

Table of Contents

1 Factorial Randomized Trials	1	Web-Based Adjudication	37
Summary	1	Conclusion	37
Introduction	1		
Randomized Clinical Trial Design Strategies with Multiple Interventions	2	7 Subgroup Analyses	39
Selecting a Factorial Randomized Design	3	Summary	39
Conclusion	6	Introduction	39
		Subgroup Analysis Defined	39
2 Expertise-Based Randomized Trials	8	Design of a Subgroup Analysis	39
Summary	8	Reporting	41
Introduction	8	Interpretation	41
Conventional RCT Design	8	Conclusion	42
Expertise-Based RCT Design	9		
Challenges of Expertise-Based RCTs	11	8 Trial Management— Advanced Concepts and Systems	44
Independent Assessor	11	Summary	44
Balanced and Consecutive or Random Contributions to Screening Pool	11	Introduction	44
Perceived Equivalence between Practices	12	Phases of Clinical Trials	44
Conclusion	12	Common Considerations in Conducting a Clinical Trial	45
		Trial Committees	48
3 Randomization Systems and Technology	14	The Search for Funding	49
Summary	14	Conclusion	50
Introduction	14		
Methods of Patient Allocation	15	9 Case–Control Studies	52
Other considerations	18	Summary	52
Conclusion	21	Introduction	52
		Definition of a Case–Control Study	52
4 Blinding and Concealment	23	Case–Control Methodology	53
Summary	23	Case–Control Studies within a Cohort Study	55
Introduction	23	Conclusion	56
Concealment	23		
Blinding	24	10 Cohort Studies	59
Conclusion	26	Summary	59
		Introduction	59
5 Composite Outcome in Orthopaedics: Understanding the Concepts	28	Cohort Studies in the Hierarchy of Evidence	60
Summary	28	Types of Cohort Study Designs	62
Introduction	28	Methods for Reducing Confounding and Assessing Causality	63
Rationale for Use of a Composite Outcome	29	A Checklist to Evaluate or Improve the Strength of Evidence	64
Limitations of Using Composite Outcomes	30	Conclusion	64
Guidelines for Creating a “Good” Composite Outcome	31		
Reporting and Interpreting Composite Outcomes	32	11 Survey Design	66
Conclusion	32	Summary	66
		Introduction	66
6 Adjudication of Outcomes— Systems and Approaches	34	Identifying a Research Question	67
Summary	34	Survey Development	67
Introduction	34	Survey Design	68
Importance of Adjudication	34	Using Existing Surveys	69
Process of Adjudication	35	Survey Validation	69
Existing Methods of Adjudication	37	Pilot Testing	70
		Survey Administration	70

