

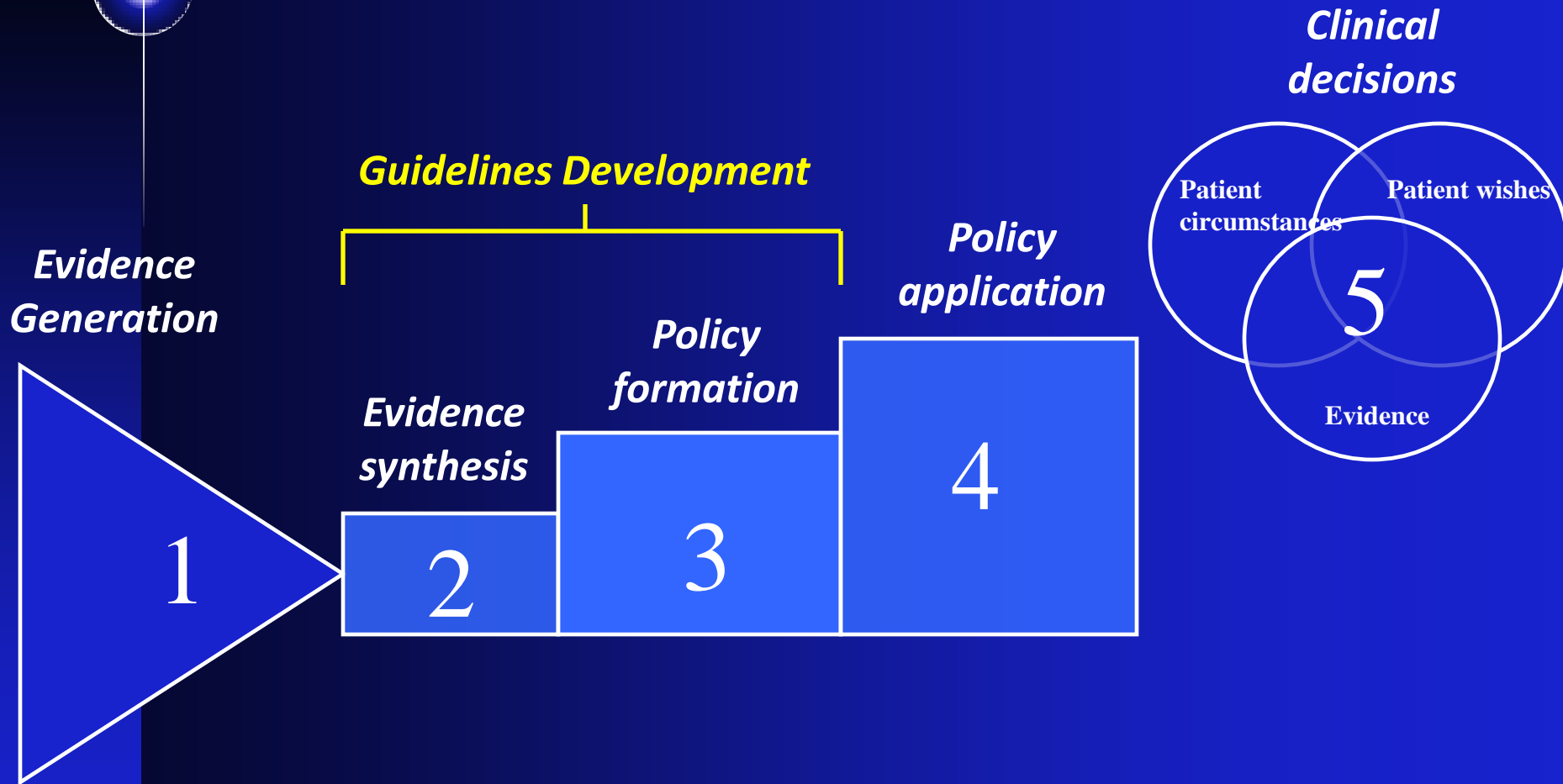
Developing Guidance for PrEP Use in the US

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Steps from evidence generation to clinical application



Developing Guidelines

- Reviewed PHS and CDC guidelines procedures
 - nPEP
 - STD
 - ARV treatment
- Reviewed the literature on guidelines
 - Strength of evidence assessment methods
 - Determining factors for “successful” guidelines
 - Implementability
 - Dissemination
 - Adoption
 - Fidelity

Clinical Practice Guidelines

- Systematically developed, scientifically supported recommendations, strategies, and information that
 - Assist practitioners to make decisions about appropriate health care for specific clinical circumstances
 - Seek to minimize harm, reduce inappropriate variations in clinical care, and produce optimal health outcomes for patients

