Anna Ridley & Dr Nicole Yager

In this interactive workshop, spread over two sessions, we will look at how the immune system functions in homeostasis, how it acts to protect us from pathogenic infection and how dysregulation of the immune system can have serious consequences.

Thursday 5th November
10:00am: Speaker: Anna Ridley
Title: Building an immune system
In this session we will examine our first line of defense; the innate immune system. Using the gut as an example we will build up a model of the innate immune system, exploring its function in homeostasis and its activation by infectious agents.

11:00am: Speaker: Nicole Yager
Title: Methods in studying the immune system
Should the innate immune system be insufficient to clear an infection the adaptive system is mobilized. In this session we will explore how and where this occurs. This session will include an introduction to some of the methods and techniques used to investigate the function of the immune system.

Thursday 12th November
10:00am: Speaker: Anna Ridley
Title: How to do a journal club
Whilst slower to respond the adaptive immune system provides a vital and specific response against infection. In this session we will focus on effector function of T and B cells, highlighting their importance by human immunodeficiencies. We will continue to explore some of the methods and techniques used to study the immune system and put this knowledge into practice with the analysis of a recent paper.

11:00am: Speaker: TBC
Title: When things go wrong
Regulation of the immune system is essential and breakdown of this control can lead to asthma, allergy, chronic inflammation and autoimmune disease. We will investigate the different mechanisms of control and what happens when this goes wrong.

Introduction To Clinical Trials 1 & 2

1. An Introduction to Study Terminology and Potential Sources of Bias

Tuesday 1st of December 2020, 9am – 12pm
Online – joining instructions to follow
Facilitators: Dr Ines Rombach and Dr Ruth Knight

A multi-centre, controlled, open-label, superiority, randomised controlled phase III parallel group trial" represents terminology commonly used in study protocols. This interactive session will explore the meaning and importance behind these terms, and discuss a variety of design approaches for randomised controlled trials (RCTs).

We will also discuss different sources of potential bias that can be introduced during the trial design, conduct, follow-up and analysis stage of RCTs. The concept of internal and external validity is introduced to establish the robustness of the research performed and its generalisability to clinical practice.

This session aims to provide participants with a good understanding of the different components of trial design, either to improve their ability to critically appraise the methods sections of RCT protocols and manuscripts or to contribute to the design of a trial. Further, the talk aims to enable participants to assess the integrity and validity of clinical trials, as well as their limitations.

The focus of this session will be on large, definitive trials, rather than early-phase research. Protocols of trials run in NDORMS will be used to illustrate and discuss various design features and their implications.

2. An Introduction to Designing and Testing Complex Healthcare Interventions in Clinical Trials

Tuesday 1st December 2020, 1pm – 3:15pm

Online

Facilitator: Dr David Keene

This session aims to introduce a range of key research design considerations when planning to develop and test a complex (non-pharmacological) intervention in healthcare. Examples from musculoskeletal surgery and rehabilitation research will be used to highlight the potential challenges that need to be addressed during the stages of intervention development, feasibility testing, large-scale evaluation in multicentre trials, and facilitating implementation into clinical practice.

The session will include:

- The biopsychosocial model of health
- Developing an complex intervention for a clinical trial and clinical practice
- Pilot and feasibility testing
- Clinical trial conduct and monitoring the quality of intervention delivery
- Using mediation analysis to understand the mechanisms of an intervention
- Qualitative methods in intervention development and implementation

Speakers will include Dr David Keene, Dr Beth Fordham, Dr Esther Williamson, Dr Hopin Lee

Next Generation Sequencing

Tuesday 15th December 2020, 10am – 4pm

Via Zoom – link will be sent prior to session

Facilitators: Dr Martin Philpott and Dr Adam Cribbs

Next Generation Sequencing (NGS) has revolutionised biological research, allowing entire systems to be simultaneously interrogated. This interactive lecture will be divided into two sessions. The first will cover an introduction to various NGS technologies, with an emphasis on the dominant Illumina sequencing by synthesis, common applications including genome sequencing, RNA-seq, ChIP-seq and single cell sequencing and the molecular biology underpinning library production. The second will highlight the importance of good experimental design for successful NGS studies and an introduction to the pipelines and statistical methods employed for the analysis of NGS data.

10am: Speaker: Martin Philpott - Molecular Biology of NGS.

Lunch Break

1pm: Speaker: Adam Cribbs - Experiment Design and Analysis of Sequence Data

Advanced Real-World Epidemiology and Machine Learning for Healthcare

Date: TBC

Facilitators: Dr Victoria Strauss and Dr Sara Khalid

10.00-10.15 Dr Victoria Strauss
Real world epidemiology recap
A brief recap of introduction in real world epidemiology.

10.15-11.30 Dr Danielle Robinson
Different approaches to minimize confounders in real world epidemiology
An interactive game will be played to facilitate teaching how different analytical approaches are used to minimize confounders in real world epidemiology that aim to understand the casual association. We will then cover the concept behind the game.

11.30-11.45 Coffee break

11.45-12.15 Dr Victoria Strauss
Real world epidemiology using multiple databases: common data model
A high level of introduction what common data model is and how they are becoming popular in real world epidemiology

12.15-13.30 Dr Danielle Robinson, Dr Victoria Strauss, Dr Annika Jodicke
A practical workshop-from a research question to analysis plan for a real world epidemiology study
A case study will be used to facilitate an interactive group to design a real world epidemiology study including statistical analysis planning.

13.30-14.15 Lunch break

14:15– 15.30 Dr Sara Khalid
Machine Learning for Healthcare
A brief overview of machine learning methods for healthcare applications including supervised and unsupervised learning, followed by real-world examples of data analysis using routinely-collected data.

