Course guide
200646 - MERC - Statistical Methods in Clinical Research

Last modified: 09/06/2023

Unit in charge: School of Mathematics and Statistics
Teaching unit: 1004 - UB - (ENG)Universitat de Barcelona.

Degree: MASTER'S DEGREE IN STATISTICS AND OPERATIONS RESEARCH (Syllabus 2013). (Optional subject).

Academic year: 2023 **ECTS Credits:** 5.0 **Languages:** Spanish

LECTURER

Coordinating lecturer: JOSEP LLUÍS CARRASCO JORDAN

Others: Segon quadrimestre:
MIQUEL CALVO LLORCA - A
JOSEP LLUÍS CARRASCO JORDAN - A
ANTONIO MONLEON GETINO - A
SARA PÉREZ JAUME - A

REQUIREMENTS

- It is necessary that students have basic knowledge of R. In the following link the materials from a course to introduction to R are available
http://www.ub.edu/stat/docencia/EADB/Curso%20basico%20de%20R.htm
- It is recommended that students have taken a course in Design of Experiments or have basic knowledge on this subject. In particular it is recommended that students know the methodology outlined in chapters 12 and 13 included in
Montgomery, DC (2001). Design and analysis of experiments, 5th edition. John Wiley & sons.

DEGREE COMPETENCES TO WHICH THE SUBJECT CONTRIBUTES

Specific:
5. CE-1. Ability to design and manage the collection of information and coding, handling, storing and processing it.
6. CE-2. Ability to master the proper terminology in a field that is necessary to apply statistical or operations research models and methods to solve real problems.
7. CE-3. Ability to formulate, analyze and validate models applicable to practical problems. Ability to select the method and / or statistical or operations research technique more appropriate to apply this model to the situation or problem.
8. CE-4. Ability to use different inference procedures to answer questions, identifying the properties of different estimation methods and their advantages and disadvantages, tailored to a specific situation and a specific context.
9. CE-5. Ability to formulate and solve real problems of decision-making in different application areas being able to choose the statistical method and the optimization algorithm more suitable in every occasion.
Translate to english
10. CE-6. Ability to use appropriate software to perform the necessary calculations in solving a problem.
11. CE-7. Ability to understand statistical and operations research papers of an advanced level. Know the research procedures for both the production of new knowledge and its transmission.
12. CE-8. Ability to discuss the validity, scope and relevance of these solutions and be able to present and defend their conclusions.
13. CE-9. Ability to implement statistical and operations research algorithms.

Transversal:
1. ENTREPRENEURSHIP AND INNOVATION: Being aware of and understanding how companies are organised and the principles that govern their activity, and being able to understand employment regulations and the relationships between planning, industrial and commercial strategies, quality and profit.

2. SUSTAINABILITY AND SOCIAL COMMITMENT: Being aware of and understanding the complexity of the economic and social phenomena typical of a welfare society, and being able to relate social welfare to globalisation and sustainability and to use technique, technology, economics and sustainability in a balanced and compatible manner.

3. TEAMWORK: Being able to work in an interdisciplinary team, whether as a member or as a leader, with the aim of contributing to projects pragmatically and responsibly and making commitments in view of the resources that are available.

4. EFFECTIVE USE OF INFORMATION RESOURCES: Managing the acquisition, structuring, analysis and display of data and information in the chosen area of specialisation and critically assessing the results obtained.

TEACHING METHODOLOGY

The theoretical concepts are introduced in lessons accompanied with practical examples by means of slides that will be available for students.
Furthermore, the appropriate software to carry out the analyses and procedures will be also introduced by solving real data examples.

LEARNING OBJECTIVES OF THE SUBJECT

To face concrete situation, the student have to know how identifying the appropriate designs, properly carry out the experimentation and analyzing the results.
To obtain theoretical and practical knowledge of some critical designs in Biostatistics.
To know the regulatory that rules the approval of generic drugs and formulations.
To know to differentiate between a situation that requires an analysis of differences from an analysis of equivalence.
To provide the concepts and approaches to carry out an analysis of bioequivalences and equivalence in general.
To provide the concepts and approaches to carry out an analysis of concordance among measurements.
To know differentiating an analysis of concordance from an association or parameter comparison analysis.
To identify the sources of disagreement.
To provide the skill of discriminating among approaches depending of the type of data and objectives.
To provide the student with the concepts and procedures necessary to carry out an assessment analysis of the diagnostic capacity of medical tests.

STUDY LOAD

Type	Hours	Percentage
Self study	80,0	64.00
Hours large group	30,0	24.00
Hours small group	15,0	12.00

Total learning time: 125 h

CONTENTS

BLOCK 1. HIERARCHICAL FACTOR MODELS, REPEATED MEASURES AND CROSS-OVER DESIGNS

Description:
1.1.1. Factor designs with random effects. Mixed effects designs.
1.1.2. Hierarchical designs with two and three factors. Bennett-Franklin algorithm.
1.1.3. Repeated measures designs. Sphericity concept and ANOVA table corrections.
1.1.4. Crossover design concept. 2x2 crossover design (AB/BA). Crossover design of superior order and its analysis.