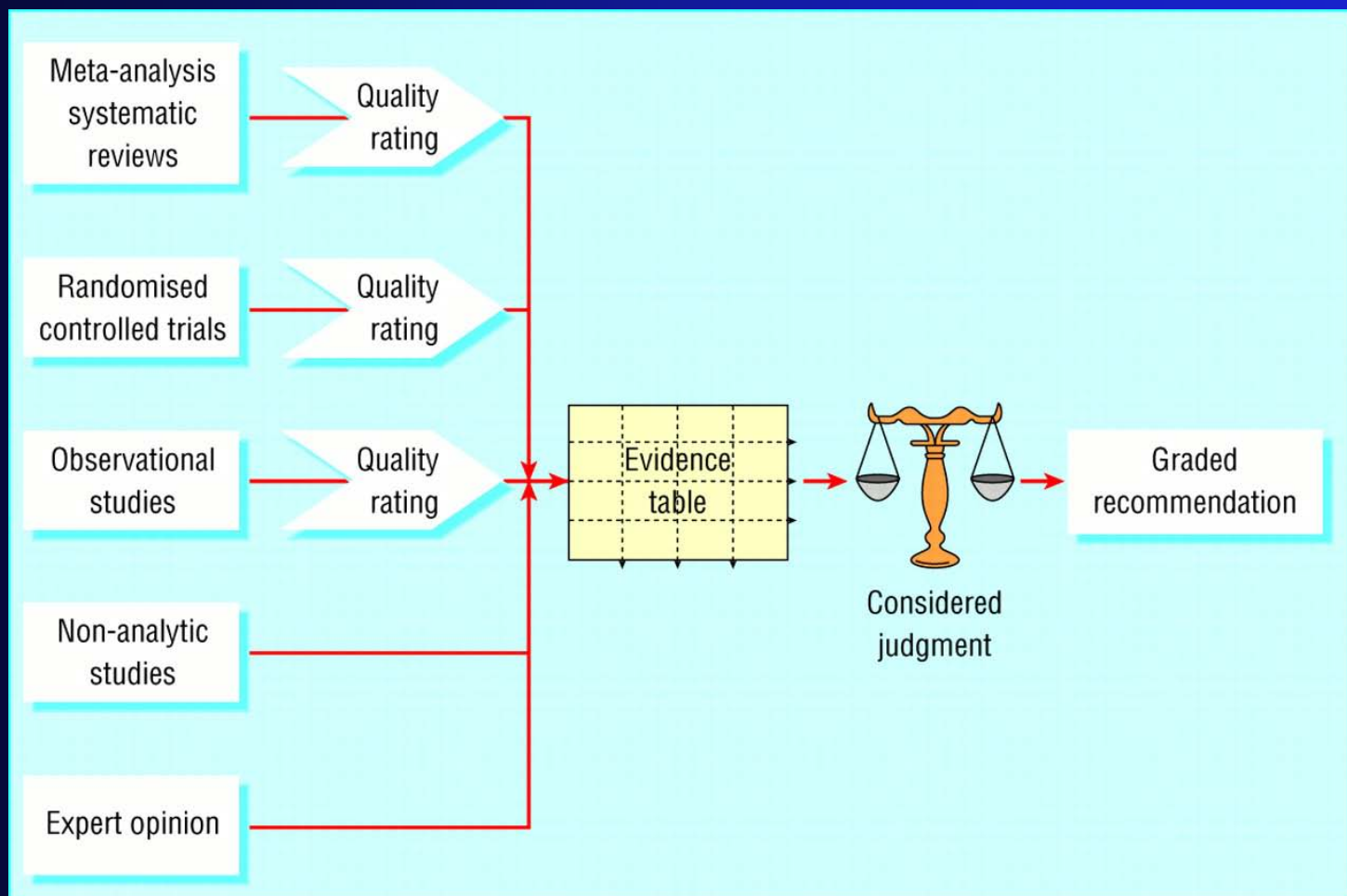
Guidelines should be explicit about

- WHEN (under what circumstances)
- WHO
- OUGHT TO
- Do WHAT
- To WHOM
- HOW
- WHY

Evidence Rating Systems

- Cochrane Collaboration (1999)
- CDC Guide to Preventive Services (2000)
- GRADE (2011) International working group

