CPIC member call-April 2026

- Housekeeping announcements
- *NAT2*/isoniazid guideline-Kelly Caudle
- Cascade testing-Kelly Caudle
- CPIC guideline proposal: BCHE and succinylcholine-Rose Donnelly, Jenny Nguyen, and Courtney Paetznick
- CPIC antipsychotic guideline: Risperidone and *CYP2D6*17*-Laura Ramsey

NAT2/isoniazid guideline

- Hoping to start soon
- Working on a collaboration with TB and ID organizations including the WHO
- Need nominations for expert panal

Open PGY-2 in PGx

- St. Jude Children's Research Hospital
  - Cyrine Haidar; Cyrine.Haidar@stjude.org
- Cleveland Clinic
  - Jennifer Hockings; HOCKINC@ccf.org
- Sanford Imagenetics
  - Natasha Petry; natasha.petry@ndsu.edu
- Endeavor Health NorthShore Hospitals
  - Dyson Wake; Dyson.Wake@endeavorhealth.org

Familial implications of high risk pharmacogenetic test results (PGENFAM)

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- **Investigators and facilitators:** Kelly Caudle, PharmD, PhD; Cyrine Haidar, PharmD
- **Study team:** Melissa Bourque, PharmD
- **Panelist:**
  - **Genetic Counselors**
    - Passant Shaker, MS, St. Jude Children's Research Hospital
    - Jason Carmichael, MS, Valley's Children's Healthcare
  - **Geneticists/Physicians**
    - Nora Urraca Gutierrez, MD, PhD, LeBonheur Children's Hospital
    - Peter Hulick, MD, Endeavor Health
    - Kristen Suhrie, MD, Indiana University School of Medicine
  - **Pharmacist**
    - Suzanne Stevens, PharmD, Mass-General Brigham Wentworth-Douglass Hospital
    - Allison Bragg, PharmD, St. Jude Children's Research Hospital
    - Emily Cicali, PharmD, University of Florida College of Pharmacy
    - D. Max Smith, PharmD, MedStar Health and Georgetown University Medical Center
    - David Gregornik, PharmD, Minnesota Children's
    - Natash Petry, PharmD, MPH, Sanford Health Imagenetics, North Dakota State University
    - Shawn Dalton, PharmD, Veterans Health Administration, National Pharmacogenomics Program
  - **Pathologist**
    - Gwen McMillin, PhD, ARUP Laboratories, University of Utah
    - Ann Moyer, MD, PhD, Mayo Clinic, Personalized Genomics Laboratory

Cascade Testing

- The process of extending genetic testing to individuals at risk within a family for inheriting a pathogenic variant previously identified in a biologic relative.
- Sometimes referred to as cascade screening.

https://www.cancer.gov/publications/dictionaries/genetics-dictionary/def/cascade-genetic-testing

Why now?

- As pharmacogenomic test results are being returned to more patients, use cases for familial implications are becoming more common:

  - DPYD intermediate or poor metabolizer → mom and/or dad are at least DPYD Intermediate metabolizer (IM), siblings/children may be at least DPYD IM
  - CYP2C19 poor metabolizer → mom and dad are at least CYP2C19 IM, siblings/children may be at least CYP2C19 IM
  - SLCO1B1 poor function → mom and dad at least have decreased SLCO1B1 function, siblings/children may have decreased SLCO1B1 function
  - G6PD deficient female → dad is G6PD deficient, mother is at least a carrier
  - RYR1/CACNA1S → mom or dad are MH susceptible, siblings/children may be susceptible

Project Aims

Provide guidance on **if, when, who, and how** cascade testing should be offered

Identifying barriers and facilitators for implementing cascade testing strategies in real-world settings.

Methods

Nominal Group Technique

- ✓ **Panel recruitment:** Panel recruited and selected by the study team. The panel consisted of 14 individuals (PharmDs, MDs and genetic counselors) with the experience in PGx implementation and reporting test results to patient and patient families (PharmD, MD, and GCs) through a pharmacogenomics clinic model.
- ✓ **Independent viewpoint development:** Panelists were asked to complete a set of questions regarding if, who, when, and how cascade testing should be offered. Panelists independently provided responses.
- ✓ **Round robin:** On a conference call, each participant was asked to share one idea from each question they responded to. One response was shared by each participant until all participants had a chance to share their ideas. Process repeated until all participant ideas had been shared and recorded.
- ✓ **Group discussion:** The study team organized ideas and guided the group through discussion to refine, clarify, and evaluate each idea (e.g., grouping/splitting ideas, adding or excluding ideas if applicable). Conversations were recorded to capture differences in opinions or perspectives from all panelists. In addition, data was collected on the group's perceived barriers and facilitators to implementing these tactics to be used in the second phase of the study.
- ✓ **Independent voting:** In the first round of voting, each participant privately prioritized each idea and ranked the feasibility and perceived effectiveness of each idea on a scale of 0 to 100. The rankings were tabulated and presented to the group and then participants revoted. Averages less than 60 were considered outliers and excluded. The process of re-ranking after discussion continued until no further changes were made to the most important ideas. Quantitative (*e.g.,* voting) and qualitative (*e.g.*, discussion points) data were captured at each step, and the individual scores were aggregated statistically to derive a group "consensus" as pre-determined by the panelists.
- ❑ **Feedback from PGx community:** After reaching consensus from the panelists, the final ideas will be publicly posted, and feedback will be solicited from CPIC members and others as determined by the panelists. Feedback will be reviewed by the panelists and participants will revote if necessary.
- ❑ **Publish results**

