

# **BIOSTATISTICS**

## **AND RESEARCH METHODOLOGY**



**Ms. Safina I. Mulla  
Mrs. Kajal M. Chougule  
Mrs. Swatikumari S. Mahadik  
Ms. Triveni S. Patil**

**Kripa Drishti Publications, Pune.**

# **BIOSTATISTICS AND RESEARCH METHODOLOGY**

**Ms. Safina I. Mulla**

Assistant Professor,

Women's College of Pharmacy,

Peth-Vadgaon, Kolhapur.

**Mrs. Kajal M. Chougule**

Lecturer,

Ashokrao Mane Institute of Pharmacy,

Vathar tarf Vadgaon, Kolhapur.

**Mrs. Swatikumari S. Mahadik**

Lecturer,

Ashokrao Mane Institute of Pharmacy,

Vathar tarf Vadgaon.

**Ms. Triveni S. Patil**

M.Pharm (Pharmaceutics)

Bharti Vidyapeeth Poona College of Pharmacy,

Pune.

**Kripa-Drishti Publications, Pune.**

**Book Title:** **Biostatistics and Research Methodology**

**Authored By:** **Ms. Safina I. Mulla, Mrs. Kajal M. Chougule,  
Mrs. Swatikumari S. Mahadik,  
Ms. Triveni S. Patil**

**Price:** ₹625

1<sup>st</sup> Edition

**ISBN:** **978-81-19149-84-1**



9 788119 149841

**Published:** Nov 2023

**Publisher:**



**Kripa-Drishti Publications**

A/ 503, Poorva Height, SNO 148/1A/1/1A,  
Sus Road, Pashan- 411021, Pune, Maharashtra, India.  
Mob: +91-8007068686  
Email: [editor@kdpublications.in](mailto:editor@kdpublications.in)  
Web: <https://www.kdpublications.in>

© Copyright Ms. Safina I. Mulla, Mrs. Kajal M. Chougule, Mrs. Swatikumari S. Mahadik,  
Ms. Triveni S. Patil

All Rights Reserved. No part of this publication can be stored in any retrieval system or reproduced in any form or by any means without the prior written permission of the publisher. Any person who does any unauthorized act in relation to this publication may be liable to criminal prosecution and civil claims for damages. [The responsibility for the facts stated, conclusions reached, etc., is entirely that of the author. The publisher is not responsible for them, whatsoever.]

## **PREFACE**

This book describes the concepts, principles, methodology, and applications of research methodologies and biostatistics as prescribed by various Universities and the Pharmacy Council of India (PCI) for the subject "**BIOSTATISTICS AND RESEARCH METHODOLOGY**" of the B.Pharm., M.Pharm., and Ph.D. programmes.

Biostatistics is a relatively new but rapidly expanding scientific field with numerous applications in pharmacy and pharmaceutical research. Pharmacy is a research-based profession. Knowledge of basic research concepts, research methodologies, experimental designs and protocols, and data analysis resulting in good and meaningful interpretation are all required for successful pharmacy research.

The subject is presented modulated and graded, beginning with basic concepts and gradually progressing from simple to advanced topics, allowing students to progress smoothly, easily, and comfortably. The textbook is unique in that it includes a number of solved problems and case studies at the end of each topic. Experiment designs and protocols for human and animal studies, design of experiments (DOE), tests of significance including non-parametric tests, analysis of variance (ANOVA), optimisation techniques, factorial experiments and optimisation by factorial designs, correlation and regression, probit analysis, and LD<sub>50</sub> and ED<sub>50</sub> determination are all covered in detail. There is also a chapter on patentable research in pharmacy and patenting procedures with examples.

