MSc. Medical Biometry/Biostatistics Guide

University of Bremen

Module Descriptions

April 2022

Contents

0.0.1 Course Schedule:

WinterSem 2022/23	**SummerSem 2023**	**WinterSem 2023/24**	**SummerSem 2024**
1. Biometrical Methods I	*1. Statistical Modeling*	*1. Biometrical Methods II*	*Master Thesis*
2. Statistical Modeling	*2. Data Management and Statistical Programming*	*2. Complex Statistical Modeling*	
3. Data Management and Statistical Programming	*3. Basic Epidemiology*	*3. Fundamentals of Medicine*	
4. Basic Epidemiology	*4. Clinical Trials and Ethics*	*4. Internship*	
5. Clinical Trials and Ethics	*5. Fundamentals of Medicine*		
6. Fundamentals of Medicine			

Course	**Credit Points**	**Facilitator**
Biometrical Methods I	6	*Dr. Marvin N. Wright*
Statistical Modeling	12	*Prof. Dr. Iris Pigeot*
Data Management and Statistical Programming	9	*Dr. Martin Scharpenberg*
Basic Epidemiology	6	*Prof. Dr. Wolfgang Ahrens*
Biometrical Methods II	15	*Prof. Dr. Werner Brannath*
Complex Statistical Modeling	6	*Dr. Martin Scharpenberg*
Clinical Trials, Laws, Guidelines and Ethics	15	*Dr. Martin Scharpenberg*
Fundamentals of Medicine	6	*Prof. Dr. Bernd Mühlbauer*
Internship	6	*Dr. Stephan Kloep*
Master Thesis	30	*Prof. Dr. Werner Brannath*

1 BioStat-A-1: Biometrical Methods

1.1 Learning Contents

- Descriptive Statistics
- Point and interval estimators
- Principle of statistical testing (decision procedure, error rates, p-values, power)
- Selected statistical testing procedures (Z-test, t-test, chi-square test, two-sample t-test)
- Sample size calculation
- Introduction to regression analysis and analysis of variance, as well as nonparametric procedures

1.2 Learning Outcomes

- Knowledge of the most important procedures of descriptive statistics
- Knowledge of general methodology of sample size calculation in biometrical studies
- Knowledge of the basic methods of inferential statistics
- Firm apprehension of several test and analysis methods based on the normal distribution or the binomial distribution
- Insight into several procedures of nonparametric statistics
- Ability to apply the learned estimation and testing procedures in SAS

2 BioStat-A-2: Statistical Modeling

2.1 Learning Contents

2.1.1 Statistical modeling I

- Introduction to probability calculation
- Discrete and continuous random variables and their parameters, density and distribution functions
- Law of large numbers, central limit theorem
- Parameter estimation and confidence intervals

2.1.2 Statistical modeling II

- Multi-dimensional distributions, correlation
- Representation using matrices and vectors
- Linear regression, in particular parametrization of explanatory variables, dummy and effect coding of factors
- Parameter estimation, least squares methods and normal equations
- Model selection and variable selection
- Regression diagnostics
- General linear models (heteroscedastic and correlated errors)

2.2 Learning Outcomes

2.2.1 Statistical modeling I

- Knowledge of the basics of biometric models
- Comprehension of variability: random and systematic effects
- Comprehension of basic probability calculation
- Comprehension of the basics of inferential statistics

2.2.2 Statistical modeling II

- Knowledge of the linear model, in particular comprehension of model assumptions, mathematical reasoning and the mathematical formulation
- Knowledge of possible sources of modeling errors
- Ability to independently plan and analyze a study applying linear models
- Competence in the interpretation of parameters and model diagnostics
- Competence in using modeling and analysis software
- Competence in variable selection, model selection and the construction of prognostic indices

3 BioStat-A-3: Data Management and Statistical Programming

3.1 Learning Contents

3.1.1 Data Management:

- Tasks and processes of data management
- Principles of designing Case Report Forms (CRF)
- Data models, data bases
- Data entry, plausibility checks, queries
- Automatic/semi-automatic data capture
- Data base freezing, data integrity, data security
- Quality management
- Randomization
- Practical work process with exercises

