

Contents

Part I Introduction to Risk Analysis

1	Quantitative Risk Assessment Goals and Challenges	3
	The Quantitative Risk Assessment (QRA) Paradigm	3
	Example: A Simple QRA Risk Assessment Model	4
	Example: Explicit QRA Reasoning Can Be Checked and Debated	6
	Against QRA: Toward Concern-Driven Risk Management	7
	Dissatisfactions with QRA	7
	Example: Use of Incorrect Modeling Assumptions in Antimicrobial Risk Assessment	8
	Example: Use of Unvalidated Assumptions in a QRA for BSE (“Mad Cow” Disease)	9
	Toward Less Analytic, More Pluralistic Risk Management	11
	Alternatives to QRA in Recent Policy Making: Some Practical Examples	13
	Concern-Driven Risk Management	15
	Potential Political Advantages of Concern-Driven Regulatory Risk Management	16
	How Effective Is Judgment-Based Risk Management?	18
	Example: Expert Judgment vs. QRA for Animal Antibiotics	18
	Performance of Individual Judgment vs. Simple Quantitative Models	19
	Performance of Consensus Judgments vs. Simple Quantitative Models	26
	Example: Resistance of Expert Judgments to Contradictory Data	26
	Example: Ignoring Disconfirming Data About BSE Prevalence	28
	Example: Consensus Decision Making Can Waste Valuable Individual Information	29
	How Effective Can QRA Be?	31
	Summary and Conclusions	32
2	Introduction to Engineering Risk Analysis	35
	Overview of Risk Analysis for Engineered Systems	35
	Example: Unreliable Communication with Reliable Components	37

Example: Optimal Number of Redundant Components	37
Example: Optimal Scheduling of Risky Inspections	38
Using Risk Analysis to Improve Decisions	39
Hazard Identification: What Should We Worry About?	39
Example: Fault Tree Calculations for Car Accidents at an Intersection	40
Structuring Risk Quantification and Displaying Results: Models for Accident Probabilities and Consequences	41
Example: Bug-Counting Models of Software Reliability	42
Example: Risk Management Decision Rules for Dams and Reservoirs	43
Example: Different Individual Risks for the Same Exceedance Probability Curve	43
Quantifying Model Components and Inputs	44
Modeling Interdependent Inputs and Events	45
Example: Analysis of Accident Precursors	46
Example: Flight-Crew Alertness	47
Some Alternatives to Subjective Prior Distributions	47
Example: Effects of Exposure to Contaminated Soil	49
Example: The “Rule of Three” for Negative Evidence	54
Example: A Sharp Transition in a Symmetric Multistage Model of Carcinogenesis	55
Dealing with Model Uncertainty: Bayesian Model Averaging (BMA) and Alternatives	56
Risk Characterization	58
Engineering vs. Financial Characterizations of “Risk”: Why Risk Is Not Variance	58
Incompatibility of Two Suggested Principles for Financial Risk Analysis	62
Challenges in Communicating the Results of PRAs	66
Methods for Risk Management Decision Making	67
Example: A Bounded-Regret Strategy for Replacing Unreliable Equipment	68
Methods of Risk Management to Avoid	69
Game-Theory Models for Risk Management Decision Making	70
Game-Theory Models for Security and Infrastructure Protection	70
Game-Theory Models of Risk-Informed Regulation	71
Conclusions	72
3 Introduction to Health Risk Analysis	73
Introduction	73
Quantitative Definition of Health Risk	75
Example: Statistical and Causal Risk Relations May Have Opposite Signs	76
A Bayesian Network Framework for Health Risk Assessment	77

Hazard Identification 80
 Example: Some Traditional Criteria for Causality Fail to Refute
 Other Explanations 83
 Exposure Assessment 85
 Example: Simulation of Exposures to Pathogens in Chicken Meat 87
 Example: Mixture Distributions and Unknown Dose-Response
 Models 88
 Dose-Response Modeling 89
 Example: Apparent Thresholds in Cancer Dose-Response Data 90
 Example: Best-Fitting Parametric Models May Not Fit Adequately 91
 Risk and Uncertainty Characterization for Risk Management 93
 Example: Risk Characterization Outputs 93
 Conclusions 96

