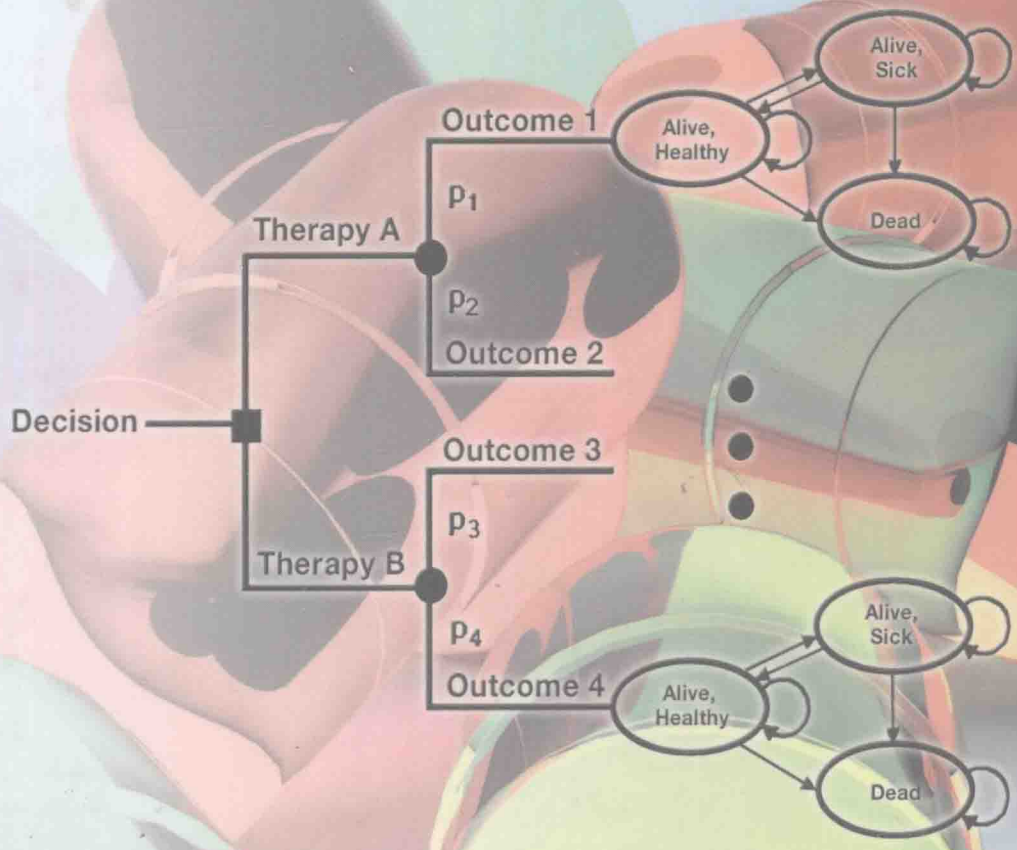
Drug Discovery Series/13

PHARMACOECONOMICS

From Theory to Practice



Edited by

RENÉE J. G. ARNOLD

CRC Press
Taylor & Francis Group

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CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number: 978-1-4200-8422-1 (Hardback)

Library of Congress Cataloging-in-Publication Data

Pharmacoeconomics : from theory to practice / editor, Renee J.G. Arnold.
p. ; cm. -- (Drug discovery series ; 13)
Includes bibliographical references and index.
ISBN 978-1-4200-8422-1 (hardcover : alk. paper)
1. Drugs--Cost effectiveness. 2. Pharmacy--Economic aspects. 3. Decision making. I. Arnold, Renee J. G. II. Title. III. Series: Drug discovery series ; 13.
[DNLM: 1. Economics, Pharmaceutical. 2. Costs and Cost Analysis. 3. Decision Making. 4. Outcome Assessment (Health Care)--economics. QV 736 P5374 2010]

RS100.P433 2010
338.4'76151--dc22 2009032763

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http://www.crcpress.com

Preface

The genesis of this book was the pharmacoeconomics research and other outcomes projects my colleagues and I have completed for our pharmaceutical company and government clients over many years. The chapter ideas came specifically from the Introduction to Pharmacoeconomics course I developed and currently teach for the Mount Sinai School of Medicine Master of Public Health program. I have collaborated extensively with many of the colleagues who have written chapters for this book, and I am truly grateful to these extremely busy people, who have contributed their valuable time and collective wisdom to make it useful and practical. Some of the views expressed herein may be controversial but, after all, experts may still disagree and some disagreement is healthy if it leads to useful dialogue and changes in practice that will benefit populations and individual patients.

