

ACIP Evidence-Based Recommendations Work Group Proposal

Wendy Carr, PhD
**CDC Lead, Evidence-Based
Recommendations
Work Group**

Advisory Committee on Immunization Practices

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ACIP and the GRADE approach

- ❑ **ACIP adopted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach in October 2010**
 - Quality of evidence for benefits and harms
 - Going from evidence to recommendations
- ❑ **Quality of evidence for benefits and harms is only one factor in developing a recommendation**
 - Other key factors include balance of benefits and harms, values, and health economic data
 - ACIP Charter states, “shall include consideration of disease epidemiology and burden of disease, vaccine efficacy and effectiveness, vaccine safety, economic analyses and implementation issues.”

The Role of Evidence Quality in Making a Recommendation

- “The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach clearly separates the certainty of evidence from the strength of recommendation. This separation allows decision-making based on lower levels of evidence. For example, despite low certainty evidence (derived from case series) regarding the association between aspirin and Reye’s syndrome in febrile children, a strong recommendation for using acetaminophen over aspirin is possible. GRADE literature also describes five paradigmatic situations in which a strong recommendation can be made based on low quality evidence”

From: Murad MH, Sultan S, Haffar S, et al. Methodological quality and synthesis of case series and case reports. BMJ Evidence-Based Medicine Published Online First: 02 February 2018. doi: 10.1136/bmjebm-2017-110853

Evidence to Decision (EtD) Frameworks

- ❑ EtD frameworks were developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group*
- ❑ Frameworks are intended to help panels:
 - structure discussion and identify reasons for disagreements,
 - be more systematic and explicit about the judgments that they make, the evidence used to inform each of those judgments, additional considerations, and the basis for their recommendations or decisions
 - make the process and basis for decisions structured and transparent
- ❑ Frameworks assist users of recommendations by enabling them to understand the judgments made by the panel and the evidence supporting those judgments

**GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction*

BMJ 2016; 353 doi: <https://doi.org/10.1136/bmj.i2016> (Published 28 June 2016)

EtD Framework Structure

- ❑ **EtD frameworks include three sections that reflect the main steps in going from evidence to a decision:**
 - formulating the question
 - making an assessment of the evidence
 - drawing conclusions
- ❑ **A key feature of EtD frameworks is that they are layered - presenting key messages in the top layer with links to more detailed information**
 - include concise summaries of the most important evidence for each criterion, summarized in a table or a paragraph of text
 - from the framework, it is possible to link to information that is more detailed – e.g., an evidence profile

EtD Framework Content

- ❑ The 3 content areas are presented in the framework as:
 - **Background (formulating the question):**
 - Details of the question and a brief summary of information to understand the question & why recommendation is needed
 - **Criteria (assessment/communication of evidence):**
 - Criteria (factors that should be considered) for making the decision
 - Judgments that must be made in relation to each criterion
 - Evidence to inform each of those judgments
 - Additional considerations that inform or justify each judgment
 - **Conclusions** that the panel must reach, based on the judgments made for all of the criteria

ACIP Evidence to Recommendation (EtR) Framework Development

- ❑ **Additional structure and clarity for the full spectrum of criteria evaluated during formulation of recommendations**
 - Factors have always been considered, but process not structured
 - Refine methods for the incorporation of additional factors that contribute to decision-making as well as GRADE evidence profiles
- ❑ **Evidence to Recommendation (EtR) framework**
 - Adapting the framework to best fit public health recommendations for vaccines
 - Piloted by Mumps and Zoster Oct meeting
 - Living document
 - Guidance document provides additional detail on development and use of the framework

Proposed EtR Framework Criteria

❑ Statement of Problem

- Public health importance
- Burden of disease

❑ Benefits and Harms

- Balance of desirable and undesirable effects
- Certainty in evidence (evidence profiles)

❑ Values and Preferences of target population

❑ Acceptability to stakeholders

❑ Resource Use

- Health Economic Analyses

❑ Feasibility

- Implementation considerations

EtR Framework Criteria

❑ For each of these Criteria the following are provided:

▪ **Judgments**

- For initial framework, draft judgements prepared by the WG that become final after review/modification by the full committee

▪ **Evidence to inform each judgment**

- May be research evidence or obtained from routine data collection
- If no peer-reviewed body of evidence is available, this should be simply stated and any additional information used to inform the judgment indicated
 - Intent is to be transparent about the information that was used to make the judgment, not to imply the need for the development of evidence when it is not available
- May include links to more detailed summaries of the evidence

▪ **Additional considerations that inform or justify each judgement**

- Can include other data, assumptions, and/or logic used to make a judgment
- Different judgments for one or more subgroups
- Dissenting views of panel members or minority opinions
- Interpretations of the evidence

Proposed ACIP EtR Framework: Question, Background, and Problem

Question: Overarching policy question to be answered by the guideline panel (ACIP) using the Evidence to Recommendations (EtR) framework.