## **Abbreviations**

Analysis of Variance (ANOVA)

Clinical Research Unit (CR0U)

Code of Federal Regulations (CFR)

Design of Experiments (DOE)

Federal Aviation Administration (FAA)

Good Clinical Practice (GCP)

Java Virtual Machine (JVM)

Key Performance Indicators (KPIs)

National Cancer Institute (NCI)

National Institutes of Health (NIH)

One Factor at A Time (OFAT)

Ordinary Least Squares (OLS)

Pharmaco Dynamics (PD)

Pharmaco Kinetics (PK)

Software Development Life Cycle (SDLC)

Statistical Package Social Sciences (SPSS)

United States Food and Drug Administration's (USFDA)

# INDEX

<b>Unit 1 .....</b>	<b>1</b>
1.1 Introduction:.....	1
1.1.1 Statistics Fundamentals: .....	2
1.1.2 Statistics in Mathematics:.....	2
1.2 Biostatistics:.....	2
1.2.1 Classification of Biostatistics: .....	4
1.2.2 Frequency Distribution:.....	5
1.3 Measures of Central Tendency: .....	6
1.4 Mean: .....	7
1.4.1 Limitations of the Mean: .....	7
1.5 Median: .....	9
1.6 Mode:.....	10
1.6.1 Limitations of the Mode: .....	11
1.7 Pharmaceutical Example: .....	12
1.8 Measures of Dispersion: .....	13
1.8.1 Dispersion:.....	13
1.8.2 Measures of Statistical Dispersion:.....	13
1.8.3 Nature of Measures of Dispersion: .....	14
1.8.4 Types of Measures of Dispersion: .....	14
1.9 Correlation: .....	19
1.9.1 Measures of Correlation: .....	20
1.9.2 Correlation Coefficient:.....	20
<b>Unit 2 .....</b>	<b>25</b>
2.1 Regression:.....	25
2.1.1 Calculating Regression:.....	25
2.1.2 Multiple Linear Regression: .....	26
2.1.3 Curve Fitting and Method of Least Squares: .....	26
2.1.4 Properties of Linear Regression:.....	28
2.1.5 Regression Coefficient: .....	28
2.1.6 Regression Line Formula: .....	30
2.2 Multiple Regression: .....	32
2.2.1 Multiple Regression Equation: .....	32
2.2.2 Standard Error of Regression: .....	34
2.3 Probability:.....	37
2.3.1 Terms Related to Probability:.....	38
2.3.2 Calculating Probability:.....	40
2.3.3 Probability Tree Diagram: .....	41

2.4 Binomial Distribution: .....	41
2.5 Normal Distribution:.....	44
2.5.1 Basic Examples of Normal Distribution: Height and Weight: .....	45
2.5.2 Importance of Normal Distribution:.....	46
2.5.3 Parameters of Normal Distribution: .....	47
2.5.4 Skewness and Kurtosis in a Normal Distribution: .....	48
2.6 Poisson Distribution: .....	48
2.6.1 Poisson Distribution Formula: .....	49
2.6.2 Poisson Distribution Mean and Variance: .....	50
2.6.3 Properties of Poisson distribution: .....	50
2.6.4 Poisson Distribution Table: .....	50
2.7 Population and Sample in Statistics: .....	52
2.7.1 Sample: .....	52
2.7.2 Population and Sample Formula:.....	54
2.8 Null Hypothesis: .....	56
2.8.1 Alternative Hypothesis: .....	58
2.8.2 Alternative Hypothesis Symbol: .....	59
2.9 Sampling: .....	59
2.9.1 Types of Sampling Methods:.....	59
2.9.2 Type I and Type II Errors: .....	62
2.10 Standard Error of Mean (SEM): .....	65
2.11 Parametric Test:.....	68
2.12 T-Test:.....	70
2.12.1 T-Test Formula: .....	71
2.12.2 T-Test Example:.....	72
2.13 ANOVA: .....	75
2.13.1 One-way ANOVA:.....	76
2.13.2 Two-Way ANOVA: .....	76
2.13.3 Least Significance Difference:.....	76

