THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI -600 032

REGULATIONS OF THE M.Sc. (BIO-STATISTICS)

(POST-GRADUATE DEGREE COURSE UNDER ALLIED HEALTH SCIENCE)

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In exercise of the powers conferred by Section 44 of the Tamil Nadu Dr.M.G.R.Medical University, Chennai Act 1987 (Tamil Nadu Act 37 of 1987) the Standing Academic Board of the Tamil Nadu Dr.M.G.R.Medical University, Chennai hereby makes the following regulations:-

1. SHORT TITLE AND COMMENCEMENT:-

These regulations shall be called as "THE REGULATIONS FOR THE MASTER OF THE SCIENCE **(BIO-STATISTICS)** " OF THE TAMIL NADU DR. MGR MEDICAL UNIVERSITY, CHENNAI.

They shall come into force from the academic year 2011-2012.

The Regulations and the Syllabus framed are subject to modification from time to time by the Standing Academic Board.

2. ELIGIBILITY FOR THE COURSE

The candidates who possess Degree in the following are eligible to get admitted into the course of M.Sc. (Biostatistics)

1. Degree with Statistics as the Main Branch (or)
2. Degree in any subject with Statistics as Ancillary/Allied

3. OBJECTIVE OF THE COURSE:

The objectives of M.Sc., Biostatistics Programme are to promote the knowledge in statistical theory, methodology and epidemiology. The Programme provides training in statistical theory, methodology, computer systems, data management and epidemiology. This programme includes a practicum, involving collaboration between health science professionals and students. A small group of students work under faculty supervision with one or more investigators. Each student in the programme has an academic advisor. The graduates from this course would be able to work in Pharma industries for drug and vaccine development and also to work in national and international institutions as faculty or scientist.

4. COMMENCEMENT OF THE COURSE

The academic year for the M.Sc. (Biostatistics) Post-graduate Degree course shall commence from 2nd May / 1st October and the candidates admitted upto 31st May / 31st October will be registered for the course.

5. DURATION

The duration of the M.Sc. (Biostatistics) course is two years and the students should complete the course in 4 years of time, failing which he/she will be discharged from the course.

6. ELIGIBILITY CERTIFICATE

The candidate who has passed any qualifying examination as stated in Regulation No.2 above other than the Tamil Nadu Dr. MGR Medical University, Madurai Kamaraj University, University of Madras, Bharathiyar University, Bharathithasan University or any other University shall obtain an "Eligibility

Certificate" from this University by remitting the prescribed fee along with the application form and required documents before seeking admission to anyone of the affiliated medical institutions. The application form is available in the University website (www.tnmmu.ac.in).

7. CUT-OFF DATE FOR ADMISSION TO EXAMINATIONS

The candidates admitted upto 31st May / 31st October shall be registered to take up their First Year examinations after fulfillment of the regulations from 15th April / 15th October of the next year.

All kinds of admissions shall be completed on or before 31st May / 31st October of the academic year. There shall not be any admissions after 31st May / 31st October, even if seats are vacant.

8. ATTENDANCE REQUIRED FOR ADMISSION TO EXAMINATIONS

(a) No candidate shall be permitted to appear in any one of the parts of M.Sc. (Biostatistics) course in Examinations unless he/she has attended the course in all the subjects for the prescribed period in an affiliated institution recognized by this University and produce the necessary certificate of study, attendance and satisfactory conduct from the Head of the institution.

(b) A candidate is required to put in a minimum of 90% of attendance out of 270 working days in both theory and practical Separately in each subject before admission to the Examinations.

(c) A candidate lacking in the prescribed attendance and progress in any one subject in theory and practical wherever necessary in the first appearance shall not be permitted for admission to the entire examinations.

9. Condonation of Lack of Attendance

There shall be no condonation of lack of attendance.

10. Working days in the academic year

Total No. of days in a year			**365 days**
No. of weekly off (Sundays)	-	52 days	
No. of Government Holidays	-	22 days	
No. of Holidays	-	21 days	
		----------	95 days
Total No. of working days including Examination period			270 days

Each academic year shall consist of not less than 270 working days.

11. EXAMINATIONS:

April 15th / October 15th

There shall be two examinations, one at the end of the I year and the other at the end of the II year. A candidate will be permitted to appear in second year examinations, only if he/she passes the first year subjects.

12. DISSERTATION

Dissertation shall be submitted by the candidate three months before the final and second year examinations.

For Dissertation Marks 200, Viva-voce on Dissertation/Presentation Marks 50 and IA 50 – Minimum mark to pass 150.

