Guidance for Health Economics Studies Presented to the Advisory Committee on Immunization Practices (ACIP)

Prepared by
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Rationale for this guidance

The Charter of the Advisory Committee on Immunization Practices (ACIP) states that, when considering recommendations for use of a vaccine, ACIP members' deliberations should include consideration of vaccine efficacy as well as cost:beneft and risk:benefit analyses. In recent years there has been a trend toward an increasing number of economic studies of vaccines presented as evidence for the Committee to consider. Precedent has been established by journals such as the *British Medical Journal* and *Vaccine*, in that they have adopted standards by which editors and reviewers should consider the quality of submitted economic studies. The Academy of Managed Care Pharmacy also has adopted guidelines for economic data submitted in support of formulary consideration. This Guidance has been developed to help ensure the quality of economic data presented to the ACIP and its work groups (WG).

To ensure the value and consistency of economic data presented to the ACIP, WG chairs are advised to involve CDC economists from the inception of the WG. Participation of CDC economists can be facilitated by the National Center for Immunization and Respiratory Diseases (NCIRD) lead economist, who can coordinate such involvement.

Objective of this guidance

It would be impossible to provide a set of standards for methods, inputs and values for inputs that would cover all the diverse vaccine-related issues that the ACIP considers. The objective of this guidance is to provide a framework for the description and presentation of methods used to examine the economics of a vaccine-related issue, such that the ACIP readily can understand the science of the analyses. To ensure that such standards have been achieved, this guidance specifically incorporates technical review of any economic materials that are to be presented to the ACIP.

GUIDANCE

Materials to be presented

All researchers (internal or external to CDC) wishing to present a health economics study (either new or revised/updated) to the ACIP (or one of its WGs) shall present the following material:

1) **Document or report providing methods and results** The document should provide a detailed description of the methods and results. The level of detail should be similar to that provided in a manuscript that would be submitted to a peer-reviewed journal. However, the document should not be bound by journal restrictions on length of the methods and results sections. There is no need for a detailed introduction section. The discussion section typically would be shorter than that found in a published manuscript. Additional details regarding the content of this document are provided below.

2) **Slide sets and other presentation materials (e.g., handouts**) The principles and template for slides intended for presentation to the ACIP which outline the methods and results, are provided in the "Guidance: format for presentation of slides" section. Additional details regarding slide content also are provided (**See attached set of "template slides.")**

Timeline for materials to be made available and review process

The report, slides, and other presentation material must be submitted to the relevant ACIP WG chair and CDC lead staff person no later than 8 weeks before the ACIP general meeting or WG meeting at which the analysis is proposed to be presented. Under extraordinary circumstance, an appeal can be made to the WG chair, the CDC lead staff person, and the NCIRD lead economist to submit the report fewer than 8 weeks before the ACIP meeting. In case of such an appeal, the lead economist will document the justification and granting of exceptions in collaboration with the WG chair and the CDC lead staff person.

The NCIRD lead economist (or designee) will work with the WG chair and CDC lead staff person to identify reviewers for an anonymous peer review. Non-CDC reviewers may be used if a particular area of expertise is not available among CDC economists. Reviewers will consult with relevant CDC subject-matter experts and return comments and questions in writing to the NCIRD lead economist (or designee) at least 4 weeks in advance of the formal presentation. These comments will be forwarded to the WG chair and CDC lead staff person who will forward them to the appropriate WG members and to the researchers submitting the economic analysis. This process will allow time for at least one round of comments and revisions or responses prior to the formal presentation. The relevant WG chair, the CDC lead staff person, and the NCIRD lead economist (or designee) will determine if revisions and responses are sufficient to allow presentation. If differences persist, the WG chair and the CDC lead staff person, in conjunction with all members of the WG, will decide if the information will be presented to the ACIP. Reviewer comments also will be provided to the WG and the ACIP to explain the differences that may exist.

GUIDANCE: Content of document

A document describing the methods and results of a health economics study for consideration by the ACIP will contain the following sections and elements:

1) Affiliations
All authors shall include their affiliations.

2) Statements of conflict or potential conflicts of interest
A separate section listing any potential conflicts of interest shall be included for each author. If there are no potential conflicts of interest, a statement to that effect must be included (e.g., Author A: No conflicts of interest).

METHODS

3) Methods: the study question
The study question must be explicitly stated in detail (e.g., In this study, we present results of a cost-effectiveness analysis of routinely vaccinating age group XX against Disease Y, using vaccine Z, using three doses given once per year over three consecutive years.)

4) Methods: the perspective
The study must be conducted from the societal perspective unless strong justification is provided for doing otherwise.

Other perspectives may be included when relevant justification is provided for their consideration.

The study perspective(s) must be explicitly stated (e.g., "The perspective used in this study is societal.")