Full-or-part-time: 31h 15m
Theory classes: 7h 30m
Practical classes: 3h 45m
Self study : 20h

BLOCK 2. BIOEQUIVALENCE

Description:
2.1. Introduction
2.1.1.Bioavailabilityt. The concept of bioequivalence between drugs. Regulatory norms.
2.1.2. TOST. The principle of confidence intervals inclusion. Confidence intervals for BE. Bayesian approach. Nonparametric approach.
2.1.3. The problem of residual effects (carryover)

2.2. Individual and multivariate Bioequivalence
2.2.1. Individual and populational bioequivalence
2.2.2. Multivariate bioequivalence.

2.3. Equivalence tests.
2.3.1. General concept of equivalence test
2.3.2. Main applications: goodness of fit, homogeneity of variances, additivity in linear models, equivalence of proportions
2.3.3. Accessories: No inferiority testing method based on statistics and distances; bioinformatics applications

Full-or-part-time: 31h 15m
Theory classes: 7h 30m
Practical classes: 3h 45m
Self study : 20h

BLOCK 3. Assessment of the diagnostic ability of medical tests

Description:
1. Introduction to medical tests
2. Assessment of binary tests
3. Assessment of continuous tests
4. Medical tests with status defined as time to event
5. Meta-analysis of medical test evaluation studies

Full-or-part-time: 41h 40m
Theory classes: 10h
Practical classes: 5h
Self study : 26h 40m

BLOCK 4. Assessment of concordance of measurements

Description:
4.1. Analysis with qualitative scale data
4.2. Analysis with quantitative scale data

Full-or-part-time: 20h 50m
Theory classes: 5h
Practical classes: 2h 30m
Self study : 13h 20m

GRADING SYSTEM

Continuous evaluation
In each one of the blocks that compose the subject the students will have to solve some exercises, which will have to be delivered in a determined term that will be announced during the course. The exercises will be scored between 0 and 10, and the average of these grades will be the grade of exercises (NEJ).
In addition, a synthesis exam will be scheduled that will cover the entire syllabus of the subject. Attendance at this exam will be optional and will be intended for those students who have not passed the continuous assessment with a NEJ of less than 5. To take the exam it will be necessary to have delivered 60% of the exercises of the continuous assessment. The synthesis exam will receive a score between 0 and 10 (NPS)

The final grade of the subject will be calculated as:
1) For those students who do not attend to the synthesis exam, the final grade of the subject will be the NEJ.
2) For those students who take the synthesis exam, the final grade of the subject will be the maximum of NPS and NEJ.

Single evaluation
Those students who want to take the single evaluation will have to communicate it to the coordinator of the subject during the first 15 school days of the subject.
The single evaluation will consist of a synthesis exam that will cover the entire syllabus of the subject. The synthesis exam will receive a score between 0 and 10 and will correspond to the final grade of the subject.

The subject will be considered passed if the final grade is higher than 5.

BIBLIOGRAPHY

Basic:
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- Vonesh, E.F., Chinchilli, V.M. Linear and nonlinear models for the analysis of repeated measurements. New York: Marcel Dekker, cop. 1997. ISBN 0824782488.
- Chow, S-C.; Liu, J-P. Design and analysis of bioavalability and bioequivalence studies. 3th ed. CRC, 2009. ISBN 0827475724.
- Shoukri, M. M. Measures of interobserver agreement. Boca Raton: Chapman & Hall/CRC, cop. 2004. ISBN 9781584883210.
- Agresti, Alan. Categorical data analysis. 2nd ed. John Wiley & Sons, 2002. ISBN 0471360937.
- Fleiss, Joseph L. The Design and analysis of clinical experiments. New York: John Wiley & Sons, 1986. ISBN 0471820474.
- Choudhary, P.K; Nagaraja, H.N. Measuring agreement : models, methods, and applications. Wiley, 2017. ISBN 9781118078587.
- Pepe, Margaret Sullivan. The Statistical evaluation of medical tests for classification and prediction. Oxford University Press, 2003. ISBN 9780198565826.

Complementary:
- Senn, Stephen. Cross-over trials in clinical research. 2nd ed. Chichester: John Wiley & Sons, Inc., cop. 2002. ISBN 0471496537.
- Patterson, Scott D., Jones, B. Bioequivalence and statistics in clinical pharmacology. Boca Raton: Chapman & Hall/CRC, 2006. ISBN 9781584885306.
- Wellek, S. Testing statistical hypotheses of equivalence. Chapman & Hall/CRC, 2003. ISBN 1584881607.
- Dunn, G. Design and analysis of reliability studies : the statistical evaluation of measurement errors. New York: Oxford University Press, 1989. ISBN 0852642970.

- Raghavarao, D.; Padgett, L.V. Block designs : analysis, combinatorics and applications. New Jersey: World Scientific, cop. 2005. ISBN 9812563601.
- De Vet, H.C.W.; Terwee, C.B.; Mokkink, L.B.; Knol, D.L. Measuement in medicine : a practical guide [on line]. Cambridge University Press, 2011 [Consultation: 05/07/2023]. Available on: https://www-cambridge-org.recursos.biblioteca.upc.edu/core/books/measurement-in-medicine/8BD913A1DA0ECCBA951AC4C1F719BCC5. ISBN 1139497812.