Evaluation of Genomic Applications in Practice and Prevention: Implementation and Evaluation of a Model Approach

Secretary's Advisory Committee on Genetics, Health, and Society

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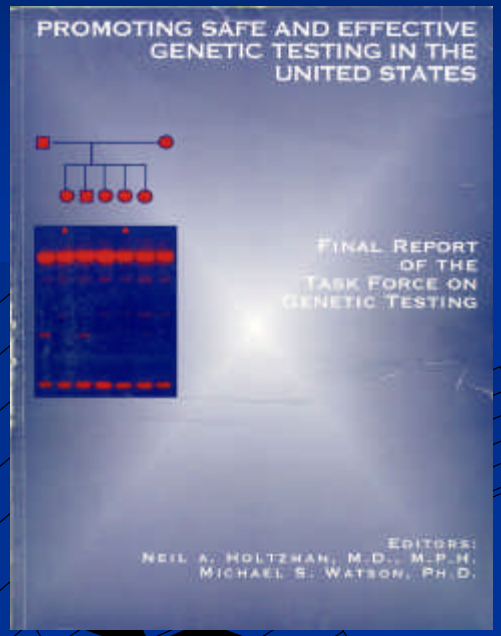
NIH-DOE Task Force on Genetic Testing

- Emphasized the need for
  - Evidence-based entry of new genetic tests into clinical practice
  - Coordinating collection of data on safety & effectiveness
  - Post-market surveillance
- Described assessment criteria
  - Analytic Validity
  - Clinical Validity
  - Clinical Utility



Final report, 1997 - http://www.nhgri.nih.gov/ELSI/TFGT_final/

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Secretary's Advisory Committee on Genetic Testing

- Affirmed Task Force assessment criteria
  - Added emphasis on social consequences
- Encouraged collaboration between laboratories and HHS agencies to
  - facilitate data collection
  - provide information to providers & consumers
- Suggested enhancements in oversight by
  - FDA – pre-market review and approval of new tests
  - CMS – augment CLIA regulations
  - CDC with other agencies – post-market collection, aggregation, and analysis of data