Population: Target population for vaccine (e.g., age range, sex, immune status, pregnancy)

Intervention: Vaccination (if applicable, dosage and schedule)

Comparison(s): No Vaccination/Placebo/Control/Standard care/An existing vaccine/Other prevention options

Outcome: Outcome(s) associated with vaccination (e.g., prevention outcomes or adverse effects)

Background: The addressed PICO question should be described in detail, and important background information for understanding the question and why a recommendation or decision is needed should be briefly provided.

	CRITERIA	JUDGMENTS	EVIDENCE	ADDITIONAL INFORMATION
		<i>No</i> <i>Probably no</i> <i>Uncertain</i> <i>Probably yes</i> <i>Yes</i> <i>Varies</i> ☐ ☐ ☐ ☐ ☐ ☐		
PROBLEM	Is the problem of public health importance?			

Proposed ACIP EtR Framework: Benefits & Harms

	CRITERIA	JUDGMENTS	EVIDENCE	ADDITIONAL INFORMATION
BENEFITS & HARMS	How substantial are the desirable anticipated effects?	<i>Trivial</i> <i>Small</i> <i>Moderate</i> <i>Large</i> <i>Don't know</i> <i>Varies</i> ☐ ☐ ☐ ☐ ☐ ☐		
	How substantial are the undesirable anticipated effects?	<i>Trivial</i> <i>Small</i> <i>Moderate</i> <i>Large</i> <i>Don't know</i> <i>Varies</i> ☐ ☐ ☐ ☐ ☐ ☐		
	Do the desirable effects outweigh the undesirable effects?	<i>Favors intervention</i> <i>Favors comparison</i> <i>Favors both</i> <i>Favors neither</i> <i>Unclear</i> ☐ ☐ ☐ ☐ ☐		
	What is the overall certainty of this evidence for the critical outcomes?	Effectiveness of the intervention <i>No included studies</i> 4 <i>Very low</i> 3 <i>Low</i> 2 <i>Moderate</i> 1 <i>High</i> ☐ ☐ ☐ ☐ ☐		
		Safety of the intervention <i>No included studies</i> 4 <i>Very low</i> 3 <i>Low</i> 2 <i>Moderate</i> 1 <i>High</i> ☐ ☐ ☐ ☐ ☐		

Proposed ACIP EtR Framework: Values

	CRITERIA	JUDGMENTS	EVIDENCE	ADDITIONAL INFORMATION
VALUES	Does the target population feel that the desirable effects are large relative to undesirable effects?	<i>No</i> ☐ <i>Probably no</i> ☐ <i>Uncertain</i> ☐ <i>Probably yes</i> ☐ <i>Yes</i> ☐ <i>Varies</i> ☐		
	Is there important uncertainty about or variability in how much people value the main outcomes?	<i>Important uncertainty or variability</i> ☐ <i>Possibly important uncertainty or variability</i> ☐ <i>Probably no important uncertainty or variability</i> ☐ <i>No important uncertainty or variability</i> ☐ <i>No known undesirable outcomes</i> ☐		

Proposed ACIP EtR Framework: Acceptability, Resource Use and Implementation

	CRITERIA	JUDGMENTS	EVIDENCE	ADDITIONAL INFORMATION
ACCEPTABILITY	Is the intervention acceptable to key stakeholders?	No Probably no Uncertain Probably yes Yes Varies ☐ ☐ ☐ ☐ ☐ ☐		
RESOURCE USE	Is the intervention a reasonable and efficient allocation of resources?	No Probably no Uncertain Probably yes Yes ☐ ☐ ☐ ☐ ☐		
FEASIBILITY	Is the intervention feasible to implement?	No Probably no Uncertain Probably yes Yes Varies ☐ ☐ ☐ ☐ ☐ ☐		

EtR Framework Conclusions

- ❑ **Conclusions should be based on the judgments made for all of the criteria and should specify:**
 - A summary of the judgements made for all criteria and implications for the decision
 - The type of decision or recommendation (e.g. Routine recommendation, individual recommendation, or not recommended)
 - The recommendation in concise, clear and actionable text
- ❑ **May include:**
 - Any subgroup considerations that the panel took into account when making a decision
 - Key implementation considerations (in addition to any that are specified in the recommendation), including strategies to address any concerns about the acceptability and feasibility of the intervention
 - Draft conclusions suggested by the WG who have prepared the framework

Adapted from DECIDE materials at <http://www.decide-collaboration.eu/evidence-decision-etd-framework>

Proposed ACIP EtR Framework: Recommendation and Additional Considerations

Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings ☐	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings ☐	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> ☐	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings ☐	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings ☐	There is insufficient evidence to determine the balance of consequences ☐
Is there sufficient information to move forward with a recommendation? Yes ☐ No ☐						
Type of recommendation	We do not recommend the intervention ☐	We recommend the intervention for individuals based on clinical decision-making ☐		We recommend the intervention ☐		
Recommendation (text)	Please provide the draft recommendations proposed to ACIP.					
Additional considerations (optional)	Please outline any significant additional considerations (e.g., aspects related to implementation, monitoring and evaluation, research priorities, etc.).					