Part II Avoiding Bad Risk Analysis

4 Limitations of Risk Assessment Using Risk Matrices 101
 Introductory Concepts and Examples 102
 A Normative Decision-Analytic Framework 104
 Logical Compatibility of Risk Matrices with Quantitative Risks 108
 Definition of Weak Consistency 109
 Discussion of Weak Consistency 109
 Logical Implications of Weak Consistency 110
 The Betweenness Axiom: Motivation and Implications 111
 Consistent Coloring 112
 Implications of the Three Axioms 113
 Example: The Two Possible Colorings of a Standard
 5 × 5 Risk Matrix 113
 Risk Matrices with Too Many Colors Give Spurious Resolution 114
 Example: A 4 × 4 Matrix for Project Risk Analysis 115
 Risk Ratings Do Not Necessarily Support Good Resource Allocation
 Decisions 117
 Example: Priorities Based on Risk Matrices Violate
 Translation Invariance 117
 Example: Priority Ranking Does Not Necessarily Support
 Good Decisions 118
 Categorization of Uncertain Consequences Is Inherently Subjective 119
 Example: Severity Ratings Depend on Subjective Risk Attitudes 119
 Example: Pragmatic Limitations of Guidance from Standards 120
 Example: Inappropriate Risk Ratings in Enterprise Risk
 Management (ERM) 121
 Discussion and Conclusions 122
 Appendix A: A Proof of Theorem 1 123

5 Limitations of Quantitative Risk Assessment Using Aggregate Exposure and Risk Models 125

What Is Frequency? 126

 An Example: Comparing Two Risks 127

 Event Frequencies in Renewal Processes 127

 Example: Average Annual Frequency for Exponentially Distributed Lifetimes 128

 The “Frequency” Concept for Nonexponential Failure Times 128

 Example: Average Annual Frequency for Uniformly Distributed Lifetimes 128

 Conflicts Among Different Criteria for Comparing Failure Time Distributions 129

 Do These Distinctions Really Matter? 130

 Summary of Limitations of the “Frequency” Concept 132

Limitations of Aggregate Exposure Metrics 133

 Use of Aggregate Exposure Metrics in Risk Assessment 134

 Aggregate Exposure Information May Not Support Improved Decisions 134

 Example: How Aggregate Exposure Information Can Be Worse Than Useless 135

 Multicollinearity and Aggregate Exposure Data 137

 Example: Multicollinearity Can Prevent Effective Extrapolation of Risk 137

 A Practical Example: Different Predictions of Asbestos Risks at El Dorado Hills, CA 138

 Summary of Limitations of Risk Assessments Based on Aggregate Exposure Metrics 140

Limitations of Aggregate Exposure-Response Models: An Antimicrobial Risk Assessment Case Study 141

 Statistical vs. Causal Relations 142

 Example: Significant Positive K for Statistically Independent Risk and Exposure 142

 Example: A Positive K Does Not Imply That Risk Increases with Exposure 143

 Example: Statistical Relations Do Not Predict Effects of Changes 143

 Prevalence vs. Microbial Load as Exposure Metrics 144

 Attribution vs. Causation 145

 Human Harm from Resistant vs. Susceptible Illnesses 147

 Summary of Limitations of Aggregate Exposure-Response Model, $Risk = K \times Exposure$ 148

Some Limitations of Risk Priority-Scoring Methods 149

 Motivating Examples 149

 Example: Scoring Information Technology Vulnerabilities 150

 Example: Scoring Consumer Credit Risks 150

 Example: Scoring Superfund Sites to Determine Funding Priorities 151

Example: Priority Scoring of Bioterrorism Agents 151

Example: Threat-Vulnerability-Consequence (TVC) Risk Scores
and Risk Matrices 152

Priorities for Known Risk Reductions 152

Priorities for Independent, Normally Distributed Risk Reductions 153

Priority Ratings Yield Poor Risk Management Strategies
for Correlated Risks 155

Example: Priority Rules Overlook Opportunities
for Risk-Free Gains 155

Example: Priority Setting Can Recommend the Worst
Possible Resource Allocation 156

Example: Priority Setting Ignores Opportunities for Coordinated
Defenses 157

Priority Rules Ignore Aversion to Large-Scale Uncertainties 158

Discussion and Conclusions on Risk Priority-Scoring Systems 159

Conclusions 160

Part III Principles for Doing Better

6 Identifying Nonlinear Causal Relations in Large Data Sets 165

Nonlinear Exposure-Response Relations 166

Entropy, Mutual Information, and Conditional Independence 168

Classification Trees and Causal Graphs via Information Theory 170

Illustration for the Campylobacteriosis Case Control Data 173

Conclusions 177

7 Overcoming Preconceptions and Confirmation Biases Using Data Mining 179

Confirmation Bias in Causal Inferences 180

Example: The Wason Selection Task 180

Example: Attributing Antibiotic Resistance to Specific Causes 181

Study Design: Hospitalization Might Explain Observed
Resistance Data 183

Choice of Endpoints 185

Quantitative Statistical Methods and Analysis 185

Results of Quantitative Risk Assessment Modeling for vatE
Resistance Determinant 193