http://www4.od.nih.gov/oba/sacgt.htm

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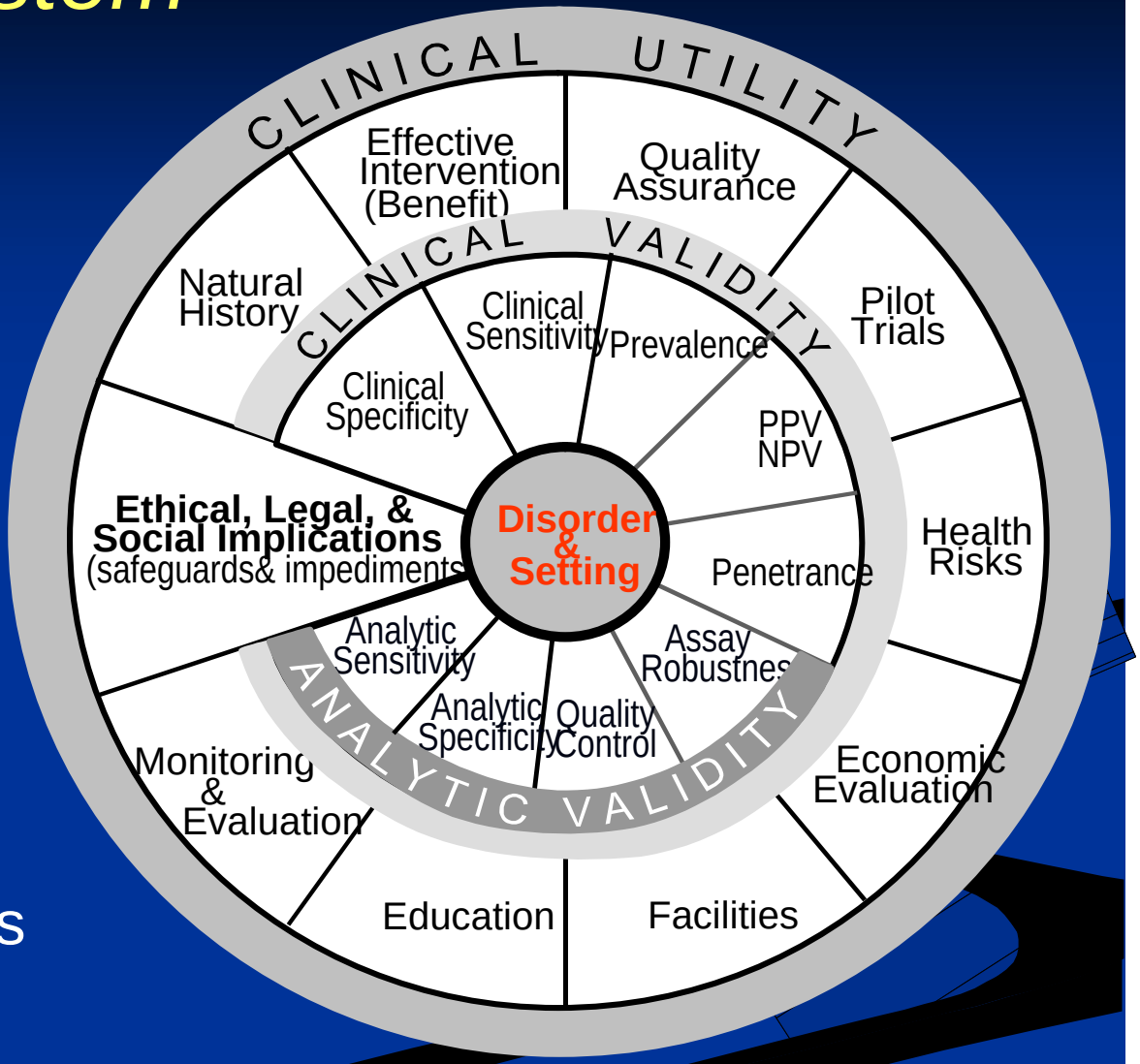
ACCE Model System

- Developed by the Foundation for Blood Research
- Name reflects four components of evaluation
- Define test, disorder, and setting
- Analytic framework – 40+ targeted questions



http://www.cdc.gov/genomics/activities/fbr.htm

ACCE Model System

- Designed to assess data on DNA-based testing for disorders with a genetic component
  - Broad focus – “first look” at all available data
  - Ad hoc approach to grading quality of evidence to extract maximum information
  - Review, analyze, and integrate data
  - Did not suggest policy or make recommendations
- Provide up-to-date, accurate and complete summaries
- Formats useful to policy-makers, health care providers and the general public

ACCE Reviews

- Prenatal Screening for Cystic Fibrosis via Carrier Testing
- Screening for Hereditary Hemochromatosis in Adults via *HFE* Mutation Testing
- Testing for Factor V Leiden and Prothrombin Mutations as a Risk Factor for Recurrent Venous Thrombosis in Adults
- Family History and BRCA1/2 Testing for Identifying Women at Risk for Inherited Breast/Ovarian Cancer
- DNA Testing Strategies Aimed at Preventing HNPCC

