# *Guideline Development in a Rapidly Evolving Field – A Look Ahead*

**Roundtable on Genomics and Precision Health:**
***Examining Clinical Guidelines for the Adoption of Genomic Testing***

**National Academies of Sciences, Engineering, and Medicine**

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## *Disclosures*

I am now retired and have no relevant conflicts of interest

## *Future Vision*

Today you have heard about the current state of guidelines for genomic testing and the many challenges we face. But I want to share my vision for a better future:

- More guidelines on more topics, all kept up to date
  - Many based on robust evidence, but others will be evolving as evidence improves.
- Data in digital formats
- Select aspects of the systematic reviews and analyses will be AI-enabled.
- Guideline recs will be computable and easily implementable.
  - Specific and clear
  - Computable derivative products
- Diverse guideline panels of all relevant stakeholder types and perspectives
  - With informaticians to ensure recommendations can be coded for EHRs
- Feedback loops
- Recommendations will go beyond population-based guidance to address outcomes and interventions for specific subgroups (*eg,* commonly occurring comorbidities) in NMA nodes.
  - Goal: To approach precision medicine
- EHRs will autopopulate with relevant recs and flag contraindications and conflicting values and preferences.
  - Patients and physicians will be able to have well-informed SDM conversations
  - Including what works for patients like them

## *Living Guidelines*

**Benefits of living guidelines:**

- Continually updated, as relevant, with modular updates
- Based on a regularly monitored systematic reviews of evidence
- Explicit and transparent methodology
- Minimizing distortions, biases, and conflicts of interest
- Multidisciplinary panels of experts and representatives from all key affected groups and all relevant perspectives.
    - Structure such that panelists remain over several iterations, maintaining the diversity of perspectives and reducing COI review time
- Living guidelines can address access and equity, including insurance coverage, as a resource consideration
- In genomic testing, evidence is advancing rapidly, but LGM guideline updates can keep pace.

## *Living Guidelines*

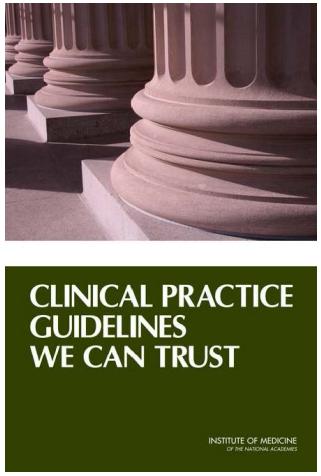
***Challenges of living guidelines:***

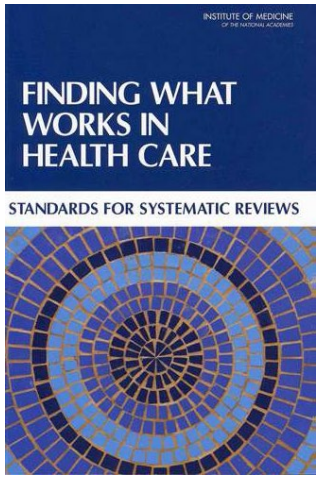
- Costs to conduct the methodologically-rigorous systematic reviews and meta-analyses,
    - Economies of scale with each update
- Costs to develop the guideline recommendations
    - Economies of scale with each update
- Challenges with guideline collaboration in the LGM:
    - Specific MOUs addressing entire process and methods is critically important from the foundational guideline through successive iterations and updates.
    - Agreements on criteria and triggers for updating.
    - What happens when one or more organizations deem a topic ready for updating but others do not? How will funding and functioning be affected?
- Time to complete each iteration, although a few lessons learned:
    - Maintaining COI-approved panelists over several iterations
    - Regularly scheduled literature monitoring and surveillance
    - Consideration of some rapid review techniques
    - Standardizing consensus-development processes

## *Updating Standards for Guidelines and Systematic Reviews*

All existing standards: review for possible revisions.
Additionally, new technologies and methods that did not exist previously:

- Artificial intelligence
- Big data analytics
- Adding equity of access and treatment
- Multiple other changes (for a different discussion)
- But now let's focus on how to answer clinical questions even when the evidence base is weak or still evolving,