If the candidate fails in the Written/Practical examination , but his/her dissertation is approved(passed), the approval of the dissertation shall be carried over to the subsequent examination.

Two copies of the evaluation report of the dissertation should be submitted by the Examiners to the Controller of Examinations of this University.

A candidate failing in either theory or practicals will have to reappear for theory, practicals and Viva voce to be able to clear the examination in subsequent attempt. However, the dissertation, if approved(passed), need not be submitted again.

13. COURSE OF STUDY

First Year

Paper - I	Probability and Distribution Theory
Paper - II	Epidemiology and Design of Experiments
Paper - III	Statistical Inference, Sampling Methods and Sample Size
Paper - IV	Demography and Health Data Management
	Practicals – I

Second Year

Paper – I	Applied Regression Methods
Paper - II	Applied Multivariate Analysis and Time Series Analysis
Paper -III	Clinical Trial and its Management
	Practicals – II
	Dissertation and Viva

14. SCHEME OF EXAMINATIONS

Examination Pattern - I year

Paper	Subjects	Internal Assessment (IA)		Theory		Practical		Viva Voice	
		Max	Min	Max	Min	Max	Min	Max	Min
I.	Probability and Distribution Theory	50	25	100	50	150	75	50	25
II	Epidemiology and Design of Experiments	50	25	100	50				
III	Statistical Inference, Sampling Methods and Sample Size	50	25	100	50				
IV	Demography and Health Data Management	50	25	100	50				

Ist Year

If the candidates fails in Practical /Viva should write all the Four papers again.

Examination Pattern - II year

Paper	Subjects	Internal Assessment (IA)		Theory		Practical		Viva Voice	
		Max	Min	Max	Min	Max	Min	Max	Min
I.	Applied Regression Methods	50	25	100	50	150	75	50	25
II	Applied Multivariate Analysis and Time Series Analysis	50	25	100	50				
III	Clinical Trial and its Management	50	25	100	50				

IInd Year

If the candidates fails in Practical /Viva should write all the Three papers again.

Dissertation	200
Oral on Dissertation	50
IA	50
Total	300
Passing Minimum	150

Papers suggested for First Year

Paper I : Probability and Distribution Theory

Probability Theory : (50%)

Sets and classes of events, Random variables, Definition of probability, Simple properties, Sample space and events, Discrete probability space, General probability space, Distribution function of a random variable, Definition of Expectation, Properties of Expectation. Inequalities: (Chebychev's, Morkov's, Holder's, Jenison's and Minkowski inequalities). Convergence in probability, Almost sure Convergence, Convergence in distribution. Moment generating function, Characteristic function, Definition and properties. Inversion formula, Convergence of distribution function and characteristic function. Independence, Multiplication properties, Central limit theorem for independently and identically distributed random variables (statement only).

Distribution Theory: (50%)

Univariate distributions:

Review of univariate distributions with special reference to biostatistics; Binomial, Poisson, Geometric, negative-binomial, Hypergeometric, Normal, Logistic, Lognormal, Exponential, χ^2, t , f , gamma and beta distributions. Their properties and applications, transformation and change of variables techniques.

Multivariate distributions:

Bivariate and Multivariate Normal Distribution, Additive properties, Characteristic functions, Conditional distributions, Marginal distributions, Estimation of mean vector and covariance matrix, Partial, Multiple correlation coefficients and their sampling distributions*, Generalised T^2 statistic, Mahalanobis D^2 statistic, Wishart distribution*, Cochran's theorem, Distributions of quadratic forms (* - statement only).

Books for study and reference:

1. Bhat BR, Modern Probability theory, 1985, Wiley Eastern Ltd.

2. Rohatgi VK and Md.Ehsanes saleh AK, An Introduction to Probability & Statistics, 2009, Wiley India..

3. Ross S, A First course in Probability, 2002, Pearson Education Inc.

4. Rao CR. Linear Statistical Inference and its Applications, 1973, John Wiley, NY.

5. Johnson NL and Kotz S. Discrete Disrtibutions,1969, John Wiley & Sons.

6. Johnson NL and Kotz S. Continuous Univariate Distributions Vol I & Vol II, 1970, John Wiley & Sons.

7. Robert. V. Hogg and Allen. T. Craig, Introduction to Mathematical Statistics, 5th edition, 1995, Pearson Education Publishing Co., Inc.