Results for Inducible Resistance 197

Discussion and Implications for Previous Conclusions 198

Summary and Conclusions 200

Appendix A: Computing Adjusted Ratios of Medians
and their Confidence Limits 201

8 Estimating the Fraction of Disease Caused by One Component of a Complex Mixture: Bounds for Lung Cancer 203

Motivation: Estimating Fractions of Illnesses Preventable by Removing Specific Exposures 203

Why Not Use Population Attributable Fractions? 204

 Example: Attribution of Risk to Consequences Instead of Causes 204

 Example: Positive Attributable Risk is Compatible with Negative Causation 205

Theory: Paths, Event Probabilities, Bounds on Causation 206

 A Bayesian Motivation for the Attributable Fraction Formula 208

The Smoking-PAH-BPDE-p53-Lung Cancer Causal Pathway 210

Applying the Theory: Quantifying the Contribution of the Smoking-PAH-BPDE-p53 Pathway to Lung Cancer Risk 212

 A Simple Theoretical Calculation Using Causal Fractions 212

 Step 1: Replace Causal Fractions with Fractions Based on Occurrence Rates 213

 Step 2: Quantify Occurrence Rates Using Molecular-Level Data 216

 Step 3: Combine Upper-Bound Surrogate Fractions for Events in a Path Set 218

Uncertainties and Sensitivities 219

Discussion 220

Conclusions 221

9 Bounding Resistance Risks for Penicillin 223

Background, Hazard Identification and Scope: Reducing Ampicillin-Resistant *E. faecium* (AREF) Infections in ICU Patients 223

Methods and Data: Upper Bounds for Preventable Mortalities 225

 Estimated Number of ICU Infections per Year 226

 Fraction of ICU Infections Caused by *E. faecium* 227

 Fraction of ICU *E. faecium* Infections That Are Ampicillin-Resistant and Exogenous (Nonnosocomial) 227

 Fraction of Vancomycin-Susceptible Cases 228

 Fraction of Exogenous Cases Potentially from Food Animals 229

 Penicillin Allergies 230

 Excess Mortalities 231

Results Summary, Sensitivity, and Uncertainty Analysis 232

Summary and Conclusions 234

10 Confronting Uncertain Causal Mechanisms – Portfolios of Possibilities 237

Background: Cadmium and Smoking Risk 238

Previous Cadmium-Lung Cancer Risk Studies 239

 Cadmium Compounds are Rat Lung Carcinogens 239

 Epidemiological Data are Inconclusive 240

Pharmacokinetic Data Show That Smoking Increases Cadmium Levels in the Human Lung 240

Biological Mechanisms of Cadmium Lung Carcinogenesis 242

 A Transition Model Simplifies the Description of Cadmium-Induced Lung Carcinogenesis 242

 Cadmium Can Affect Lung Carcinogenesis via Multiple Mechanisms 244

 Smoking and Cd Exposures Stimulate Reactive Oxygen Species (ROS) Production 245

 Cadmium Inhibits DNA Repair and Is a Co-Carcinogen for PAHs 248

Quantifying Potential Cadmium Effects on Lung Cancer Risk 251

 Polymorphism Evidence on Lung Cancer Risks from Different Mechanisms 252

 Quasi-Steady-State Analysis 252

 A Portfolio Approach to Estimating the Preventable Fraction of Risk for Cd 256

Discussion and Conclusions 257

Appendix A: Relative Risk Framework 258

11 Determining What Can Be Predicted: Identifiability 261

 Identifiability 262

 Example 1: A Simple Example of Nonidentifiability 262

 Example 2: Unique Identifiability in a Two-Stage Clonal Expansion Model 262

 Multistage Clonal Expansion (MSCE) Models of Carcinogenesis 266

 Nonunique Identifiability of Multistage Models from Input-Output Data 270

 Example 3: Counting 5×5 Matrices with Sign Restrictions 270

 Example 4: Two Equally Likely Effects of Reducing a Transition Rate 271

 Discussion and Conclusions 275

 Appendix A: Proof of Theorem 1 277

 Appendix B: Listing of ITHINK™ Model Equations for the Example in Figure 11.3 279

Part IV Applications and Extensions

12 Predicting the Effects of Changes: Could Removing Arsenic from Tobacco Smoke Significantly Reduce Smoker Risks of Lung Cancer? 283