Recommendation		Key Implementation Barriers
Counseling and Communication		
Institutional workflows for cascade testing	1 . Institutions should implement clear pre- and post-test workflows to integrate the discussion of familial implications and the sharing of relevant information with the proband to facilitate downstream cascade testing.	Limited pharmacogenomics-trained workforce; lack of internal champions; uncertainty about cascade testing value; resource allocation tensions; competing institutional initiatives; unclear ownership of counseling workflows.
Multidisciplinary counseling leadership	2. Cascade testing counseling should be led by a pharmacogenomics-trained healthcare practitioner (e.g., pharmacists, genetic counselors, or the ordering clinician), ideally in a multidisciplinary framework.	Limited PGx-trained professionals; specialist shortages; scheduling limitations; lack of direct patient contact in some PGx implementation models; fragmented care delivery; clinician uncertainty about when to refer.
Patient autonomy and privacy	3. Patient autonomy and privacy must be protected, including honoring patient preferences regarding testing and result disclosure, ensuring informed consent prior to discussing results with relatives, and complying with institutional and legal protections for genetic information.	Variable patient health literacy; complexity of genetic privacy implications; lack of standardized documentation fields to capture disclosure preferences; variation in institutional or state policies; clinician uncertainty about disclosure boundaries.
Pre-test counseling	4. Pre-test counseling for the proband should raise awareness of familial implications (inheritance patterns, risks for first-degree relatives, and benefits and risks of testing including protections such as GINA), with more detailed counseling provided if actionable results are found.	Variable genetic literacy among patients; limited retention of pre-test education; heterogeneity in clinician genetics training; limited counseling time; lack of reimbursement structures; competing clinical priorities.
Post-test counseling and documentation	5. After reviewing the familial implications of the proband's test result, the proband's institution should provide portable documentation (e.g., test reports, family letters, guideline summaries) that can be shared by the proband with relatives and their healthcare providers.	Patients may be unwilling or hesitant to share results; limited understanding of documentation; loss or underutilization of materials; EHR build requirements; lack of automation; competing IT priorities.
Criteria for cascade testing		
Prioritization based on clinical risk	6. Cascade testing should be prioritized when the therapeutic context carries high risks associated with severe adverse outcomes (e.g., DPYD–5FU, CYP2C19–clopidogrel, RYR1/CACNA1S–anesthetics, HLA alleles).	Additional counseling time required to determine which relatives qualify; lack of structured prioritization tools; rural access limitations; limited PGx-trained workforce; competing institutional priorities; need for leadership engagement.
Identification of family members	7. First-degree relatives (parents, siblings, children) should be the primary candidates for cascade testing; however, cascade testing may also extend to other relatives when clinically appropriate based on anticipated medication exposure.	Family estrangement or weak family ties; adoption or unknown biological relatives; sensitive family dynamics; lack of standardized documentation; limited provider familiarity with cascade testing.
Testing requirements	8. Cascade testing must at least detect the variant(s) identified in the proband and ideally include additional variants per evidence-based recommendations.	Uncertainty in test selection; differences across laboratories in variant detection; lack of standardized order sets; cross-system incompatibility; insurance coverage variability; prior authorization burdens.
Reassessment over time	9. Education should indicate that cascade testing be revisited over time as family members age, medical circumstances change, or guidelines are updated.	Limited follow-up infrastructure; difficulty maintaining longitudinal engagement with families; competing clinical priorities.
When cascade testing occurs within the same institution		
Workflow support for relatives	10. Practitioners may consider maintaining workflows to support testing logistics for relatives seeking cascade testing.	Rare-event workflow sustainability; staff turnover; cross-system referral complexity; lack of interoperability; difficulty tracking families longitudinally.
Resource allocation models	11. Institutions should establish resource allocation models internally to ensure cascade testing is equitable, accessible and sustainable across diverse populations.	Limited institutional budgets; competing strategic priorities; lack of reimbursement clarity; healthcare system fragmentation; leadership reluctance to fund services for non-enrolled individuals.
Electronic health record integration	12. Electronic health record integration should be used for documenting cascade testing and enabling use of decision support for practitioners.	Need for privacy safeguards and consent tracking; leadership approval required for CDS tools; genomic module limitations; interoperability challenges across systems.
When cascade testing occurs outside the institution		
Practical guidance for relatives	13. During post-test counseling, the proband's institution should discuss cascade testing of family members with the proband and consider providing practical steps to pursue testing.	Ambiguity regarding institutional responsibility; limited counseling time; lack of reimbursement for navigation; variable patient follow-through; family dynamics and privacy concerns.