8. Anderson TW. An Introduction to Multivariate Statistical Analysis, 1984, John Wiley & Sons.

9. Johnson RA and Wichern DW. Applied Multivariate Statistical Analysis, 1984, John Wiley & sons.

10. Mardia KV, Kent JT and Bibby JM. Multivariate Analysis, 2003, Academic press.

Paper II : Epidemiology and Design of Experiments

Epidemiology (60%)

Introduction to epidemiology: Definition, agent, host and environment, Mode of transmission, Incubation period, Spectrum of disease, Herd immunity, Classification of cause of death, measure of mortality. Measure of morbidity, morbidity surveys, issues and problems. Risk, cause and bias. Observational studies: retrospective, cross-sectional and prospective studies. Reliability and Validity.

Diagnostic tests Definition, reliability, validity, sensitivity, specificity, predictive values, likelihood ratio test, selection and interpretation of diagnostic test. Deciding on the best therapy, ROC curves, multiple and parallel test. Screening for disease, critical appraisal, meta- analysis.

Genetic Epidemiology Basic concept of human genetics- Chromosomes-DNA-inheritance in families, Modes and types of Pedigree diagram, their analysis-Genetic of common disorders – single gene and polygenic inheritance- Randomly mating population-Hardy Weinberg Equilibrium and its application- Non-random matting and other violation of Hardy-Weinberg law - Inbreeding and its affects - Computation of Wright's confection F and other inbreeding coefficients Selection - Mutations – Segregation analysis – Twin studies Genetic demography – Genetic epidemiology – models of multi factorial inheritance and path analysis applied to Quantitative traits.

Design of Experiments (40%)

Design, Replication, Randamization, Assignable cause, Chance causes, Analysis of CRD, RBD and LSD. Missing values in RBD, CRD and LSD. Design of clinical trials, Single and double blind trials. Type of control, Design of studies with matched controls.

Setting up of experiment with the following designs and their analysis:

Factorial Design – 2^n, 3^2, 2x3x4, Confounding in factorial designs, total and partial confounding. Balanced lattice design, Connected balanced design, Cross-over design, Orthogonal Latin square, Balanced Incomplete Block design(BIBD), Split plot design, Analysis of Covariance .

Books for study and reference:

1. Lilienfeld AM and Lilienfeld DC, Foundations of epidemiology, 1980, Oxford University Press.

2. Gordis L, Epidemiology, 2004, Elsevier Saunders.

3. Montgomery DC, Design and Analysis of Experiments, 1984, John Wiley & Sons, Inc.

4. Das MN and Giri NC, Design and Analysis of clinical Experiments, 1979, Wiley
Eastern Ltd.

5. Haynes RB, Sackett DL, Guyatt GH and Tugwell P. Clinical Epideomiology: How to do Clinical Practice Research, 2006, Lippincot Williams & Wilkins.

6. Fletcher RH, Fletcher SW and Wagner EH. Clinical Epidemiology: The Essentials, 2nd edition, 1982

7. Thompson JS and Thompson MW. Genetics in Medicine, 1986, Icaku-Shoin Saunders International Edition, 4th edition.

Paper III : Statistical Inference, Sampling Methods and sample size

Statistical Inference (50%)

Estimation Theory: (25%)

Properties of point estimators, Minimum variance unbiased estimator, Best linear unbiased estimator, Interval estimation. Confidence interval for mean, variance of normal distribution, Proportions, Correlation and Regression coefficients. Confidence interval of mean and variance for small samples.

Illustration of Cramer-Rao inequality,Bhatacharya inequality, Rao-Blackwell inequality, Maximum likelihood estimators, Method of moments, Method of minimum Variance, Method of chi-square, Method of modified minimum chi-square, Method of least squares.

Testing of Statistical Hypothesis: (25%)

Critical region and level of significance, Test of a simple hypothesis against simple alternative, composite hypothesis, Neymen Pearson test of hypothesis, UMP test, UMP unbiased test, Likelihood ratio test, Test on the mean of normal population, Difference between the mean of two normal populations, Test on the variance of normal populations, χ^2 test, χ^2 goodness of fit test and test of independence of contingency tables. Test of proportion, Test of correlation and regression coefficient, Trends of proportion, Test based on t and f, Multiple comparisons.

Sequential Analysis and Sequential probability ratio test Non-parametric tests-Wilcoxon Mann Whitney, Kolmogorov Smirnov tests (two sample tests). Quantile tests, multiple range test.

Sampling Theory (50%)

Definitions, Sample, Sampling – advantages of sample studies. Types of samples – The convenience sample – Judgment sample and the probability sample –Simple random sampling with and without replacement – Systematic sampling –Stratified sampling- Estimation of mean, Proportion and standard error using the above probability sampling– Sources of error in surveys.