3.1.2 Statistical Programming

- Performance spectrum of statistical analysis programs
- Efficient organization of data management tasks
- Solving analysis exercises in SAS-programming including the usage of macros
- Knowledge of areas of application, possibilities and limitations of software solutions
- Insight to the possibilities to extent the biometrical methodology in the software, in particular to the implementation of methodology which is not already included in the software
- Planning and analysis of data management tasks and conduct of analyses in SAS using generated data

3.2 Learning Outcomes

3.2.1 Data Management:

- Knowledge of tasks and processes of the data management in a clinical trial
- Knowledge of purpose and content of essential documents that are produced by data management in the course of a clinical trial
- Knowledge of guidelines for the design of such documents
- Knowledge of typical software to process the tasks of data management in a clinical trial

3.2.2 Statistical Programming

- Ability to execute the tasks of data management in a clinical trial
- Ability to use software relevant for data management and analysis tasks
- Knowledge of possibilities to extent the biometrical methods already included in software packages

4 BioStat-A-4: Basic Epidemiology

4.1 Learning Contents

- Basic Epidemiology, in particular goals and methods of epidemiology
- Definitions, fundamental concepts, as well as typical problems and approaches of epidemiology
- Interpretation and assessment of epidemiological studies using publications

4.2 Learning Outcomes

- Knowledge of epidemiological study designs
- Knowledge of descriptive and comparative epidemiological measures and standardization
- Understanding of sources of error, bias and confounding, misclassification
- Knowledge of experimental and observational study designs
- Knowledge of data sources and data acquisition
- Knowledge of methods for quality assurance and good epidemiological practice
- Ability interpret and critically assess epidemiological study results with regard to methods, presentation of results and discussion
- Ability to present study results
- Ability to moderate a scientific discussion

5 BioStat-A-5: Biometrical Methods – Special Aspects

5.1 Learning Contents

5.1.1 Multiple Testing Problems

- Basics and theory of multiple testing
- Methods for comparisons of multiple groups and subgroup analyses for multiple endpoints
- Graphical multiple tests

5.1.2 Survival Analysis

- Basics: Censoring, Survival function, hazard and cumulative hazard
- Nonparametric, semiparametric and parametric methods
- Complex modeling approaches
- Sample size calculation

5.1.3 Nonparametric Methods

- Ideas and basics of nonparametric methods (methods without distributional assumptions)
- Methods for paired and unpaired samples, for two or more groups, for multi factorial designs

5.1.4 Bayes Statistics

- Multivariate, marginal and conditional distributions and Bayes' Rule (discrete and continuous)
- Principle of Bayesian inference
- Conjugate Priors with examples (e.g. Beta-binomial model for a proportion, Poisson-gamma model for a rate, Normal-normal model for a mean)
- Mixtures of conjugate priors
- Improper, objective, Jeffrey and reference priors
- Computational approaches (e.g. Markov Chain Monte Carlo (MCMIII. method, Gibbs sampling, Metropolis-Hastings (MH) sampling, MCMIII.
- Empirical Bayes (optional)
- Frequentist properties of Bayesian methods (optional)
- Application of Bayesian methods in clinical trials and medical studies

5.1.5 Problems of biometrical research

- Current examples of biometrical research, based on the particular interests of the students with regard to their master thesis. An oral presentation is given which approaches the topic of the master thesis systematically:
  i. General overview over the medical and methodological problem
  ii. Narrowing the topic to a relevant core
  iii. Approach and working program for the work on the problem

5.2 Learning Outcomes

- Knowledge of the differentiation and specialization of the biometrical methodology to specific questions
- Ability to apply these methods to clinical practice and to interpret the results
- Competence in the application of corresponding software

6 BioStat-A-6: Complex Statistical Modeling

6.1 Learning Contents

- Theory of the generalized linear model, in particular:
- Univariate and multiple logistic regression
- Logit-transformation, odds ratio
- Parameter estimation (maximum likelihooIV., interpretation of the parameters of the generalized linear model
- Model selection, variable selection, quality criteria, diagnostics
- Exponential families, link function, canonical link
- Poisson regression
- Proportional odds model, logistic regression with multiple categories
- Introduction to generalized estimating equations
- Introduction to the generalized linear mixed model
- Introduction to propensity score methods