General Approach



PHS ARV Treatment Guidelines

Recommendations Ratings

Strength of Recommendation

- **A** Strong
- **B** Moderate
- **C** Optional

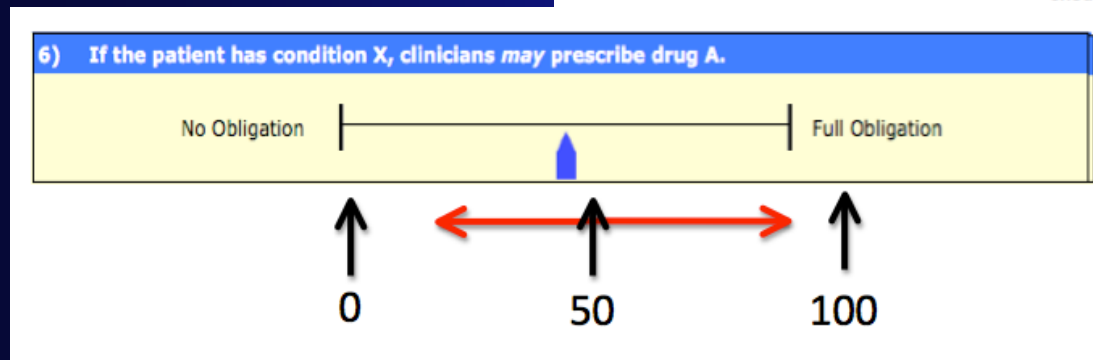
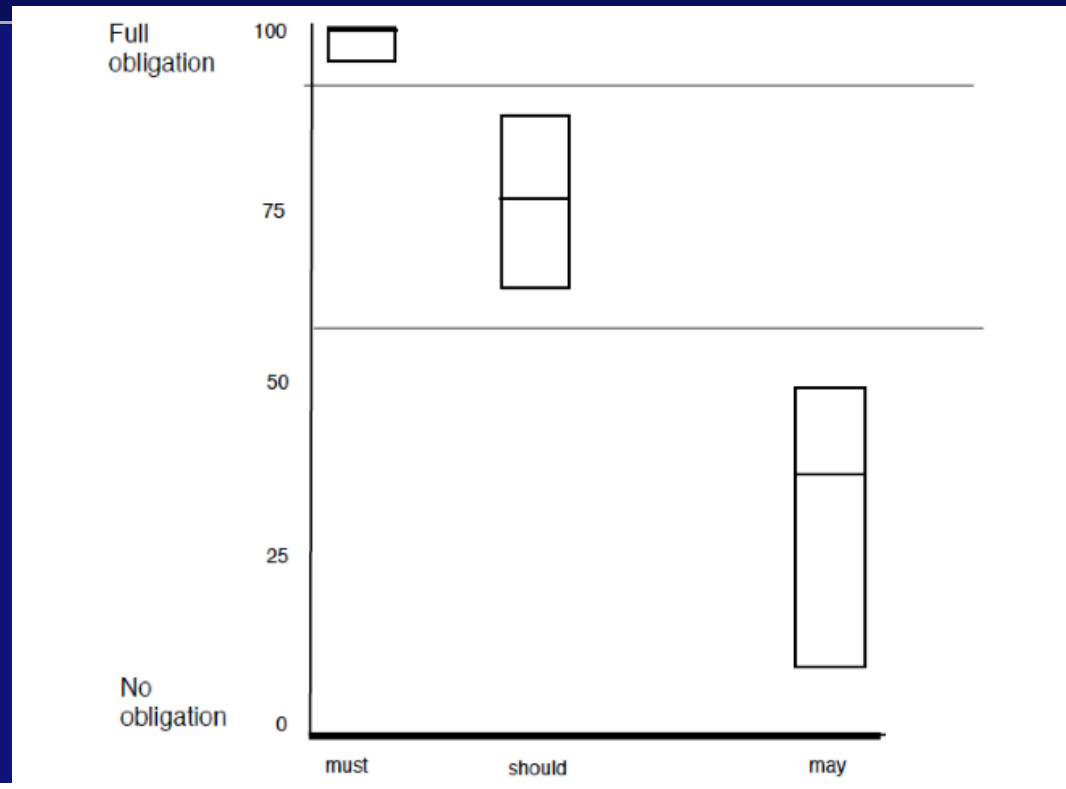
Quality of Evidence

- **I** ≥ 1 RCT with clinical outcomes and/or validated laboratory endpoints
- **II** ≥ 1 well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
- **III** Expert opinion

Some caveats

- Formal grading of strength of evidence
 - primarily assesses efficacy and safety findings
- Implementation concerns are addressed in guidelines but not included directly in the strength of evidence assessment
 - Screening and diagnosis for intervention indications
 - Adherence
 - Adjunctive procedures (e.g., counseling, safety monitoring)
- Feasibility, implementation cost, and cost-effectiveness may determine whether guidelines are issued at all in specific circumstances

Language of “obligation”



Unclear Language

- **Ambiguous**
 - Interpretable in more than one discrete way
 - “MS” – morphine sulfate, magnesium sulfate...
- **Vague**
 - Lack a crisp threshold in a single dimension
 - “high fever”
- **Underspecified**
 - Lack specificity in multiple dimensions
 - “sufficiently ill to warrant immediate antimicrobials”