Estimation of mean proportion and standard error in Cluster Sampling, Multistage and multiphase Sampling, Ratio estimate, Regression estimate, Quota Sampling for proportions, Double Sampling, Interpenetrating subspace.
Estimation of sample size for clinical experiments

Books for study and reference:

1. Casella G and Berger RL, Statistical Inference 2nd edition, 2002, Duxbury

2. Hogg RV and Craig AT, Introduction to Mathematical Statistics,5th ed., 1995, Pearson Education Publishing Co., Inc.

3. Rohatgi VK and Md.Ehsanes saleh AK, An Introduction to Probability & Statistics, 2009, Wiley India.

4. Siegel S and Castellan NJ. Non-parametric Statistics for the Behavioral Sciences, 1988, McGraw-hill book company.

5. Sharon. L. Lohr, Sampling Design and Analysis, 1999, Duxbury Press.

6. Kish L, Survey Sampling, 1995, John Wiley & Sons,inc.

7. Levy PS and Lemeshow S, Sampling of Populations: Methods & Applications,1991, John Wiley & Sons.

8. Machin D, Campbell MJ, Fayers PM and Pinol APY. Sample Size Tables for Clinical Studies, 2nd edition, 1997, Blackwell science ltd.

9. Chow SC, Shao J and Wang H. Sample size calculations in clinical research, 2008, Chapman & Hall, CRC press.

Paper IV : Demography and Health Data Management

Demography (20%)

Introduction to demographic data: Census, vital events, registration, survey, extent of under registration. Chandrasekar Deming index. Mortality measurements: crude and specific rates, direct and indirect methods of standardization, Life tables – construction and uses, Abridged Life table – construction and uses, concept of model life table. Determination of mortality.

Population growth, Composition and Distribution: Population pyramid, Aging of population, Rejuvenation of population, Age ratios and Sex ratio, effect of fertility, mortality and migration on age structure.

Health Data Management

MS Excel (20%)

Introduction to MS Excel, creating a data file, data manipulations, simple statistical analysis using Excel, making graphs and charts.

Statistical package for Social Sciences (SPSS Version 16.0) (30%)

Data view and variable view, importing a file, Data transformations (compute, recode, count, If, yrmoda). Sort cases, merging and appending data, Frequencies, descriptive statistics, crosstabulations. Statistical analysis: independent samples 't' test, paired 't' test, ANOVA, chi square, Fisher's exact test, McNemar chi-square test, correlation and regression. Non-parametric methods: Mann Whitney U test, Wilcoxon Signed rank test, Spearman's correlation.

Statistical Analysis System (SAS 9.0) (30%)

Data Input and Output. Data manipulation commands. Date functions. Frequencies, descriptive statistics, crosstabulations. Statistical analysis: independent samples 't' test, paired 't' test, ANOVA, chi square, Fisher's exact test, McNemar chi-square test, correlation and regression. Non-parametric methods: Mann Whitney U test, Wilcoxon Signed rank test, Spearman's correlation.

Macro writing. Running Query Language.

PRACTICALS : 1 (100%)

Distributions: Fitting of binomial, Poisson, Normal, negative binomial, hypergeometric, lognormal distributions.

Statistical inference: Critical regions and power curves concerning testing of hypothesis on the parameters of binomial and normal distributions(one and two sided), test for correlation coefficient, test for trends of proportion, multiple comparison test, chi-square test of independence and goodness of fit, test for homogeneity, fisher's exact test, Sequential Probability ratio tests for parameters of binomial, poisson and exponential distributions.

Design of experiments: Analysis of variance- Two way classification, missing plot technique, RBD, LSD, mixed up plots technique, interaction model, unequalcell frequency, factorial experiment 2^3, 3^2,and 2x3x4 types. Confounding (partial/full), split plot design, BIBD.

Epidemiology: Analysis of 2x2 tables for relative risk and odds ratio, Mantel-Haenszel test, Constrution of ROC curve.

Second Year

Paper V : Applied Regression Methods

Regression Analysis – Multiple, Logistic Regression Analyses, Diagnostics, and Generalized Linear Models: (40%)

Multiple regression: Continuous variables, dummy variables, residual analysis, multicollinearity.

