CONTENTS

PREFA	ACE TO THE THIRD EDITION	vi
ACKN	OWLEDGMENTS	ix
СНАР	TER 1. THE SCIENTIFIC METHOD	1
1.1		1
	Variability of Phenomena Requires Statistical Analysis	6
1.3	· · · · · · · · · · · · · · · · · · ·	Ü
1.0	of the Scientific Method	7
14	Design of Studies	8
	How to Quantify Variables	10
	The Null Hypothesis	11
	Why Do We Test the Null Hypothesis?	12
	Types of Errors	14
1.9	• •	15
	Consequences of Type I and Type II Errors	16
CHAP	TER 2. A LITTLE BIT OF PROBABILITY	19
2.1	What Is Probability?	19
	Combining Probabilities	20
	Conditional Probability	23
2.4	Bayesian Probability	24
2.5	Odds and Probability	25
2.6	Likelihood Ratio	26
2.7	Summary of Probability	27
СНАР	TER 3. MOSTLY ABOUT STATISTICS	29
	Chi-Square for 2×2 Tables	29
	McNemar Test	34
3.3	Kappa	35

••	_
X11	Contents

3.4	Description of a Population: Use of the Standard	
	Deviation	36
3.5	Meaning of the Standard Deviation: The Normal	
	Distribution	40
3.6	The Difference Between Standard Deviation and	
	Standard Error	42
3.7	Standard Error of the Difference Between Two Means	46
3.8	Z Scores and the Standardized Normal Distribution	47
3.9	The t Statistic	51
3.10	Sample Values and Population Values Revisited	52
	A Question of Confidence	53
3.12	Confidence Limits and Confidence Intervals	55
3.13	Degrees of Freedom	56
3.14	Confidence Intervals for Proportions	57
3.15	Confidence Intervals Around the Difference Between	
	Two Means	58
3.16	Comparisons Between Two Groups	60
3.17	Z-Test for Comparing Two Proportions	60
3.18	t-Test for the Difference Between Means of Two	
	Independent Groups: Principles	62
3.19	How to Do a t-Test: An Example	64
3.20	Matched Pair t-Test	66
3.21	When Not to Do a Lot of t-Tests: The Problem of	
	Multiple Tests of Significance	67
3.22	Analysis of Variance: Comparison Among Several	
	Groups	69
3.23	Principles	69
3.24	Bonferroni Procedure: An Approach to Making	
	Multiple Comparisons	72
3.25	Analysis of Variance When There Are Two Independent	
	Variables: The Two-Factor ANOVA	74
3.26	Interaction Between Two Independent Variables	75
3.27	Example of a Two-Way ANOVA	76
	Kruskal-Wallis Test to Compare Several Groups	77
	Association and Causation: The Correlation Coefficient	78
3.30	How High Is High?	79

Contents	xiii
3.31 Causal Pathways	79
3.32 Regression	82
3.33 The Connection Between Linear Regression and the	
Correlation Coefficient	84
3.34 Multiple Linear Regression	84
3.35 Summary So Far	86
CHAPTER 4. MOSTLY ABOUT EPIDEMIOLOGY	87
4.1 The Uses of Epidemiology	87
4.2 Some Epidemiologic Concepts: Mortality Rates	88
4.3 Age-Adjusted Rates	90
4.4 Incidence and Prevalence Rates	92
4.5 Standardized Mortality Ratio	94
4.6 Person-Years of Observation	94
4.7 Dependent and Independent Variables	96
4.8 Types of Studies	96
4.9 Cross-Sectional Versus Longitudinal Looks at Data	97
4.10 Measures of Relative Risk: Inferences From	
Prospective Studies: the Framingham Study	101
4.11 Calculation of Relative Risk from Prospective Studies	103
4.12 Odds Ratio: Estimate of Relative Risk from	
Case-Control Studies	104
4.13 Attributable Risk	107
4.14 Response Bias	109
4.15 Confounding Variables	111
4.16 Matching	112
4.17 Multiple Logistic Regression	113
4.18 Confounding By Indication	116
4.19 Survival Analysis: Life Table Methods	117
4.20 Cox Proportional Hazards Model	120
4.21 Selecting Variables For Multivariate Models	122
4.22 Interactions: Additive and Multiplicative Models	124
Summary:	127

•	
XIV	Contents

CHAPTER 5. MOSTLY ABOUT SCREENING 5.1 Sensitivity, Specificity, and Related Concepts 5.2 Cutoff Point and Its Effects on Sensitivity and Specificity	129 129 136
CHAPTER 6. MOSTLY ABOUT CLINICAL TRIALS 6.1 Features of Randomized Clinical Trials 6.2 Purposes of Randomization 6.3 How to Perform Randomized Assignment 6.4 Two-Tailed Tests Versus One-Tailed Test 6.5 Clinical Trial as "Gold Standard" 6.6 Regression Toward the Mean 6.7 Intention-to-Treat Analysis 6.8 How Large Should the Clinical Trial Be? 6.9 What Is Involved in Sample Size Calculation? 6.10 How to Calculate Sample Size for the Difference Between Two Proportions	141 141 143 144 145 146 147 150 151 153
6.11 How to Calculate Sample Size for Testing the Difference Between Two Means	158
CHAPTER 7. MOSTLY ABOUT QUALITY OF LIFE 7.1 Scale Construction 7.2 Reliability 7.3 Validity 7.4 Responsiveness 7.5 Some Potential Pitfalls	161 162 162 164 165 167
CHAPTER 8. MOSTLY ABOUT GENETIC EPIDEMIOLOGY 8.1 A New Scientific Era 8.2 Overview of Genetic Epidemiology 8.3 Twin Studies 8.4 Linkage and Association Studies 8.5 LOD Score: Linkage Statistic 8.6 Association Studies 8.7 Transmission Disequilibrium Tests (TDT) 8.8 Some Additional Concepts and Complexities of Genetic Studies	171 171 172 173 175 178 179 181

Contents	XV
CHAPTER 9. RESEARCH ETHICS AND STATISTICS	189
9.1 What does statistics have to do with it?	189
9.2 Protection of Human Research Subjects	190
9.3 Informed Consent	192
9.4 Equipoise	194
9.5 Research Integrity	194
9.6 Authorship policies	195
9.7 Data and Safety Monitoring Boards	196
9.8 Summary	196
Postscript A FEW PARTING COMMENTS ON THE IMPACT OF EPIDEMIOLOGY ON HUMAN	
LIVES	197
Appendix A. CRITICAL VALUES OF CHI-SQUARE, Z, AND t	199
Appendix B. FISHER'S EXACT TEST	201
Appendix C. KRUSKAL-WALLIS NONPARAMETRIC TEST TO COMPARE SEVERAL GROUPS	203
Appendix D. HOW TO CALCULATE A CORRELATION COEFFICIENT	205
Appendix E. AGE-ADJUSTMENT	207
Appendix F. CONFIDENCE LIMITS ON ODDS RATIOS	211
Appendix G. "J" OR "U" SHAPED RELATIONSHIP BETWEEN TWO VARIABLES	213
Appendix H. DETERMINING APPROPRIATENESS OF CHANGE SCORES	217
Appendix I. GENETIC PRINCIPLES	221

xvi	Contents	
REFERENCES		227
SUGGESTED READING	S	233
INDEX		237