### **Unit 3.....**

3.1 Non-Parametric Test:.....	80
3.1.1 Non-Parametric Paired T-Test: .....	80
3.1.2 Non-parametric Test Methods: .....	80
3.1.3 Non-parametric Test Formula:.....	81
3.1.4 Advantages and Disadvantages of Non-Parametric Test: .....	81
3.1.5 Applications of Non-Parametric Test:.....	81
3.1.6 Types of Non-parametric Test: .....	81
3.2 Wilcoxon Rank Sum Test: .....	82
3.3 Mann-Whitney U Test: .....	84
3.3.1 Assumptions of the Mann-Whitney: .....	84
3.3.2 Procedure to conduct Mann-Whitney Test:.....	84
3.4 Kruskal-Wallis Test: .....	87
3.5 Friedman Test:.....	89
3.6 Introduction to Research:.....	93

3.7 Need for Research: .....	94
3.8 Need for Design of Experiments:.....	95
3.8.1 Types of Experimental Designs:.....	96
3.9 Quasi-Experimental Design: .....	96
3.10 Randomized Block Design: .....	97
3.11 Plagiarism: .....	97
3.12 Graphs:.....	99
3.12.1 Types of Graphs in Statistics:.....	100
3.13 Designing the Methodology:.....	110
3.13.1 Sample Size Determination and Power of a Study: .....	111
3.14 Report Writing and Presentation of Data:.....	115
3.14.1 Report Writing: .....	115
3.15 Presentation of Data: .....	117
3.15.1 Types of Data Presentation:.....	117
3.16 Protocol:.....	118
3.16.1 The Written Protocol:.....	119
3.16.2 Format for the protocol: .....	119
3.17 Cohort Study: .....	121
3.17.1 The Cohort at Baseline: .....	122
3.17.2 Advantages of a Cohort Study:.....	124
3.18 Observational Studies: .....	125
3.18.1 Observational Study Example: .....	126
3.19 Experimental Studies: .....	129
3.20 Observational Study vs. Experiment: .....	130
3.21 Designing Clinical Trial: .....	130
3.21.1 Designs: .....	130
3.22 Phases of Clinical Trials: .....	131
3.23 The Phase of the Study and Clinical Trial Designs:.....	132
<b>Unit 4 .....</b>	<b>136</b>

4.1 Introduction:.....	136
4.2 Blocking:.....	137
4.2.1 Confounding:.....	138
4.3 Regression Modeling:.....	143
4.3.1 Types of Regression:.....	143
4.4 Hypothesis Testing: .....	147
4.4.1 Procedure of Hypothesis Testing:.....	148
4.4.2 Types of Hypothesis Testing: .....	148
4.4.3 Hypothesis Test for Simple Linear Regression: .....	149
4.4.4 Research Hypotheses: .....	150
4.5 Multiple Regression Analysis: .....	151
4.6 Introduction to Practical Components of Industrials Clinical Trials Problems: .....	152
4.6.1 Clinical Trials: .....	152
4.7 Statistical Analysis Using Excel: .....	155