5) Methods: intervention strategies
Intervention strategies must be clearly identified and completely described. A baseline strategy must be included.

Authors must describe all relevant interventions. If the analysis does not include all possible interventions, the authors shall provide the rationale for including or excluding them. For example, the authors of an analysis of vaccination of adults against pertussis would discuss the rationale for inclusion or exclusion of a selective strategy of vaccinating care providers of young infants.

6) Methods: time frame and analytic horizon
The time frame and analytic horizon for each strategy must be defined clearly, complete with appropriate justification (e.g., "We analyzed benefits and costs over a ten year period. The analytic horizon was selected because available data suggest that after XX years, vaccine-

induced immunity may wane to the point where a large proportion of vaccinees would require a booster dose to maintain adequate levels of immunity.").

7) Methods: the economic model
a) The analytic method used must be specified (e.g., cost-benefit, cost-effectiveness, or cost-utility analysis). The summary measure must be defined/ identified.

b) The basic model used in the analysis must be explained in the text without use of mathematical notation. Authors may consider enhancing the written description with a word "equation". If deemed necessary by the authors, an equation, or set of equations, using mathematical notation also can be provided in a technical appendix.

8) Methods: health outcomes of interest
Health outcomes must be clearly identified (e.g., deaths, hospitalizations, outpatient visits, quality adjusted life years).

Authors must ensure that health outcomes are relevant to the perspective. Although almost any health outcome may be relevant for a societal perspective, some health outcomes may be irrelevant for any additional perspectives.

9) Methods: inclusion of epidemiologic models
When an epidemiologic model is an integral part of a health economics study to be presented to the ACIP, the authors shall include a description of the model. The authors must include a schematic diagram illustrating the model. Annotation in such a diagram must be done without use of mathematical notation. Authors are directed to ensure that such schematic diagrams can be readily understood without extensive reading of the main text (i.e., can "stand alone").

The authors must state the time step used in the epidemiologic model. "Time step" refers to the time associated with the probabilities used in the model. For example, if the authors use probabilities of death per unit population per year, then the *de facto* time step of such a model would be one year. Probabilities, and time step, can be in almost any unit of time. The total number of time steps must match the time frame of the economic model unless a specific explanation is given.

Authors should note that it is insufficient merely to reference another source (e.g., reference a previously published paper).

10) Methods: Inputs: values and sources
a) Probabilities: Values and sources must be presented. Authors must make sure that probabilities used in the analysis are "reasonable."

b) Costs: Values and sources must be presented. The study shall differentiate between direct medical, direct non-medical, indirect (i.e., productivity), and intangible costs (included when relevant). The year of cost data also must be stated. Authors must make sure that included costs are relevant to the stated perspective.

c) Other inputs: Values and sources of any other inputs (e.g., Quality Adjusted Life Years) must be presented.

Each value used in the model must have at least one clearly identified source. Values that are assumed, or calculated (e.g., a residual probability), or the results of expert opinion shall be identified as such.

Authors are advised that the greatest clarity is often achieved by presenting all input values and sources in tabular format. Such tables must include sufficient footnotes to enable a reader to readily understand the table without extensive reading of the main text (i.e., such tables must "stand alone").

11) Methods: discounting

All future costs and benefits shall be discounted to present value. This includes future health outcomes (e.g., future lives saved must be discounted to present).

The discount rate used must be specified, and authors must ensure that the discount rate is relevant to the stated perspective.

12) Methods: sensitivity analyses

The general goal of sensitivity analyses is to demonstrate how conclusions might change with changes in input values.

Sensitivity analyses, including appropriate threshold analyses, shall be conducted and reported on cost and incidence variables. The type of sensitivity analysis conducted must be described.

Authors are strongly encouraged to conduct sensitivity analyses that allow them to identify which variables within the model are most influential in determining the overall results.

The ranges and sources of the values used in the sensitivity analyses must be clearly reported. Authors shall report values used in sensitivity analyses in the same table in which they report values of all inputs (see Point 10).

Univariate sensitivity analyses (altering only one value at a time, and keeping all other values fixed at original values) are unlikely to be considered adequate. Authors shall present some form of multivariate sensitivity analysis or an explanation as to why such analysis is not presented.

Authors must use sensitivity analysis ranges that are based on clinically relevant or policy relevant cutoffs rather than those based on arbitrary changes in input values (e.g., plus or minus 10% of initially used values).

As a form of sensitivity analysis, in addition to presenting results that have been discounted to present values (see Point 11), undiscounted costs and benefits may be presented.

13) Methods: independent replication

In general, information must be presented that would allow a researcher, with sufficient interest and relevant skills, to independently replicate the study..

In order to meet such a standard, where necessary, authors may provide additional details in a technical appendix.

