6.1.5 Blinding and Masking 89
6.1.5.1 Blinding 89
6.1.5.2 Concealment of Allocation 89
6.1.5.3 Masking 90
6.2 Issues in Clinical Trials 90
6.2.1 Outcome Assessment 90
6.2.1.1 Specification of End Points or Outcome 90
6.2.1.2 Causal Inference 91
6.2.1.3 Side Effects 91
6.2.1.4 Effectiveness versus Efficacy 92
6.2.1.5 Pragmatic Trials 92
6.2.2 Various Equivalences in Clinical Trials 92
6.2.2.1 Superiority, Equivalence, and Noninferiority Trials 92
6.2.2.2 Therapeutic Equivalence and Bioequivalence 93
6.2.3 Designs for Clinical Trials 94
6.2.3.1 n-of-1, Up-and-Down, and Sequential Designs 94
6.2.3.2 Choosing a Design for a Clinical Trial 95
6.2.4 Designs with Interim Appraisals 95
6.2.4.1 Designs with Provision to Stop Early 96
6.2.4.2 Adaptive Designs 96
6.2.5 Biostatistical Ethics for Clinical Trials 97
6.2.5.1 Equipoise 97
6.2.5.2 Ethical Cautions 98
6.2.5.3 Statistical Considerations in a Multicentric Trial 98
6.2.5.4 Multiple Treatments with Different Outcomes in the Same Trial 98
6.2.5.5 Size of the Trial 99
6.2.5.6 Compliance 99
6.2.6 Reporting the Results of a Clinical Trial 99
6.2.6.1 CONSORT Statement 99
6.2.6.2 Registration of Trials and Open Access 100
6.3 Trials Other than for Therapeutics 101
6.3.1 Clinical Trials for Diagnostic and Prophylactic Modalities 101
6.3.1.1 Diagnostic Trials 101
6.3.1.2 Prophylactic Trials in Clinics 102
6.3.2 Field Trials for Screening, Prophylaxis, and Vaccines 102
6.3.2.1 Screening Trials 102
6.3.2.2 Prophylactic Trials in the Field 102
6.3.2.3 Vaccine Trials 103
6.3.3 Issues in Field Trials 103
6.3.3.1 Randomization and Blinding in Field Trials 103
6.3.3.2 Designs for Field Trials 104
References 104
Exercises 105

7. Numerical Methods for Representing Variation 107
7.1 Types of Measurement 107
7.1.1 Nominal, Metric, and Ordinal Scales 107
7.1.1.1 Nominal Scale 107
7.1.1.2 Metric Scale 108
7.1.1.3 Ordinal Scale 108
7.1.1.4 Grouping of a Metric Scale (Categorizing Continuous Measurements) 109
7.1.2 Other Classifications of the Types of Measurement 110
7.1.2.1 Discrete and Continuous Variables 110
7.1.2.2 Qualitative and Quantitative Data 111
7.1.2.3 Stochastic and Deterministic Variables 111

7.2 Tabular Presentation ... 111
7.2.1 Contingency Tables and Frequency Distribution ... 112
7.2.1.1 Empty Cells ... 113
7.2.1.2 Problems in Preparing a Contingency Table on Metric Data ... 113
7.2.1.3 Features of a Table ... 113
7.2.2 Other Types of Statistical Tables ... 114
7.2.2.1 Multiple Responses Tables ... 114
7.2.2.2 Statistical Tables ... 115
7.2.2.3 What Is a Good Statistical Table? ... 115
7.3 Rates and Ratios ... 115
7.3.1 Proportion, Rate, and Ratio ... 115
7.3.1.1 Proportion ... 116
7.3.1.2 Rate ... 116
7.3.1.3 Ratio ... 116
7.4 Central and Other Locations ... 117
7.4.1 Central Values: Mean, Median, and Mode ... 117
7.4.1.1 Understanding Mean, Median, and Mode ... 118
7.4.1.2 Calculation in the Case of Grouped Data ... 118
7.4.1.3 Which Central Value to Use? ... 120
7.4.1.4 Geometric Mean ... 121
7.4.1.5 Harmonic Mean ... 121
7.4.2 Other Locations: Quantiles ... 122
7.4.2.1 Quantiles in Ungrouped Data ... 123
7.4.2.2 Quantiles in Grouped Data ... 123
7.4.2.3 Interpretation of Quantiles ... 124
7.5 Measuring Variability ... 125
7.5.1 Variance and Standard Deviation ... 126
7.5.1.1 Variance and Standard Deviation in Ungrouped Data ... 126
7.5.1.2 Variance and Standard Deviation in Grouped Data ... 128
7.5.1.3 Variance of Sum or Difference of Two Measurements ... 128
7.5.1.4 Measuring Variation in Skewed and Nominal Data: Interquartile Range and Variation Ratio ... 128
7.5.2 Coefficient of Variation ... 129
References ... 131
Exercises ... 131

8. Presentation of Variation by Figures: Data Visualization ... 133
8.1 Graphs for Frequency Distribution ... 133
8.1.1 Histogram and Its Variants ... 134
8.1.1.1 Histogram ... 134
8.1.1.2 Stem-and-Leaf Plot ... 134
8.1.1.3 Line Histogram and Dot Plot ... 136
8.1.2 Polygon and Its Variants ... 136
8.1.2.1 Frequency Polygon ... 136
8.1.2.2 Area Diagram ... 136
8.1.3 Frequency Curve ... 136
8.2 Pie, Bar, and Line Diagrams ... 136
8.2.1 Pie Diagram ... 137
8.2.1.1 Useful Features of a Pie Diagram ... 138
8.2.1.2 Donut Diagram ... 138
8.2.2 Bar Diagram ... 138
8.2.3 Scatter and Line Diagrams ... 140
8.2.3.1 Scatter Diagram ... 140
8.2.3.2 Bubble Chart ... 140
8.2.3.3 Line Diagram ... 142
8.2.3.4 Complex Line Diagram ... 142