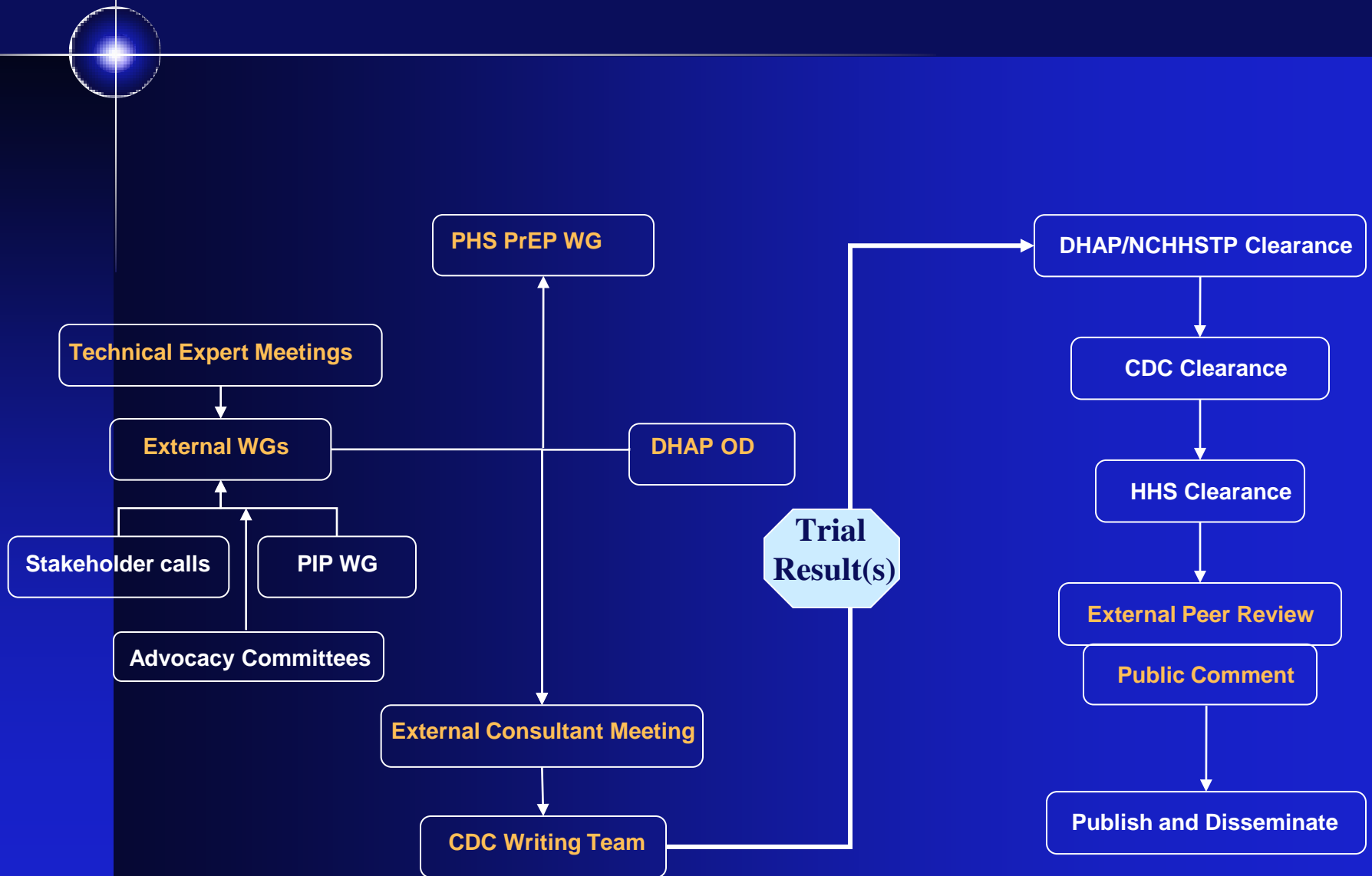
Types of PrEP Guidance

- **Brief statement on principles of use**
 - “Immediately” after any positive trial result
 - “Dear Colleague Letter” and/or MMWR “Notice to Readers”
- • **PHS guidelines**
 - Wide stakeholder engagement and public comment
 - Cleared by key HHS agencies
 - Basis for program monitoring and evaluation
- **Program implementation guidance**
 - Series of “how-to” documents
 - For demo projects, health departments, and trainers
 - Specific to settings, populations, and providers

PrEP Guidelines

- The strength of evidence determination for PHS guidelines will include:
 - **PrEP RCT efficacy and safety outcomes**
 - Informed by:
 - Other human ARV prophylaxis and treatment data
 - Human pharmacology studies (e.g., concentration of drugs in the genital tract)
 - Expert opinion obtained via formal consultations and public comment periods

Process



Planned Format

- PrEP use in the US
 - Sections for transmission risk populations
- Modest size
 - Supplementary documents
- Posted to guidelines website(s)
- Prompt updates as science develops

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"The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention."