

# Swiss Epidemiology Winter School 2019



## Mendelian randomization: moving from the one-sample to two-sample approach

January 24<sup>th</sup> – 26<sup>th</sup>, 2019

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### Faculty

#### **Prof. George Davey Smith**

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### Venue

#### **CH – 3823 Wengen | SWITZERLAND**

Hotel Sunstar (see map on <http://www.epi-winterschool.org/hotels>)

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### Description

Mendelian randomization is an approach which uses genetic variants as instrumental variables to test the causal effect of a (non-genetic) risk factor on a disease or health related outcome. Since the approach was first formally outlined 2003 it has been increasingly used to determine population causal effects using observational data. Academics working in the MRC Integrative Epidemiology Unit (IEU) at the University of Bristol, including those who are tutors on the course, have been at the forefront of developing methods for assessing and limiting potential biases with this approach.

This course aims to provide an introduction to the conduct, assumptions, strengths and limitations of Mendelian randomization, including up-to-date methods for applying Mendelian randomization using summary-level genetic data and sensitivity analyses that explore likely violation of Mendelian randomization assumptions. Participants will also gain practical experience of applying the two-sample Mendelian randomization approach (and up-to-date sensitivity analyses) to real data using the MR Base platform and “TwoSampleMR” R package developed by researchers at the MRC Integrative Epidemiology Unit. Practical examples ranging from pharmaceutical target validation, through conventional biomarkers to health behaviours and social factors (such as education) will be presented.

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### Contact:

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## Objectives

By the end of this course participants will:

- understand the principles and assumptions of instrumental variable analyses;
- understand the properties of genetic variants that make them suitable to be used as instrumental variables;
- understand the strengths and limitations of one-sample and two-sample Mendelian randomization for addressing population health causal questions;
- be able to complete a two-sample Mendelian randomization analysis using summary-level genetic data;
- understand the concepts behind sensitivity analyses to test for potential violation of the key assumptions of Mendelian randomization;
- be able to apply up-to-date sensitivity analyses in Mendelian randomization to explore violation of the key assumptions

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## Target audience

Prior experience with Mendelian randomization is not required, but participants should have an understanding of aetiological epidemiological principles and basic biostatistics. Participants must have experience of using R (or have completed an introductory online R course\*) as all practicals on the course will be run in R. The focus of these practicals will be on Mendelian randomization (and not learning how to use this statistical software). The course will not include any genetic epidemiology teaching or how to undertake a genome wide association study. However, genetic epidemiology training and the ability to complete a genome-wide association study are NOT a prerequisite for being able to follow this course. Introductory reading material for the course will be provided in good time to allow participants to be up to speed.

\* Suitable courses include

<https://www.rstudio.com/online-learning/#r-programming>

<http://www.ucl.ac.uk/lifelearning/courses/statistical-computing-r-programming-introduction>

<https://www.coursera.org/learn/r-programming>

<https://www.class-central.com/course/datacamp-introduction-to-r-7630>

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## Outline

The course will run over three days and consist of lectures, group work and computer practical sessions. We start early in the morning with a review of the previous day. During the extended break in the afternoon participants review course materials, catch up on emails or go skiing. We reconvene at 4:30 pm for the computer sessions.

### **Thursday, January 24<sup>th</sup> (8:00 – 12:00 | 16:30 – 18:30)**

- Introduction to causal analysis in epidemiology
- Introduction to Mendelian randomization and its assumptions
- One vs. two-sample Mendelian randomization
- Two-sample MR using the MR-Base web platform
- Power calculations in Mendelian randomization

### **Friday, January 25<sup>th</sup> (8:00 – 12:00 | 16:30 – 18:30)**

- Data harmonization in two-sample MR
- Testing the assumptions of two-sample Mendelian randomization
- Mendelian randomization and pleiotropy
- Two-sample MR using R
- Sensitivity analyses for MR using R

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**Saturday, January 26<sup>th</sup> (8:00 – 12:00 | 16:30 – 18:30)**

- Two-sample MR: Avoiding the downsides of a powerful, widely applicable but potentially fallible technique (critical appraisal)
- Use of MR in drug discovery and target validation
- Future directions in MR methodology (two-step and multivariable MR)
- MR and Triangulation
- Group practical on study design

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**Credits** 1.0 ECTS

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**To bring along** Students should bring their own portable computers. A course license for Stata® will be available, to be installed before arrival. University of Bern IT staff onsite can provide help upon request per e-mail ([it@ispm.unibe.ch](mailto:it@ispm.unibe.ch))

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**Course fee** SSPH+ students: CHF 0 \*)  
Academic: CHF 900  
Industry: CHF 2000  
\*) except students from University of Geneva (cohort 4) and Lucerne

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**Registration** You can register on the Winter School website [www.epi-winterschool.org](http://www.epi-winterschool.org).

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**Accommodation** Participants must book their accommodations themselves. Please see our recommendations on [www.epi-winterschool.org/hotels](http://www.epi-winterschool.org/hotels) for special prices.

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