

Format for Formulary Submissions

A Format for Submission of Clinical and Economic Data
In Support of Formulary Consideration
by Managed Health Care Systems in the United States



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Acknowledgements

The Academy of Managed Care Pharmacy gratefully acknowledges the contributions of many individuals who have devoted much time, expertise, and commitment in the preparation of this valuable pharmacy tool.

AMCP's *Format for Formulary Submissions* is the result of a voluntary collaboration between talented authors experienced in the challenges presented by the complex task of appropriate formulary decision making: Joseph A. Gricar, M.S., former pharmacoeconomics fellow with Parke-Davis, now with Pfizer Pharmaceuticals; Paul Langley, PhD, 3M Corporation; Bryan Luce, PhD, President and CEO of MED-TAP International; Alan Lyles, ScD, MPH, Assistant Professor Johns Hopkins University School of Hygiene and Public Health; and Sean D. Sullivan, PhD, Associate Professor, University of Washington Department of Pharmacy.

The *Format* would not have come about without the pioneering work of Dwight S. "Pete" Fullerton, PhD and the pharmacy services staff at Regence BlueShield; as well as Dell B. Mather, PharmD, Prime Therapeutics. Their efforts in improving the evidentiary requirements for rational drug selection in managed care organizations served as a practical basis for evaluating the items considered for inclusion in this document. These guidelines have benefited directly and indirectly from their efforts.

As the *Format* evolved through progressive iterations, the Academy was well served by a task force of members who agreed to act as an expert review panel. We are indebted for the sage advice and constructive comments that helped mold this document given by: Chad Green, PharmD, MBA, Aventis Pharmaceuticals; Brenda R. Motheral, RPh, MBA, PhD, Director, Outcomes Research, Health Management Services; Vera E. Person-Aaron, RPh, MS, Associate Director, Managed Care, Sanofi-Synthelabo Inc.; C.E. (Gene) Reeder, RPh, PhD, Associate Dean, University of South Carolina Center for Outcomes Research and Evaluation; Louise J. Sargent, RPh, MS, Medical Information Scientist, AstraZeneca Pharmaceuticals, and James Shaw, PharmD, MS, Pre-Doctoral Fellow in Pharmaceutical Policy, The University of Arizona College of Pharmacy.

Special recognition is due Richard Fry, Senior Director of Pharmacy Affairs for AMCP. Richard's diligence in shepherding the *Format* from inspiration to implementation made it a reality. His personal commitment, perseverance, and expertise are at the root of this fine tool for managed care pharmacy. ♦

Preface

The Academy of Managed Care Pharmacy (AMCP) has developed AMCP's *Format for Formulary Submissions*. The *Format* is a tool for the pharmacy director to use in obtaining and arraying useful clinical and pharmacoeconomic data that will enable a Pharmacy & Therapeutics (P&T) Committee to draw evidence-based decisions that will guide the treatment options available to the covered population. It is intended as a template for pharmaceutical and medical device manufacturers to use to construct a formulary submission dossier designed to make the product evaluation process in formulary development more rational. As the *Format* becomes widely adopted by health care organizations establishing formularies, manufacturers will be able to standardize the framework within which they present population-specific data.

The *Format's* process has been designed to maintain a high standard of objectivity and will achieve two important goals. First, the timeliness, scope, quality, and relevance of information available to the P&T Committee will likely be improved. Take for example the requirement of submitting unpublished studies and information regarding anticipated off-label uses of the product. This request improves access to material that has been difficult to obtain in the past. It also enables manufacturers to submit such data within regulatory constraints mandated by the Food and Drug Administration. Further, by assessing the health plan impact of using a product, the models requested can improve the P&T Committee's ability to assess the effects of formulary alternatives on clinical outcomes and economic consequences for the entire health plan.

Secondly, the *Format* will streamline the data acquisition and review process for health plan staff pharmacists. By clearly specifying the standards of evidence implicit in the existing formulary process, the submission guidelines furnish pharmaceutical manufacturers with consistent direction concerning the nature and format of information that is expected. In addition, the standardized format allows clinical staff to formally evaluate the completeness of submissions received and to easily add the results of the plan's literature reviews and analysis.

Effective formulary deliberations require accurate, complete product dossiers best developed by manufacturers in partnership with health plans. Therefore, implementation of the *Format* calls for resource and communication commitments by both health plans and manufacturers.

Health plans can facilitate the *Format* process by providing manufacturers with guidance on criteria that the health plan uses to determine formulary acceptance. These criteria should include data specific to the health plan's population so that the information requested from the manufacturers will be valid and more germane to the plan's needs.

Health plan requirements for the successful implementation of the process include, but are not limited to:

- a) Human, technical (IT), and financial resources to support the process within the plan;

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- b) Clear communication of *Format* requirements to pharmaceutical industry representatives;
- c) Health plan pharmacy staff training in interpreting and integrating the data presented into the formulary process; and
- d) Accessibility to health plan staff by industry representatives for presentations on data and economic models.

Since modeling processes used by manufacturers can be complex and numerous, a health plan should request a detailed description of the structure of the model used and an explanation of its findings. In order to analyze the model, health plans can use an assessment based on the guidelines for authors and peer reviewers reported in the *British Medical Journal (Drummond and Jefferson, 1996)*¹ (see Appendix 7.1), that provides a checklist for health plans as a consistent measure of the quality and comprehensiveness of the report.

Part of the health plan's use of the *Format* should include critical evaluations of the data supplied by manufacturers to validate it prior to its submission to the P&T Committee. The review should include an analysis of the model and its findings by one trained in pharmacoeconomics.

Under the *Format*, the pharmaceutical industry will have the opportunity to justify the price of a new agent in terms of its health value to the health plan. The *Format* does not specify methods for economic evaluation. It is the submitter's responsibility to utilize appropriate techniques and data sources in order to demonstrate:

- ♦ Disease description and agent's role in therapy;
- ♦ Clinical efficacy, safety, and effectiveness;
- ♦ Economic evaluations;
- ♦ Modeling; and
- ♦ Clinical value.

Under the *Format*, manufacturers have increased responsibility for providing data, particularly economic impact information. The economic data requirements are for disease-based models only, not random clinical trial-specific models. The economic data called for must be broadly applicable to the health plan population and address the system-wide impact of formulary changes on both clinical outcomes and resource utilization and costs.

In response to requests from Australia, Canada, and other countries, major pharmaceutical manufacturers are already submitting outcomes modeling data as part of submissions to national formularies. The *Format's* requirements mirror these requests. The formalized system suggested in AMCP's *Format* should be seen as a dynamic, rather than static, process. It is anticipated that increased standardization of economic evaluations and outcomes modeling will lead to progressive improvement in the quality of submissions over time.

Products should only be considered for formulary review when the manufacturer can submit a complete dossier. When evidence is missing, the manufacturer should provide the health plan with a detailed explanation of what evidence is missing and a

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plan that addresses this deficiency within a specific time limit. If a dossier is not submitted, the plan should reserve the right either (i) to use its own internal resources or contract with experts to perform the necessary analysis, or (ii) to place the product on a prior authorization status until such time as an acceptable dossier is submitted.

AMCP's *Format for Formulary Submissions* is a template or guide, not a mandate or standard. As such, it does not claim to establish a standard of practice for managed care pharmacy. Since many of the provisions of the document test relatively uncharted waters, AMCP intends to gather comments on the *Format's* use over the next year and edit it as necessary based on those comments. Please submit ideas and comments you have to Steve Avey, FMCP Executive Director at (703) 683-8416, ext 346 or at savey@FMCPnet.org. We also intend to test the *Format* in specific sites and, if warranted, offer training for those interested.

As we look down the road, once there is broad acceptance and use of standards for formally evaluating and incorporating health economics information into product adoption decisions for day-to-day plan management, health plans are encouraged to adopt the larger *societal* perspective that classic pharmacoeconomics argues should be the base of decision making. In the interim, we consider this format to represent the minimum expected information to accompany a formulary submission. It permits industry scientists and consultants, using a reasonable scientific framework, to submit additional information (e.g. indirect and non-medical cost impacts) to demonstrate the broad value of their products when compared to usual treatments. It will provide the managed care pharmacist with data often unavailable in the past. ♦

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Section I — Overview

1.0 Drug/Product Formulary System

Rational product adoption decisions employing clinical, economic, and humanistic data are built on the foundation of a sound formulary system. These precepts are affirmed by the recently approved guidance “Principles of a Sound Drug Formulary System” (U. S. Pharmacopeia, August 2000) endorsed by the Academy of Managed Care Pharmacy, Alliance of Community Health Plans, American Medical Association, American Society of Health-System Pharmacists, Department of Veterans Affairs, Pharmacy Benefits Management Strategic Healthcare Group, the National Business Coalition on Health, and U. S. Pharmacopeia. (See Appendix 7.2)

Drug products should be subjected to a rigorous clinical review (and periodic re-review) based on evidence from the clinical literature. Efficacy, safety, effectiveness and cost-effectiveness provide the foundation for this review. Where feasible, comparisons should be made relative to existing products rather than to placebo. The goal of the process is optimal patient care, taking into account the reality of constrained budgets. For products proven equivalent, decisions will be made primarily on net acquisition cost.

1.1 The Role of Guidelines

Formulary guidelines support the informed selection of optimal treatment choices by a) standardizing information requirements, b) formalizing their impact on both the health plan and its enrolled patient population, and c) making the assumptions and evidence influencing the choice(s) clear and verifiable.

AMCP’s *Format*, as proposed here, has the potential to move managed care away from the pharmacy silo-budgeting approach typically utilized for formulary decisions to a total cost and health impact approach to health care delivery. Guidelines generally have been used to support categorical pharmacy drug cost impact models, which have failed to communicate the value of pharmaceuticals and, at best, are of limited use to health plans.

AMCP’s *Format* offers a template for managed care pharmacists to use for product formulary submissions. These guidelines are intended to rationalize the formulary decision process and to support informed decisions to obtain value from pharmaceutical products. This document contains the information requirements for a comprehensive and systematic evaluation of pharmaceutical products. It is emphasized in the *Format* that economic considerations follow clinical concerns of safety and efficacy. Importantly, manufacturers should understand that submission of information in the format recommended herein does not guarantee approval of their product for listing on the health plan’s drug formulary.

These guidelines offer a clear, shared vision of the formulary process and information requirements to facilitate the partnership necessary between the managed care plan and the manufacturer. The *Format* describes the minimum information requirements necessary to support a comprehensive assessment of the proposed product.

**Section I —
Overview
*continued***

1.2 Format Overview

A formulary submission dossier includes the following sections:

- a) Product Information
- b) Supporting Clinical and Economic Information
- c) Impact Model Report
- d) Clinical Value and Overall Cost
- e) Supporting Information: Bibliography, Checklist and Appendices

1.3 Methods

These guidelines are not intended to restrict dossiers to a specific analytic technique, but the methodology adopted by the manufacturer and the techniques employed should be consistent with the health plan's objective. It is recommended that the manufacturer collaborate with the health plan's representatives to obtain data and to agree on assumptions (*see 6.4: Agenda for Pre-Submission Meeting*).

