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.

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.
200628 - DAIC - Advanced Experimental Design in Clinical Research

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 in-person lessons consist of sessions in the classroom where the theoretical concepts are introduced 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.

Study load

<table>
<thead>
<tr>
<th>Total learning time: 125h</th>
<th>Hours large group: 30h 24.00%</th>
<th>Hours medium group: 0h 0.00%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total learning time: 125h</td>
<td>Hours small group: 15h 12.00%</td>
<td>Guided activities: 0h 0.00%</td>
</tr>
<tr>
<td>Study load</td>
<td>Self study: 80h 64.00%</td>
<td></td>
</tr>
</tbody>
</table>

The in-person lessons consist of sessions in the classroom where the theoretical concepts are introduced 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.
## 200628 - DAIC - Advanced Experimental Design in Clinical Research

### Content

<table>
<thead>
<tr>
<th>BLOCK 1. HIERARCHICAL FACTOR MODELS, REPEATED MEASURES AND CROSS-OVER DESIGNS</th>
<th>Learning time: 31h 15m</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description:</strong></td>
<td>Practical classes: 12h</td>
</tr>
<tr>
<td>1.1.1. Factor designs with random effects. Mixed effects designs.</td>
<td>Guided activities: 8h</td>
</tr>
<tr>
<td>1.1.2. Hierarchical designs with two and three factors. Bennett-Franklin algorithm.</td>
<td>Self study: 11h 15m</td>
</tr>
<tr>
<td>1.1.3. Repeated measures designs. Sphericity concept and ANOVA table corrections.</td>
<td></td>
</tr>
<tr>
<td>1.1.4. Crossover design concept. 2x2 crossover design (AB/BA). Crossover design of superior order and its analysis.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BLOCK 2. BIOEQUIVALENCE</th>
<th>Learning time: 31h 15m</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description:</strong></td>
<td>Practical classes: 12h</td>
</tr>
<tr>
<td>2.1. Introduction</td>
<td>Guided activities: 8h</td>
</tr>
<tr>
<td>2.1.1. Bioavailability. The concept of bioequivalence between drugs. Regulatory norms.</td>
<td>Self study: 11h 15m</td>
</tr>
<tr>
<td>2.1.2. TOST. The principle of confidence intervals inclusion. Confidence intervals for BE. Bayesian approach. Nonparametric approach.</td>
<td></td>
</tr>
<tr>
<td>2.1.3. The problem of residual effects (carryover)</td>
<td></td>
</tr>
<tr>
<td>2.2. Individual and multivariate Bioequivalence</td>
<td></td>
</tr>
<tr>
<td>2.2.1. Individual and populational bioequivalence</td>
<td></td>
</tr>
<tr>
<td>2.2.2. Multivariate bioequivalence.</td>
<td></td>
</tr>
<tr>
<td>2.3. Equivalence tests.</td>
<td></td>
</tr>
<tr>
<td>2.3.1. General concept of equivalence test</td>
<td></td>
</tr>
<tr>
<td>2.3.2. Main applications: goodness of fit, homogeneity of variances, additivity in linear models, equivalence of proportions</td>
<td></td>
</tr>
<tr>
<td>2.3.3. Accessories: No inferiority testing method based on statistics and distances; bioinformatics applications</td>
<td></td>
</tr>
</tbody>
</table>
BLOCK 3. ASSESSMENT OF THE DATA QUALITY: RELIABILITY AND CONCORDANCE OF MEASUREMENTS

Learning time: 62h 30m
- Theory classes: 22h 30m
- Practical classes: 24h
- Guided activities: 16h

Description:
3.1. INTRODUCTION
- Model of measurement. Types of measurement errors.
- Concepts: validity, accuracy, reliability and calibration.
- Classification of the approaches to evaluate agreement.

3.2. ANALYSIS WITH QUALITATIVE DATA
- Concordance index: kappa index and weighted kappa y kappa. Kappa index extended to k observers.

3.3. ANALYSIS WITH CONTINUOUS DATA
- Components of discordance: bias, association and heteroscedasticity.
- Coefficient of concordance: definition and generalization.
- Intraclass correlation coefficient: reliability, consistency and concordance.
- Procedures based on probability criteria: tolerance intervals and total deviation index. Bland-Altman approach. Other approaches to assess concordance.
- Assessment of individual bioequivalence as a concordance among measurements issue.

Qualification system
Overall mark will be obtained as an average of:
1) Proposed exercises (50%)
2) Test about theoretical concepts treated along the course (50%)
Bibliography

Basic:


Complementary:


