
Table of Contents

Foreword	xxi
Preface	xxv
About the Editor-in-Chief	xxvii

Introduction	1
---------------------------	----------

*Quentin G. Eichbaum, MD, PhD, MPH, MFA, MMHC, MA, MSc, MMed,
FCAP, FASCP*

A Personal Journey	1
A Needed Resource	2
Scope and Structure	2
Conclusion	3
Reference	3

RESEARCH PREPARATION

*Section Editors: Quentin G. Eichbaum, MD, PhD, MPH, MFA, MMHC, MA, MSc, MMed,
FCAP, FASCP, and Bethany Brown, PhD, MSCS*

1. The Role of Philosophy and Theory in Research	5
---	----------

*Michelle P. Zeller, MD, MHPE, DRCPSC, FRCPC; Tara Minor, PhD, MAT,
MA; Kelly Holloway, MSc, PhD; and Quentin G. Eichbaum, MD, PhD, MPH,
MFA, MMHC, MA, MSc, MMed, FCAP, FASCP*

Learning Objectives	5
Overview	6
Ontology, Epistemology, and Philosophical Paradigms	6
Theories and Research	9
Research Methodologies, Designs, and Methods	10
Conclusions	11
References	13

2. Identifying Knowledge Gaps and Crafting Answerable Research Questions	15
---	-----------

*Bethany Brown, PhD, MSCS; Simon Stanworth, PhD, FRCPath; and
Carlos Villa, MD, PhD*

Introduction	16
Understanding the Research Landscape and Identifying Knowledge Gaps	17

Crafting Answerable Research Questions	18
Conclusions	20
References	21
3. Considerations for Selecting the Appropriate Research Design	23
<i>Bethany Brown, PhD, MSCS; Heather Pidcock, MD, MSCI, PhD; and Richard Cook, PhD</i>	
Introduction	24
Observational Studies in Transfusion Medicine	26
Experimental Study Designs	28
Qualitative Research Designs	30
Mixed-Methods Designs	30
Additional Methods	31
Levels of Evidence	31
Key Considerations in Selecting the Research Design	31
Strengths and Weaknesses of Different Study Designs	33
Conclusions	37
References	41
4. Using Available Evidence—Literature, Databases, and Theory	43
<i>Johnathan Mack, MD, MSc, FRCPC</i>	
Introduction	44
Defining Medical Evidence	44
Primary, Secondary, and Tertiary Sources	44
Importance of Using Available Evidence	45
Finding (Relevant) Medical Evidence	45
Formulating a Search Using Boolean Operators	46
Filtering and Appraising the Evidence	46
Peer-Reviewed vs Non-Peer-Reviewed Evidence	47
Hierarchy of Medical Evidence	47
Critical Appraisal	48
Summary	51
Online Resources	51
5. Choosing the Right Statistical Analysis Plan	53
<i>Richard J. Cook, PhD; Bethany L. Brown, PhD, MSCS; and Lily Zou, PhD(c)</i>	
Introduction	54
Statistical Methods for Continuous Outcomes	54
Analysis of Binary Responses	57
Considerations Regarding Correlated Responses	58
Event and Time Analyses	58
Topics in the Design and Analysis of Randomized Trials	60
Some Common Errors	61

Discussion	62
References	63
6. Writing and Publishing the Results of Research	65
<i>Jeffrey McCullough, MD, and Miquel Lozano, MD, PhD</i>	
Considerations for Getting Started	66
Steps in Manuscript Preparation	69
After Submission to a Journal	75
Acceptance for Publication	75
References	76
7. Principles of Building Effective and Diverse Research Teams	77
<i>Heather Pidcoke, MD, MSCI, PhD; Audra L. Taylor, MS, SBB(ASCP); Tina Ipe, MD, MPH; and Raquel R. Bunge, RN, BSN, CCRC</i>	
Learning Objectives	77
Introduction	78
Effectiveness in the Research Team	78
The Case for Diversity in the Research Team	80
Building an Effective and Diverse Team	82
Standards in Research Conduct and Staff Competency	84
Summary	88
References	88
8. Ethical Considerations for Designing Human Research in Transfusion Medicine	93
<i>Nicole Mozden Dungee, MS, CIP; Claire L. Barrett, MBChB, MMed, PG Dipl (Transfusion Medicine), FCP(SA); and Stephen Wagner, PhD</i>	
Learning Objectives	93
Overview	94
How Did We Get Here?	94
The Belmont Report	97
When Is Ethics Committee Review Required, and What Are the Criteria for Approval?	97
Differentiating Research from Practice	100
Informed Consent	100
Vulnerable Populations	108
Children in Research	109
Sound Research Design	110
Biobanks	110
Disseminating Research Results	111
Recruitment and Compensation	112
Role Duality and Therapeutic Misconception	113
Importance of Acknowledging Local Researchers	114
References	114