http://www.cdc.gov/genomics/activities/fbr.htm

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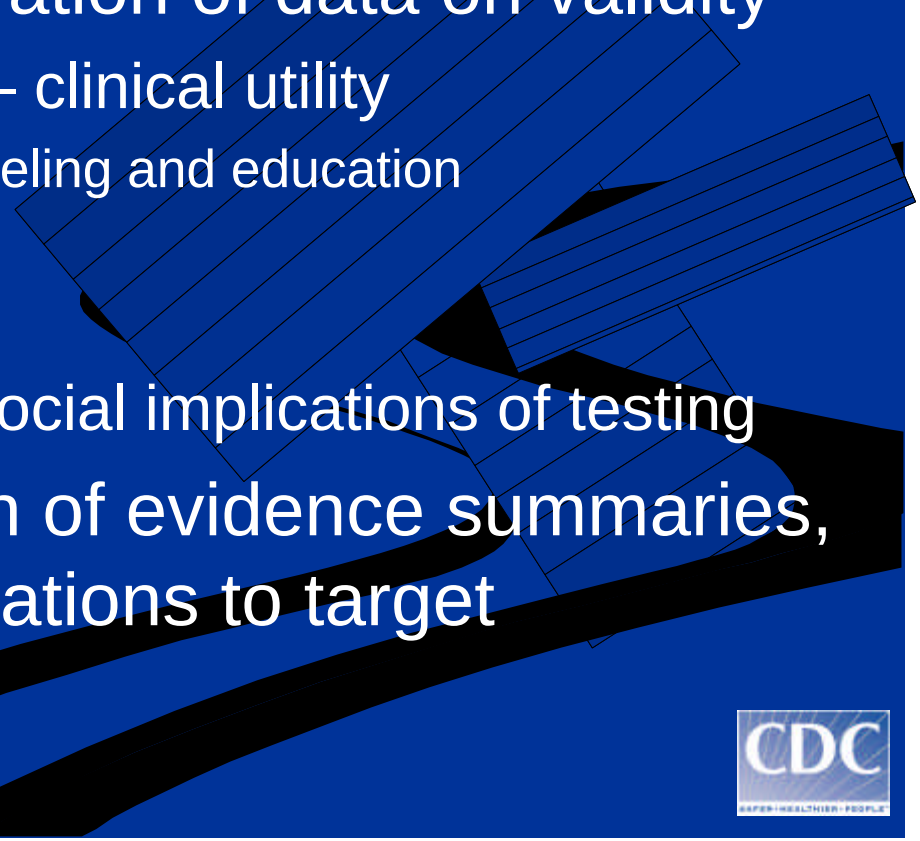
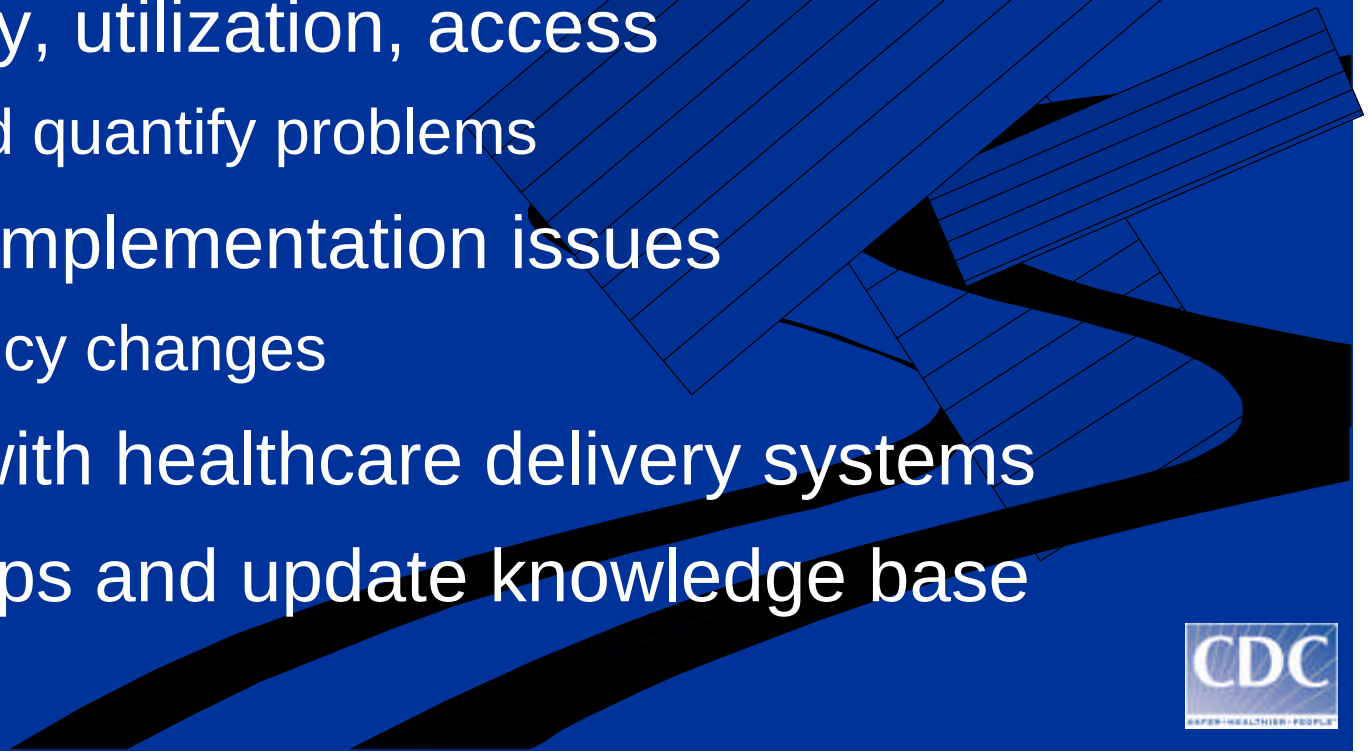
Transition from research to clinical and public health practice

