

Clinical Guidelines for Genomic Testing: Evidence Synthesis Considerations

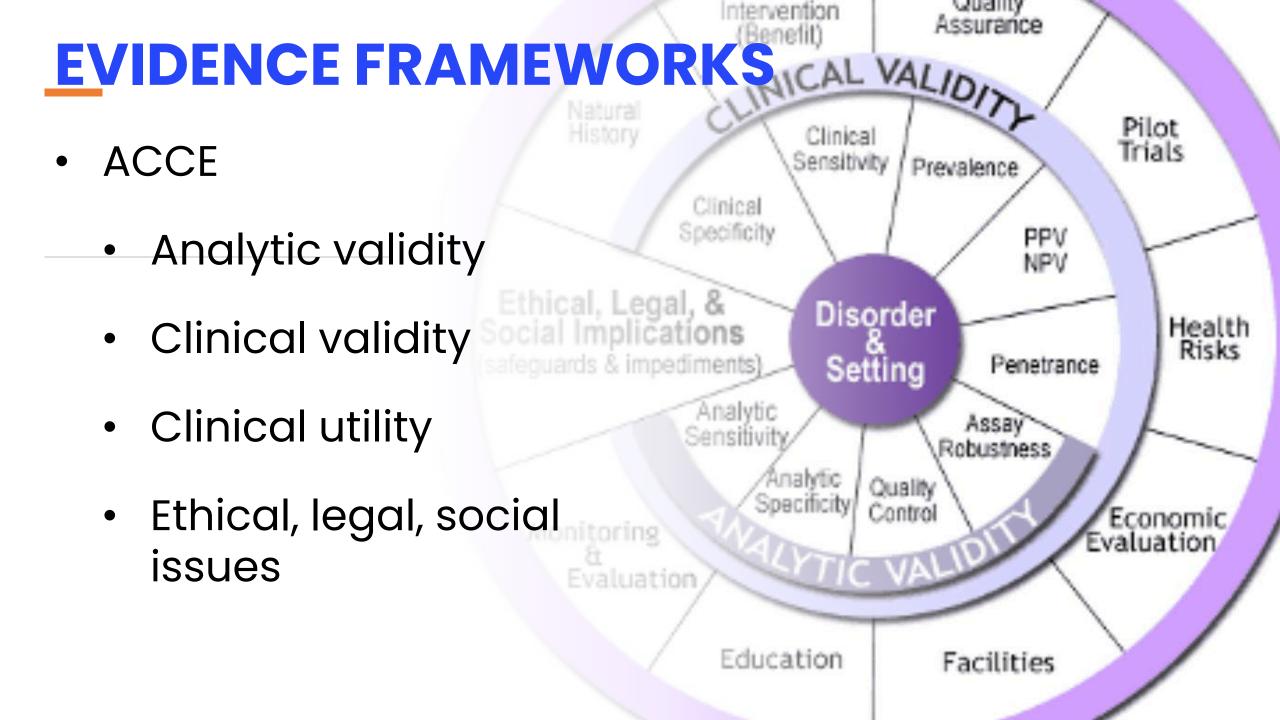
Examining Clinical Guidelines for the Adoption of Genomic Testing: A Workshop

SESSION VI: Guideline Development in a Rapidly Evolving Field – A Look Ahead

Karli Kondo, PhD, MA October 29, 2024

DECLARATIONS

No conflicting affiliations or financial interests



EVIDENCE FRAMEWORKS

Lin et al. BMC Medical Informatics and Decision Making 2012, 12:117 http://www.biomedcentral.com/1472-6947/12/117



CORRESPONDENCE

Evaluating genomic tests from bench to bedside: a practical framework

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Abstract

The development of genomic tests is one of the most significant decades. As these tests become increasingly available evaluate the evidence base and evidence gaps in order to describe such a framework that can provide a common I genomic testing. Each stakeholder can use this framework making, depending on their perspective and particular necessary.