9. Community-Based Participatory Research Approaches 117

Jennie Haw, PhD; Hayley Evans, PhD, BSc (Hons); Aditi Khandelwal, MDCM, DRCPSC, MSc, BSc (Hons), FRCPC; and Shana D. Hughes, PhD, MPH

Overview 118
 Ethical Considerations 119
 Building Community Partnerships 121
 What to Consider When Conducting a CBPR Study 124
 Challenges and Tensions 126
 Conclusions 128
 References 129

OBSERVATIONAL STUDIES

Section Editors: Brian Custer, PhD, MPH, and Simon Stanworth, PhD, FRCPath

10. Introduction to Observational Studies 131

Le Thi Phuong Thao, PhD, and Zoe McQuilten, MD

Bias and Confounding in Observational Studies 134
 Statistical Strategies to Mitigate Bias 135
 Planning and Reporting Observational Studies 138
 Conclusion 138
 References 138

11. Cross-Sectional and Survey Studies 141

Richard R. Gammon, MD, and Bryan R. Spencer, PhD, MPH

Cross-Sectional Studies 141
 Survey Studies 147
 References 157
 Appendix 11-1. Example Article and Commentary 161

12. Case Series, Case-Control, and Cohort Studies 165

Suzanne F. Fustolo-Gunnink, MD, PhD

Introduction 165
 Case Reports 168
 Case-Control Studies 169
 Cohort Studies 172
 References 175
 Appendix 12-1. Example Article and Commentary 177

13. Performing Database-Driven Transfusion Research Using Electronic Health Records181

Shebaryar Raza, MD, FRCPC; Matthew Karafin, MD, MS; and Ruchika Goel, MD, MPH, CABP

Introduction 181

Description of the Design 182

Data Sampling and Collection 184

Steps and Considerations in Using the Design 185

Data Analysis 188

Database Architecture: The REDS-IV-P Study 189

Strengths and Weaknesses of the Design 191

Conclusions 193

References 193

Appendix 13-1. Example Article and Commentary 195

14. Genotype-Phenotype Studies in Transfusion Medicine197

Celina Montemayor, MD, PhD, and Margaret A. Keller, PhD

Introduction 197

Case or Family Studies 198

Phenotype-Driven Studies 200

Population-Based Studies 202

References 205

Appendix 14-1. Example Article and Commentary 208

15. Mitigating Bias in Observational Analyses209

Richard J. Cook, PhD, and Lily Zou, PhD(c)