- Evidence-based review to establish safety and efficacy before widespread use
- Systematic review / integration of data on validity
  - Assess risks and benefits – clinical utility
    - Resources for testing, counseling and education
    - Results of pilot trials
    - Cost effectiveness analysis
  - Identify ethical, legal and social implications of testing
- Appropriate dissemination of evidence summaries, guidelines, & recommendations to target audiences



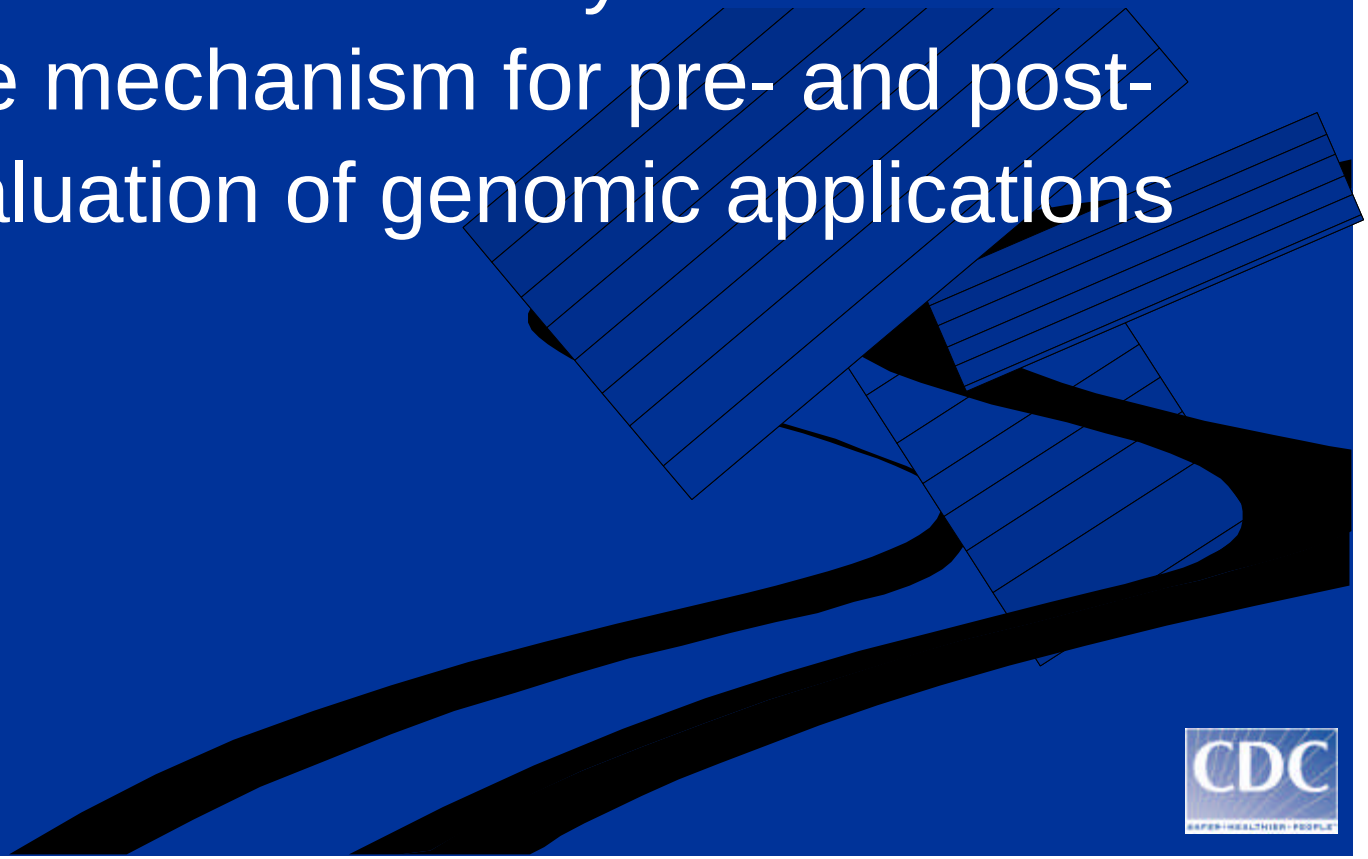
Data collection and monitoring in the post-implementation period