 Biologically Based Risk Assessment Modeling 283

 Arsenic as a Potential Human Lung Carcinogen 284

 Data, Methods, and Models 287

A Multistage Clonal Expansion (MSCE) Framework for Lung Field
 Cancerization 287
 A Mathematical Model of Field Carcinogenesis 291
 Modeling the Effects on Lung Cancer Risk of Reductions
 in Carcinogenic Constituents 293
 Linking Biomarker Data to Model Transition Parameters 295
 Results 296
 Limitations of Modeling Assumptions and Calculations 298
 Sensitivities, Uncertainties, Implications, and Conclusions 298
 Appendix A: Listing for TSCE Model of Smoking and Lung Cancer 300
 Appendix B: Listing for MSCE Lung Cancer Model with Field
 Carcinogenesis 301

**13 Simplifying Complex Dynamic Networks: A Model of Protease
 Imbalance and COPD Dynamic Dose-Response 303**
 Background on COPD 304
 A Flow Process Network Model of Protease-Antiprotease
 Imbalance in COPD 305
 Mathematical Analysis of the Protease-Antiprotease Network 308
 Some Possible Implications for Experimental and Clinical COPD 313
 Is the Model Consistent with Available Human Data? 314
 Summary and Conclusions 316
 Appendix A: Equilibrium in Networks of Homeostatic Processes 317
 Representing Biological Knowledge by Networks of Flow Processes . . . 317
 Example: ODE and ITHINK[®] Representations
 of a Single Process 319
 Reducing Chains of Coupled Processes to Simpler Equivalents 320

**14 Value of Information (VOI) in Risk Management Policies
 for Tracking and Testing Imported Cattle for BSE 325**
 Testing Canadian Cattle for Bovine Spongiform Encephalitis (BSE) 327
 Methods and Data 330
 Formulation of the Risk Management Decision Problem
 as a Decision Tree 330
 Estimated Economic Consequences of Detecting Additional
 BSE Cases 333
 Scenario Probabilities 339
 Solution Algorithms 342
 Results 343
 Optimal Decision Rule for the Base Case 343
 Sensitivity Analysis Results 343
 Discussion 346
 Epilogue and Conclusions 347
 Appendix: Market Impact Assumptions and Calculations 349

15 Improving Antiterrorism Risk Analysis 351

 The *Risk = Threat × Vulnerability × Consequence* Framework 351

 RAMCAP™ Qualitative Risk Assessment 353

 Limitations of RAMCAP™ for Quantitative Risk Assessment 354

 Example: Distortions Due to Use of Arithmetic Averages
 on Logarithmic Scales 355

 Example: Limited Resolution 355

 Example: Manipulating Vulnerability Estimates by Aggregating
 Attack Scenarios 355

 Example: Nonadditive Vulnerabilities 356

 Example: Product of Expected Values Not Equal to Expected
 Value of Product 356

 Risk Rankings Are Not Adequate for Resource Allocation 357

 Example: Priority Ranking May Not Support Effective Resource
 Allocation 358

 Some Fundamental Limitations of *Risk = Threat ×*
 Vulnerability × Consequence 358

 “Threat” Is Not Necessarily Well Defined 359

 “Vulnerability” Can Be Ambiguous and Difficult to Calculate
 via Event Trees 360

 “Consequence” Can Be Ambiguous and/or Subjective 367

 Discussion and Conclusions 367

16 Designing Resilient Telecommunications Networks 371

 Introduction: Designing Telecommunications Infrastructure Networks
 to Survive Intelligent Attacks 372

 Background: Diverse Routing, Protection Paths, and Protection
 Switching 372

 Automated Protection Switching (APS) for Packets and Light Paths . . . 373

 Demands Consist of Origins, Destinations, and Bandwidth
 Requirements 373

 Multiple Levels of Protection for Demands 374

 A Simple Two-Stage Attacker-Defender Model 376

 Results for Networks with Dedicated Routes (“Circuit-Switched”
 Networks) 377

 Designing Networks to Withstand a Single ($k = 1$) Link Cut 377

 Designing Networks to Withstand $k = 2$ Link Cuts 380

 Results for the General Case of k Cuts 380

 Statistical Risk Models and Results for Scale-Free Packet Networks 381

 Real-World Implementation Challenges: Incentives to Invest
 in Protection 384

 Example: An N-Person Prisoner’s Dilemma for Network
 Maintenance 385

 Example: Nash Equilibrium Can Be Inadequate for Predicting
 Investments 386

Example: A Network Collusion Game with an Empty Core 387

Example: A Tipping Point 388

Summary 388

Epilogue 389

References 391

Index 423



<http://www.springer.com/978-0-387-89013-5>

Risk Analysis of Complex and Uncertain Systems

Cox Jr., L.A.

2009, XXVIII, 436 p., Hardcover

ISBN: 978-0-387-89013-5