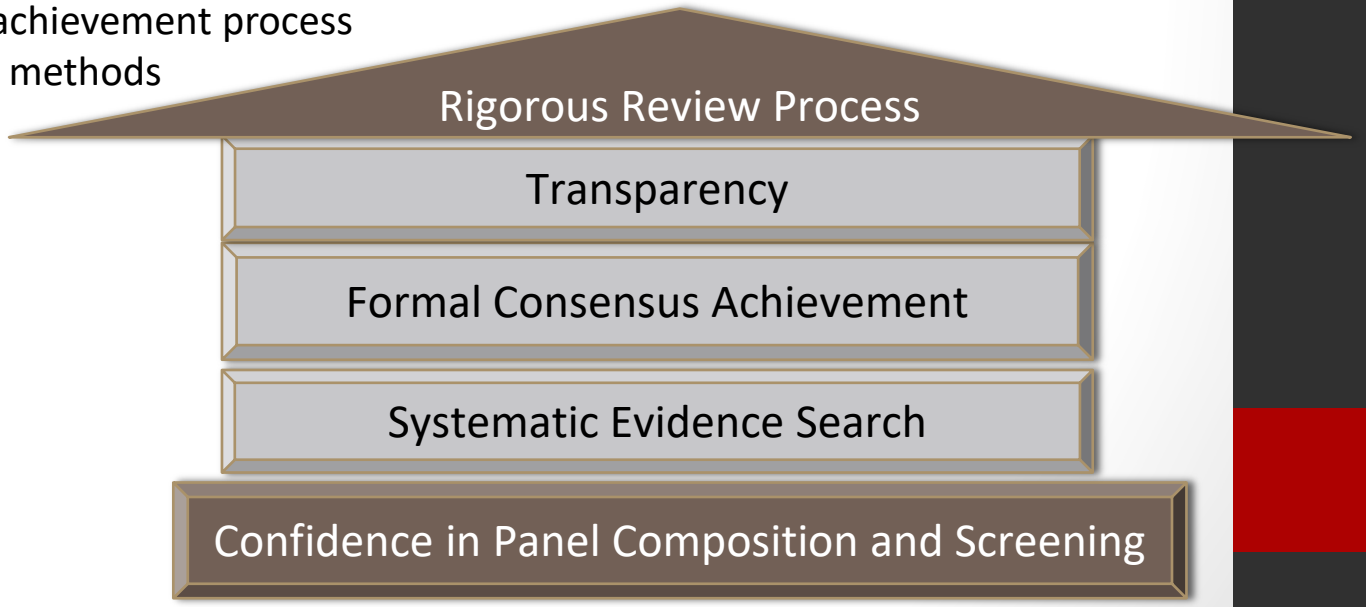
## *Updating Standards for Guidelines and Systematic Reviews*

How to create guidance in new and emerging fields or when the total body of evidence is of lower quality?

- When data do not support meta-analyses
- TCBS process
  - high quality
  - reliable
  - evidence-informed and consensus-based

***5 pillars of the TCBS process:***

- Panel structure and panelist approval criteria (foundation of trust)
- Comprehensive and systematic literature searches
- Delphi-based consensus achievement process
- Transparency of data and methods
- Thorough review

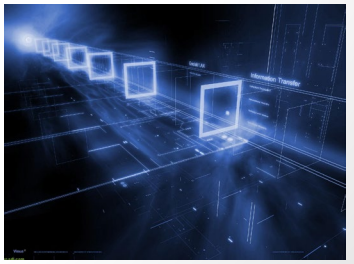



Lewis SZ. Developing Trustworthy Consensus-Based Guidelines When Only Low-Quality Evidence Exists. presented at: Guidelines International Network; September 22, 2023; Glasgow, Scotland.

# *Updating Standards for Guidelines and Systematic Reviews*

## *Artificial Intelligence*

- The use of AI to monitor and screen new and emerging evidence and other time-intensive tasks requires:
    - Objective review
    - Oversight
    - Accuracy and reliability checks
    - Replicability
- Value-based judgements considering uncertainty and differing perspectives still require humans.



## *Current Guidelines*

### *Improvements to the Existing State:*

Addressing fragmented or incomplete adoption and barriers to interoperability:

- Conflicting and divergent interpretations of guideline recommendations
  - Develop joint guidelines with relevant organizations
  - MOUs - long term consequences for living guidelines
  - Co-development → funding
- Include specificity as the evidence will support → actionable
  - Important for digital guidelines with computable recommendations
  - Recs: Who, What, When, Where, and How (not Why)
  - Informaticians on all guideline panels
- Resolve existing controversies with methodological rigor and all relevant stakeholder perspectives
- Policies and procedures → acceptable methods
- Computable guidelines with improved adoption of health IT standards

However, many guideline developing organizations not culturally ready for change and/or lack financial resources and appropriate expertise.

## *Computable Guidelines*

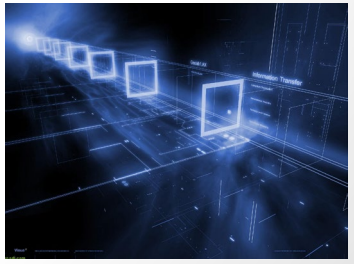
### *We need to build the tools to Make Guidelines Computable*

Boxwala et al's levels of knowledge framework:

- Level 1 represents knowledge in a narrative format
- L2 is in a semi-structured format
- L3 is in a structured format
- L4 is in an executable format

To facilitate the L4 executable state:

- Develop and implement computable guidelines employing a universally accepted standard enabling interoperable electronic health data exchange
- US Department of Health and Human Services Office of the National Coordinator for Health IT endorses FHIR® standards from Health Level Seven International (HL7®)
- EBMonFHIR uses FHIR resources related to clinical research evidence and clinical practice guideline development
- CPG-on-FHIR also for guidelines




- Boxwala AA, Rocha BH, Maviglia S, et al. A multilayered framework for disseminating knowledge for computer-based decision support. J Am Med Inform Assoc. 2011;18(Suppl 1):i132–i139.