- Demonstrate acceptable performance in practice
  - Confirm or update performance estimates
- Assess public health impact – including quality, acceptability, utilization, access
  - Define and quantify problems
- Document implementation issues
  - Inform policy changes
- Assess fit with healthcare delivery systems
- Resolve gaps and update knowledge base



Evaluation of Genomic Applications in Practice and Prevention (EGAPP): A Three-Year Model Project

- Establish and evaluate a systematic and sustainable mechanism for pre- and post-market evaluation of genomic applications in the US



EGAPP: A Three-Year Model Project

- Respond to recommendations for action
- Use knowledge gained from ACCE model project
- Interact with
  - existing processes for evaluation and appraisal
  - international health technology assessment community
  - other projects
    - Quality assurance – CDC process to obtain and distribute QC materials for genetic testing
    - North American Rare Disease Laboratory Network
    - Policy initiatives

EGAPP: A Three-Year Model Project

- Provide clear linkage between the evidence and recommendations
  - Minimize conflicts of interest
  - "*Evidence-based* requires that the linkage be transparent, explicit, and publicly accountable; not that it be *objective*." Al Berg
- Develop a plan for dissemination of information and communication with target audiences

Are genetic tests different?

- Basic similarities in assessment
  - Concerns about potential use to discriminate, stigmatize, cause harms to individuals and families
- Increased awareness of genetic testing and public perception that is “different”
  - EGAPP addresses a current public health issue
- Knowledge gained about successful evaluation approaches, methodologies and infrastructure applicable to the assessment of other emerging health technologies

Support for the model project

- Provided by CDC under a contract for *Program and Policy Assessments and Policy Design*
- Award to RTI International August, 2004

EGAPP Working Group

Independent
Non-Federal
Multidisciplinary

- 10-12 experts
  - Health care
  - Genomics
  - Epidemiology
  - Health technology assessment (HTA)
  - Public health
- Scheduled meetings

Roles of Working Group

- Define protocols for evidence-based reviews (EBR) and development of recommendations
- Consider input from stakeholders, develop criteria, select and prioritize topics
- Request EBR, oversee quality review of reports
- Develop recommendations based on reports
- Consider needs and strategies for post-implementation monitoring and data collection
- Take part in evaluation of the project
  - Process, products, and value/impact

Stakeholders

Health care providers

Consumers

Professional organizations

Policy makers

Public health

Industry / biotechnology

Health care payers & purchasers

Laboratories

Regulatory groups

- Identify & engage
- Needs assessment
  - Specific topics for immediate consideration
  - Content and format of information needed and useful from their perspectives
- Content experts
  - Technical assistance, peer review of reports
  - Development of informational messages for key target audiences