8.2.4 Choice and Cautions in Visual Display of Data 143
8.2.5 Mixed and Three-Dimensional Diagrams 144
8.2.5.1 Mixed Diagram 144
8.2.5.2 Box-and-Whiskers Plot 144
8.2.5.3 Three-Dimensional Diagram 145
8.2.5.4 Biplot 146
8.2.5.5 Nomogram 146
8.3 Special Diagrams in Health and Medicine 146
8.3.1 Diagrams Used in Public Health 147
8.3.1.1 Epidemic Curve 148
8.3.1.2 Lexis Diagram 148
8.3.2 Diagrams Used in Individual Care and Research 148
8.3.2.1 Growth Chart 148
8.3.2.2 Partogram 150
8.3.2.3 Dendrogram 150
8.3.2.4 Radar Graph 150
8.4 Charts and Maps 152
8.4.1 Charts 152
8.4.1.1 Schematic Chart 152
8.4.1.2 Health Infographics 152
8.4.1.3 Pedigree Chart 153
8.4.2 Maps 154
8.4.2.1 Spot Map 154
8.4.2.2 Thematic Choroplethic Map 154
8.4.2.3 Cartogram 154
References 156
Exercises 156

9. Some Quantitative Aspects of Medicine 159
9.1 Some Epidemiological Measures of Health and Disease 159
9.1.1 Epidemiological Indicators of Neonatal Health 160
9.1.1.1 Birth Weight 160
9.1.1.2 Apgar Score 161
9.1.2 Epidemiological Indicators of Growth in Children 161
9.1.2.1 Weight-for-Age, Height-for-Age, and Weight-for-Height 161
9.1.2.2 Z-Scores and Percent of Median 162
9.1.2.3 T-Score 163
9.1.2.4 Growth Velocity 163
9.1.2.5 Skinfold Thickness 164
9.1.2.6 Other Indicators of Growth 164
9.1.3 Epidemiological Indicators of Adolescent Health 164
9.1.3.1 Growth in Height and Weight in Adolescence 164
9.1.3.2 Sexual Maturity Rating 165
9.1.4 Epidemiological Indicators of Adult Health 165
9.1.4.1 Obesity 165
9.1.4.2 Smoking 166
9.1.4.3 Physiological Functions 168
9.1.4.4 Quality of Life 168
9.1.5 Epidemiological Indicators of Geriatric Health 169
9.1.5.1 Activities of Daily Living 169
9.1.5.2 Mental Health of the Elderly 169
9.2 Reference Values 169
9.2.1 Gaussian and Other Distributions 169
9.2.1.1 Properties of a Gaussian Distribution 170
9.2.1.2 Other Distributions 171

9.2.1.3 Checking Gaussianity: Simple but Approximate Methods 172
9.2.2 Reference or Normal Values 174
9.2.2.1 Implications of Normal Values 174
9.2.3 Normal Range 175
9.2.3.1 Disease Threshold 175
9.2.3.2 Clinical Threshold 175
9.2.3.3 Statistical Threshold 176
9.3 Measurement of Uncertainty: Probability 177
9.3.1 Elementary Laws of Probability 177
9.3.1.1 Law of Multiplication 178
9.3.1.2 Law of Addition 178
9.3.2 Probability in Clinical Assessments 179
9.3.2.1 Probabilities in Diagnosis 179
9.3.2.2 Forwarding Diagnosis 180
9.3.2.3 Assessment of Prognosis 180
9.3.2.4 Choice of Treatment 181
9.3.3 Further on Diagnosis: Bayes' Rule 181
9.3.3.1 Bayes' Rule 181
9.3.3.2 Extension of Bayes' Rule 182
9.4 Validity of Medical Tests 183
9.4.1 Sensitivity and Specificity 184
9.4.1.1 Features of Sensitivity and Specificity 185
9.4.1.2 Likelihood Ratio 186
9.4.2 Predictivities 186
9.4.2.1 Positive and Negative Predictivity 186
9.4.2.2 Predictivity and Prevalence 187
9.4.2.3 Meaning of Prevalence for Predictivity 188
9.4.2.4 Features of Positive and Negative Predictivities 189
9.4.3 Combination of Tests 190
9.4.3.1 Tests in Series 190
9.4.3.2 Tests in Parallel 190
9.4.4 Gains from a Test 191
9.4.4.1 When Can a Test Be Avoided? 192
9.5 Search for the Best Threshold of a Continuous Test: ROC Curve 192
9.5.1 Sensitivity–Specificity-Based ROC Curve 192
9.5.1.1 Methods to Find the Optimal Threshold Point 194
9.5.1.2 Area under the ROC Curve 195
9.5.2 Predictivity-Based ROC Curve 197
References 198
Exercises 199

10. Clinimetrics and Evidence-Based Medicine 203
10.1 Indicators, Indices, and Scores 203
10.1.1 Indicators 203
10.1.1.1 Merits and Demerits of Indicators 203
10.1.1.2 Choice of Indicators 204
10.1.2 Indices 204
10.1.3 Scores 204
10.1.3.1 Scoring System for Diagnosis 205
10.1.3.2 Scoring for Gradation of Severity 206
10.1.3.3 APACHE Scores 207
10.2 Clinimetrics 208
10.2.1 Method of Scoring 208
10.2.1.1 Method of Scoring for Graded Characteristics 208
10.2.1.2 Method of Scoring for Diagnosis 209