1.4 Standards of Care and Data Source

Any cost and outcomes assessment must reflect the characteristics of the health plan's treatment environment. Analyses based on clinical trials or data from other health plans often are not sufficient unless the manufacturer shows them to be directly applicable to the health plan. It is recommended that resource utilization and cost impact assessments focus on medical services provided directly by the health plan (or by the contracted medical providers who are deemed to be within the limit of appropriate medical care). In some cases, there may be differences of opinion as to what constitutes appropriate standards of care. If this is the case, the analysis should also be based on the health plan's practice patterns.

1.5 Disclosure of Potential Reporting Bias

To minimize the potential for bias in formulary submissions, manufacturers should follow generally-accepted rules of scientific conduct (*Task Force on Principles for Economic Analysis of Health Care Technology*; Hillman, et al., 1991)^{2,3}. At a minimum, the following should be disclosed:

- a) Identify all investigators and give the details of their affiliations
- b) All financial or contractual relations that might impact on the independence of the investigators
- c) All key assumptions

Section I — Overview *continued*

1.6 Recommended Formulary Submission Process (see 6.5)

The following steps are recommended for a submission:

Step 1: A letter (*Notice of Intention to Submit*) should be sent to the attention of the health plan's Pharmacy Director or Formulary Manager, to notify the manufacturer's intent to submit a product for formulary consideration at least 6 months prior to submission. This letter should include the timelines for the submission and permit the health plan to schedule a review and assign the submission to a subcommittee.

Step 2: The manufacturer should schedule an initial pre-submission meeting(s) with representatives of the health plan to review the *Format's* requirements and to identify any data that might be required to establish a baseline for product impact assessment. Required data will be identified and decisions on how to capture these data will be addressed (see 6.4: *Agenda for Pre-Submission Meeting*).

Step 3: At least 2 months prior to the formulary committee's meeting, copies of the submission should be received by the health plan's designee. This submission should be accompanied by an executive summary, a completed checklist (*section 6.5*), and justification for incomplete or missing data.

Step 4: The health plan's designee will review the submission. Based on the initial review, the manufacturer may be asked to submit additional information to complete the submission dossier.

Step 5: At least 2 weeks prior to the Pharmacy and Therapeutics Committee meeting, the manufacturer will be informed in writing whether the dossier is considered complete and whether it will be abstracted for the Pharmacy and Therapeutics Committee's consideration. If it is not considered to be complete or useful, it will be returned to the manufacturer citing the reasons why it was not submitted.

Step 6: The health plan's designee submits a summary of the manufacturer's submission to the Pharmacy and Therapeutics Committee, presents the principal arguments for and against listing the product on formulary, and any conditions which may apply.

Step 7: The manufacturer is informed in writing of the Pharmacy and Therapeutics Committee's recommendation for the product's formulary listing and any recommendations for restricting access. The health plan will provide a detailed rationale to the manufacturer for a product's denial or restriction as well as guidance for reconsideration or appeal.

1.7 Role and Responsibilities of the Health Plan

The manufacturer is encouraged to solicit data and information from the health plan to facilitate complying with the requested dossier.

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**Section II —
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1.8 The Formulary Submission Dossier

A completed formulary submission will use this format to integrate the relevant published and unpublished data evaluating the efficacy, safety, economic impact, and other medical outcomes associated with the use of the manufacturer's product. It should contain the following items:

Complete sections II–V, presented in the order listed. Where data are unavailable or incomplete, the manufacturer should indicate and explain why it is missing and when it will be provided.

Provide the following additional information:

- a) A comprehensive list of references for all studies cited and for information sources from which estimates were drawn for use in the economic evaluation for section 3.3.
- b) Identify the author(s) of the submission document (*see 1.5*).
- c) Identify the author(s) of primary economic evaluations conducted for section 3.3. of this document (*see 1.5*).
- d) Identify a contact person who can answer questions and provide additional information regarding the submission materials for health plan reviewers.

2.1 Product Description [10 pages maximum]

Detailed knowledge about the characteristics of the product is required. The new product should be compared with other agents commonly used to treat the condition, whether or not these products are currently on the health plan's formulary. The product description consists of information that traditionally has been incorporated in a product monograph and includes the following:

- a. Generic, brand name and therapeutic class of the product,
- b. All dosage forms, including strengths and package sizes,
- c. The National Drug Code (NDC) for all formulations,
- d. A copy of the official product labeling/literature, and
- e. The (AWP) cost per unit size (the plan contract price, if available, should be included as well).

Additional required product information includes:

- f. DPS/AHFS Drug Classification
- g. FDA Approved and other Studied Indication(s): A detailed discussion of the approved Food and Drug Administration (FDA) indications and the date approval was granted (or is expected to be granted) must be included. Data on off-label use, if available, should be included.
- h. Pharmacology

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*continued***

- i. Pharmacokinetics
- j. Contraindications
- k. Warnings/Precautions
- l. Adverse Effects
- m. Interactions, with suggestions on how to avoid them
 - ♦ Drug/Drug
 - ♦ Drug/Food
 - ♦ Drug/Disease
- n. Availability, Dosing and Administration
- o. Co-Prescribed / Concomitant Therapies, including dosages
- p. Comparison with the pharmacokinetic/pharmacologic profile of other agents in the therapeutic area. The material should include a discussion of comparator product(s) or services that the proposed product is expected to substitute for, or replace (including drug and non-drug interventions). This information should be presented in tabular form.

2.2 Place of the Product in Therapy [3 pages maximum]

To assess the impact of a new product effectively, the clinical condition being treated and the role of the product in its treatment must be clearly understood. The disease description should include the disease and characteristics of the patients who are treated for the condition. Present a brief summary of information from the literature for each topic. When information from studies is presented, strongly consider reporting the results in tabular form. Next, an attempt should be made to generalize these findings to the health plan's population. Discuss the implications of any differences that exist between the literature and the health plan's practice patterns and patient population. When more than one disease is addressed, complete the description for each separate condition.

Specific disease descriptive information requested: **[No more than 2–3 pages per disease]**

- a. Epidemiology and relevant risk factors
- b. Pathophysiology
- c. Clinical presentation
- d. Approaches to treatment — principal options/practice patterns
- e. A description of alternative treatment options (both drug and non-drug)
- f. The place of the proposed therapy in treatment (e.g. first line)
- g. The expected outcomes of therapy
- h. Other key assumptions and their rationale

The manufacturer will be responsible for determining the relevant treatment options for comparison, although the determination should be made with assistance and guidance from the health plan. Consequently, this topic should be part of the manufacturer's initial meeting with the health plan.

Section III — Supporting Clinical and Economic Information

Submit the key clinical and economic studies that have been conducted, whether published or not, for clinical safety, efficacy, and economic evaluations. Economic evaluation studies include prospective cost-efficacy studies, prospective cost-effectiveness studies, cross-sectional or retrospective economic evaluations, review articles and meta-analyses. For each of the categories below, present summaries of the studies **(maximum one page per study; maximum five studies per category)**.

Studies reported in this section should be summarized in a clear, concise format; presenting data from multiple studies in tabular form within a category is strongly encouraged. All of the following that apply should be included (*asterisk items are only necessary for economic studies*):

- a. Name of the clinical trial or study, location and study date;
- b. Trial design, randomization and blinding procedures;
 - * Research question(s);
 - * Type of economic study;
 - * Study perspective;
- c. Washout, inclusion and exclusion criteria;
- d. Sample characteristics (demographics, size, disease severity, co-morbidities);
 - * Treated population (actual or assumed)
- e. Patient follow-up procedures (e.g., if an intention-to-treat design is used, were drop-outs followed);
 - * Treatment period
- f. Treatment and dosage regimens;
 - * Treatment framework
 - * Resource utilization classification
 - * Unit costs;
- g. Clinical outcome(s) measures;
 - * Outcomes evaluated;
- h. Other outcome measures (e.g., quality of life);
 - * Principal findings
- i. Statistical significance of outcomes and power calculations;
- j. Validation of outcomes instrument (if applicable);
- k. Compliance behavior;
- l. Generalizability of the population treated;
 - * Relevance to [PLAN NAME]'s enrolled populations being treated
- m. Publication citation(s)/references used.

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Information
*continued***

3.1 Presenting Clinical Study Results [1 page maximum per study]

Formulary decisions should use all the necessary data for an evidence-based technology assessment of a new product. The manufacturer should provide a summary of pivotal safety and efficacy trials for the product (**maximum five studies**) and any head-to-head comparison clinical studies between the proposed product and the principal comparators. Summaries of principal trial results of key comparator products are desirable but not required.

In the appendix, include a reprint of each study discussed or referenced. Discuss important study findings and comment on their implications for the health plan's patient population. Information from all known studies on the product should be summarized in a spreadsheet format (*item f below*), noting which studies were presented previously (*items a through d*).

- a) Pivotal safety and efficacy trials [**No more than 1 page per study**]
- b) Prospective effectiveness (e.g. large simple) trials [**No more than 1 page per study**]
- c) Additional prospective studies examining other non-economic endpoints such as health status measures and quality of life. If the instruments utilized in these studies are supported by previous validation and reliability studies, also reference these studies. [**No more than 1 page per study**]
- d) Retrospective studies [**No more than 1 page per study**]
- e) Summarize review articles and meta-analyses, with particular emphasis on the inclusion and exclusion criteria and main outcome measure(s) for studies analyzed.
- f) Spreadsheet of all published and unpublished trials addressing the following data elements:

| | | |
|----------------------------|--------------------------------|-------------|
| ♦ Citation, if published | ♦ Sample size | ♦ Endpoints |
| ♦ Study dates | ♦ Treatments | ♦ Results |
| ♦ Design | ♦ Inclusion/exclusion criteria | |
| ♦ Statistical significance | | |

3.2 Clinical and Disease Management Intervention Strategies [3 pages maximum]

Identify and summarize any studies or reports that evaluate the impact of the product being proposed as part of a disease or care management intervention strategy.

3.3 Economic Evaluation Supporting Data [1 page maximum per study]

Economic evaluations permit the selection from a number of analytic designs, including prospective studies piggy-backed onto pivotal clinical trials, naturalistic comparative studies, retrospective studies or modeling studies. Since the focus of this portion

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*continued***

**Section IV —
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[maximum of
15 pages]**

of the document is a comprehensive assessment of available evidence, the number of studies considered will not be restricted by imposing methodological standards. However, the health plan will judge the merit of individual studies based on published standards for conducting and reporting these analyses.⁴⁻¹⁴

4.1 Model Overview

Properly constructed pharmacoeconomic models can combine estimates of the treatment effectiveness, the resources consumed (and, thus, costs) by each treatment process, and a measure of uncertainty in these estimates to predict the system-wide consequences of formulary changes. Models developed in this manner can aid decisions regarding the addition of a new product to the formulary, help define its specific role in the health plan's environment, and assist in creating benchmarks against which the product's future performance can be measured.

