

Development of ACIP/CDC vaccine recommendations using GRADE

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Advisory Committee on Immunization Practices

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ACIP EBRWG Terms of Reference

Charge: To develop a uniform approach to making explicit the evidence base for ACIP recommendations



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ACIP EBRWG Activities

- On 28 October 2010, ACIP unanimously voted to adopt a methodology to assist in the development of clear and uniform evidence assessment and reporting for future ACIP recommendations
 - based on a modification of GRADE pertaining to the labeling of evidence and recommendation categories not the underlying methodology
- The EBRWG has now officially disbanded following completion of the specified terms of reference set forth by ACIP



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ELSEVIER

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journal homepage: www.elsevier.com/locate/vaccine



Review

Methods for developing evidence-based recommendations by the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (CDC)

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How good is the evidence?

Design: Review of all original clinical research in 3 major general clinical journal or high-impact specialty journals from 1990-2003 that were cited more than 1000 times

Results: Of 49 highly cited studies, 45 claimed that the intervention was effective

- 7 (16%) contradicted by subsequent studies
- 7 (16%) found effects stronger than those of subsequent studies
- 20 (44%) were replicated
- 11 (24%) remained largely unchallenged

Source: Ioannidis JPA. JAMA 2005;294:218-228.



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*“Poor fool with all this sweated lore,
I stand no wiser than I was before.”*

Johann Wolfgang von Goethe
Faust - Part One, 1806



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Implementation of GRADE by ACIP Work Groups

- WGs that have used GRADE
 - Meningococcal
 - HPV
 - Hepatitis B
 - Pneumococcal
 - Influenza



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Informal SWOT Analysis

- Strengths
 - Weaknesses/Limitations
 - Opportunities
 - Threats
-
- Conducted with CDC lead staff on ACIP Work Groups



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Perceived GRADE Deficits

- Structural -

- Grading of Evidence may not address key factors
 - Burden of Disease
 - Indirect Benefit
- Limitations with Safety Assessments
 - Observational in nature
 - Rare events
- Limitation in Categories of Recommendations
 - Types
 - Alignment with strength of evidence



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Perceived GRADE Deficits

- Procedural -

- Arbitrariness
 - incorporating values
 - Thresholds for upgrading / downgrading
 - Expert guidance
- Over-reliance on RCTs
 - Inherent lower quality of observational studies
- Reliance on External Methodology Experts
 - From outside of CDC



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Areas for Clarification

- Guidance
 - Ranking importance of outcomes
 - Determining values and preferences
 - Assignment of recommendation category
 - Drafting language
 - Upgrading / Downgrading evidence
 - “bias” in industry-sponsored studies
 - blinding
 - statistical approaches
 - levels of limitation (serious vs. minor vs. no)



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Areas for Clarification

- Additional categories
 - “no recommendation for or against due to insufficient evidence”
 - Time limited
- Adjustment of Evidence Tables
- Issues with use of Safety Evidence
 - Post-licensure



Practicality

“Recommendations that may be helpful but do not need grading are typically those in which it is sufficiently obvious that desirable effects outweigh undesirable effects that no direct evidence is available because no one would be foolish enough to conduct a study addressing the implicit clinical question.”

GRADE guidelines 1

http://www.ceb-institute.org/fileadmin/upload/refman/j_clin_epidemiol_2011_64_383_guyatt.pdf



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*“I was just guessing
at numbers and figures
pulling the puzzles apart*

*Questions of science
science and progress
do not speak as loud as my heart”*

Coldplay – “The Scientist”

A Rush of Blood to the Head - 2002



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