This book is meant to provide an introduction to the major concepts and principles of pharmacoeconomics, with particular emphasis on modeling, methodologies, and data sources and application to real world dilemmas. Readers will learn about the international use of pharmacoeconomics in drug regulation, drug approval, and pricing. They are also given examples of pharmacoeconomic models used to support these purposes in government, the pharmaceutical industry, and healthcare settings (e.g., pharmacoeconomic analyses of a public health vaccination program). In particular, the example of collaboration among members of the pharmaceutical industry, academia, and government in the development of the recently approved human papillomavirus vaccine is used as a running theme through the majority of the chapters to demonstrate the full range of ethical and moral issues, as well as overall public health and commercial concerns that are often involved in decisions entailing pharmacoeconomic issues. Lest readers think these issues esoteric or untimely, they are referred to a recent Institute of Medicine Report (Institute of Medicine of the National Academies, Roundtable on evidence-based medicine: Learning healthcare system concepts, 2008) that stated that the best value is derived by "applying the evidence we have about the medical care that is most effective" and also by improving our "timely generation of evidence on the relative effectiveness, efficiency, and safety of available and emerging interventions." These principles are being embodied, for example, in the much-discussed potential U.S. Institute for Comparative Effectiveness Research (interestingly, the same acronym as an oft-used concept in pharmacoeconomics, that of the incremental cost-effectiveness ratio, or ICER) and in guidances rendered by the U.K.'s National Institute for Health and Clinical Excellence (NICE). Pharmacogenomics, or the use of personalized medicine, will be combined with cost-effectiveness analyses to inform and improve healthcare decision-making. For example, a recent theoretical Markov model showed pharmacogenomic-guided dosing for anticoagulation with warfarin to not be cost effective in patients with nonvalvular atrial fibrillation. Interestingly, another recently published algorithm using logistic regression from international retrospective databases showed that incorporating pharmacogenetic information was more likely to result in

a therapeutic international normalized ratio (INR), the major method of determining anticoagulation, than use of clinical data alone. However, the data used to inform the Markov model were published studies that did not include the latter study, and the algorithm did not indicate the clinical diagnoses, nor the clinical outcomes, of the patients who were more or less likely to be within a therapeutic INR. Thus, improved and cost-effective decisions, using the best available evidence-based medicine, will require that both clinical and economic expertise, as epitomized in this book, be used.

Acknowledgments

I gratefully acknowledge my colleague and friend, Dr. Sean Ekins, who prompted me to write this book and also contributed a chapter. In addition, the expert assistance of Kirsten Groesser, a graduate student in the Mount Sinai School of Medicine Master of Public Health program, was particularly appreciated.

Editor

Renée J. Goldberg Arnold completed her undergraduate training at the University of Maryland and received her Doctor of Pharmacy degree from the University of Southern California in Los Angeles. She also completed a one-year post-doctoral residency at University Hospital in San Diego, which is affiliated with the University of California at San Francisco School of Pharmacy. Dr. Arnold was previously President and Co-Founder of Pharmacon International, Inc. Center for Health Outcomes Excellence; Senior Vice President, Medical Director, William J. Bologna International, Inc., a pharmaceutical marketing and advertising agency; and Assistant Professor of Clinical Pharmacy at the Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University (LIU) in Brooklyn, New York. Her research interests at that time were plasma amino acid concentrations in very low birth weight infants and home-infusion total parenteral nutrition.

Dr. Arnold is currently President and CEO, Arnold Consultancy & Technology LLC, with headquarter offices in New York City, where she develops and oversees outcomes research and affiliated software for the pharmaceutical, biotech, and device industry, and federal government programs. Her special interest in evidence-based health derives from her research that deals with use of technology to collect or model real-world data for use in rational decision-making by healthcare practitioners and policy makers. For example, the company recently developed and published the results of an interactive decision tree model to compare the cost and diagnostic abilities of ultrasound performed with and without the use of an oral contrast material. An interactive program was developed that was used to train 200 representatives nationwide on formulary issues associated with use of the contrast material and was also used in discussions with reimbursement officials (CMS) in the U.S. government.