Introduction, model fitting, Logistic Regression analysis: Conditional and Unconditional models, Estimating Odds Ratio- Interpretation of the results. Logistic Regression for Ordinal, Polytomous data. Count data and Poisson regression

Categorical Data Analysis (30%)

Sampling distribution for discrete data. Analysis of contingency tables: Hypothesis of homogeneity and Independence. Measure of association: relative risk, odds ratio and confidence interval. Mantel-Haenszel procedures. Measure of agreement: Kappa and weighted Kappa. Loglinear models for two and three way tables. Collapsibility and model building. Logistic regression: conditional and unconditional probability models for binary variable. Logistic regression for ordinal, polytomous data (concepts only).

Survival Analysis (30%)

Survival and hazard functions. Types of censoring. Kaplan-Meier estimates, log-rank and generalized Wilcoxon test for censored and uncensored data. Parametric distribution: exponential and Weibull, Cox's proportional hazard model, time dependent covariate, log (log (survival)) plot and stratified analysis.

Books for study and reference

1. Draper NR and Smith H, Applied Regression Analysis, 1981, John Wiley & Sons.

2. Jobson JD, Applied Multivariate Data Analysis Vol 1. Regression & Experimental, 1991, Springer Verlag.

3. Hosmer DW and Lemeshow S, Applied Logistic Regression, 1989, Wiley John & Sons.

4. Clayton D and Hills M, Statistical Models in Epidemiology, 2001, Oxford University Press.

5. Flesis JL. Statistical Methods For Rates and Proportions, 1981, John Wiley & Sons.

6. Agresti A, Categorical Data Analysis, 1990, John Wiley & Sons.

7. Kleinbaum DG, Kupper LL and Morgenstern H, Epidemiologic Research, 1982, Van Nostrand Reinhold Co. Ltd.

8. Hosmer DW and Lemeshow S, Applied Logistic Regression, 1989, Wiley John & Sons.

9. Collett D, Modelling Survival Data in Medical Research, 1997, Chapman & Hall.

10. Cox DR and Oakes D, Analysis of Survival data, 1984, Chapman & Hall.

11. Lee ET, Statistical Methods for Survival Data Analysis, 1992, John Wiley & Sons.

12. Hosmer DW and Lemeshow S, Applied Survival Analysis: Regression Modeling of Time to Event Data, 1999, John Wiley & sons.

13. Kleinbaum DG and Klein M. Survival Analysis: A self-learning text, 2nd edition, 2005, Springer science & business media Inc.

Paper VI : Applied Multivariate and Time Series Analysis

Applied Multivariate Methods (50%)

Multiple Classification analysis, Discriminant analysis, Path analysis, Principal component analysis, Factor analysis and Cluster analysis.

Time Series Analysis (50%)

Application of time series analysis in epidemiology- Simple descriptive techniques for detecting seasonal, cyclical, secular and random variations- Transformations- Trend analysis-Auto correlation-Forecasting spectral analysis.

Books for study and reference

1. Johnson RA and Wichern DW, Applied Multivariate Statistical Analysis, 1984, John Wiley & sons.

2. Chatfield C. and Collins AJ. Introduction to Multivariate Analysis., 1980, Chapman & Hall.

3. Anderson TW. An Introduction to Multivariate Statistical Analysis, 1984, John Wiley & Sons

4. Seber, GAF, Multivariate Observations, 2004, Wiley series in probability and statistics.

5. Diggle PJ. , Time Series: A Biostatistical Introduction, 1990, Clarendon Press, Oxford.

6. Chatfield C., The Analysis of Time Series – An Introduction, 1989, Chapman & Hall.

Paper VII : Clinical Trials and its management (100%)

Clinical trials. Method of randomization, Ethical issues, Crossover trials. Factorial design. Sequential and group sequential trials. Interim analysis, multiple testing and stopping rules. Equivalence trials. Meta Analysis. Trial and data management principles. Data safety monitoring board: concepts and management.

Books for study and reference

1. Friedman LM, Furberg CD and DeMets DL. Fundamentals of Clinical Trials, 3rd edition, 1998, Springer-Verlag, NY, Inc.

2 Cook TD and DeMets DL, Introduction to Statistical Methods for Clinical Trials, 2008, Chapman & Hall CRC press.

3. Piantadosi S. Clinical Trials: A methodological perspective, 2nd edition, 2005, John Wiley & Sons, Inc.

4. Susan S. Ellenberg, Thomas RF and DeMets DL. Data Monitoring committees in Clinical Trials: A practical perspective, John Wiley & Sons, Inc.

Practicals II : Health Data Analyses using SPSS (100%)

Analyses of data which need multiple regression, Logistic regression (bivariate and Ordinal) analyses, Poisson regression. Sample size calculation based on stopping rules in Non-inferiority trials. Meta Analyses using REVMAN software. Time Series analysis

Dissertation and viva voce