Development of an analytic model as described in this section is important for the health plan to evaluate the impact which the new product, if adopted, is likely to have on its costs and the clinical and humanistic outcomes of the plan's enrolled population. Even though the specific formats utilized by individual models may vary, each should incorporate a comprehensive disease-based analytical model (*Langley and Sullivan, 1996*) that is tailored to the plan and depicts the following:

- a. Disease or condition, its natural history, and clinical course and outcomes.
- b. Primary treatment options and the treatment process for each option. Each process of treatment utilizing a specific product or other intervention is called a Clinical Pathway. If the health plan employs a treatment guideline for this condition, this framework should be followed. Alternative Clinical Pathways presented by the manufacturer may also be considered.
- c. Proportion and characteristics of patients being treated by the Clinical Pathway.
- d. Product and other medical resources used to support each Clinical Pathway.
- e. Costs of product and other medical resources consumed within each Clinical Pathway.
- f. Outcomes of therapy for each Clinical Pathway, including expected proportion of treatment failures and mean or median time to failure, if known. These outcomes can be broadly and uniquely defined by the manufacturer and can be modeled from other data sources. The manufacturer should address the relevance of the selected outcomes measure and generate both baseline and projected outcome impact assessments.
- g. Incremental cost and outcomes analysis presented in either cost/consequences tables or as cost-effectiveness ratios.

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[maximum of
15 pages]
*continued***

In addition, the manufacturer is requested to:

- h. Separate the volume of resources utilized and the unit costs for each resource.
- i. Perform sensitivity analyses on pivotal estimates and assumptions.
- j. Consult with the health plan in the early stages of model development to ensure the incorporation of appropriate comparator products and endpoints.
- k. Present the following information in tabular form: total resource utilization, total costs, total effectiveness, incremental costs, and incremental effectiveness. Measures of total and incremental effectiveness should incorporate natural units as well as quality-adjusted life years when possible.

The model should be based on the clinical trial and economic data, as modified by realistic expectations of the plan, practice patterns within the plan and the particular enrolled patient population. For the model to be realistic, it will commonly be necessary for the manufacturer either to obtain data or information from the health plan or, if that is not available, to provide their best estimates and a supporting rationale. The manufacturer is encouraged to contact the formulary manager in the early stages of model development to discuss the availability of data. Other information sources include randomized controlled trials, retrospective analyses, case-control studies, cross-sectional surveys, case reports, and expert opinion.

The model framework should consider recommendations published by the Panel on Cost-Effectiveness in Health and Medicine convened by the U.S. Public Health Service.⁷ Although no standard model approach is proposed, good modeling practices should always be followed.⁹ The model's time frame is a critical element. For chronic illnesses, a one-year period should be adopted as well as a longer period, as appropriate for the clinical problem and its resolution. For this longer period, a final health outcome determination is recommended. For acute illness, shorter periods may be appropriate.

4.2 Clinical Trials: Claims for Safety and Efficacy [10 page maximum]

The primary considerations for adding a product to a formulary are the safety and the effectiveness of the product for the managed care system's eligible population. Efficacy, as determined by clinical trial results, must be translated into effectiveness. The best quantitative estimates of effectiveness are required, with the uncertainty in the estimate(s) being handled analytically via sensitivity analysis. If these data are not available, manufacturers should provide their best estimate of the expected effectiveness outcomes in usual practice. Translation of claims from an efficacy to an effectiveness context should also be considered when:

- a. The model's treatment period extends beyond that represented by the clinical trial;
- b. Outcomes supported by the trial are intermediate or surrogate in nature;

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15 pages]
*continued***

- c. Compliance, dosing, co-morbid conditions and the population of interest (e.g., children, elderly) are expected to differ from the efficacy trial data.

Poor compliance, especially for chronic conditions, can undermine claims that are based exclusively on clinical trials. All claims made for new products (whether they are in therapeutic or economic terms) state clearly the assumptions concerning patient compliance. It is recommended that manufacturers provide documentation of anticipated compliance patterns from populations similar to the managed care plan's treatment population if available.

Additional issues pertaining to clinical trial data used to support a formulary submission include:

- a. Establishing a clinical trial's external validity;
- b. Controlling for provider and patient behavioral characteristics. While clinical trials typically focus on a product's efficacy, the relevant outcome for modeling purposes is effectiveness.

4.3 Incidence and Prevalence Impact Assessments

An analytic model should reflect a *prevalence* framework rather than *incidence* when modeling chronic diseases. The prevalence framework represents the patterns of treatment experienced by the health plan over a specified length of time (i.e., 12-month period), irrespective of the disease state reached by individual members. Incidence analysis, however, can be an acceptable modeling perspective for some acute diseases.

Outcomes should be differentiated by incidence and prevalence. Typically, in incidence analysis a cohort of patients is tracked from initiation of therapy to an intermediate or final outcome. The manufacturer should translate such point-estimate impact claims into prevalence based claims, if possible, to clarify how the outcomes are achieved and how they are distributed within the treated population. If this is not possible, the manufacturer should work with the health plan to estimate the net effect of treatment across the entire patient population.

4.4 Optimizing Patient Care

The impact assessment should start with an assessment of resource utilization and associated medical costs at baseline for the designated therapy area, using data aggregated from service claims. This will allow the manufacturer to describe treatment options, determine patterns of resource utilization and determine imputed costs for pharmacy and medical claims.

Treatment pattern models should characterize the health plan's population and reflect best practice(s) as promulgated by task forces, learned societies or appropriate government agencies. If these utilization patterns differ from actual practice, the actual treatment patterns should also be modeled. It is desirable for the model to depict both scenarios when it is believed that actual and best practices differ.

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[maximum of
15 pages]
*continued***

Evidence for care pathway impacts on patient outcomes, resource utilization, costs and therapy options must be provided, as available: (a) under the evidence supporting clinical and pharmacoeconomic claims; and, (b) under the model assumptions chosen for the impact assessment. Direct evidence of health outcomes often may not be available, however, and will require agreement between the health plan and the manufacturer on which approach or assumptions will be accepted by the health plan. All assumptions of the analysis must be presented and justified consistent with the prevalence framework of the analysis. These assumptions may be justified using known characteristics of patient population, epidemiological profiles and clinical trials, meta-analyses and literature reviews, and expert panels.

When a product is to be used in the treatment of more than one disease, its impact should be modeled in each therapeutic area. Because of the complexity involved in constructing a model that simultaneously addresses several therapeutic areas, we recommend using a separate model for each condition.

4.5 Presentation of Model Results

Results should be presented as follows:

- a. Estimates must include the cost of any additional resources associated with implementing the therapy (e.g., disease management). Costs should be presented as total net costs of introduction of the new product.
- b. Based on discussions between the plan and the manufacturer, the submission should include recommendations on the use of medical and pharmacy data to monitor costs, patient outcomes and validate claims.
- c. Impact assessments should be estimated for the first three budget periods following product launch.

4.6 Exceptions

In some situations, a pre-existing model developed for another health plan may eliminate the need to develop a new model for this submission. To be acceptable, the existing model should follow the general framework described in this document and must be able to demonstrate the system-wide impact of introducing the product to the health plan's formulary. It will be the manufacturer's responsibility to justify the adequacy of pre-existing substitutes for the model described above.

**Section V —
Clinical Value
and Overall Cost
[2 page
maximum]**

This section of the submission requirements represents the principal opportunity for a manufacturer to communicate the value of its product in the health plan environment. The manufacturer should briefly summarize the information presented, state the expected per unit product cost, and estimate the health plan's expenditures for the product. Based on this information, a value argument should then be articulated to justify expenditures on this product in the context of its anticipated effects on clinical and health-related quality of life outcomes and then economic consequences for the health plan and its clients and members. Through this process, product value is redefined as both parties move beyond cost containment to focus on optimizing drug utilization in an environment of limited resources.

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6.1 References Contained in Dossiers

Submissions should list and provide copies of all clinical and pharmacoeconomic references made in Sections **II through IV** above.

6.2 Spreadsheet Models

Media: In addition to the written report, the manufacturer must provide a transparent, unlocked copy of the model without the graphical interface. It should be presented on a 3.5" disk or other electronic media as an Excel workbook, ASCII tab-delimited file or an alternative format that is agreed upon by the health plan and the manufacturer. The model should be transparent, thus designed to allow the health plan staff to investigate assumptions and calculations, and to perform independent sensitivity analyses by varying individual parameters. This model will be retained by the health plan for internal analyses and will not be released to any other party. Referenced articles are to be attached as appendices. The completed dossier is to be sent to the formulary manager at the health plan.

6.3 Data and Information Availability from the Health Plan

Specific data elements are not listed at this time since their availability will vary from plan to plan and the specific data needed will have some variability from model to model. As health plans and manufacturers develop more experience with the use of this *Format* and results from pilot projects are analyzed, AMCP will develop a core data set, from which each plan would add or delete as part of their discussions with the manufacturer.

6.4 Agenda for Pre-Submission Meeting

This meeting(s) should take place at least 4-to-6 months before the actual date of formulary review to allow time for the manufacturer to gather the necessary data for the health plan. This meeting will also serve as a forum to discuss the consequences

**Section VI —
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*continued***

of missing information deemed necessary by the health plan. This agenda can serve as a discussion guide to ensure that relevant topics are raised.

Manufacturer Responsibilities

The representatives for the manufacturer should provide a copy and be prepared to discuss the following at the first meeting(s):

- a) List of intended indications
- b) Summary of all studies to be included in the formulary submission. This will include:
 - ♦ Clinical trials (experimental and non-experimental)
 - ♦ Outcomes studies
 - ♦ Meta analysis
 - ♦ Retrospective studies
 - ♦ Pharmacoeconomic models
- c) A general description of how your cost and outcomes impact assessments will be developed. This should include:
 - ♦ List of data sources (studies, databases, etc.),
 - ♦ Discussion of conversion of efficacy to effectiveness for both drug and comparators,
 - ♦ Approach to modeling the environment of the health plan,
 - ♦ Assumptions and suggested approach for determining patient characteristics for switching.
- d) Summary of anticipated studies to be completed within 1–3 years
- e) A filled out submission checklist

Agenda Topics

- a) Review of intended indications
- b) Review of clinical studies
 - 1) Explanation of comparators used and determination of their appropriateness
 - 2) Determine level of data needed for efficacy claims
 - ♦ If not enough, discuss the use of non-experimental data to supplement?
 - ♦ Determine if submission can proceed without the additional data?
- c) Review of cost impact assessment
 - 1) Evaluation of cost data and how it compares to health plan
 - 2) Level of patient switching: how does this influence overall costs?
 - 3) Discuss future studies and enhancements
 - 4) Discuss incorporation of health plan data
 - 5) Determine level of data needed for submission
 - 6) Determine if submission can proceed without the additional data

**Section VI —
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- d) Review of outcomes impact assessment
 - 1) Evaluate outcome markers used
 - 2) Level of anticipated patient switching
 - 3) Level of patient compliance
 - 4) Discussion of conversion of efficacy to effectiveness
 - 5) Modeling assumptions appropriateness
 - 6) Discuss of future outcomes monitoring
 - 7) Determine level of data needed for submission
 - 8) Determine if submission can proceed without the additional data

6.5 Formulary Submission Checklist

A completed formulary submission checklist should accompany each submission. A brief explanation for all missing data should also be included.