6.2 Learning Outcomes

- Knowledge of definitions, properties and mathematical basics of complex models, in particular of generalized linear models
- Overview of differentiation and specialization of the models covered regarding special questions
- Knowledge of the areas of application, possibilities and limits of the models
- Establishing connections between modeling and methods of planning and analysis of studies
- Knowledge of the corresponding model related theories of analysis (estimation, testing)
- Knowledge of the corresponding methods of sample size calculation
- Ability to choose appropriate models in complex designs
- Ability to assess the appropriateness of a chosen model
- Ability to independently perform the biometrical planning, analysis and interpretation in such models

7 BioStat-B-1: Clinical / Diagnostic Trials, Laws, Guidelines and Ethics

7.1 Learning Contents

7.1.1 Clinical Trials I

- Study types from observational studies to randomized trials
- Causality, stochastics, evidence, question, hypotheses, trial design
- Determination of target population, criteria for evaluation and parameters
- Randomization and blinding
- Sample size calculation

7.1.2 Clinical Trials II

- Principles of conducting randomized therapy trials: Organization, documentation and data management, clinical monitoring
- Analysis and interpretation of randomized trials
- Analysis populations: Per protocol, full analysis set, intention to treat principle
- Estimands
- Overview of common statistical procedures
- Handling of drop outs and missing data
- Analysis of follow-up data
- Interim analysis strategies
- Subgroup analyses
- Confirmatory vs. exploratory analyses

7.1.3 Diagnostic Studies

- Definition and examples for diagnostic tests and medical screening/classification tools
- The development and investigation of diagnostics tests and medical screening/classification tools
- Measures of test and classification accuracy (e.g. accuracy, sensitivity, specificity, ROC curve)
- Statistical methods for the estimation of accuracy
- Definition and estimation of positive and negative predictive values
- Statistical methods for the comparison of diagnostic tests
- Study designs and hypothesis tests for diagnostics studies
- Methods to account for covariate effects on diagnostic tests
- Statistical methods for biomarker selection and biomarker combination

7.1.4 Laws & Guidelines

- Basic legal terms
- Overview of national and international regulations and standards in clinical research
- International Conference on Harmonization (ICH) guidelines
- Special conditions and requirements for special populations (e.g. children, persons who are incapable of giving consent)

7.1.5 Ethics

- Basic ethical requirements
- Bioethics
- Declaration of Helsinki
- Ethical reasoning for the quality assurance in clinical research
- Ethical principles of good clinical practice (GCP)

7.2 Learning Outcomes

7.2.1 Clinical Trials I

- Knowledge of general basics and the design of clinical trials
- Ability to biometrically plan clinical trials according to legal and regulatory requirements
- Competence in elaboration of trial designs and aspects of trial planning, as well as the ability to impart those to an inderdisciplinary team
- Ability to conduct the quality management of a clinical trial and to critically assess scientific publications of study results

7.2.2 Clinical Trials II

- Knowledge of basic aspects of the conduct, analysis and interpretation of clinical trials in special consideration of legal environment as well as the methodological and organizational aspects
- Ability to plan, support and correctly analyze biometrical trials according to legal and regulatory requirements Knowledge of the corresponding statistical methods
- Knowledge of the measures for securing equality of observation and treatment
- Ability to identify confounding effects and bias
- Competence in imparting study aspects in an interdisciplinary team

7.2.3 Diagnostic Studies

- To understand basic and more advanced principles for the investigation and evaluation of diagnostic tests and medical screening/classification tools.
- To be able to describe and estimate test and classification accuracy
- To know how to plan and analyze a typical diagnostic study
- Basic knowledge of statistical methods for biomarker selection and combination