4.7.1 Pivot Tables: .....	155
4.7.2 Using Excel for Statistical Analysis: Descriptive Statistics: .....	156
4.7.3 Using Excel for Statistical Analysis: ANOVA (Analysis of Variance): .....	158
4.7.4 Using Excel for Statistical Analysis: Moving Average: .....	160
4.7.5 Using Excel for Statistical Analysis: Rank and Percentile:.....	160
4.7.6 Using Excel for Statistical Analysis: Regression: .....	161
4.7.7 Using Excel for Statistical Analysis: Random Number Generator: 162	
4.7.8 Using Excel for Statistical Analysis: Sampling: .....	165
4.7.9 Some Excel Worksheet Functions for Statistical Analysis: .....	166
4.7.10 Excel Array Functions for Statistical Analysis: .....	167
4.7.11 Excel Data Analysis Tools: .....	168
<b>4.8 Statistical Analysis Using SPSS:.....</b>	<b>169</b>
4.8.1 Features of SPSS:.....	169
4.8.2 Statistical Methods of SPSS: .....	171
4.8.3 Types of SPSS: .....	172
4.8.4 Data Manipulation:.....	173
4.8.5 SPSS Installation:.....	174
4.8.6 SPSS by Industry: Use Cases: .....	175
4.8.7 Advantages of Using SPSS:.....	176
<b>4.9 Statistical Analysis Using MINITAB:.....</b>	<b>177</b>
4.9.1 Minitab in Six Sigma: .....	178
4.9.2 Minitab's Uses Within the Industry: .....	178
4.9.3 There Are Eight Basic Vital Features of Minitab: .....	179
<b>4.10 Design of Experiments:.....</b>	<b>180</b>
4.10.1 Trial-And-Error Method: .....	182
4.10.2 One Factor at A Time (OFAT) Method: .....	183
<b>4.11 R-Online Statistical Software to Industrial and Clinical Trial Approach Notes:</b> .....	<b>186</b>
4.11.1 Reasons Why R Can Be a Potential Powerful Tool for Data Analysis: .....	187
4.11.2 R Packages for Clinical Trial Design, Monitoring, and Analysis: 188	
4.11.3 R Implementation in Pharma – Real-Time Examples:.....	188
4.11.4 R Validation Hub: Enabling Use of R in Regulatory Setting:.....	190
<b>Unit 5.....</b>	<b>192</b>
<b>5.1 Introduction: .....</b>	<b>192</b>
5.2 Two Factor Factorial Designs: .....	197
5.2.1 Advantages of Factorial Design:.....	200
5.3 Response Surface Methodology: .....	201
5.4 Approximate Model Function: .....	202
5.5 Central Composite Designs:.....	203
5.6 Historical Designs: .....	207
5.7 Optimization Techniques: .....	208
5.7.1 Complicating Factors in Optimization: .....	209

5.7.2 Constrained versus Unconstrained Optimization: .....	210
5.7.3 Techniques:.....	212
<b>References.....</b>	<b>213</b>

## ABOUT THE AUTHORS



**Ms. Safina I. Mulla**

She is presently working as a Assistant professor at Women's College of Pharmacy, Peth-Vadgaon, Kolhapur. She has completed B. Pharm from Gourishankar Institute of Pharmaceutical Education & Research, Satara (Shivaji University, Kolhapur) and M. Pharm in Pharmaceutics from Yashoda Technical Campus, Satara (Shivaji University Kolhapur). She is having more than 5 years of experience in academics. Her research interest in nanoparticles and hydrogels. She published review as well as research papers in various journals.



**Mrs. Kajal M. Chougule**

*She is presently working as a lecturer at Ashokrao Mane Institute of Pharmacy, Vathar tarf Vadgaon, Kolhapur. She has completed B. Pharm from Ashokrao Mane College of Pharmacy, Peth Vadgaon (Shivaji University, Kolhapur) and M. Pharm in Quality Assurance Technique from Ashokrao Mane College of Pharmacy, Peth Vadgaon (Shivaji University Kolhapur). She published review as well as research papers in various journals. She is having 5 years of experience in academics.*



**Mrs. Swatikumari S. Mahadik**

*She is presently working as a lecturer at Ashokrao Mane Institute of Pharmacy, Vathar tarf Vadgaon. She has completed her B pharm at Ashokrao Mane Institute of Pharmacy Peth Vadgaon (Shivaji University, Kolhapur). She is having 1 year experience in academics.*



**Ms. Triveni S. Patil**

*She has completed M. Pharm in Pharmaceutics from Bharati Vidyapeeth Poona College of Pharmacy, Pune (Savitribai Phule University, Pune) and did research article on polymer grafting method and their uses in floating drug delivery. She has completed B. Pharm in Bharati Vidyapeeth College of Pharmacy, Kolhapur (Shivaji University Kolhapur). She is having 1.5 years of experience in academics.*



Kripa-Drishti Publications

A-503 Poorva Heights, Pashan-Sus Road, Near Sai Chowk,  
Pune - 411021, Maharashtra, India.

Mob: +91 8007068686

Email: editor@kdpublications.in

Web: <https://www.kdpublications.in>

Price: ₹ 625

ISBN: 978-81-19149-84-1



9 788119 149841