| A. Submission Process | Yes | No |
|--|------------|-----------|
| A.1 Have you met with [PLAN NAME] staff to review the submission process? | | |
| A.2 Have you agreed to the submission date with [PLAN NAME]? | | |
| A.3 Have you requested summary data to identify baseline characteristics of the plan population? | | |
| A.4 Have you included an explanation for any missing data? (Check yes if not applicable) | | |
| B. Product Information | Yes | No |
| B.1 Have you provided a product description for the product? | | |
| B.2 Have you provided a list of approved indications for the product? | | |
| B.3 Have you identified the place of this product in therapy for each indication? | | |
| B.4 Have you provided copies of treatment guidelines for this product? | | |
| B.5 Have you listed the intermediate and final outcomes of therapy for this product? | | |
| B.6 Have you listed any co-prescribed drugs for this product by indication? | | |
| B.7 Have you identified the comparator drugs for this product by indication? | | |
| C. Supporting Clinical Information | Yes | No |
| C.1 Have you identified all relevant clinical and other experimental studies for the product? | | |
| C.2 Have you identified all relevant clinical and other experimental studies for the product's comparator therapies? | | |
| C.3 Have you included copies of all studies identified in the submission package? | | |
| C.4 Have you provided a spreadsheet summary of all studies identified? | | |

**Section VI —
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| | | |
|---|------------|-----------|
| C. Supporting Clinical Information | Yes | No |
| C.5 Have you translated the outcomes to effectiveness terms? | | |
| C.6 Have you included these translations in the submission? | | |
| C.7 Have you included all relevant non-experimental studies for the product? | | |
| C.8 Have you included all relevant non-experimental studies for its proposed comparator therapies? | | |
| C.9 Have you provided a spreadsheet summary of all non-experimental studies? | | |
| C.10 Have you translated the outcomes in non-experimental studies to effectiveness terms? | | |
| C.11 Have you included these translations in the submission? | | |
| D. Supporting Economic Information | Yes | No |
| D.1 Have you identified all relevant pharmacoeconomic studies for the product? | | |
| D.2 Have you justified the relevance of these pharmacoeconomic studies (PE) for this population? | | |
| D.3 Have you provided a spreadsheet summary of these PE studies, detailing their relevance? | | |
| D.4 Have you developed a therapy intervention framework for this product for each indication? | | |
| D.5 Have you confirmed the therapy intervention framework with the health plan? | | |
| D.6 Have you identified the characteristics of patients to be switched to this product? | | |
| D.7 Have you identified the patient characteristics that would exclude patients from your drug? | | |
| D.8 Have you provided electronic copies of all spreadsheets or models used? | | |
| D.9 Will a disease or care management strategy be utilized with the introduction of this product? | | |
| D.10 Have you included documentation on this intervention program in the submission? | | |
| E. Impact Model Assessments Costs | Yes | No |
| E.1 Have you included a baseline prevalence analysis of resource utilization and cost? | | |
| E.2 Have you structured these baseline estimates in terms of your therapy intervention framework? | | |
| E.3 Have you detailed the scenarios for cost impact assessment? | | |
| E.4 Have you highlighted the assumptions made for projecting patient switching behavior? | | |
| E.5 Have you justified the scenarios and assumptions for this plan's patient population? | | |
| E.6 Have you provided aggregate cost impact assessments for the next 3 years? | | |
| E.7 Have you provided a breakdown of the costs by medical resource utilization and drug categories? | | |

**Section VI —
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| | | | |
|-----------|---|------------|-----------|
| E.8 | Have you included a proposal on how these cost impact projections might be monitored? | I | I |
| E.9 | Have you explained how differences between projections and actual costs might be resolved? | I | I |
| E.10 | Have you included the cost of your proposed intervention program in the cost assessment? | I | I |
| F. | Clinical | Yes | No |
| F.1 | Have you included a baseline prevalence analysis of patient outcomes? | I | I |
| F.2 | Have you structured these baseline estimates in terms of your therapy intervention framework? | I | I |
| F.3 | Have you detailed the scenarios for outcome impact assessment? | I | I |
| F.4 | Have you detailed the assumptions made for projecting patient switching behavior? | I | I |
| F.5 | Have you justified the scenarios and assumptions for this plan's population? | I | I |
| F.6 | Have you provided aggregate patient outcome impact assessments for the next 3 years? | I | I |
| F.7 | Have you included a proposal on how patient outcomes might be monitored? | I | I |
| F.8 | Have you explained the differences between the projected and actual patient outcomes? | I | I |

6.6 Terms and Definitions

Care pathways: A general method of using predetermined, time-staged, evidence-based actions for managing the care of patients who have clearly defined diagnoses or require certain procedures. Ideally, care pathways should be applicable to the management of patients moving among a managed health care systems multiple levels of care and practice settings. Other terms for care pathways include clinical care plans, clinical pathways, critical pathways, care guides, and care maps.

Cost and Outcome Modeling: A quantitative modeling method used to estimate the impact of formulary changes on: 1) potential health outcomes; 2) total costs of drug and medical care in a population. One possible use of cost and outcome modeling, for example, is to extrapolate trial-based efficacy data into effectiveness and cost-effectiveness endpoints of relevance to health plans. Cost and outcomes impact data from models can then be used to assess the health and overall fiscal *consequences* of health plan formulary changes. The estimated impact of a new product on the total costs and outcomes of care for health plan members are preferable.

Dossier: A detailed report for each product submitted by the manufacturer for consideration that contains (1) clinical and economic data from published and unpublished studies and (2) a disease-based economic model to project the potential impact that introducing the product would have on health and economic consequences occurring across the entire health plan system.

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Effectiveness: The actual effects of treatment by the drug under “real life” conditions [patients not always remembering to take their doses, physicians often not prescribing the lowest FDA recommended doses, side effects not all controlled, etc]. ‘Head to head’ effectiveness studies with similar medications are preferable.

Efficacy: The potential effects of treatment by the drug under optimal circumstances [e.g. patients all taking their doses at the right times, physicians prescribing correct doses, side effects appropriately monitored, etc]. Efficacy studies are typically the foundation of new drug submissions to the FDA. Studies that compare the efficacy of similar drugs, rather than just efficacy compared to placebo are preferable.

Formulary: A continually updated list of medications, related products and information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health.

Formulary system: An ongoing process whereby a health care organization, through its physicians, pharmacists and other health care professionals, establishes policies on the use of drugs, related products and therapies, and identifies drugs, related products and therapies that are the most medically appropriate and cost effective to best serve the health interests of a given patient population.

6.7 References

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***BMJ* 1996;313:275–283 (3 August)**

M F Drummond, *chair of working party*

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on behalf of the BMJ Economic Evaluation Working Party

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Over the past decade interest in the economic evaluation of health care interventions has risen.¹ Reviews of published studies have, however, shown gaps in the quality of work.^{2,3,4,5} As far back as 1974 Williams listed the essential elements of economic evaluations,⁶ and more recently Drummond and colleagues set out the methodological areas generally agreed among economists.⁷ Guidelines for economic evaluations have been promulgated and reviewed by many bodies,^{8,9,10,11,12,13,14} but few medical journals have explicit guidelines for peer review of economic evaluations or consistently use economist reviewers for economic papers even though they are a major publication outlet for economic evaluations.^{15,16,17} In January 1995 the BMJ set up a working party on economic evaluation to improve the quality of submitted and published economic articles.

It was not our intention to be unduly prescriptive or stifle innovative methods; our emphasis is on improving the clarity of economic evaluations. We also did not address those issues of conduct that have been emphasised in other guidelines.^{13,14,15,16,17,18}

The working party's methods

The working party's objectives were to improve the quality of submitted and published economic evaluations by agreeing acceptable methods and their systematic application before, during, and after peer review. Its task was to produce: (a) guidelines for economic evaluation, together with a comprehensive supporting statement which could be easily understood by both specialist and non-specialist readers; (b) a checklist for use by referees and authors; and (c) a checklist for use by editors.

In producing the guidelines the working party has concentrated on full economic evaluations comparing two or more health care interventions and considering both costs and consequences.¹⁹ Articles sent to the BMJ and other medical journals are often more broadly based "economic submissions,"²⁰ which comprise essentially clinical articles that report approximate cost estimates or make statements that a given treatment was "cost effective."

We took the view that submissions reporting partial evaluations, such as a costing study or an estimate of the value to individuals of improved health, should adhere to the relevant sections of the guidelines given below, as should anecdotal reports or commentaries drawing economic conclusions about alternative forms of care. In addition to a referees' (and authors') checklist, therefore, the working party has produced shorter checklists to help BMJ editors distinguish between full economic evalu-

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ations and other types of economic submission and to help them decide which articles should be sent to referees. The main checklist and the editors' checklists are given in the boxes and a flow chart explaining their use is given in figure 1. The checklists do not replace the need for an overall judgment on the suitability of a paper.

Drafts of the guidelines and their supporting statement and the checklists have been circulated to health economists and journal editors and were debated at the biannual meeting of the UK Health Economists' Study Group in January 1996. A survey of members attending the meeting was used to identify those items of the full referees' checklist that should be used by editors.

The final document reflects a broad consensus among the working party. Any differences reflect different perspectives on the role of economic evaluation and the extent of members' interests in particular aspects of methodology rather than basic differences over the need to improve standards of reporting.

Finally, in drafting the guidelines, the working party recognised that authors may not be able to address all the points in the published version of their paper. This being so, they may care to submit supplementary documents (containing, for example, the details of any economic model used) or refer the reader to other published sources.

Guidelines for submission of economic evaluations

The guidelines are given below, grouped in 10 sections under three headings: study design, data collection, and analysis and interpretation of results. Under each section is a commentary outlining the reasons for the requirements and the main unresolved methodological issues and explaining why firm guidelines cannot be given in some cases. The guidelines are designed to be read in conjunction with other more general guidance to authors from the BMJ and the existing BMJ guidelines on statistical methods.²¹

Study design (I) STUDY QUESTION

- The economic importance of the research question should be outlined.
- The hypothesis being tested, or question being addressed, in the economic evaluation should be clearly stated.
- The viewpoint(s) — for example, health care system, society — for the analysis should be clearly stated and justified.

The research question, or hypothesis, needs to satisfy three criteria.

Firstly, the question should be economically important (in terms of its resource implications) and be relevant to the choices facing the decision maker. The question "Is health promotion worthwhile?" does not meet this criterion because it fails to specify alternatives — worthwhile compared with what? Furthermore, any alternatives need to be realistic. An option of "doing nothing," or maintaining the status quo, should be included when appropriate.

Secondly, the question should be phrased in a way that considers both costs and out-

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comes. The research question “Is drug X more costly than the existing therapy?” will provide incomplete information because the decision maker also needs to consider comparative effectiveness.

| <i>Different forms of economic evaluation</i> | | |
|--|---|--|
| Study type | Measurement of benefits | Question posed |
| Cost minimisation analysis | Benefits found to be equivalent | Which is the most efficient way of achieving a given goal (or objective)? |
| Cost effectiveness analysis Cost-utility analysis | Natural units (eg life years gained) or Healthy years (eg quality adjusted life years, healthy years equivalents) | What is the most efficient way of spending a given budget? |
| Cost-benefit analysis | Monetary terms | Should a given goal (or objective) be pursued to a greater or lesser extent? |

Thirdly, the research question should clearly state the viewpoint of the economic evaluation, and this should be justified. Possible viewpoints include those of the provider institution, the individual clinician or professional organisation, the patient or patient group, the purchaser of health care (or third party payer), and society itself. For example, hospital and other providers may need information to help in making procurement and related technology management decisions; individual clinicians to inform patient care decisions; health insurers or purchasers to support decisions on whether to pay for a procedure or which services to develop; and patients to know the level of costs they may incur in travelling to hospital or providing informal nursing care at home. The viewpoint chosen will in turn influence both the costs included in the evaluation — for example, whether to limit these to a given department, hospital, or locality and whether patient costs are included — and the types of outcome measured — for example, disease specific outcomes or generic measures of patients’ quality of life.