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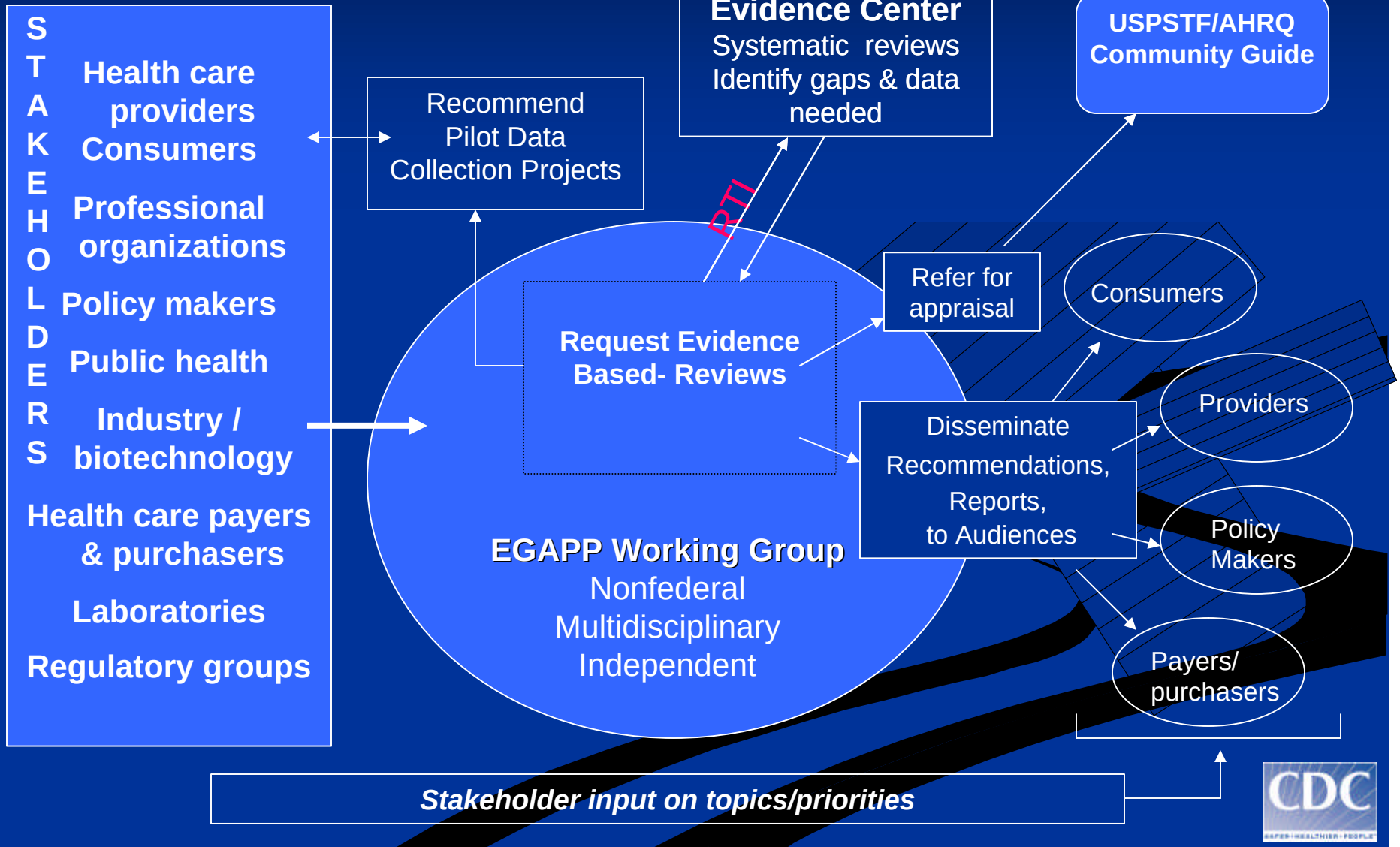
