

Criteria Work Group: Update on the Nominating and Review Process

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12-18-06 *ACHDGDNC*



Criteria Work Group (10/05 -)

- Group of *ACHDGDNC* members, appointed by Dr. Howell
- Goal: to develop a structured nomination process by which additional disorders could be considered by the *ACHDGDNC*
 - HRSA staff: Michele Puryear, Marie Mann,
 - Dr. Howell, *Ex officio*



Nomination Process - concepts

- Broad access to the process
- Considered review
- Streamlined process
- Transparency
- Consistent criteria throughout nomination process
- 3 main areas: Condition, Test, Treatment
- **Current focus:**
 - *Evidence-based review to inform ACHDGDNC*

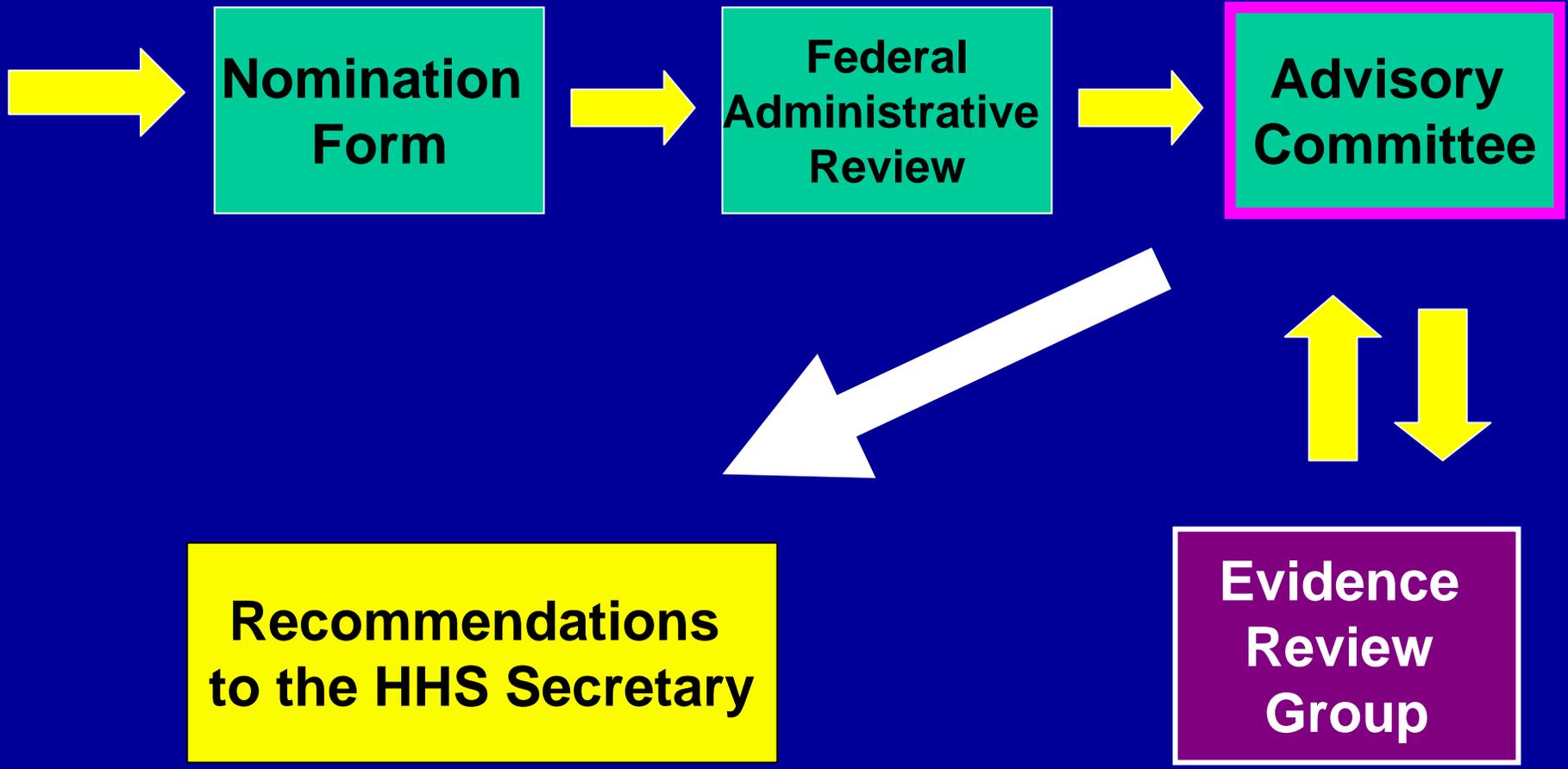


3 Proposed Steps for Nominations

- Step #1: The Nomination Form
- Step #2: Federal administrative review
- Step #3: Review by *ACHDGDNC*
 - A) *ACHDGDNC* review
 - ** B) External evidence-based review
 - C) *ACHDGDNC* review and decision