Dr. Arnold's academic titles include Adjunct Associate Professor, Master of Public Health program, Department of Community and Preventive Medicine at the Mount Sinai School of Medicine, where she has developed the pharmacoeconomics coursework and is a preceptor for MD/MPH students completing their MPH practicums. She is also Full Adjunct Professor, Division of Social Sciences and Administrative Sciences, at LIU. In that capacity, she serves as a preceptor for undergraduate and graduate students completing rotations in health outcomes and pharmacoeconomics research. Dr. Arnold also initiated internship and postdoctoral fellowship programs in pharmacoeconomics at Arnold Consultancy & Technology LLC and is a founding member and former Chair of the Education Committee of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), as well as current Chair

of the Health/Disease Management Special Interest Group. In addition, she is a licensed pharmacist. Dr. Arnold is the author of numerous articles in the areas of pharmacology, pharmacoeconomics, and cost containment strategies and is a co-author of five book chapters, one in cardiovascular therapeutics, another in pharmacoeconomic analyses in cardiovascular disease, the third in computer applications in pharmaceutical research and development, the fourth in quality of life and cost of atopic dermatitis and the fifth in the reliability and validity of claims and medication databases as data sources for health/disease management programs.

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1 Introduction to Pharmacoeconomics

William F. McGhan

CONTENTS

> The desires to consume medicines and use pharmacoeconomics are perhaps the greatest features that distinguish humans from animals.
>
> **—Adapted from William Osler**

1.1 INTRODUCTION

Practitioners, patients, and health agencies face a multitude of conundrums as the development of new therapies seems boundless, while the money to purchase these cures is limited. How does one decide which are the best medicines to use within restricted budgets? The continuing impact of cost-containment is causing administrators and policy makers in all health fields to examine closely the costs and benefits of both proposed and existing interventions. It is increasingly obvious that purchasers and public agencies are demanding that health treatments be evaluated in terms of clinical and humanistic outcomes against the costs incurred.

Pharmacoeconomics is the field of study that evaluates the behavior or welfare of individuals, firms, and markets relevant to the use of pharmaceutical products, services, and programs.[1] The focus is frequently on the cost (inputs) and consequences (outcomes) of that use. Of necessity, it addresses the clinical, economic, and humanistic aspect of health care interventions (often diagrammed as the ECHO Model,

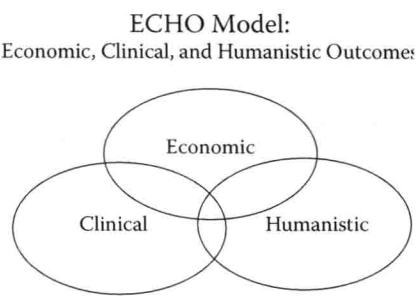

FIGURE 1.1 ECHO Model. (Kozma, CM et al. Economic, clinical, and humanistic outcomes: A planning model for pharmacoeconomic research. *Clin Ther.* 15: (1993): 1121–32.)

Figure 1.1)[2] in the prevention, diagnosis, treatment, and management of disease. Pharmacoeconomics is a collection of descriptive and analytic techniques for evaluating pharmaceutical interventions, spanning individual patients to the health care system as a whole. Pharmacoeconomic techniques include cost-minimization, cost-effectiveness, cost-utility, cost-benefit, cost of illness, cost-consequence, and any other economic analytic technique that provides valuable information to health care decision makers for the allocation of scarce resources. Pharmacoeconomics is often referred to as "health economics" or "health outcomes research," especially when it includes comparison with non-pharmaceutical therapy or preventive strategies such as surgical interventions, medical devices, or screening techniques.