Health economists generally advocate adopting the broader societal viewpoint when possible. This is because data can usually be disaggregated and the analysis carried out from a number of viewpoints. Also, the additional cost of adopting a broader perspective at the outset of a study is probably less than the cost of attempting to gather additional information later. Researchers should therefore identify key potential decision makers (government, purchaser, or provider) at the outset and be able to show that the research question posed will meet the needs of all key groups.

(2) SELECTION OF ALTERNATIVES

- The rationale for choice of the alternative programmes or interventions for comparison should be given.
- The alternative interventions should be described in sufficient detail to enable the reader to assess the relevance to his or her setting — that is, who did what, to whom, where, and how often.

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The choice of the alternative must be designed to help get as close a measure as possible of the opportunity cost of using the new treatment. In principle the comparator should be the most cost effective alternative intervention currently available. In practice the comparator is usually the most widely used alternative treatment. Unless current practice is “doing nothing,” it is usually best not to use placebo as the comparator. Such a study could, however, if well conducted and reported, provide information for use in conjunction with studies of other treatments also compared with placebo.

The alternatives being compared should be described in enough detail to enable the reader to relate the information on costs and outcomes to the alternative courses of action. The use of decision trees and other decision analytic techniques (discussed in section 7) can help to clarify the alternative treatment paths being followed and provide a framework for incorporating cost and outcome data. Clear exposition of alternative treatment paths and the probabilities, cost, and outcomes linked to them should enable decision makers to use those parts of the analysis that are relevant to their viewpoint.

(3) FORM OF EVALUATION

- The form(s) of evaluation used — for example, cost minimisation analysis, cost effectiveness analysis — should be stated.
- A clear justification should be given for the form(s) of evaluation chosen in relation to the question(s) being addressed.

There are two types of question which require the use of different forms of evaluation (see box).

The first is: “Is it worth achieving this goal?” or “How much more or how much less of society’s resources should be allocated to pursuing this goal?” Such questions can be answered formally only by the use of cost-benefit analysis. Looking at one intervention alone, cost-benefit analysis addresses the question of whether its benefits are greater than its costs — that is, the best alternative use of the resources. When several competing interventions are being considered the costs and benefits of each should be examined and that combination which maximises benefits chosen.

The main practical problem with cost-benefit analysis is that of valuing benefits, such as the saving of life or relief of pain, in money units. However, if we are to examine whether more or less should be spent on health care, we need to find a way of comparing the costs (benefits forgone elsewhere) with the benefits of improved health and any other resulting benefits. Even when all benefits cannot be measured in terms of money, cost-benefit analysis provides a useful framework for structuring decision making problems.

The second type of question is: “Given that a goal is to be achieved, what is the most efficient way of doing so?” or “What is the most efficient way of spending a given budget?” Such questions are addressed by cost effectiveness analysis, which can take one of two forms. In the first the health effects of the alternatives are known to be equal, so only the costs need to be analysed, and the least costly alternative is the

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most efficient. This type of analysis is often referred to as cost minimisation analysis. Secondly, alternatives may differ in both cost and effect, and a cost effectiveness ratio (cost per unit of health effect) is calculated for each. For example, given a fixed budget for dialysis, the modality (home dialysis, hospital dialysis, or continuous ambulatory peritoneal dialysis) with the lowest cost per life year saved would, if implemented, maximise the amount of life years produced by the dialysis programme. In practice, however, the selection of the most efficient mix of programmes, given a budget constraint, is more complicated: it depends on whether alternative programmes are mutually exclusive and whether the scale of programmes can be changed without changing their incremental cost effectiveness ratios.

The concept “within a given budget” is also crucial. Often authors produce a ratio of extra costs per extra unit of health effect for one intervention over another and argue that a low cost effectiveness ratio, relative to other existing health care programmes, implies that a given intervention should be provided. However, judgment is still required as the resources to meet such extra costs would inevitably come from another programme, from within or outside health care. (This point is returned to in section 10.)

The third category of evaluation, cost-utility analysis, lies somewhere between cost effectiveness and cost benefit analysis. It can be used to decide the best way of spending a given treatment budget or the health care budget. The basic outcome of cost-utility analysis is “healthy years.” Years of life in states less than full health are converted to healthy years by the use of health state preference values, resulting in generic units of health gain, such as quality adjusted life years (QALYs) or healthy years equivalents.²² (These approaches are discussed in section 5.)

Data Collection (4) EFFECTIVENESS DATA

- If the economic evaluation is based on a single effectiveness study — for example, a clinical trial — details of the design and results of that study should be given — for example, selection of study population, method of allocation of subjects, whether analysed by intention to treat or evaluable cohort, effect size with confidence intervals.
- If the economic evaluation is based on an overview of a number of effectiveness studies details should be given of the method of synthesis or meta-analysis of evidence — for example, search strategy, criteria for inclusion of studies in the overview.

Economic evaluation of interventions relies on the assessment of their clinical effectiveness. The data can come from a single clinical study, a systematic overview of several studies, or an ad hoc synthesis of several sources. Any limitations which weaken the assessment of effectiveness weaken any economic evaluation based on it. The gold standard for assessing the efficacy of interventions is the randomised, double blind controlled trial. This design has the highest internal validity — that is, freedom from bias.

In most clinical trials the primary assessment is based on an intention to treat analysis, which assesses the clinical outcomes of all randomised patients, whether or not

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they completed their allocated treatment. Other analyses serve as secondary or exploratory analyses in clinical studies and should be justified if used as the primary analysis for the economic evaluation.

Clinical trials may include active or placebo controls. In active controlled studies the appropriate comparator for economic analysis is the most cost effective available therapy, or the most widely used therapy. In placebo controlled studies the economic analysis should indicate whether there are active comparators that could be considered as alternative therapies.

The generalisability of the study population is important in assessing the results of clinical trials and hence their suitability for economic evaluations. Factors that can limit generalisability include: differences across countries or health systems; costs and benefits resulting only from the trial protocol but which would not arise in practice; unrealistically high compliance rates; or the appropriateness of usual practice in clinical studies that compare a therapy with best usual care. Clinical data from studies employing a “pragmatic” protocol are often more generalisable and hence preferable for economic evaluation.

In a pragmatic trial subjects are still randomised to treatment groups, but the patient and doctor may not necessarily be blind to the treatments. The treatment protocol is also kept as close to normal care as possible and monitoring kept to a minimum. Such trials are attractive for economic analysis since they reflect what may happen in practice, but the results apply only to similar settings. Unfortunately many clinical studies are still performed under fairly restrictive conditions, so some adjustments may be required for economic evaluation (discussed below).

Clinical data can also be generated from overviews or syntheses of clinical literature. Before the data from any such overview are used in economic assessments the methods used for the overview, including the search strategy and the criteria for inclusion and exclusion of studies, need reporting.

Effectiveness data from overviews have the advantage that the confidence interval around the point estimate of clinical effect is usually narrower than that from an individual trial and the result may be more generalisable.²³ Typically the economic analyst would take the point estimate of effect from the overview as the base case value and use the confidence interval as the relevant range for sensitivity analysis (see section 9).

Sometimes clinical trial data may be insufficient for economic evaluation because some of the relevant endpoints have not been measured, patients have not been followed for long enough, or the design was not pragmatic. In such cases it may be possible to adjust or supplement the data by modelling.

Ad hoc synthesis of effectiveness data from several sources, including expert opinion, is justifiable when no relevant well controlled clinical studies have been performed.²⁴ In many cases the economic evaluation may be based on a previously published clinical trial or systematic overview. In such a case it would be sufficient to provide a brief summary, addressing the points in the guidelines, and to refer the reader to the published source.

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(5) *BENEFIT MEASUREMENT AND VALUATION*

- The primary outcome measure(s) for the economic evaluation should be clearly stated — for example, cases detected, life years, quality adjusted life years (QALYs), willingness to pay.
- If health benefits have been valued details should be given of the methods used — for example, time trade off, standard gamble, contingent valuation — and the subjects from whom valuations were obtained — for example, patients, members of the general public, health care professionals.
- If changes in productivity (indirect benefits) are included they should be reported separately and their relevance to the study question discussed.

In cost effectiveness analysis benefits are usually measured in natural units. For programmes whose main effect is to extend life the usual measure is life years gained. When the main effect is on quality of life a disease specific or generic quality of life index might be used.

Sometimes the benefit measure may be an intermediate marker rather than a final outcome. For example, in comparing programmes for preventing coronary heart disease reductions in blood pressure might be used. Similarly, if two antenatal screening programmes are being compared cases detected might be chosen. Such intermediate endpoints need to be justified, however, as they may be poor surrogates for final outcomes.

Only a single measure can be used in the calculation of a given cost effectiveness ratio. It cannot reflect the effects of a particular intervention on both quantity and quality of life; nor can more than one aspect of quality of life be expressed. This restriction is the main limitation of cost effectiveness analysis, as other important benefits may be overlooked. Nevertheless, several cost effectiveness ratios could be calculated relating to different outcomes — but this may lead to problems of interpretation. Authors using cost effectiveness analysis should explain why they have chosen a particular outcome measure for calculation of the ratio and reassure the reader that important outcomes are not being overlooked.

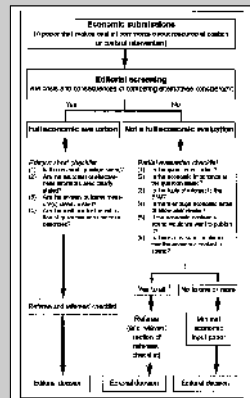
In cost-utility analysis the outcome is healthy years. Quality adjusted life years measure healthy years by combining data on the life years gained by programmes with a value (usually obtained from samples of patients or the population in general) reflecting the quality of those years. Two years of life in a health state judged to be halfway between death and full health would be equivalent to one year in full health. Incremental health gain is given by the difference in quality adjusted life years produced by one intervention as compared to another.

Rather than obtaining valuations for each health state and then multiplying by the time spent in each, the use of healthy years equivalents requires a scenario of a specified sequence of health states and their duration. Respondents are asked how many healthy years of life this scenario is equivalent to — hence the term “healthy years equivalents.”

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Most methods of measuring quality adjusted life years and healthy years equivalents are based on the notion of sacrifice. In economics something is not of value unless one is prepared to give up something else in order to get it. For example, using a time trade off a respondent is asked how many years of life in a health state he or she would be prepared to give up to be in full health. Using a “standard gamble” the respondent is asked to choose between a certain health state and a gamble with two possible outcomes (one worse and the other better than the health state being valued).