Overview 209

Variables, Directed Graphs, and Statistical Models 212

Propensity Scores 214

Biases Due to Selection Effects 216

Other Methods: Instrumental Variables 219

Dealing with Time-Varying Processes 220

Discussion 221

References 222

Appendix 15-1. Example Article and Commentary 224

RANDOMIZED STUDY DESIGNS

Section Editors: Jose A. Cancelas, MD, PhD, and Magali Fontaine, MD, PhD

16. Introduction to Randomized Study Designs—Complexities and Limitations225

Jose A. Cancelas, MD, PhD, and Magali Fontaine, MD, PhD

Overview 225

Preclinical Studies	226
Pilot Studies	226
Inferring Cause and Effect through Randomized and Experimental Design	227
References	227
17. Preclinical Research Design	229
<i>Felicia Ciuculescu, MD, PhD</i>	
Overview	229
Description of the Design	230
Considerations for Preclinical Studies	230
Role and Scope of Preclinical Research	232
Preclinical Research Study Objectives	232
Regulatory Resources	234
Conclusions	235
References	235
Appendix 17-1. Example Article and Commentary	237
18. Pilot and Feasibility Studies in Transfusion Medicine	239
<i>Carlos H. Villa, MD, PhD</i>	
Overview	239
Description of the Design	241
Outcomes	243
Use of a Data Safety Monitoring Board	244
Examples in Transfusion Medicine	244
Progression to Definitive RCTs	245
Conclusions	246
References	246
Appendix 18-1. Example Article and Commentary	248
19. Inferring Cause and Effect through Randomized and Experimental Design	251
<i>Bethany Brown, PhD, MSCS; Richard Cook, PhD; Claire Barrett, MBChB, MMed; and Heather Pidcoke, MD, MSCI, PhD</i>	
Introduction	251
Description of the Design	253
What to Consider in the Design	257
Data Sampling and Collection	261
Data Analysis	263
Strengths and Weaknesses of RCT Design in Transfusion Medicine	264
More Specialized Topics on Experimental Design	265
Conclusion	266
References	267
Appendix 19-1. Example Article and Commentary	270

QUALITATIVE RESEARCH DESIGNS

Section Editors: Jennie Haaw, PhD, and Michelle Zeller, MD, MHPE, DRCPSC, FRCPC

20. Introduction to Qualitative Methodologies	273
<i>Jennie Haaw, PhD; Shana Hughes, PhD, MPH; and Kelly Holloway, MSc, PhD</i>	
Overview	273
The Use of Theory in Qualitative Research	274
What Kinds of Questions Can Be Answered by Qualitative Research?	277
Design Checklist	277
Assessing the Quality of Qualitative Research	280
Conclusion	281
References	282
21. Designing Applied Qualitative Research in Transfusion Medicine	285
<i>Rachel Thorpe, PhD; Jennie Haaw, PhD; and Kelly Holloway, PhD</i>	
Overview	285
Approaches to Applied Qualitative Research	286
Description of the Design	287
Data Sampling and Collection	288
Data Analysis	293
Strengths and Weaknesses of the Design	295
Conclusions	296
References	296
Appendix 21-1. Example Article and Commentary	298
22. Ethnographic Opportunities for Transfusion Medicine Research: A Practical Introduction to Rapid Ethnographies	301
<i>Cecilia Vindrola-Padros, PhD; Syka Iqbal, PhD; Qanita Fatima, MSc; Saeeda Arshad, MSc; and Shana D. Hughes, PhD, MPH</i>	
Overview	301
What Is Ethnography Anyway?	302
Overview of Rapid Ethnography	304
Rapid Ethnography Research Procedures	306
Rapid Ethnographies: Strengths and Challenges	313
Conclusions	314
References	314
Appendix 22-1. Example Article and Commentary	318
23. Narrative Inquiry	321
<i>Kelly Holloway, PhD</i>	
What Is Narrative Inquiry?	321
Description of the Design	322

Practicing Narrative Inquiry	324
Potential for Use of Narrative Inquiry in Transfusion Medicine	327
Strengths and Weaknesses of Narrative Inquiry	328
Establishing Quality and Rigor in Narrative Inquiry	328
Conclusion	329
References	329
Appendix 23-1. Example Article and Commentary	331

24. Other Qualitative Designs: Phenomenology, Grounded Theory, and Case Studies 333

Quentin Eichbaum, MD, PhD, MPH, MFA, MMHC, MA, MSc, MMEd, FCAP, FASCP

Introduction	333
Phenomenology	334
Grounded Theory	336
Case Studies	338
Summary	339
References	341
Appendix 24-1. Example Article and Commentary: Grounded Theory	342

MIXED-METHOD RESEARCH DESIGNS

Section Editors: Lauren Crowder, PHD, MPH, CPH, and Shauna Hughes, PhD, MPH

25. Introduction to Mixed-Method Research 345

Lauren A. Crowder, PhD, MPH, CPH, and Shana D. Hughes, PhD, MPH

Overview	345
What Is Mixed-Method Research?	346
Theory in Mixed-Method Research	346
Design Checklist	346
Resourcing an MMR Project	350
Dissemination of MMR	350
Limitations of MMR	350
Conclusion: Overview of Chapters and Utility in Transfusion Medicine	351
References	351