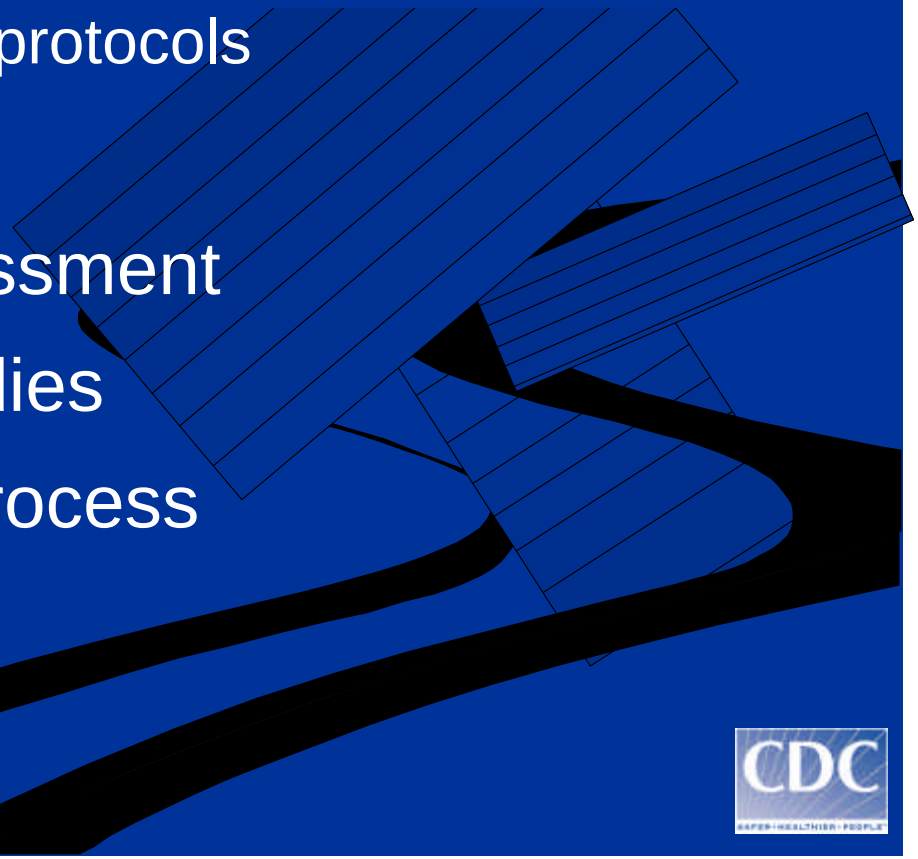
EGAPP overview