Estimates obtained by time trade off methods reflect respondents’ attitudes to time as well as their attitudes to the health state being valued. Likewise, estimates obtained by standard gamble methods reflect respondents’ attitudes to risk as well as their attitudes to the health state being valued. Economists are still debating which approach is most desirable.



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Another cheaper approach is to include in the clinical trial a generic health state preference instrument, such as the EuroQoL (EQ5D)²⁵ or McMaster health utilities index.²⁶ The responses from patients to a simple questionnaire can then be expressed as a health state preference value by reference to pre-scaled responses (obtained by standard gamble or time trade off) from a relevant reference group.

Values can be provided by the population at large or by a sample of patients with the condition for which the treatment is being evaluated. The choice depends on the perspective of the study. If the issue is allocating resources between competing programmes the former might be used; if it is deciding the best way to treat a given condition the latter might be used. In reporting their results authors should explain why a particular source of values has been used.

In cost-benefit analysis the benefits of health care are traditionally valued in money terms by using either the human capital approach or the willingness to pay approach. The former values a health improvement on the basis of future productive worth to society from being able to return to work. Values have to be imputed for activities such as homemaking, so the human capital approach suffers from problems of how to value health improvements for retired and unemployed people.²⁷ This fairly narrow view of the value of improved health is rarely used nowadays.

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Debate continues about whether productivity gains from improved health (“indirect benefits”) should be included alongside other measures of the value of improved health. Some analysts argue it introduces inequalities between those interventions that are aimed at individuals who could potentially return to productive activity and those that are not. Other researchers are concerned about the potential for double counting if indirect benefits are calculated alongside another method of valuing improved health. Finally, some researchers are concerned about the standard method of measuring productivity gains, which values work days lost by gross earnings. Koopmanschap et al have proposed an approach for measuring productivity changes, called the friction cost method, which recognises that the amount of production lost due to disease depends on the time an organisation needs to restore the initial production level.²⁸ Whatever estimation method is used, indirect benefits should be reported separately so that readers can decide whether or not they should be included in the overall result of the study.

The other approach values health improvement (or types of health care) on the basis of people’s willingness to pay for them — usually associated with individuals’ ability to pay. If diseases affect rich and poor in different proportions, and if richer people tend to have different preferences from poor people, then treatment of diseases of the rich may appear to be “valued” more highly. A willingness to pay value will, to an extent, reflect ability to pay as well as strength of preference. It is the latter (strength of preference) which reflects “values,” so when using willingness to pay a check is needed for its association with income and social class.

Willingness to pay has advantages over techniques like quality adjusted life years since the latter focuses on valuation of health gains only, while willingness to pay permits respondents to take into account other factors (such as the value they attach to the process of care). In some cases health gain is not even an issue. For example, two different ways of screening may simply provide information in different ways from those screened,²⁹ and respondents will still have preferences which can be assessed by use of willingness to pay. Also, in some situations individuals other than the patient may be willing to pay for improved health — for example, in the case of communicable diseases.

(6) COSTING

- Quantities of resources should be reported separately from the prices (unit costs) of those resources.
- Methods for the estimation of both quantities and prices (unit costs) should be given.
- The currency and price date should be recorded and details of any adjustment for inflation, or currency conversion, given.

Costing involves estimating the resources used — for example, days in hospital — and their prices (unit costs). These estimates must be reported separately to help the reader judge their relevance to his or her setting. When there are many cost items reporting should concentrate on the main costs.

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When economic evaluations are undertaken alongside clinical trials data on physical quantities may be gathered as part of the trial. The interpretation of resource use resulting from the trial protocol may, however, prove difficult. One view is that everything done to a patient during a clinical trial could potentially influence outcome, so the costs of all procedures should be included. On the other hand, procedures such as clinic visits solely for data collection would not take place in regular clinical care and may seem unlikely to affect outcome. Authors should consider whether the procedures followed in the trial are typical of normal clinical practice and should justify any adjustments they make to the actual observed resource use.

Outside the context of a trial, estimates of resource quantities should be based on data on real patients, collected either prospectively or retrospectively from medical records. The use of physician “expert panels” to estimate resource quantities, while common, runs the risk that respondents may give inaccurate estimates or specify the resources required for ideal care, rather than that provided in practice.

Prices of resources can be obtained from the finance departments of particular institutions or from national statistics, but charges (or fees) can differ from real costs. The authors of studies should comment on the extent to which the use of charges may bias their estimates.

Guidelines on economic appraisal rarely discuss in detail whether the interventions being compared should be costed at marginal or average cost. Marginal costs are the additional costs of changes in the production of a service. Some authors claim the superiority of marginal costing over average costing, but this choice can be related to context and timeframe. In the short run few costs may be variable if a change in treatment is introduced, whereas over longer periods all resources, including buildings, can be switched to other uses.

Thus if the study relates to a decision of a hospital manager the short run marginal costs of the various options in his or her hospital may be the relevant costs in the current budget period. If the decision relates to a matter of national policy, however, average costs may be more appropriate as these reflect the true variable costs when many services are provided in a large number of facilities across the country.

Finally, the dates of both the estimates of resource quantities and prices should be recorded, along with details of any adjustments to a more recent price level. Also, attention should be paid to the generalisation of cost estimates, since relative prices and the opportunities to redeploy resources may differ from place to place.³⁰ Currency conversions should, when possible, be based on real purchasing power, rather than financial exchange rates, which fluctuate according to money market changes.^{31 32}

(7) MODELLING

- Details should be given of any modelling used in the economic study — for example, decision tree model, epidemiology model, regression model.
- Justification should be given of the choice of the model and the key parameters.

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Modelling techniques enable an evaluation to be extended beyond what has been observed in a single set of direct observations. The model will necessarily be simplified, and the extent to which the simplification is appropriate will be a matter of judgment. Modelling may involve explicit and recognised statistical or mathematical techniques. It may, however, simply bring together data from a variety of sources into a formal prespecified conceptual framework, such as a decision analysis model incorporating best available evidence from a wide variety of sources. It may be “what if” modelling, exploring what values for particular uncertain parameters would be needed for a treatment to be cost effective.

Modelling may be required (a) to extrapolate the progression of clinical outcomes (such as survival) beyond that observed in a trial — for example, the progression of disease in patients with asymptomatic AIDS³³; (b) to transform final outcomes from intermediate measures — for example, survival and coronary heart disease events from cholesterol concentrations³⁴; (c) to examine the relation between inputs and outputs in production function models to estimate or apportion resource use — for example, in a cost analysis of neonatal intensive care³⁵; (d) to use data from a variety of sources to undertake a decision analysis — for example, of screening options for prostate cancer³⁶; (e) to use evidence from trials, or systematic reviews of trials, to reflect what might happen in a different clinical setting or population — for example, treatments for respiratory distress syndrome in preterm infants.³⁷

The key requirements are that the modelling should be explicit and clear. The authors should explain which of the reported variables/parameters have been modelled rather than directly observed in a particular sample; what additional variables have been included or excluded; what statistical relations have been assumed or derived; and what evidence supports these assumptions or derivations.

All this information may not be included in the published paper, but it should be available to the reviewer. The overall aim of published reports should be to ensure transparency so that the importance and applicability of the methods can be clearly judged (see section 9).

Analysis and interpretation of results (8) ADJUSTMENTS FOR TIMING OF COSTS AND BENEFITS

- The time horizon over which costs and benefits are considered should be given.
- The discount rate(s) should be given and the choice of rate(s) justified.
- If costs or benefits are not discounted an explanation should be given.

The time horizon should be long enough to capture all the differential effects of the options. It should often extend to the whole life of the treated individuals and even to future generations. If the time horizon is shortened for practical reasons this decision should be justified and an estimate made of any possible bias introduced. Justifying a short time horizon on the grounds of the duration of the available empirical evidence may be fallacious.³⁸ If the relevant horizon for the decision is long term additional assumptions may need to be made.

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In health care there is a still debate on discounting.^{39,40} Most analysts agree that costs should be discounted in any study having a time horizon longer than one year. At present most recommendations seem to vary between 3 and 6%, and a common rate in the literature is 5% per year. Certainly the analyst should use the government recommended rate, probably as the baseline value, and provide a sensitivity analysis with other discount rates. It is also helpful to provide the undiscounted data to allow the reader to recalculate the results using any discount rate.

Most analysts argue that health benefits should be discounted at the same rate as costs in the baseline analysis, even if they are expressed in non-monetary units, such as life years or quality adjusted life years. A zero discount rate — or one lower than that used for costs — can be introduced in the sensitivity analysis. A lower rate is advocated so as not to penalise preventive programmes and also because the results of some studies seem to suggest it.³⁹

However, there is no a priori economic reason to favour preventive programmes and the comparisons may be between them. Imagine two programmes having the same discounted costs and the same total (undiscounted) amount of benefits, say 100 life years, but programme A obtains these benefits between years 2 and 3 and programme B between years 52 and 53. Not discounting health benefits would result in both programmes having the same cost effectiveness ratio, which seems absurd. Moreover, if the absolute benefits of programme B were 100 years and 1 day, it would be preferred — again absurdly.

It is doubtful if there is enough empirical evidence on which to base a decision on the appropriate discount rate. Moreover, if the empirical argument is accepted it should also be applied to the discounting of costs. In favour of a single discount rate for costs and benefits are, firstly, consistency between cost effectiveness and cost-benefit analysis and, secondly, the idea that it is always possible to transform wealth (resources) into health at any point in time. Then, if resources are discounted, why should health not be discounted?

Given the current debates about discounting, the main emphasis should be on transparency in reporting the methods used.

(9) ALLOWANCE FOR UNCERTAINTY

- When stochastic data are reported details should be given of the statistical tests performed and the confidence intervals around the main variables.
- When a sensitivity analysis is performed details should be given of the approach used — for example, multivariate, univariate, threshold analysis — and justification given for the choice of variables for sensitivity analysis and the ranges over which they are varied.

A recent review suggested that one in four published economic evaluations failed to consider uncertainty at all, and only one in eight handled it well. Without proper consideration of uncertainty the reader may be unable to judge whether conclusions are meaningful and robust.⁴¹

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At least three broad types of uncertainty are recognised.⁴²

Uncertainty relating to observed data inputs — When observed data have been sampled from an appropriate population standard statistical methods should be used. Typically, confidence intervals might be presented. When both costs and effects have been derived from a single set of individual patient data a stochastic approach may be used to the presentation of the confidence intervals surrounding the cost effectiveness ratio.^{43 44 45} When data come from a sample attention should also be given to sample size and power. In many studies alongside clinical trials sample size may have been determined entirely by clinical endpoints. In some cases a subsample is assumed to be adequate for collecting data on resource use, but in many cases the variability in resource use data is greater than for clinical parameters, and the distribution of values is often non-normal. Attention must be paid to whether sample sizes are adequate for the economic analyses. Ideally power calculations should be presented.

Uncertainty relating to extrapolation — When data have been extrapolated or modelled (see section 7) the uncertainty inherent in that process is best handled by appropriate sensitivity analysis.

Uncertainty relating to analytical methods — Uncertainties may stem from the existence of alternative analytical methods. Some issues will be avoided by an explicit statement of the approach to be adopted, but others may be usefully handled by using sensitivity analysis — for example, to present results for different discount rates, or with and without indirect costs.