Type of Recommendation

- ❑ **Draft includes 3 types of recommendation**
 - “We do not recommend the Intervention”
 - “We recommend the intervention for individuals based on clinical decision-making”
 - “We recommend the intervention”
- ❑ **These types of recommendation will replace former “Category A” and “Category B” labeling of recommendations**

Use of the ACIP EtR Framework

- ❑ **This is a proposed update to the current ACIP evidence-based recommendation process consistent with expansion of GRADE methodology guidance**
 - Precise language subject to continued improvement
 - Guidance will be updated as experience is gained
 - Additional supporting documents being developed
- ❑ **Previous recommendations will not be retroactively put into the EtR format but the framework will be used when recommendations are periodically updated**
- ❑ **Completed EtR frameworks will be published online**

Evidence-Based Recommendations

Work Group Members

ACIP Members

Grace Lee (Chair)

Paul Hunter

Liaison Representatives

AAP – Sean O’Leary

AAFP – Margot Savoy

ACP – Amir Qaseem

FDA – Roshan Ramanathan

NACI – Nadine Sicard and Shainoor Ismail

SHEA – David Weber

Previous ACIP members

Arthur Reingold

Jon Temte

Doug Campos-Outcalt

Lorry Rubin

CDC Contributors

EBRWG Lead - Wendy Carr (NCIRD)

ACIP Work Group leads - Tamara Pilishvili
and Kathleen Dooling

Immunization Services Division - Carolyn
Bridges and Megan Lindley

Consultants

US GRADE Network - Rebecca Morgan

SAGE - Charles Wiysonge and Melanie
Marti

Robert Koch Institute STIKO - Thomas
Harder IDSA - Valéry Lavergne

Ned Calonge

Vote

- ❑ **The EBRWG proposes that an Evidence to Recommendation framework be adopted and used by ACIP to support decision making**
 - Note: The terminology is NOT being voted on as it will likely evolve over time
 - Enhancements may be made to the framework in the future

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	INTREPRETATION OF EVIDENCE
PROBLEM	Is the problem a public health priority?	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☐ Yes ☒ Varies ☐	Annual rate ~4 HZ cases per 1000 population (1 million cases annually)^{1,2} Incidence increases with age, ranging from <1 case/1000 children to >15 cases/1000 population 80 years and older^{2,3} The incidence among people 60 years of age and older is about 10 cases per 1,000 U.S. population annually^{1,2} In a study using administrative data, the annualized incidence of herpes zoster was 4.6, 6.9, 9.5, and 10.9 per 1000 people aged 50–59, 60–69, 70–79, and 80 years, respectively⁴ Risk of herpes zoster increases with age, and among persons who experience herpes zoster, older persons are more likely to also experience PHN⁴, non-pain complications⁴, hospitalizations⁵, and interference with activities of daily living⁶ For adults 50 years and older with HZ, 10-18% will go on to develop PHN. Incidence of PHN increases significantly with age⁷ For adults 50-59 years old with HZ, , an estimated 5-8% will go on to develop PHN^{8,9} ZVL, the current licensed and recommended herpes zoster vaccine, is 51% and 67% effective in preventing herpes zoster and PHN, respectively, among adults aged ≥60	Burden of herpes zoster increases with age, with steep increases occurring after age 50 years Although incidence is lower in 50-59 year olds compared to those over 60 yrs, ~21% of all HZ episodes occur in this age group annually. However, 50-59 year olds are less likely to experience complications due to herpes zoster compared to elderly adults. Complications from herpes zoster, including PHN and ocular complications, can be severe and debilitating. Likelihood of complications increases significantly with age. PHN and pain-associated with zoster, can have a significant negative impact on quality of life can cause chronic fatigue, sleep disorders, social isolation, depression and anxiety, and can interfere with basic activities of daily living The current zoster vaccine is only 51% effective at preventing herpes zoster, leaving a substantial number of individuals who receive the vaccine still at risk for disease.

¹ Jumaan et al., JID, 2005, 191:2002-7.

² Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9.

³ Insinga et al., J Gen Intern Med. 2005, 20:748-53.

⁴ Insinga et al., J Gen Intern Med. 2005, 20:748-53.

⁵ Lin F, Hadler JL. J Infect Dis 2000;181:1897–905.

⁶ Schmader KE, Johnson GR, Saddier P, et al. J Am Geriatr Soc 2010;58:1634–41.

⁷ Johnson, RW, and McElhaney, J. Int J Clin Pract. 2009 Sep; 63(9): 1386–1391.

⁸ Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9.

⁹ Gauthier et al 2009, Epidemiol Infect. 2009; 137:38-47