7.2.4 Laws & Guidelines

- Knowledge of the legal basics for clinical research in German, European and international law, as well as the relevant regulatory provisions and guidelines
- Knowledge of the main laws and guidelines and their application
- Knowledge of the principles of quality assurance
- Competence in dealing with exceptional cases
- Competence in working alongside regulatory authorities and legal practitioners
- Ability to independently make out legal texts

7.2.5 Ethics

- Knowledge of ethical principles of medical research
- Ability to introduce ethical aspects in the planning of clinical trials
- Ability to critically assess the ethical aspects of study concepts
- Knowledge of ethical aspects of quality assurance
- Ethical competence in dealing with exceptional cases

8 BioStat-B-2: Fundamentals of Medicine

8.1 Learning Contents

8.1.1 Medical Basics

- Introduction to general medical terminology, nomenclature and medical approaches
- Anatomy and function of muscles and bones
- Anatomy and function of internal organs (e.g. cardiovascular system, liver, pancreas, gastrointestinal tract, kidneys and urinary tract
- Neuroanatomy and neurophysiology
- Physiology of sensory perception
- Trauma and growth

8.1.2 Molecular Medicine

- Cell metabolism at the example of glucose
- Birth and death of a cell, regulation of cell functions: hormones, signal transduction
- Gene expression
- Hederitary diseases (basics and perinatal diagnostics)
- Hemostasis
- Medical analytical laboratory
- Basics of microbiology: Parasites, Bacteria, Fungi
- Diagnostic in microbiology

8.1.3 Pharmacotherapy

- Demarcation of experimental and clinical pharmacology
- Basics of pharmacodynamics and pharmacokinetics, PK/PD modeling
- Choosing a efficient and rational drug therapy
- Adiposis, Diabetes, Dyslipidemia
- Sytematology and pharmacotherapeutic approaches to neurological diseases
- Systematology of psychiatric drugs
- Clinic and therapy of mental disorders
- Drug therapy of Asthma and COPD
- Drugs for pain therapy, principles of anesthesia
- Bone diseases
- Clinic and therapy of gastrointestinal diseases
- Clinic and therapy of infectious diseases

8.1.4 Special Areas of Medicine (e.g. Oncology)

- Medical terminology and basic principles of a special area of medicine

8.2 Learning Outcomes

8.2.1 Medical Basics

1. Knowledge and understanding of basic medical terminology
2. Knowledge of basic anatomy, physiology, as well as knowledge of organ systems
3. Knowledge of key medical terms of internal medicine
4. Competence in applying medical vocabulary in dialogues with physicians an in the planning, conduct and analysis of clinical trials.

8.2.2 Molecular Medicine

1. Knowledge of basic molecular medicine

2. Basic knowledge of cell functions, hemostasis and laboratory medicine

8.2.3 Pharmacotherapy

1. Knowledge of key terms of pharmacokinetics, pharmacodynamics and pharmacogenomics
2. Knowledge of the tools of experimental and clinical pharmacology for medical research

8.2.4 Special Areas of Medicine

1. Knowledge of key terms of a special area of medicine (e.g. oncology)
2. Knowledge of common therapy appraoches in that area

9 BioStat-C-1: Internship

9.1 Learning Contents

Students shall experience working situations and job requirements in a pertinent professional field of activity inside or outside the university. They should learn to define and analyze the occurring problems and tasks based on their professional qualification acquired until then.

Furthermore, they should learn to develop and realize approaches to those problems and tasks.

9.2 Learning Outcomes

1. Develop and promote the professional orientation
2. Imparting deepened knowledge of the organization and functioning of a professional field
3. Apply the knowledge and skills acquired in the studies. Promote the development of practical questions in the studies
4. Give an insight and contacts to possible professional fields

10 BioStat-D-1: Module Master Thesis

10.1 Learning Contents

1. Scientific work under supervision
2. Specialization in a subject of biostatistics

10.2 Learning Outcomes

1. Ability to work independently and scientifically, in particular:

- Independently search for and becoming acquainted with relevant literature
- Reflection of current state of research
- Development of own research results if possible
- Adherence to rules of good scientific practice

2. Ability to write a comprehensive academic work
3. Ability to present the research work orally