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BRIEF REPORT

Genetics in Medicine

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Evidence synthesis and guideline development in genomic medicine: current status and future prospects

Sheri D. Schully, PhD¹, Tram Kim Lam, PhD, MPH¹, W. David Dotson, PhD², Christine Q. Chang, MPH¹, Naomi Aronson, PhD³, Marian L. Birkeland, PhD⁴, Stephanie Jo Brewster, MS⁵, Stefania Boccia, PhD⁶, Adam H. Buchanan, MS⁷, Ned Calonge, MD, MPHጾ, Kathleen Calzone, MSN, RN⁶, Benjamin Djulbegovic, MD, PhD¹⁰,¹¹, Katrina A.B. Goddard, PhD¹², Roger D. Klein, MD¹³, Teri E. Klein, PhD¹⁴, Joseph Lau, MD¹⁵, Rochelle Long, PhD¹⁶, Garv H. Lvman. MD. MPH¹⁷. Rebecca L. Morgan. MPH¹ጾ. Christina G.S. Palmer. CGC, PhD¹⁶,

Genetics inMedicine

SPECIAL ARTICLE

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Improving the efficiency and relevance of evidence-based recommendations in the era of whole-genome sequencing: an EGAPP methods update

David L. Veenstra, PharmD, PhD¹, Margaret Piper, PhD, MPH², James E. Haddow, MD³, Stephen G. Pauker, MD⁴, Roger Klein, MD, JD⁵, Carolyn Sue Richards, PhD⁶, Sean R. Tunis, MD, MSc⁻, Benjamin Djulbegovic, MD, PhD⁶, Michael Marrone, MPH⁶,¹⁰, Jennifer S. Lin, MD, MCR¹¹, Alfred O. Berg, MD, MPH¹² and Ned Calonge, MD, MPH¹³; on behalf of the EGAPP Working Group

ANALYTIC FRAMEWORKS

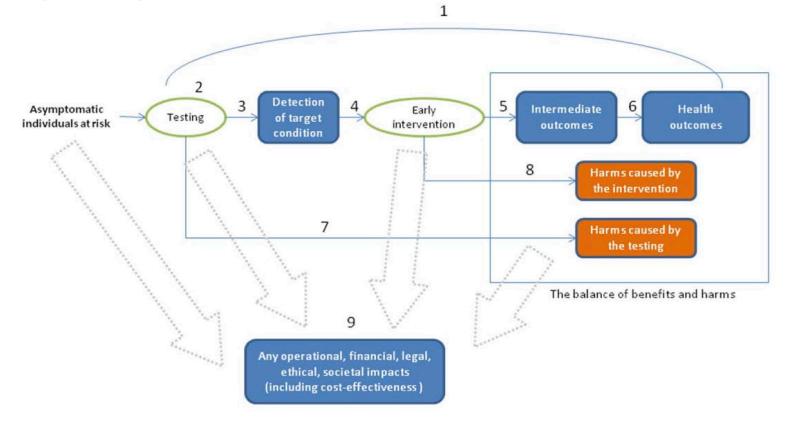
Methods Research Report

Addressing Challenges in Genetic Test Evaluation

Evaluation Frameworks and Assessment of Analytic Validity

Prepared for:

Agency for Healthcare Research and Quality U.S. Department of Health and Human Services 540 Gaither Road Rockville, MD 20850 www.ahrq.gov



EVIDENCE FRAMEWORKS

Phase 0: Marker identification & Assay Development

Discovery, establish association between biomarker(s) and outcome(s) of interest

Develop assay based on identified biomarker(s)

Phase 1: **Initial Test Performance** and Assay Refinement

Determine test performance of defined assay in targeted population

Refine assay based on initial test performance

Test Validation

Determine test performance and feasibility in intended

population

Phase 2:

Phase 3: **Clinical Test Performance** Generalizability & Health **Impacts**

> Determine effects (benefits and harms) on important decision making and health outcomes

Phase 4: Comparison with Existing **Tests**

Determine comparative effectiveness (benefits and harms)

Phase 5: **Population Impacts**

Determine health. cost effects at a population or health systems level

Determine feasibility of implementing testing programs, and legal/ethical implications for society

Clinical Phases (Includes clinical validity/utility)

Pre-Clinical Phases (Includes analytic validity)

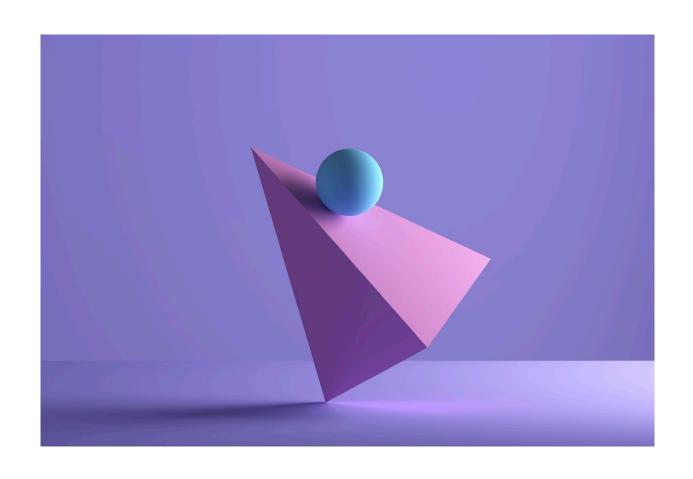
Lin et al., BMC Medical Informatics and Clinical Decision Making, 2012, 12:117

