New Framework for Developing Evidence-Based Recommendations by the ACIP

Faruque Ahmed, PhD

1st National Immunization Conference Online
March 26-28, 2012

National Center for Immunization & Respiratory Diseases
Immunization Services Division

Outline

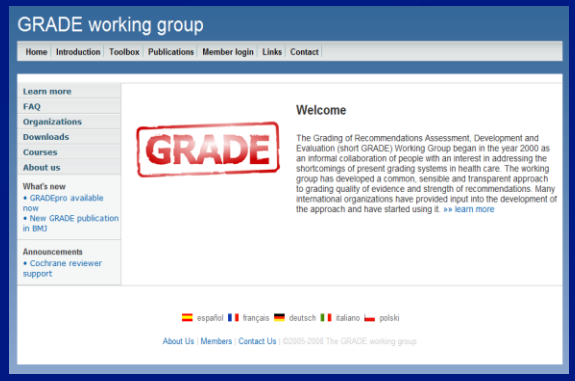
- Overview of new evidence framework of the U.S. Advisory Committee on Immunization Practices (ACIP)
- Evaluating evidence type or quality
- Going from evidence to recommendations

New ACIP Evidence Framework

- **ACIP unanimously voted to adopt 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

GRADE Uptake

- Agency for Health Care Research and Quality (AHRQ)
- American College of Chest Physicians
- American College of Physicians
- American Thoracic Society
- Allergic Rhinitis in Asthma Guidelines
- Infectious Diseases Society of America
- UpToDate
- British Medical Journal
- Canadian Cardiovascular Society
- Clinical Evidence
- Cochrane Collaboration
- European Society of Thoracic Surgeons
- National Institute Clinical Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)



ACIP Recommendation Categories

- **Category A: Applies to all persons in an age or risk group**
  - Desirable effects outweigh undesirable effects (recommendation for)
  - Undesirable effects outweigh desirable effects (recommendation against)
- **Category B: Individual clinical decision-making**
- **No recommendation/unresolved issue**

Desirable: benefits, savings. *Undesirable:* harms, costs.

ACIP Wording of Recommendations

- **Category A**
  - Use words like "recommend," "recommend against," "should," "should not"
- **Category B**
  - Use words like "may," "suggest against"

Evidence Type or Quality

1. Randomized controlled trials (RCTs), or overwhelming evidence from observational studies
2. RCTs with important limitations, or exceptionally strong evidence from observational studies
3. RCTs with notable limitations, or observational studies
4. RCTs with several major limitations, observational studies with important limitations, or clinical experience and observations

Evidence Type

- **The four evidence types represent a general hierarchy reflecting confidence in the estimated effect of vaccination on health outcomes (benefits, harms)**
  - Randomization minimizes potential bias and confounding, and randomized controlled trials (RCTs) are considered the gold standard for assessing vaccine efficacy
  - However, observational studies may provide more relevant information for rare or long-term outcomes
  - Observational studies provide useful information of the effect of vaccination under the conditions of everyday practice and when RCTs are not ethical or feasible

Going from Evidence to Recommendations

- Deliberate separation of type or quality of evidence from recommendation category
- No automatic one-to-one connection as in other grading systems
- Other factors beyond the type of evidence influence the recommendation category

Considerations for Formulating Recommendations

Key Factors	Explanation
Evidence type for benefits and harms	The higher the confidence in the estimated effect of vaccination on health outcomes, the more likely is a category A recommendation.
Balance between benefits and harms	The larger the difference between the benefits and harms, the more likely is a category A recommendation. The smaller the net benefit and the lower certainty for that benefit, the more likely is a category B recommendation.
Values	The greater the variability in values and preferences, or uncertainty in values and preferences, the more likely is a category B recommendation.
Health economic data (e.g., cost-effectiveness)	The lower the cost-effectiveness, the more likely is a category B recommendation.

Methodology for Categorizing Evidence

Study design	Initial evidence type	Criteria for downgrading	Criteria for upgrading	Final evidence type
Randomized Controlled Trial (RCT)	1	Risk of bias Inconsistency Indirectness Imprecision Publication bias	Strength of association Dose-Response Direction of all plausible residual confounding or bias	1 2
Observational study	3			3 4

http://www.gradeworkinggroup.org/

Balance Between Benefits and Harms

- **Smaller net benefit**
  - Low burden of disease
  - Small absolute effect of vaccination
  - Small relative effect of vaccination

Values

- Relative importance of outcomes related to benefits, harms, and costs
- Values should reflect those of the people affected

Health Economic Analyses

- Health economic analyses based on modeling often presented to the ACIP
- The above methodology for categorizing the type or quality of evidence is not intended to be applied to economic modeling studies

Example:
ACIP Recommendations for Adults with Diabetes

- Hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A; evidence type 2)
- Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥60 years (recommendation category B; evidence type 2)

MMWR 2011;60(50):1709-11

Considerations for Formulating Recommendations: Adults with Diabetes

Key factors	Comments
Balance between benefits and harms	Benefits are greater than potential harms
Evidence type for benefits and harms	2
Values	High values on preventable outcomes for persons <60 years and moderate to high values for persons ≥60 years
Cost-effectiveness	Vaccination is most cost effective for adults with diabetes for ages <60 years

Summary

- Widespread adoption of GRADE, thereby unifying meaning of recommendations across organizations
- Clear separation between quality of evidence and strength of recommendations
- Explicit, comprehensive criteria for downgrading and upgrading quality of evidence ratings
- Transparent process of moving from evidence to recommendations
- Explicit acknowledgment of values and preferences
- Balance between simplicity and methodological comprehensiveness

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: http://www.cdc.gov

National Center for Immunization & Respiratory Diseases
Immunization Services Division