DPhil 8 - session module

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Observational research: Introduction to epidemiology, real-world data, prognostic models and health economics

One of the key principles of evidence-based medicine is that there exists a hierarchy of evidence, often represented by a pyramid with study types ordered according to their comparative level of validity. Systematic reviews and meta-analyses sit at the top, followed by randomised controlled trials (RCTs) and then various observational study designs. The high costs and limitations of RCTs, together with the ever-growing availability of observational data and the strengths and increasingly refined methods of observational studies are making them more relevant in evidence-based medicine and healthcare decision-making. The Centre for Statistics in Medicine at NDORMS houses various teams conducting observational research, currently producing studies that advance healthcare practice and policy focusing on improving safety, vigilance, equity, effectiveness and cost-effectiveness. Topics of interest include prognosis, clinical predictions, analysis of routinely-collected health data, and health economics and outcomes research. This 8-session module will provide DPhil students with an introduction to the methods and practice of observational research which can help support their research and will enhance their skills in their future research careers.

Overview

This module will provide students with the opportunity to learn about the foundations of a series of key related topics in observational research over eight consecutive session. Generally, there will be two sessions per week with occasional work to be done between sessions to help prepare and enrich the level of discussion in subsequent sessions. The module will cover basic and real-world epidemiology, sources of real-world data in the UK, development and validation of prognostic models, machine learning, foundations of health economics, and economic analyses of MSK diseases and interventions.

Learning outcomes

With the series of eight sessions in this module we aim to help students become familiar with some of the key methods, data sources, strengths, limitations and applications of observational research, with particular attention to their use in musculoskeletal diseases and interventions.

By the end of this 8-session module, students will:

- be familiar with the principles and scope of epidemiology, the benefits and limitations of various epidemiological studies, and understand how causal associations can be examined by real world epidemiology;
- understand the role, strengths and weaknesses of real-world big clinical sources, with special attention to the UK setting, as well as recognise challenges and identify solutions to give observational studies robust foundations;
- understand what prediction models are as well as the processes required to develop and validate them, and be able to critically appraise the methodological quality of studies reporting on those;
- be familiar with machine learning methods in healthcare and their application using real-world data;
- understand the basic rationale of health economic analyses as well as how and why economic evaluations are used to inform decision-making in healthcare, especially for the assessment of MSK interventions using routinely-collected data.

Sessions

Session 1 – Introduction to Epidemiology

Dr Victoria Strauss, Dr Sam Hawley, Maria Sanchez-Santos

Students will learn the principles and scope of epidemiology and examine the benefits and limitations of epidemiological studies. Concepts such as 'PICO', 'confounding' and 'bias' will be introduced and the differences between various study designs such as cohort and case-control examined. Leading to the following session, students will be introduced to real-world epidemiology.

Session 2 – Real-world Epidemiology

Dr Victoria Strauss, Dr Danielle Robinson, Dr Annika Jodicke

Students will learn about real-world data and how the causal association can be examined by real world epidemiology. The definitions of exposures, outcomes and confounders will be examined as well as specific bias inherent in these type of data. We will provide a high level introduction of approaches used to deal with confounders in real-world epidemiologic studies. The advantages and disadvantages of cohort and case-control study designs in real world epidemiology will be discussed through a group debate, closing with a discussion on the challenges and pitfalls of real-world epidemiology.

Session 3 – Real-world data sources in the UK: CPRD (GOLD AND AURUM), ONS and HES

Dr Antonella Delmestri

Students will learn about the most influential data sources available in the UK: why they are collected, how they are structured and linked, and how to gain permission to use them, including ISAC applications. The challenges of real-world big clinical data will be made apparent together with solutions through the usage of DataBase Management Systems

(DBMS, e.g. MySQL) and high-level programming languages (e.g. Python) to implement advanced data curation and variable extraction.

Session 4 – Development of prognostic models

Dr Michael Schlussel, Dr Paula Dhiman

Prediction models are widely used to inform clinical practice and to help guide physicians' treatment decisions. To be effective in improving patient care, prediction models need be robustly developed to provide accurate predicted probabilities for the health outcome of interest. In this two-session talk on prediction modelling, we will first cover the study design, analysis and reporting considerations when developing a prediction model. This will include how to handle predictors, modelling techniques, and options for simplifying a prediction model so it is presented in an easy-to-use format.

Session 5 – Validation of prognostic models

Dr Michael Schlussel, Dr Paula Dhiman

In this second session, we will build on previously presented concepts of developing a prediction model, and introduce the study design, analysis, and reporting considerations when validating a prediction model. This will include how to predict from the model, how to estimate a model predictive performance using the same or different individuals from those used to develop the model (internal or external validation, respectively), and how to interpret the predictive accuracy of a model.

Session 6 – Introduction to machine learning

Dr Sara Khalid

This session will offer a brief overview of machine learning methods for healthcare applications including supervised and unsupervised learning, followed by real-world examples of data analysis using routinely-collected data.

Session 7 – Health economics: the basics

Assoc Prof Rafael Pinedo-Villanueva

Treatment effects are key outcomes of clinical research, but when it comes to healthcare systems making decisions about their implementation then treatment costs, and relevant outcomes, must be assessed together to help inform the decision-making process. We will explore why and how this is done, and introduce the foundations of economic evaluations in healthcare, including the concept of quality-adjusted life years.

Session 8 – Economic analyses of MSK diseases and interventions

Assoc Prof Rafael Pinedo-Villanueva

Many MSK diseases are chronic and this requires assessments that consider long periods of time. It is also often the case that evaluations must be conducted using evidence from various

studies. We will introduce the basics of decision-analytic modelling in health economics, which offer a framework to conduct simulations over the lifetime of patients and using different sources of data. We will discuss examples of economic analyses of MSK diseases and interventions using descriptive analysis and modelling methods.