Paradigm for Committee Consideration of Additional Disorders



Step #1: Nomination Form

Steps to date



-
- Drafted by Criteria Work Group
 - Reviewed by *ACHDGDNC*
 - Input from consumers and professionals
 - Piloted
 - Modified
 - Approved by *ACHDGDNC*
 - Considered by “Evidence” group
 - Help entire process to maintain consistency

Suggestions for the submission process from the 6/06 *ACHDGDNC* meeting

- 1) Need a cover letter of guidance to NF
- 2) Sample completed form – MCAD (Dr. Rinaldo)
- 3) Define Evidence-Based Review –
Practice and principles
- 4) Streamline process - funnel multiple applications on same or linked disorders



Previous *ACHDGDNC* meeting (continued)

- 5) Only the *ACHDGDNC* can reject an NF application, even with expedited review
- 6) Conflict-of-interest disclosure for nominating process
- 7) How to prioritize?
 - May want to start with those 84 disorders that were on the ACMG's original list
- 8) Consider economic impact of screening in the EBR step.

Nomination Process:

Evidence-based Review

Meeting 10/23/06: Setting the framework for evidence-based review (EBR):

- Chair – Dr. James Perrin

 - Professor of Pediatrics, Harvard Medical School

- Attendees: Several AC members, EBR experts

- Major accomplishment:

 - Outlined guiding principles of EBR in NBS



Evidence Review Meeting (continued)



- Nomination process and NF – overall supported
- Advised some additions to the NF:
 - May need some clarity regarding:
 - test sensitivity/specificity and
 - level of available evidence
 - Needs to be accompanied by good NF model (MCAD) and a cover letter
- Described a framework for application of EBR in NBS

Framework for EBR in NBS

- Similar, though not identical to USPSTF or ACIP
 - Types of available data
 - For example, RCTs rare or not possible
 - Relatively scant data for unusual disorders, including the impact of early intervention vs. the natural history of the disorder and later intervention
- Apply consistent decision analysis (*decision tree*)
- Focus on:
 - Outcomes of screening and their implications: True positive, true negative, false positive, false negative
 - What disorders and what spectrum does screening identify?
 - How to assess the impact of treatment?

DRAFT Decision Tree for Evidence-Based Analysis for a Disorder in NBS

★ *At a discernible level of evidence*

Disease
Defined entity?
Age of onset?
Severity?
Natural history?

NO



Research gaps

↓ YES

Research gaps

NO



Screening test
DSB? (not essential)
Performance?
Risks?

YES



Diagnostic test
Accurate?
Reasonable?
Available?

NO



Research gaps

↓ YES

Research gaps

NO



Screening Pilot
Population-based?
Specificity?
Sensitivity?
Clinical utility?

YES



Treatment
Efficacy?
Urgency?
Risks?
Available?
Cost vs. no Rx?

↓ YES

YES



Impact on the family?

NO



Research gaps

Recommendations: - More research to ACHDGDNC
- Pilot(s)
- Universal NBS



ACHDGDNC
Liaison group

↙ YES

EBR Framework in NBS (continued)



- Additional questions that need to be addressed:
 - How to weigh evidence, especially where sparse or inconclusive?
 - What kind of minimum pilot studies are needed?
 - How does cost analysis influence decisions?
 - Cost of screening and Rx vs. Not screening and Rx
 - How to define and prioritize the benefits from NBS?

Evidence Review Group: What expertise would be needed?