EVIDENCE CONSIDERATIONS



- Rapid development
 - Potential need to inform interest-holders with "less than ideal" evidence
 - Insufficient evidence due to:
 - Single studies
 - Small samples, etc.

EVIDENCE CONSIDERATIONS



Study Designs: "lower level"

- Observational, diagnostic accuracy
- Case series, case studies
- Grey literature

— INFORMATION SOURCES

- Published literature
- Grey literature
 - Preprints
 - Media, newsletters
 - FDA 510k, device submissions
 - Other federal agencies
 - International sources



— INFORMATION SOURCES

- Test developers, laboratories
 - Scientific Information Packets
- ClinicalTrials.gov
- Professional societies
- Interest holder review and feedback



KEEPING IT CURRENT: LIVING REVIEWS

- Increasingly common
- Enables the currency of conclusions
 - Multiple data/evidence sources
 - Iterative process provides flexibility
 - Continual or regular surveillance
- Equity and implementation considerations

KEEPING IT CURRENT: HEALTH EQUITY SEARCH FILTER

Development across multiple reviews avoids overfitting to a single context.

- Systematic Review A
- Systematic Review B
- Systematic Review C

Develop

Test & Validate

- Gold standard across reviews
- Infrastructure in place

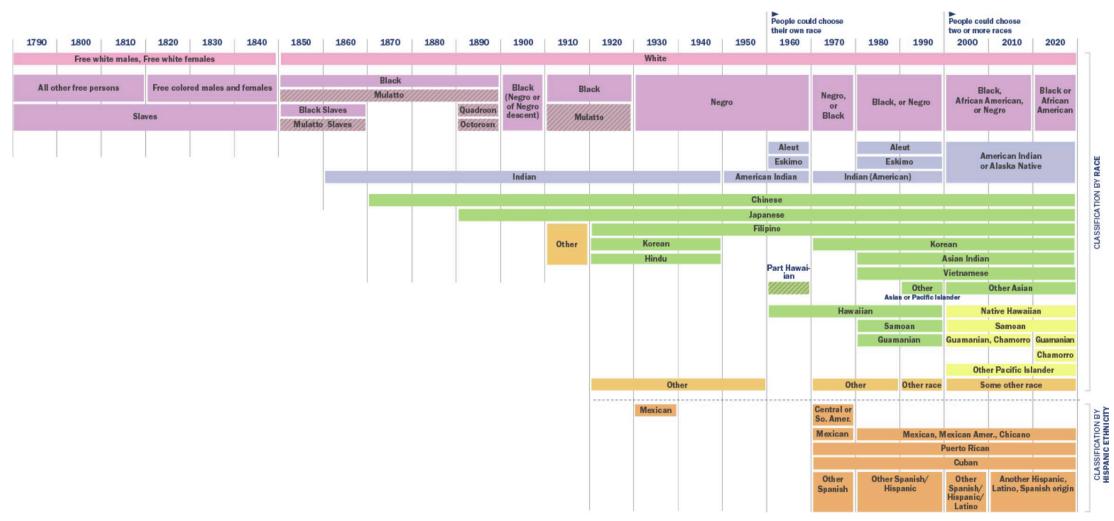
- Planned review
- MeSH updates

Revise

Planned revisions keeps search from becoming outdated due to semantic drift and leverages improved indexing.



KEEPING IT CURRENT: POPULATION DESCRIPTORS



Adapted from: "What Census Calls Us, A Historical Timeline" Pew Research Center, Washington, D.C.

Racial categories changed over time due to shifts in scientific, political and social thinking about race and ethnicity.

KEY POINTS

Established frameworks exist: rapidly evolving field

Use published & other evidence sources (FDA, SIP CT.gov, interest holders)

Living reviews: continuous surveillance keeps conclusions up to date Importance of equity & implementation, & social, ethical, & legal implications

THANK YOU! For questions or further discussion: karli.kondo@cancer.org