Except for sampled data, uncertainty is usually handled using some form of sensitivity analysis. Simple sensitivity analysis (one way or multi-way), threshold analysis, analysis of extremes, and probabilistic sensitivity analysis may each be appropriate in particular circumstances.⁴² The ranges of values tested need to be justified and ideally should be based on evidence or logic.

Authors and reviewers should pay particular attention to whether the important question is the precision of the quantitative results or the robustness of the conclusions drawn from them. Firm conclusions may be shown to hold despite considerable uncertainty; on the other hand, relatively tight estimates of parameters may still leave substantial uncertainty about the policy implications of the study.

(10) PRESENTATION OF RESULTS

- An incremental analysis — for example, incremental cost per life year gained — should be reported, comparing the relevant alternatives.
- Major outcomes — for example, impact on quality of life — should be presented in a disaggregated as well as aggregated form.
- Any comparisons with other health care interventions — for example, in terms of relative cost effectiveness — should be made only when close similarity in study methods and settings can be demonstrated.
- The answer to the original study question should be given; any conclusions should follow clearly from the data reported and should be accompanied by appropriate qualifications or reservations.

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The main emphasis in the reporting of study results should be on transparency. The main components of cost and benefit — for example, direct costs, indirect costs, life years gained, improvements in quality of life — should be reported in a disaggregated form before being combined in a single index or ratio.

The results of economic evaluations are usually presented as a summary index such as a cost effectiveness or cost-utility ratio. When two or more interventions are being compared in a given study, the relevant ratio is the one that relates the additional (or incremental) benefits to the additional costs. Reporting disaggregated data allows the reader to calculate other ratios that he or she sees fit.

Beyond the individual study the reporting and interpretation of cost effectiveness ratios need to be handled with care. For example, authors often compare the cost effectiveness ratios generated in their own study with those for other interventions evaluated in previous studies in “league tables,” where rankings are produced, ranging from the intervention with the lowest cost per life year (or cost per quality adjusted life year) gained to the one with the highest.

Referees’ checklist (also to be used, implicitly, by authors)

| Item | Yes | No | Not Clear | Not Appropriate |
|-------------|------------|-----------|------------------|------------------------|
|-------------|------------|-----------|------------------|------------------------|

Study design: (1) The research question is stated (2) The economic importance of the research question is stated (3) The viewpoint(s) of the analysis are clearly stated and justified (4) The rationale for choosing the alternative programmes or interventions compared is stated (5) The alternatives being compared are clearly described (6) The form of economic evaluation used is stated (7) The choice of form of economic evaluation is justified in relation to the questions addressed

Data collection: (8) The source(s) of effectiveness estimates used are stated (9) Details of the design and results of effectiveness study are given (if based on a single study) (10) Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies) (11) The primary outcome measure(s) for the economic evaluation are clearly stated (12) Methods to value health states and other benefits are stated (13) Details of the subjects from whom valuations were obtained are given (14) Productivity changes (if included) are reported separately (15) The relevance of productivity changes to the study question is discussed (16) Quantities of resources are reported separately from their unit costs (17) Methods for the estimation of quantities and unit costs are described (18) Currency and price data are recorded (19) Details of currency of price adjustments for inflation or currency conversion are given (20) Details of any model used are given (21) The choice of model used and the key parameters on which it is based are justified

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Analysis and interpretation of results

- (22) Time horizon of costs and benefits is stated
- (23) The discount rate(s) is stated
- (24) The choice of rate(s) is justified
- (25) An explanation is given if costs or benefits are not discounted
- (26) Details of statistical tests and confidence intervals are given for stochastic data
- (27) The approach to sensitivity analysis is given
- (28) The choice of variables for sensitivity analysis is justified
- (29) The ranges over which the variables are varied are stated
- (30) Relevant alternatives are compared
- (31) Incremental analysis is reported
- (32) Major outcomes are presented in a disaggregated as well as aggregated form
- (33) The answer to the study question is given
- (34) Conclusions follow from the data reported
- (35) Conclusions are accompanied by the appropriate caveats

Two sets of objections may be raised to such rankings. Firstly, different studies may have used different methods. Differences in cost per quality adjusted life year could arise from differences in methodological approach, rather than real differences in the interventions themselves.⁴⁶ Secondly, a simplistic interpretation of league tables may be misleading. For example, each cost effectiveness or cost-utility ratio in the league would have been generated by reference to a comparison programme. In some cases this would have been doing nothing; in others it would have been current care. The incremental ratio will therefore vary in relation to the comparison chosen, which may not itself be an efficient intervention.

Birch and Gafni argue that, in deciding whether or not to adopt a particular intervention, the decision maker needs to assess the opportunity cost for the health care budget.⁴⁷ Whether or not the total health care budget should grow is a question for cost-benefit analysis, not cost effectiveness or cost-utility analysis. On the other hand, Johannesson argues that cost effectiveness analysis is best viewed as a subset of cost benefit analysis and that, to interpret and use cost effectiveness analysis as a tool to maximise the health effects for one specified real world budget, would be inconsistent with a societal perspective and likely to lead to major problems of suboptimisation.⁴⁸

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Editors' short checklist and partial evaluation checklist

| Item | Yes | No | Not Clear | Not Appropriate |
|--|------------|-----------|------------------|------------------------|
| Short checklist | | | | |
| (1) Is the research question stated? | | | | |
| (2) Are the source(s) of effectiveness estimates used clearly stated? | | | | |
| (3) Are the primary outcome measure(s) clearly stated? | | | | |
| (4) Are the methods for the estimation of quantities and unit costs described? | | | | |
| Partial evaluation checklist | | | | |
| (1) Is the question important? | | | | |
| (2) Is the economic importance of the question stated? | | | | |
| (3) Is the topic of interest to the BMJ? | | | | |
| (4) Is there enough economic detail to allow peer review? | | | | |
| (5) If the economic content is sound would we want to publish it? | | | | |
| (6) Is there a reasonable chance that the economic content is sound? | | | | |

In practice, the answer may lie in the way the results of economic evaluations are interpreted. Published data are inevitably specific to a context and will need some reinterpretation by decision makers in other settings. Transparency in reporting can help decision makers generalise results from one setting to another .

Finally, apart from being modest about the generalisability of their results, authors should ensure that their analysis is relatively conservative. Sensitivity analysis plays an important part here, and enough results should be presented to enable the reader to assess the robustness of the study conclusions.

Evaluating the guidelines

We intend to evaluate the guidelines. The options are still under discussion, but the evaluation will probably focus on four questions:

- (1) Do the guidelines help BMJ editors filter out unpublishable economic studies at an early stage? This has two components: (a) distinguishing full economic evaluations from other types of economic submissions and (b) avoiding wasting time refereeing papers that are fundamentally flawed. This question could be answered by undertaking a study of economic submissions before and after the publication of the guidelines.
- (2) How satisfied are editors, reviewers, and authors with their respective checklists? This question could be answered by assessing the checklists with a questionnaire.

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- (3) Do the guidelines improve the quality of referees' reports on economic evaluations? This question could be answered by a prospective study to compare reports from reviewers who had and had not been asked to apply the referees' checklist.
- (4) Do the guidelines improve the quality of the economic evaluations that are eventually published? This is probably the most difficult question to answer, since it requires a view to be taken about the methodological principles of economic evaluation. However, the evaluation might focus on the transparency of reporting of results, since the main objective of the guidelines is to improve this. Again, a prospective evaluation would be required, comparing the version of economic evaluations submitted to the BMJ with the version eventually published. We foresee two practical problems with this component of the evaluation. Firstly, the BMJ currently receives only a limited number of full economic evaluations, so a prospective study might take some time. Secondly, it will be difficult to separate out the distinctive contribution of the guidelines from the benefits of the peer review process more generally.

Members of the working party were: M Buxton, London; V Demicheli, Pavia, Italy; C Donaldson, Aberdeen; M Drummond (chair), York; S Evans, London; TO Jefferson (secretary), Aldershot, UK; B Jonsson, Stockholm; M Mugford, Oxford; D Rennie, Chicago; J Rovira, Barcelona; F Rutten, Rotterdam; K Schulman, Washington, DC; R Smith (editor, BMJ), London; A Szczepura, Warwick, UK; A Tonks (assistant editor, BMJ), London; G Torrance, Hamilton, Canada; A Towse, London.

We thank Vanessa Windass and Gaby Shockley for secretarial help and an anonymous referee for helpful comments.

Funding: Since no funding was sought for this project we thank our own institutions for bearing the cost.

Conflict of interest: None.

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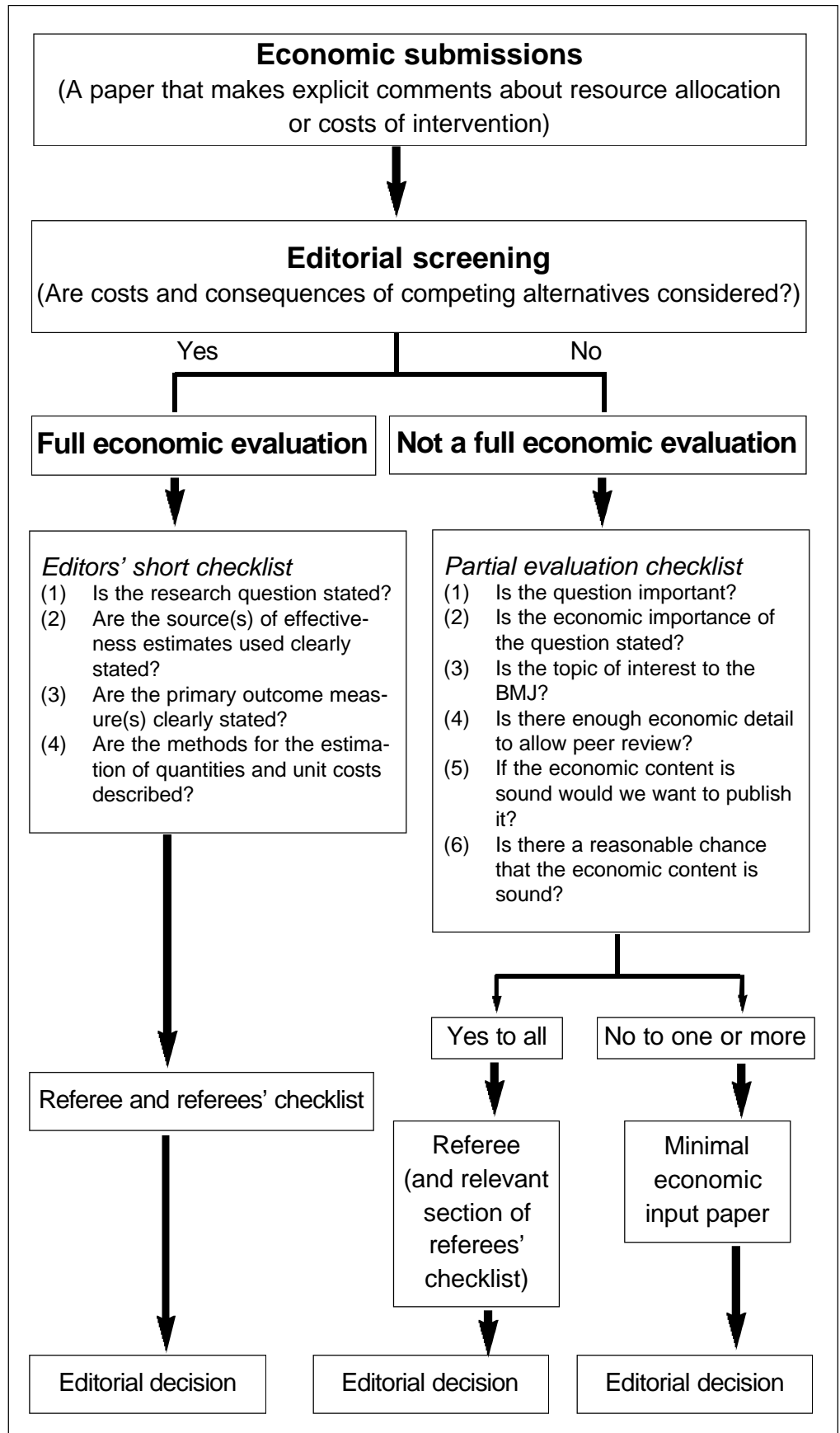
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**Appendix A —
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**Appendix A —
Guidelines for
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the *British
Medical Journal***