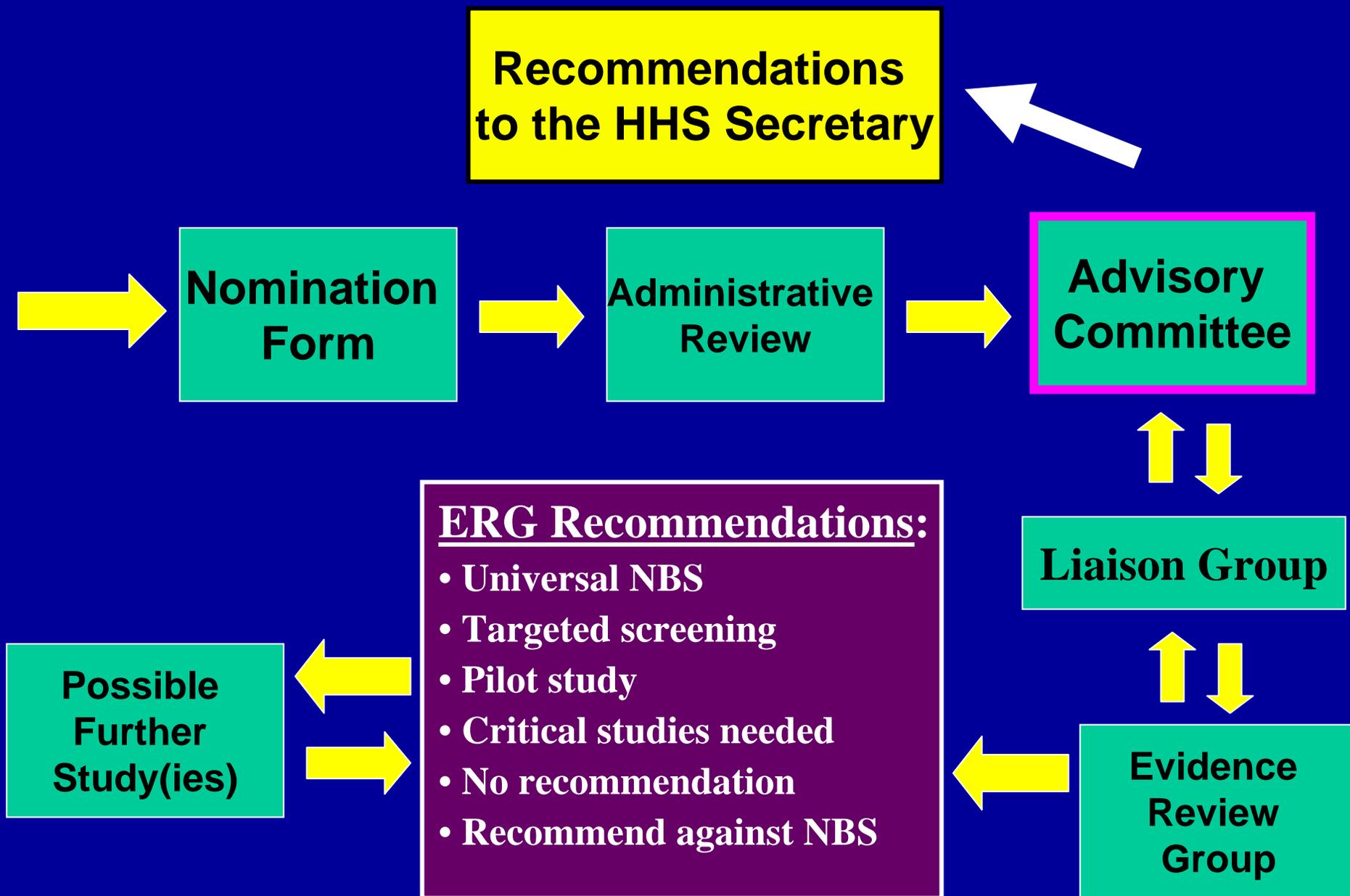
- Presumably a stable core:
 - Clinical (genetics, pediatrics, other?), Evidence Review expertise, Epidemiology, Public Health, Consumers, Laboratory
- *Ad hoc* expertise – For specific disorder or group of disorders (e.g. LSDs, Immune deficiency, Infectious disease, etc.
- AC members (2) as liaison to *ACHDGDNC*

Range of Evidence Group Recommendations to the *ACHDGDNC*

- Accept for universal NBS
- Unacceptable for NBS
- Reservations:
 - Need to improve screening or diagnostic test
 - Need more data on natural history
 - Need more data on the impact of Rx
 - Need more pilot data, especially trials of population-based screening (e.g. at state or local level)
- Likely need to have an iterative process between *ACHDGDNC* and ERG



Consideration of Additional Disorders for NBS



EBR Meeting: Conclusions



- EBR can be applied to NBS
- Can follow many of the EBR principles
- May need to weigh evidence differently
- Evidence review group = Advisory role to the *ACHDGDNC*, with a *Liaison group between the 2*
- *Help determine needed research, including pilot(s)*
- Additional questions to be addressed:
 - Define benefits of intervention
 - Costs analysis – Screening vs. not screening

Recommendations to *ACHDGDNC*

- Include formal EBR step in nomination process
- Evidence Group composition: To be defined
 - Probably: Stable core plus *ad hoc* experts
 - Explicit conflict-of-interest policy
- ERG to report its recommendations to the *ACHDGDNC*
- *ACHDGDNC* would recommend next steps:
 - Research, pilot(s), or implementation



Nomination Process: Next steps

- *ACHDGDNC* to review and ratify EBR concept and proposed framework
- Define Evidence Review Group –
 - Responsibilities, Composition, Operating principles and format
- Establish priorities for disorders to enter the nomination process