## *Computable Guidelines*

### *WHO SMART Guidelines*

- WHO used CPG-on-FHIR to develop Standards-based, Machine-readable, Adaptive, Requirements-based, and Testable (SMART) Guidelines
- To transform guideline adaptation and implementation preserving fidelity and accelerating uptake
- SMART guidelines for antenatal care, HIV, family planning, TB, and child health in humanitarian emergencies with additional topics in development

### *Adapting Clinical Guidelines for the Digital Age*

- Centers for Disease Control and Prevention
- Sought to redesign and improve the process of guideline development, implementation, and FHIR-based standardization
- While WHO started with an existing guideline to make it computable, CDC did the reverse -- improving the process for development of a computable guideline. Both groups worked collaboratively and leveraged their experiences.


- Michaels M. Adapting Clinical Guidelines for the Digital Age: Summary of a Holistic and Multidisciplinary Approach. American Journal of Medical Quality. 2023;38(5S):S3–S11. doi:10.1097/JMQ.0000000000000138
- World Health Organization. SMART Guidelines. Accessed October 21, 2024. https://www.who.int/teams/digital-health-and-innovation/smart-guidelines
- World Health Organization. SMART Guidelines. The Lancet Digital Health. 2024;2024(October 21)

## *Computable Guidelines*

***Accelerating Care Transformation (***ACT)

- Led by Jerry Osheroff and a steering committee
- Many work group volunteers
- Initially funded by AHRQ to explore how to make its evidence, guidance, resources, and tools (along with others) more findable, accessible, interoperable, reusable, computable, and useful
- Based on the Vision for Healthcare in 2030
- Aim: to advance interoperable digital knowledge platforms to support the Learning Health System cycle and the quintuple aim
- HL7 standards and working with:
    - EHR vendors
    - Payor organizations
    - Evidence and guidance organizations
    - Public health
    - Federal agencies
    - Other standards groups
- Several high priority clinical and public health improvement topics in development
    - Additional topics to be added


- Itchhaporia D. The Evolution of the Quintuple Aim: Health Equity, Health Outcomes, and the Economy. J Am Coll Cardiol. November 22 2021;78(22):2262–2264. doi:https://doi.org/10.1016/j.jacc.2021.10.018
- Osheroff JA. AHRQ evidence-based Care Transformation Support (ACTS). https://digital.ahrq.gov/acts

# *Computable Guidelines*

## *Health Evidence Knowledge Accelerator (HEvKA)*

- Governed by an oversight board and lead by Brian Alper and a small project management team but primarily volunteer driven, with 15 working groups and a few grants
- Establishing mechanisms for computable guidelines compatible with GRADE, WHO, and other guideline development processes by addressing the need for a standard for terminology for evidence and guidance:
    - More than 2/3 the way through a multiyear, multidisciplinary effort to define close to 600 terms for study design, risk of bias and statistics, called the Scientific Evidence Code System (SEVCO).
    - Engaged in similar efforts with GRADE to define terms for certainty of evidence, strength of recommendation and evidence-to-decision framework judgements for GRADE Ontology.
- Employing EBMonFHIR standards to create 16 specialized software tools for computability that will not require users to learn FHIR or underlying technical specifications including:
    - Recommendation Authoring Tool
    - Guideline Authoring Tool
    - Converter Tools to transform data from MEDLINE, ClinicalTrials.gov, and MAGICapp to FHIR.
- Goal: for the output to be usable, easy to understand, and user-friendly


- Soares A, Schilling AM, Richardson J, et. al. Making Science Computable Using Evidence-Based Medicine on Fast Healthcare Interoperability Resources: Standards Development Project. J Med Internet Res. 2024;26(e54265):1-12.

## *Key suggestions:*

***How can we get to our ideal future vision from here?***

- Living guidelines
- Controversies addressed through rigorous methodological analyses of current evidence
- TCBS guideline processes funded for areas such as genomic testing
- Panels including all relevant stakeholder perspectives
- Include informaticians with implementation and FHIR standards experience
- Feedback mechanisms
- More research on minority populations and subgroups with varying genetic propensities.
- Computable clinical practice guidelines to accelerate the evidence-to-practice (bench-to-bedside) time gap by increasing adoption of guidelines at the point of care.

**Improve the evidence base**:

- Require digital databases and digitized results available the day of publication
    - International Committee of Medical Journal Editors requirement
    - Encourage replication of results
    - Reduce the need to ask original authors and statisticians for clarity or specificity

**Increase funding for systematic reviews and living guidelines**

- Make all government-funded reviews useful for guidelines with aligned topics that address identified targets.
- Provide funding mechanisms for guideline developers
- Including nonprofit organizations such as medical professional societies

## *Next Steps:*

- Update the standards for both SRs and CPG, including:
  - Living guidelines methods
  - TCBS processes
  - Equity and access
  - Leveraging AI to advance the timeline
- Create a guideline repository with unbiased assessments based on established evaluative criteria that are widely recognized and validated.
- Require digitized data and encourage more research, especially for impacted subgroups.
- Guidelines need to be computable.

**The number 1 way to help: increase funding!**

- We need more guidelines, better guidelines, and must keep them living!

# QUESTIONS?

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