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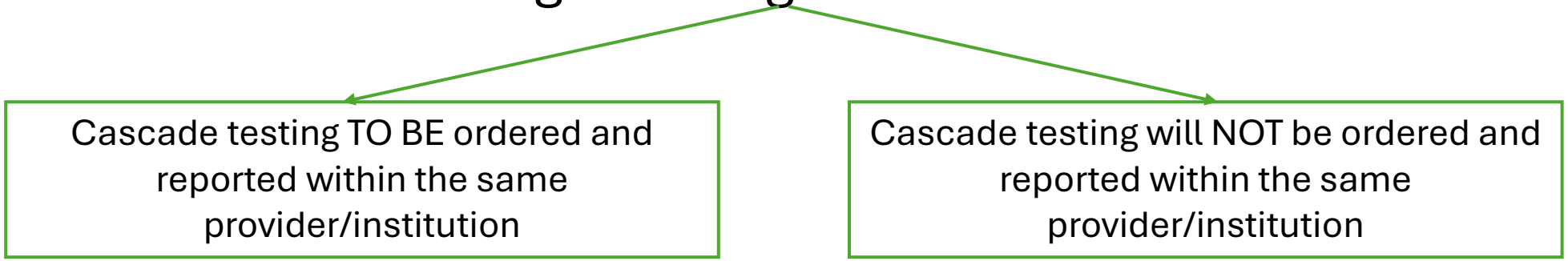
If recommending cascade testing

We thought through two scenarios



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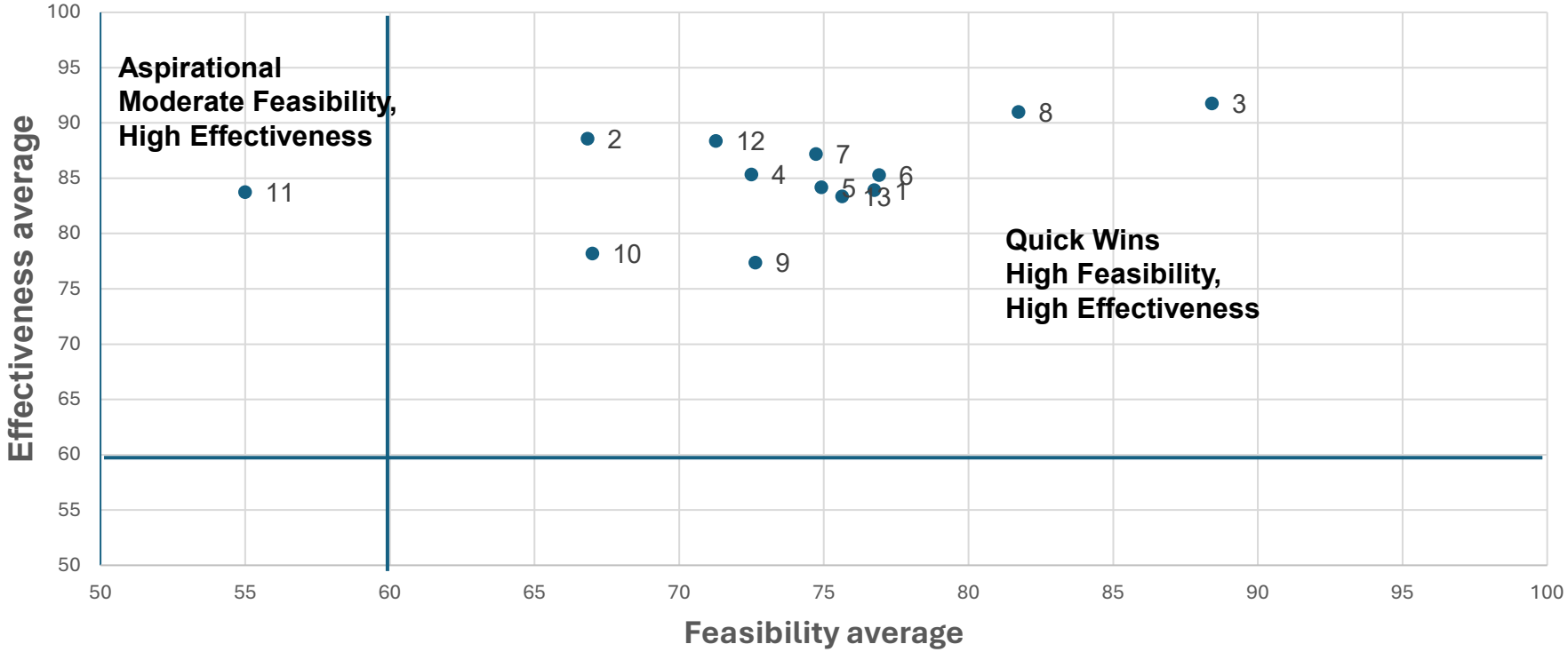

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