RESULTS

14) Results: summary measures

Results that answer the study question must be identified. The summary economic measure(s) that answers the study question must be presented.

The summary measure must be appropriate for the perspective used in the study.

If deemed necessary, authors also may wish to present other results calculated during the analysis, such as total number of cases averted.

15) Results: tables and graphs

All tables and graphs used to present results must be readily understood without extensive reading of the main text (i.e., such graphs and tables can "stand alone"). Authors must include footnotes that will help a reader understand each table and graph.

Tables and graphs must add value to the report. Graphs or tables that contain results not central to the summary measure (see Point 16) may be included in a technical appendix.

Graphs shall be drawn using the standard guidelines for graphical representation of data. Detailed guidelines can be found in texts such as Tufte (Tufte ER. *The Visual Display of Quantitative Information*. Graphics Press, Cheshire Connecticut, 1983: pp. 197). Examples of such guidelines include:

1) Pie charts are almost always unacceptable.
2) Horizontal and vertical grid lines usually are not needed.
3) For line charts, typically only 4 lines (variables) drawn per chart.
4) For column and bar charts, typically only 4 bars (variables) included per chart. Avoid using "stacked" bars or columns (e.g., a column that has several elements that add to 100%).
5) To allow easy printing and copying, graphs and figures should be drawn in gray-scale. Color in graphs and figures should be used sparingly, if at all.

16) Results: sensitivity analyses and influential variables

Authors shall present their sensitivity analyses in a clearly identified section, complete with relevant tables and graphs.

Authors shall, whenever possible, present a list of "most influential" variables as identified through sensitivity analysis (see Point 12).

DISCUSSION

17) Discussion: overall
The discussion section should be more limited than that typically found in a peer-reviewed manuscript.

18) Discussion: limitations
Study limitations must be discussed. Limitations shall include accuracy of any epidemiologic model and input data (see Points 9 and 10).

Any implicit assumptions, such as an adequate supply of vaccine, should be mentioned.

19) Discussion: relation to other relevant studies
Results must be discussed in relation to other similar studies if such studies are available.

20) Discussion: how results may change
There must be an explicit discussion, typically drawing from the results of the sensitivity analyses, of how results would change if key assumptions or values were to change.

21) Discussion: no policy implications
Unless otherwise requested by the relevant WG chair, the report must NOT include a discussion of the policy implications of the results and limitations. Because it is CDC's and ACIP's responsibility to make policy interpretations, such discussion will be deleted if included in the document distributed for ACIP discussion, unless the WG chair specifically requests it be included.

22) Details not addressed in this guidance
For further guidance regarding methods and results, researchers may follow the recommendations described in the following standard texts (or equivalent):

1) *Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation, 2d. Ed.* Anne Haddix, Steven Teutsch, and Phaedra Corso, editors. (New York: Oxford University Press, 2003)

2) *Cost-Effectiveness in Health and Medicine.* Joanna Siegel, Louise Russell, Milton Weinstein, and Marthe Gold, editors. (New York: Oxford University Press, 1996).

23) Additional information

1) Link to the Community Guide Economic Evaluation abstraction form where all of the important components of an EE analysis are presented. The form has a quality rating of EEs at the end. www.thecommunityguide.org/methods/econ-abs-form.pdf

2) Many standards for conducting economic evaluations are also on the CDC on-line Economic Evaluation course. www.cdc.gov/owcd/EET/Preface/Preface.html

3) The Guide to Community Preventive Services book, chapter 11 is titled "Interpreting and Using Economic Evidence".

4) Detsky AS, Laupacis A. Relevance of cost-effectiveness analysis to clinicians and policy makers. JAMA. 2007;298:221-4.

GUIDANCE: format for presentation of slides

Principles for presenting a health economics study to ACIP:
After the document has been peer-reviewed internally, and the WG chair and CDC lead staff person have reviewed and discussed the contents of the document and the relevant analysis, they will decide whether to proceed with inviting a presentation to the ACIP or WG.

It is realistic to assume that many ACIP members will not have had the opportunity to read the document. Further, the ACIP general meetings (but not WG meetings) are open to the public. Thus, the presenter of the health economics study should realize that most of the audience at the presentation will not be aware of the study, and that the audience members have diverse backgrounds. Further, especially for presentations at an ACIP general meeting, it is likely that a relatively short amount of time will be allotted for the presentation, typically 20-30 minutes including time for questions. A presentation made in the closed setting of a WG teleconference or meeting may be longer and more detailed.

Template slides:
The attached set of template slides provides an outline of the type of slides and suggested layout of each type of slide. The subject matter of the slides in the template is designed so that a presenter can be assured of presenting the main facts as they relate to the methods, results and limitations of the study.