**Summary of External Scientific Panel/Steering Committee Meeting: April 2024**

April 18, Zoom

1. **HCP survey update & plans | Ingrid Holm (BCH), Georgia Wiesner (VUMC)** 
   1. Most previous healthcare provider (HCP) surveys about genetics/genomics are not based on experience but hypothetical situations.
   2. Based on the HCP survey from eMERGE 3, most HCP did not feel confident about their knowledge or ability to explain monogenic results to their patients.
   3. The primary aim of this version of the HCP survey is to gauge their perception of the GIRA report as useful for clinical care.
   4. Several workgroup and subgroup leads were involved in the development and implementation of the HCP survey.
   5. The survey workflow begins with the survey link being created in the R4 Portal.
      1. If a participant gets a high risk GIRA, the site will log the HCP information in a local database.
      2. An invitation email with the survey link is sent to the HCP in roughly 2-4 weeks after return of results.
      3. The HCP completes the survey.
      4. The site will maintain a log of HCPs who completed the survey.
   6. Only one survey per HCP is sent to avoid inundating provider in-boxes.
   7. A not at high risk GIRA will not generate a HCP survey due to various difficulties in implementation, tracking, etc.
      1. Qualitative interviews are planned and hope to address HCP perceptions of not at high risk GIRA reports.
   8. The HCP survey started on January 16, 2024 with all sites sending surveys out by 4/16/2024.
   9. As of 4/3/2024, 257 surveys have been sent to HCP with 50 responses (19% response rate).
      1. Lower response rates seem to come from sites that recruit from multiple sites.
   10. The GIRA is uploaded to the EHR, but sites are informing the HCP listed by the participant (or clinic inbox, depending on clinic instructions) by email regarding the survey.
2. **Manual chart review & outcomes | Lisa Martin (CCHMC), Jen Pacheco (NU), Nita Limdi (UAB), Dave Veenstra (UW)** 
   1. Manual chart review will be used to validate novel EHR-based algorithms and outcomes data.
   2. Another benefit is having cases for training and testing Large Language Models for extracting data.
   3. There is a collaboration between the Provider Uptake & Outcomes, Phenotyping, and QA/QC taskforce workgroups in order to develop a chart review approach and validate algorithms.
   4. Three topics for evaluation have been identified.
      1. Referrals: Six conditions are being investigated for a novel EHR algorithm.
      2. Procedures: Condition leads have identified algorithms, including Hi-TAG algorithms developed in eMERGE 3.
      3. Diagnoses: Most diagnoses have validated algorithms.
   5. Time-frame specific phenotyping algorithms may need to be developed due to a short observation time frame compared to existing algorithms.
   6. The scope of manual chart review has been decided.
      1. Each site will review 30 charts.
         1. Adult focused sites will review 25 adult charts and 5 pediatric charts.
         2. Child focused sites will review 25 pediatric charts and 5 adult charts.
      2. A general binomial distribution was used to establish the number of charts to review.
   7. One pediatric site and one adult site will beta test manual chart review and provide feedback and lessons learned in order to develop a manual to harmonize this process across the Network.
3. **Accelerating GIRA return | Iftikhar Kullo (Mayo), Cindy Prows (CCHMC)** 
   1. Site enrollment numbers will be determined by the number of biospecimens collected.
   2. Enrollment ends on 6/30/2024 and sample submission to labs ends on 8/31/2024.
   3. The last GIRA returns (date GIRA is uploaded to the EHR) are to happen by 10/31/2024.
   4. There have been some issues that have delayed return to date.
      1. Technical and lab issues have slowed returns down at times.
      2. Outside partners, such as CanRisk and BOADICEA, have also had issues that created delays in returns.
      3. GIRA generation in R4 has been slow at times, but timing of generations during slower REDCap usage times has helped improve the time for generating these reports.
   5. The RoR process can take a lot of time due to scheduling, no shows, or needing to reschedule appointments.
   6. One method that has helped with contact is to “cold call” participants. If there is no answer, the staff member calls right back with good success in talking to the participant.
   7. Inadequate FTEs at some sites have been addressed by diverting recruitment staff to returning results to help improve return numbers.
4. **Questions/discussion | Rex Chisholm (NU)**
   1. The last several in-person meetings have been extremely productive in identifying and overcoming barriers for returning results.
   2. Sites are allowed up to five contact attempts before the participant is considered lost to follow up or not interested in learning of the results.
   3. The use of certified letters are listed as an option in the consent but sites aren’t currently using this method for mailing returns.
      1. The GIRA is uploaded to the EHR, even if the participant doesn’t answer reach out attempts/mailings.
5. **Input and feedback from the ESP**
   1. The ESP is pleased with the progress made at this point in time of the study.
   2. The ESP recognizes the difficulty in contacting the large number of participants for returns by the proposed deadline.
   3. Regarding the GIRA return presentation: It will be important to acknowledge/identify the differences and challenges between obtaining results, analyzing data, returning results in a research context vs. a real-world context.
   4. The ESP strongly encourages the eMERGE Network to, despite the heterogeneity across sites in several process level items, that innovations on solving Network related issues to report on these as a Network and not as one-off reports from individual sites.
      1. There is a robust manuscript concept sheet process that allows for all sites to contribute and/or become authors for publications.
6. **Official ESP Recommendations**