Pharmacoeconomic tools are vitally important in analyzing the potential value for individual patients and the public. These methods supplement the traditional marketplace value as measured by the prices that the patient or patron is willing to pay. With government agencies and third parties' continuing concern about the higher expenditures for prescriptions, pharmaceutical manufacturers and pharmacy managers are highly cognizant that pharmaceutical interventions and services require comparative cost-justification and continual surveillance to assure cost-effective outcomes.[3–6]

From pharmaceutical research, we have seen significant therapeutic advances and breakthroughs. From health care delivery entrepreneurs we have seen numerous expanding roles for pharmacists, nurses, and physician assistants, with services such as home intravenous therapy, drug-level monitoring, parenteral nutrition management, hospice care, self-care counseling, and genetic screening for customizing therapy, among other innovations. The use of valid economic evaluation methods to measure the value and impact of new interventions can increase acceptance and appropriate use of such programs by third-party payers, government agencies, and consumers.[7–9]

There is increasing scrutiny over all aspects of health care as we attempt to balance limited finances and resources against optimal outcomes. Cost-effectiveness evaluations of pharmaceutical options are becoming mandatory for attaining adequate reimbursement and payment for services.[10,11] Pharmacoeconomic methods help document the costs and benefits of therapies and pharmaceutical services, and establish priorities for those options to help in appropriately allocating resources in ever-changing health care landscapes.

1.2 ANALYTICAL PERSPECTIVES

Point of view is a vital consideration in pharmacoeconomics. If a medicine is providing a positive benefit in relation to cost in terms of value to society as a whole, the service may not be valued in the same way by separate segments of society. For example, a drug therapy that reduces the number of admissions or patient days in an acute care institution is positive from society's point of view but not necessarily from that of the institution's administrator, who depends on a high number of patient admissions to meet expenses. Thus, one must determine whose interests are being served when identifying outcome criteria for evaluation. When considering pharmacoeconomic perspectives, one must always consider who pays the costs and who receives the benefits. A favorable economic analysis that showed savings in clinic utilization from the employer perspective would probably not be viewed positively from the clinic's budget perspective. More broadly, what is viewed as saving money for society may be viewed differently by private third-party payers, administrators, health providers, governmental agencies, or even the individual patient. It is generally agreed among health economists that the societal perspective should always be discussed in an evaluative report, even though the focus of the report might deal with other segments such as hospitals or insurance agencies. In the United States, with many different health care delivery and payer approaches, this can be complicated, and analyses are often done from multiple perspectives to assist adjudication by multiple stakeholders.

1.3 CODE OF ETHICS

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has published a code of ethics that is vital to the honesty and transparency of the discipline.[12] The code encourages pharmacoeconomists to maintain the highest ethical standards because the academy recognizes that activities of its members affect a number of constituencies. These include but are not limited to: (1) Patients who are ultimately going to experience the greatest impact of the research; (2) practitioners who will be treating or not treating patients with therapies, medications, and procedures made available or not made available because of the research; (3) governments, employers, decision-makers, and payers who must decide what is covered so as to optimize the health of the patient and resource utilization; (4) professional outcomes researchers; (5) colleagues, where relationships in conducting research and related activities are particularly critical; (6) research employees concerned about how they are regarded, compensated, and treated by the researchers for whom they work; (7) students who work for researchers, where respect and lack of exploitation are important because they are the future of the discipline; and (8) clients for whom the research is conducted, and the researchers' relationships with them.

The ISPOR code of ethics lists many standards for researchers, but a sample section of the code related to "design and research practices" is as follows:

1. Maintain a current knowledge of research practices.
2. Adhere to the standards of practice for their respective fields of research and identify any official guidelines/standards used.

3. Research designs should be defined a priori, reported transparently, defended relative to alternatives, and planned to minimize all types of bias.
4. Respect the rights of research subjects in designing and conducting studies.
5. Respect the reputations and rights of colleagues when engaged in collaborative projects.
6. Maintain and protect the integrity of the data used in their studies.
7. Not draw conclusions beyond those which their data would support.

1.4 OVERVIEW OF ECONOMIC EVALUATION METHODS

This section will introduce the reader with a brief overview of the methodologies based on the two core pharmacoeconomic approaches, namely cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). Table 1.1 provides a basic comparison of these methods with cost-of-illness, cost-minimization, and cost-benefit analysis. One can differentiate between the various approaches according to the units used to measure the inputs and outcomes, as shown in the table. In general, the outputs in CEA are related to various natural units of measure, such as lives saved, life-years added, disability-days prevented, blood pressure, lipid level, and so on. Cost-benefit analysis (CBA) uses monetary values (e.g., euros, dollars, pounds, yen) to measure both inputs and outputs of the respective interventions. Further discussion and examples of these techniques have been presented elsewhere.[1–3,13–21] It is hoped that the evaluation mechanisms delineated further in this book will be helpful in managing pharmaceutical interventions toward improving societal value and generate greater acceptance by health authorities, administrators, and the public. Using the human papillomavirus (HPV) vaccine as an example for case studies, other chapters in this book will further illustrate the various analytical methodologies related to CEA, CUA, CBA, etc.