EGAPP - Year 1

- Process development
  - Recruitment of Working Group
  - Two organizational meetings
  - Development of working protocols
- Methodology meeting
- Preliminary needs assessment
- Pilot data collection studies
- Evaluation – focus on process



EGAPP - Years 2 and 3

- Continuing support of Working Group
- Commissioning / oversight of EBRs
- Dissemination of reports, Working Group recommendations, and informational messages
- Ongoing dialogue with stakeholders
  - Development of informational messages for target audiences
  - Feedback on the value of the process and products
- Pilot data collection studies
- Evaluation - process, products and impact
- Mechanisms to sustain a validated evaluation process

Why talk about methodology?

- Standard processes / methodologies not as effective
  - Conditions are often less common
  - Interventions and clinical outcomes not well defined
  - Limited evidence base
    - Data collected after introduction into clinical practice
    - Argument for efficacy based on descriptive evidence, no clinical trials
  - Ethical, legal, and social issues less amenable to evidence-based approach
  - Influence of advocacy from industry and patient interest groups

Methodology meeting – January 2005

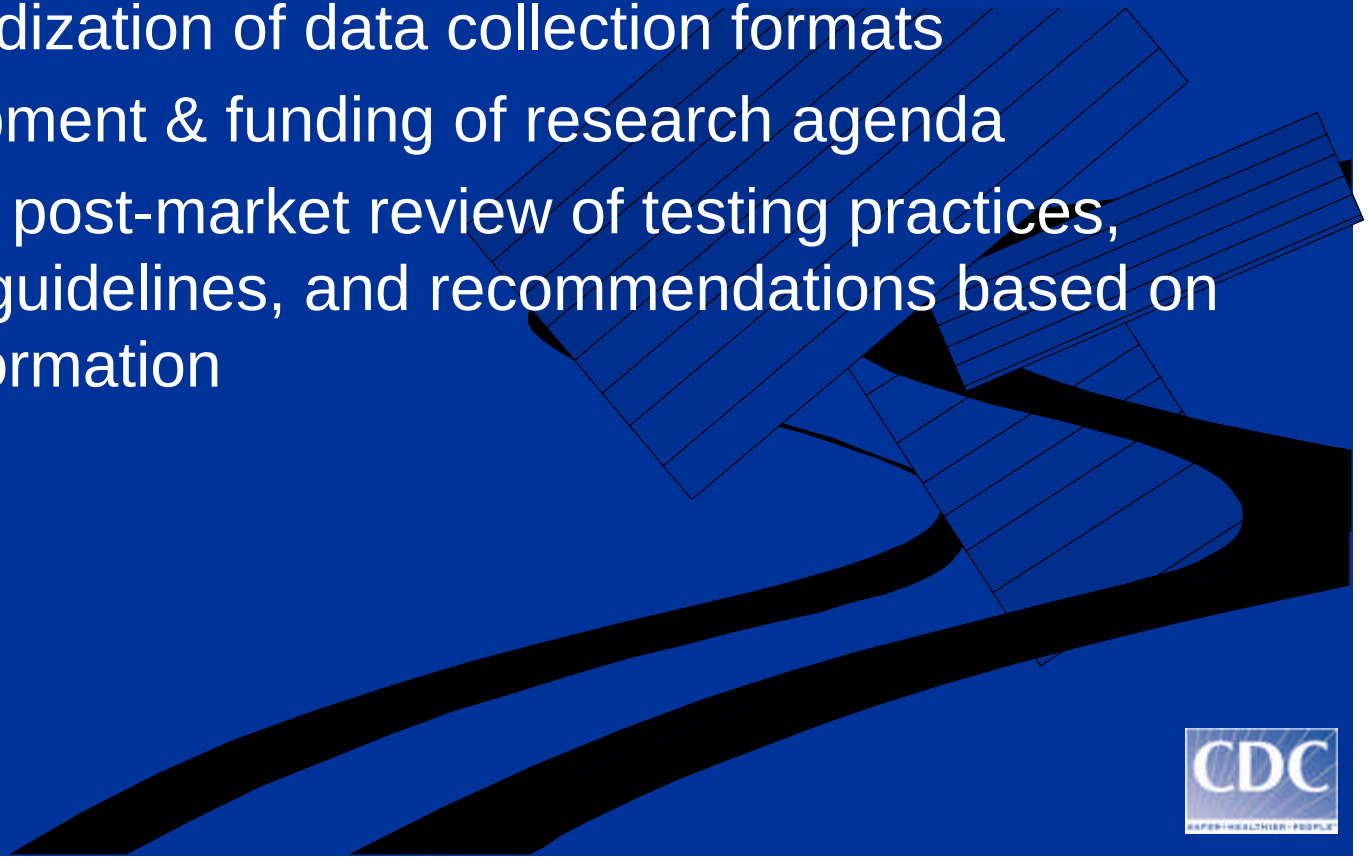
- Experts in EBR, HTA, epidemiology, genomics
- Focus on elements of evaluation process
  - Define the test, the disorder, the setting
  - Analytic framework for EBR
  - Literature search and synthesis
  - Grading quality of evidence
  - Evidence to recommendations
- Seek agreement on minimum standards
  - When is a test “ready” to move into clinical practice?
    - Amount of information? Threshold for quality of evidence?
  - How do we optimize the quality of data to be collected in the future?

Rationale for EGAPP

- Now is the time
  - Genetic tests are increasing in number and complexity
  - New applications are anticipated
  - Testing will move into primary care
  - Health care providers and the public need a source of objective advice about appropriate use of tests
- Short-term - provide information to address questions posed by SACGT and SACGHS
  - Oversight of genetic technologies
  - Coverage and reimbursement
  - Access, public awareness and understanding

Rationale for EGAPP

- Long-term
  - Create an expectation that a certain level of review will occur prior to acceptance in routine practice
  - Standardization of data collection formats
  - Development & funding of research agenda
  - Support post-market review of testing practices, clinical guidelines, and recommendations based on new information



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- The EGAPP project is supported by the CDC Office of Genomics and Disease Prevention through a contract with RTI International (200-01-00123 TO36)