Ethical Considerations	72	18 Uncovering Publication Bias	114
Financial Considerations	72	Summary	114
Conclusion	73	Introduction	114
12 Qualitative Studies	75	Authors and Publication Bias	115
Summary	75	Detecting and Adjusting for Publication Bias	115
Introduction	75	Minimizing the Effect of Publication Bias	116
What Is Qualitative Research?	75	A Possible Solution: Trial Registers	116
How Is Qualitative Research Done?	77	Conclusion	117
Conclusion	80	19 Statistical Pooling—Programs and Systems	118
13 Economic Analysis	82	Summary	118
Summary	82	Introduction	118
Introduction	82	Selecting the Appropriate Programs and Systems: Factors to Consider	119
Theoretical Background	83	Review of Programs and Systems	120
Conducting Health Economics Studies	85	Types of Programs and Systems	120
Conclusion	89	Recommendations	123
14 Literature Searches	90	Conclusion	123
Summary	90	20 Meta-analysis of Observational Studies	126
Introduction	90	Summary	126
When to Conduct a Literature Search	91	Introduction	126
How to Conduct a Literature Search	91	The Observational Data Dilemma	126
Study Selection	92	Conclusion	130
Assessing Methodological Quality of Studies	93	21 Meta-regression	132
Data Extraction and Analysis	93	Summary	132
Conclusion	94	Introduction	132
15 Understanding Effect Sizes	95	Heterogeneity and Meta-regression	132
Summary	95	Meta-regression Mechanics	133
Introduction	95	Interpreting a Meta-regression	135
The <i>P</i> Value Does Not Assess the Magnitude of a Treatment Effect	95	Limitations of Meta-regression	137
The Challenge of Comparing Results Across Studies	96	Conclusion	137
Types of Effect Sizes	96	22 Preparing a Statistical Analysis Plan	139
Confidence Intervals for Effect Sizes	99	Summary	139
Use of Effect Size in Meta-analysis	99	Introduction	139
Conclusion	101	Data Management	139
16 Fixed Effects versus Random Effects	102	Statistical Procedures	139
Summary	102	Data Safety and Monitoring Board	140
Introduction	102	Sample Size	140
The Data Pool: Fixed Effects versus Random Effects	102	Interim Analysis	140
Deciding Which Model to Use	103	Reports to Investigators	141
Conclusion	105	Sensitivity Analysis	141
17 Heterogeneity	106	Tables for Presentation and Publication	141
Summary	106	Software	141
Introduction	106	Reporting Guidelines	141
Heterogeneity Defined	106	General Policies	142
Identifying Heterogeneity	107	Privacy Considerations	142
Dealing with Heterogeneity	107	Appendices	142
Conclusion	112	What Is in the Literature about SAP?	142
		Conclusion	142

23 Regression Analysis	144	28 Randomized Trials Reporting Checklists	183
Summary	144	Summary	183
Introduction	144	Introduction	183
Linear Regression	145	Consort Statement	184
Logistic Regression	147	Nonpharmacological Trials	188
Proportional Hazards Regression	149	NPT Extension to Consort Statement	190
Goodness of Fit	152	CLEAR NPT	191
Conclusion	152	Conclusion	191
24 Survival Analysis	153	29 Observational Studies Reporting Checklists	193
Summary	153	Summary	193
Introduction	153	Introduction	193
Documenting Time-to-Event (Survival) Data	154	Checklist for Observational Studies:	
The Rationale for Time-to-Event (Survival)		The STROBE Statement	194
Analysis	154	Guide to Investigators:	
Methods for Survival Analysis	155	How to Use the STROBE Statement	197
Comparing Groups	158	The STROBE Statement:	
Practical Considerations in the Design of		Explanations of Checklist Items	198
Time-to-Event Studies	160	Conclusion	200
Conclusion	161	30 Meta-analysis Reporting Checklists	202
25 Interim Analyses in Randomized Trials	162	Summary	202
Summary	162	Introduction	202
Introduction	162	Meta-analysis Reporting Checklists	202
Interim Analysis Defined	162	Conclusion	207
Design of an Interim Analysis	162	Resources and Contacts for Surgical Research	209
Data Monitoring Committees	165	Summary	209
Consequences of Stopping Early for Benefit	166	Introduction	209
Conclusion	167	Mentorship	209
26 Conflicts of Interest Reporting	168	Graduate Programs	209
Summary	168	Online Courses	210
Introduction	168	Textbooks and Journals	210
Legal Implications	169	Courses and Workshops	211
Types of Conflict of Interest	170	Contract Research Organizations	212
Who Should Disclose Conflicts of Interest?	170	Conclusion	213
When Must Conflicts of Interest Be Disclosed? . . .	170	Glossary of Terms	214
Guidelines and Recommendations		Index	222
for Disclosure	170		
Why Must Personal Financial Interests			
Be Disclosed?	170		
Alternatives to Disclosure Policies	171		
Conclusion	171		
27 Authorship—			
Modern Approaches and Reporting	173		
Summary	173		
Introduction	173		
Academic Stream	173		
Educational Stream	176		
Industrial Stream	178		
Popular Media Stream	180		
Conclusion	182		