26. Convergent Mixed-Method Design 353

Lauren A. Crowder, PhD, MPH, CPH, and Anthony J. Messina, PhD, MSHS

Overview	353
Description of the Design	354
When to Consider This Design	355
Data Sampling and Collection	355
Data Analysis	355

Table of Contents

Strengths and Challenges of the Design	356
Conclusions	356
References	358
Appendix 26-1. Example Article and Commentary	359
27. Sequential Mixed-Method Designs	361
<i>Quentin Eichbaum, MD, PhD, MPH, MFA, MMHC, MA, MSc, MMed, FCAP, FASCP, and Shana D. Hughes, PhD, MPH</i>	
Overview	361
Explanatory Sequential Design	362
Exploratory Sequential Design	366
Conclusions	371
References	371
Appendix 27-1. Example Article and Commentary	373
28. The Delphi Research Design	377
<i>Quentin Eichbaum, MD, PhD, MPH, MFA, MMHC, MA, MSc, MMed, FCAP, FASCP</i>	
Introduction	377
Description of the Design	378
Key Features of the Delphi Design	378
Data Sampling and Collection	379
Data Analysis	379
Strengths and Weaknesses of the Design	380
Conclusions	381
References	381
Suggested Readings	381
Appendix 28-1. Example Article and Commentary	382
29. Implementation Science	385
<i>Anthony J. Messina, PhD, MSHS, BSc, and Lauren A. Crowder, PhD, MPH, CPH</i>	
Overview	385
Implementation Science Research Designs and Methods	387
Measurement and Evaluation in Implementation Science	389
Conclusion	392
References	393
Suggested Readings/Additional Resources	394
Appendix 29-1. IMPACT Checklist: Implementation Methods for Planning, Adoption, Context, and Translation	395
Appendix 29-2. Example Article and Commentary	396

LITERATURE REVIEW RESEARCH DESIGNS

Section Editors: Bruce Sachais, MD, PhD, and Bethany Brown, PhD, MSCS

30. Introduction to Literature Review Research	397
<i>Bruce Sachais, MD, PhD, and Bethany Brown, PhD, MSCS</i>	
Overview	397
Conducting Traditional/Narrative Reviews	398
Other Types of Literature Reviews	399
31. Scoping Reviews and Overviews of Reviews	401
<i>Ryan A. Metcalf, MD, and Sandra K. White, MS, MS</i>	
Overview	401
Description of the Design	403
Data Sampling and Collection	403
Data Analysis	404
When to Consider This Design	404
Conclusions	405
References	405
Appendix 31-1. Example Article and Commentary	407
32. Systematic Literature Review Methodology	409
<i>Bethany Brown, PhD, MSCS; Lise Estcourt, MB BChir, MA(Cantab), MA(MEL), MSc, DLSHTM, DPhil, FRCP, FRCPath; and Janice Hodge, MLIS</i>	
Overview	409
Steps to Conduct a Systematic Literature Review	410
Strengths of Systematic Literature Reviews in Transfusion Medicine	415
Conclusions	415
References	417
Appendix 32-1. Example Article and Commentary	418
33. Analysis of Systematic Literature Reviews (Including Meta-Analyses and Assessment of Certainty of Evidence)	421
<i>Carlos Zaror, DDS, MSc, PhD, and Romina Brignardello-Petersen, DDS, MSc, PhD</i>	
Overview	421
Deciding Whether Studies Can Be Combined Together in a Single Synthesis	422
Measures of Effect	422
Meta-Analysis	423
Network Meta-Analysis	427
Narrative Synthesis	428
Certainty of Evidence	429
Drawing Conclusions from Systematic Reviews	431

Table of Contents

Conclusions	435
References	435
34. Developing Evidence-Based Clinical Practice Guidelines	439
<i>Ryan A. Metcalf, MD, and Simon J. Stanworth, MD, DPhil</i>	
Introduction	439
Guidelines in Transfusion Medicine	440
The Need for Robust Guidelines	440
Methodology for Robust Guidelines	441
Evidence Synthesis	441
Making Recommendations	442
Use of Other Literature beyond Randomized Trials	442
Summary of Platelet Transfusion Guideline Recommendations	443
Conclusion	444
References	444
Appendix 34-1. Example Article and Commentary	446
Index	447