**Appendix B —
Principles of a
Sound Drug
Formulary
System**

Principles of a Sound Drug Formulary System

These principles have been endorsed by the following organizations:

- Academy of Managed Care Pharmacy
- Alliance of Community Health Plans
- American Medical Association
- American Society of Health-System Pharmacists
- Department of Veterans Affairs,
Pharmacy Benefits Management
Strategic Healthcare Group
- National Business Coalition on Health
- U. S. Pharmacopeia

October 2000

**Appendix B —
Principles of a
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*continued***

1 Principles of a Sound Drug Formulary System

Principles of a Sound Drug Formulary System

PREAMBLE

A coalition of national organizations representing health care professionals, government, and business leaders formed a working group (See Appendix III) to develop a set of principles specifying the essential components that contribute to a sound drug formulary system. The Coalition was formed in September 1999 in response to the widespread use of drug formularies in both inpatient and outpatient settings and the lack of understanding about formularies among the public. Also, proposed federal legislation that would provide a prescription drug benefit for Medicare beneficiaries has brought increased attention to the appropriate role and management of drug formulary systems within drug benefit programs.

The formulary system, when properly designed and implemented, can promote rational, clinically appropriate, safe, and cost-effective drug therapy. The Coalition has enumerated these principles, however, because it recognizes that patient care may be compromised if a formulary system is not optimally developed, organized and administered. This document contains "Guiding Principles" that the Coalition believes must be present for a drug formulary system to appropriately serve the patients it covers. The absence of one or more of these "Guiding Principles" should be cause for careful scrutiny of a formulary system. A glossary (See Appendix I) and bibliography (See Appendix II) are included with the "Guiding Principles" to clarify terminology and to provide additional resources, respectively.

The Coalition believes that the presence of consensus-based Formulary System Principles can assist decision-makers who must balance the health care quality and cost equation. Further, the Guiding Principles will be a valuable educational tool for national, state and local public policy makers, health care system administrators, purchasers and third party payers, practitioners, and consumers and patient advocates. These parties all have an interest in designing formulary systems that ensure patients have access to rational, clinically appropriate, safe, and cost-effective therapy and which supports an affordable and sustainable drug benefit program.

DEFINITIONS

Drug Formulary System - an ongoing process whereby a health care organization, through its physicians, pharmacists, and other health care professionals, establishes policies on the use of drug products and therapies, and identifies drug products and therapies that are the most medically appropriate and cost-effective to best serve the health interests of a given patient population.

Drug Formulary - a continually updated list of medications and related information, representing the clinical judgement of physicians, pharmacists and other experts in the diagnosis and/or treatment of disease and promotion of health.

Appendix B — Principles of a Sound Drug Formulary System *continued*

Principles of a Sound Drug Formulary System 2

GUIDING PRINCIPLES

Formulary system decisions are based on scientific and economic considerations that achieve appropriate, safe and cost effective drug therapy.

The formulary system encompasses drug selection, drug utilization review, and other tools to foster best practices in prescribing, dispensing, administration, and monitoring of outcomes.

- ❖ Clinical decisions are based on the strength of scientific evidence and standards of practice that include, but are not limited, to the following:
 - ♦ Assessing peer-reviewed medical literature, including: randomized clinical trials (especially drug comparison studies), pharmacoeconomic studies, and outcomes research data.
 - ♦ Employing published practice guidelines, developed by an acceptable evidence-based process.
 - ♦ Comparing the efficacy as well as the type and frequency of side effects and potential drug interactions among alternative drug products.
 - ♦ Assessing the likely impact of a drug product on patient compliance when compared to alternative products.
 - ♦ Basing formulary system decisions on a thorough evaluation of the benefits, risks and potential outcomes for patients; risks encompass adverse drug events (adverse drug reactions and medication errors, such as those caused by confusing product names or labels).

- ❖ Economic considerations include, but are not limited, to the following:
 - ♦ Basing formulary system decisions on cost factors only after the safety, efficacy and therapeutic need have been established.
 - ♦ Evaluating drug products and therapies in terms of their impact on total health care costs.
 - ♦ Permitting financial incentives only when they promote cost management as part of the delivery of quality medical care. Financial incentives or pressures on practitioners that may interfere with the delivery of medically necessary care are unacceptable.

- ❖ The formulary system:
 - ♦ Provides drug product selection and formulary maintenance (see above).
 - ♦ Provides drug use evaluation (also called drug utilization review) to enhance quality of care for patients by assuring appropriate drug therapy.
 - ♦ Provides for the periodic evaluation and analysis of treatment protocols and procedures to ensure that they are up-to-date and are consistent with optimum therapeutics.
 - ♦ Provides for the monitoring, reporting, and analysis of adverse results of drug therapy (e.g., adverse drug reactions, medication errors) to continuously improve the quality of care.

Appendix B — Principles of a Sound Drug Formulary System *continued*

3 Principles of a Sound Drug Formulary System

GUIDING PRINCIPLES

The Pharmacy and Therapeutics (P&T) Committee, or equivalent body, comprised of actively practicing physicians, pharmacists and other health care professionals, is the mechanism for administering the formulary system, which includes developing and maintaining the formulary and establishing and implementing policies on the use of drug products.

Physicians, pharmacists, and other health care professionals provide oversight of the formulary system.

The formulary system must have its own policies, or adhere to other organizational policies, that address conflicts of interest and disclosure by P&T committee members.

❖ The Pharmacy and Therapeutics Committee:

- ♦ Objectively appraises, evaluates, and selects drugs for the formulary.
- ♦ Meets as frequently as is necessary to review and update the appropriateness of the formulary system in light of new drugs and new indications, uses, or warnings affecting existing drugs.
- ♦ Establishes policies and procedures to educate and inform health care providers about drug products, usage, and committee decisions.
- ♦ Oversees quality improvement programs that employ drug use evaluation.
- ♦ Implements generic substitution and therapeutic interchange programs that authorize exchange of therapeutic alternatives based upon written guidelines or protocols within a formulary system. (Note: Therapeutic substitution, the dispensing of therapeutic alternates without the prescriber's approval, is illegal and should not be allowed-See Glossary.)
- ♦ Develops protocols and procedures for the use of and access to non-formulary drug products.

- ♦ Health care organization policies should ensure appropriate oversight of the P&T Committee and its decisions by the medical staff or equivalent body.

❖ Formulary system policies should:

- ♦ Require P&T committee members to reveal, by signing a conflict of interest statement, economic and other relationships with pharmaceutical entities that could influence Committee decisions.
- ♦ Exclude product sponsor representatives from P&T committee membership and from attending P & T committee meetings.
- ♦ Require P&T committee members to adhere to the formulary system's policy on disclosure and participation in discussion as it relates to conflict of interest.

Appendix B — Principles of a Sound Drug Formulary System *continued*

GUIDING PRINCIPLES

The formulary system should include educational programs for payers, practitioners, and patients concerning their roles and responsibilities.

The formulary system should include a well-defined process for the physician or other prescriber to use a non-formulary drug when medically indicated.

❖ The formulary system should:

- ♦ Inform physicians, pharmacists, other health care professionals, patients, and payers about the factors that affect formulary system decisions, including: cost containment measures; the procedures for obtaining non-formulary drugs; and the importance of formulary compliance to improving quality of care and restraining health care costs.
- ♦ Proactively inform practitioners about changes to the formulary or to other pharmaceutical management procedures.
- ♦ Provide patient education programs that explain how formulary decisions are made and the roles and responsibilities of the patient, especially the importance of patient compliance with drug therapy to assure the success of that therapy.
- ♦ Disclose the existence of formularies and have copies of the formulary readily available and accessible.
- ♦ Provide rationale for specific formulary decisions when requested.

❖ The formulary system should:

- ♦ Enable individual patient needs to be met with non-formulary drug products when demonstrated to be clinically justified by the physician or other prescriber.
- ♦ Institute an efficient process for the timely procurement of non-formulary drug products and impose minimal administrative burdens.
- ♦ Provide access to a formal appeal process if a request for a non-formulary drug is denied.
- ♦ Include policies that state that practitioners should not be penalized for prescribing non-formulary drug products that are medically necessary.

**Appendix B —
Principles of a
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*continued***

**APPENDIX I
GLOSSARY**

Drug Formulary System - an ongoing process whereby a health care organization, through its physicians, pharmacists and other health care professionals, establishes policies on the use of drug products and therapies, and identifies drug products and therapies that are the most medically appropriate and cost effective to best serve the health interests of a given patient population.

Drug Formulary - a continually updated list of medications and related information, representing the clinical judgement of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health.

Pharmacy & Therapeutics (P&T) Committee - an advisory committee that is responsible for developing, managing, updating, and administering the drug formulary system.

Generic Substitution - the substitution of drug products that contain the same active ingredient(s) and are chemically identical in strength, concentration, dosage form, and route of administration to the drug product prescribed.

Therapeutic Alternates - drug products with different chemical structures but which are of the same pharmacological and/or therapeutic class, and usually can be expected to have similar therapeutic effects and adverse reaction profiles when administered to patients in therapeutically equivalent doses.

Therapeutic Interchange - authorized exchange of therapeutic alternates in accordance with previously established and approved written guidelines or protocols within a formulary system.

Therapeutic Substitution - the act of dispensing a therapeutic alternate for the drug product prescribed without prior authorization of the prescriber. This is an illegal act because only the prescriber may authorize an exchange of therapeutic alternates.

Drug Utilization Review (Drug Use Review, DUR, and Drug Use Evaluation) - process used to assess the appropriateness of drug therapy by engaging in the evaluation of data on drug use in a given health care environment against predetermined criteria and standards.

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APPENDIX II

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**Appendix B —
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**APPENDIX III
COALITION
WORKING GROUP**

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Public Comment Requested

To ensure that knowledgeable and interested parties beyond the Coalition Working Group had an opportunity to contribute to the Principles development process, a preliminary set of principles was distributed for public comment to 50-plus organizations in February 2000. Comments received were thoroughly reviewed and considered by the Coalition Working Group.