1.5 QUALITY OF LIFE AND PATIENT PREFERENCES

Significant components in pharmacoeconomics are patient outcomes and quality of life (QoL) with an expanding list of related factors to consider (Table 1.2).[14,15] Although it is recognized that there are physical, mental, and social impairments associated with disease, there is not always consensus on how to accurately measure many of these factors. Consequently, the concept of satisfaction with care is often overlooked in cost-effectiveness studies and even during the approval process of the U.S. Food and Drug Administration (FDA). Generally, pharmacoeconomic and outcomes researchers consider QoL a vital factor in creating a full model of survival and service improvement. QoL is related to clinical outcomes as much as drugs, practitioners, settings, and types of disease. The question becomes how to select and utilize the most appropriate instruments for measuring QoL and satisfaction with care in a meaningful way.

The quality-adjusted life year (QALY) has become a major concept in pharmacoeconomics. It is a measure of health improvement used in CUA, which combines mortality and QoL gains and considers the outcome of a treatment measured as the number of years of life saved, adjusted for quality.

TABLE 1.1
Comparison of Pharmacoeconomic Methods and Calculations

Method	Abbr	Basic Formula	Discounting Math	Input	Output	Results Expressed	Goal Determine:	Advantage / Disadvantage	Example
Cost of Illness	COI	(DC+IC)	$\sum_{t=1}^{n}[C_t/(1+r)^t]$	$	$	Total cost of illness	Total cost of illness	Does not look at TXs separately	Cost of migraine in U.S.
Cost Minimization Analysis	CMA	C_1-C_2 or [Preferred Formula] $(DC_1+IC_1) - (DC_2+IC_2)$	$\sum_{t=1}^{n}[C_t/(1+r)^t]$	$	Assumed Equal	Net cost savings	Lowest cost TX	Assume both TXs have same effectiveness	Assume two antibiotics have the same effects for killing infection but differ on nursing and intravenous cost
Cost-Effectiveness Analysis	CEA	$(C_1-C_2) / (E_1 - E_2)$ or [Preferred Formula] $(DC_1+IC_1) - (DC_2+IC_2) / (E_1 - E_2)$	$\sum_{t=1}^{n}[C_t/(1+r)^t] / \sum_{t=1}^{n}[E_t/(1+r)^t]$	$	Health Effect	Incremental cost against change in unit of outcome	TX attaining effect for lower cost	Compare TXs that have same type of effect units	Compare two HTN prescriptions for life years
Cost–Benefit Analysis or Net Bv enefit	CBA	$(B_1 - B_2) / (DC_1+IC_1) - (DC_2-IC_2)$ or [Preferred Formula] Net Benefit = $(B_1-B_2) - (DC_1+IC_1) - (DC_2+IC_2)$	$\sum_{t=1}^{n}[B_t/(1+r)^t] / \sum_{t=1}^{n}[C_t/(1+r)^t]$ or $\sum_{t=1}^{n}[(B_t-C_t)/(1+r)^t]$	$	Dollars	Net benefit or ratio of incremental benefits to incremental costs	TX giving best net benefit or higher B/C ratio (or return on investment)	TXs can have different effects, but must be put into dollars	Compare two cholesterol prescriptions and convert life years to wages
Cost-Utility Analysis	CUA	$(C_1-C_2) / (U_1-U_2)$ or [Preferred Formula] $(DC_1+IC_1) - (DC_2+IC_2) / (U_1 - U_2)$	$\sum_{t=1}^{n}[C_t/(1+r)^t] / \sum_{t=1}^{n}[U_t/(1+r)^t]$	$	Patient Preference	Incremental cost against change in unit of outcome adjusted by patient preference	TX attaining effect (adjusted for patient preference) for lower cost	Preferences are difficult to measure	Compare two cancer prescriptions and use QoL adjusted life years gained

Note: DC = direct cost; IC = indirect cost; r = discount rate; t = time; HTN = hpertension; QoL = quality of life; TX = treatment or intervention.