Meeting Summary

eMERGE Network- External Scientific Panel and Steering Committee

*Executive Session – 04/18/2024*

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| **ESP** | **Dan Rader,** University of Pennsylvania **- Chair**  **Kimberly Doheny,** Johns Hopkins University  **Stanley Huff,** Intermountain Healthcare\*  **Janina Jeff,** Illumina  **Brendan Lee,** Baylor College of Medicine\*  **Lisa Parker,** University of Pittsburgh  **John Witte,** Stanford University | **NGHRI** | **Teri Manolio**  **Jahnavi Narula**  **Robb Rowley**  **Rene Sterling**  **Nephi Walton** |

\*was not able to attend the ESP meeting

Scientific Panel (ESP) met with NHGRI program staff during the executive sessions of the eMERGE ESP Teleconference held on April 18, 2024. The ESP was pleased and enthusiastic about the progress the Network has made, especially with recruitment and the plans for increasing GIRA return. The ESP had a few comments on the present status of the Network and provided observations and recommendations about aspects of future publications and communication of results. Initial feedback is elaborated upon in the summary below.

**The Network should discuss what challenges are research-specific and what challenges will continue to exist when implementing GIRA outside of the research setting.**

During the call, there were discussions about the challenge of contacting participants and obtaining timely responses, along with concerns about meeting deadlines. The ESP requested that the Network distinguish—or at least highlight—the differences between the challenges that exist in the research setting, such as certain deadlines, and those anticipated in routine clinical implementation of the GIRA. That is not to suggest that there is no urgency in the clinical context; in some cases, there might be less urgency, while in others there might be more. However, it is crucial to understand which challenges are inherent to the current state of the health care system, the EHR environment, and broader structures. This understanding helps ensure that challenges are not misattributed to the wrong areas, potentially misleading interpretation of the results as irrelevant to clinical practice.

**The Network should focus on Network-wide publications, especially when considering heterogeneity across sites.**

Many Network processes that address the challenges of this multifaceted project are incredibly important to help the community understand how to implement GIRA/PRS into clinical practice. The ESP believes that single-site publications will be limited in utility because they will not include the wide range of settings in which the Network has implemented GIRA. This includes—and even emphasizes—places where the Network might be heterogeneous. For example, some sites were able to place structured data in the EHR and others weren’t. Understanding the variability in how the sites managed this can help future implementation of GIRA within other health care systems. It is important to understand what the requirements and limitations were by site, as well as to compare and contrast the effectiveness of the processes. The ESP were pleased to hear of the Network’s robust manuscript concept sheet (MCS) process that encourages all sites to contribute and that the Network was confident that the MCS process would enable compare/contrast papers as in eMERGE III.

**The Network should continue their current efforts around GIRA return.**

The ESP was impressed with the Network’s analysis of the issues around GIRA return and were confident that the Network would be able to return all GIRA reports by the October 2024 deadline. The Network should keep up their current efforts as it looks towards refining questions and outcomes at the June Steering Committee meeting.

**ESP Recommendations for the Network:**

1. The Network should discuss what challenges are research-specific and what challenges will continue to exist when implementing GIRA outside of the research setting.

2. The Network should focus on Network-wide publications, especially when considering heterogeneity across sites.

3. The Network should continue their current efforts around GIRA return.