**Summary of External Scientific Panel/Steering Committee Meeting: April 2022**

April 14, Zoom

[**ESP Meeting**](https://docs.google.com/document/d/1O202IB077QxhSD8ajyBb7UtYBXiuJEJO658V3tCKkSo/edit#bookmark=id.exkpowu9xt4q)

* [R2, ELSI, sIRB initial recruitment updates |Wendy Chung (Columbia), Digna Velez-Edwards (VUMC), Ingrid Holm (BCH)](#sdnpqc8tjmy9)
* [Provider uptake and outcomes final study design | Noura Abul-Husn (Mount Sinai) and Nita Limdi (UAB)](#koli9satif8z)
* [EHRI and CDS progress: Provider notifications and report integration | Bob Freimuth (Mayo), Luke Rasmussen (NU), Eta Berner (UAB) and Emma Perez (MGB)](#j69rkuu62f6z)
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1. **R2, ELSI, sIRB initial recruitment updates | Wendy Chung (Columbia), Digna Velez-Edwards (VUMC), Ingrid Holm (BCH)** 
   1. Seven clinical sites are recruiting currently.
   2. Participants are able to progress through pre-screening and consenting into the baseline and pre-RoR surveys.
   3. MeTree data collection and blood or saliva sample collection can be done at the same time if consenting is done in person.
   4. Samples can be collected currently but cannot be sent to Invitae or Broad at this time.
   5. Workgroup accomplishments to date include the development of the protocol, sIRB approval, staff training sessions and materials, provider education materials, and a study website (pending sIRB approval).
   6. Participant education materials for eMERGE include infographics, videos, written materials (FAQs), and other modalities.
   7. Study staff and provider education materials include written materials, self-guided content and live webinars, and EHR integrated Decision Support Tools.
   8. As of the ESP call, CHOP, CCHMC, Columbia, UAB, and Northwestern were actively recruiting participants.
   9. Participant retention methods will include reminders being sent out at various time points after consent, which may include automated emails and/or postcard mail outs.
   10. The automated emails/reminders are one-way (institute to participant) and will include site contact information so the participant can reach out if needed.
2. **Provider uptake and outcomes final study design | Noura Abul-Husn (Mount Sinai) and Nita Limdi (UAB)**
   1. In response to the ESP feedback from October 2021, the Outcomes group has focused on consolidating the outcomes of interest across phenotypes to create a cohesive analysis plan for the eMERGE study.
   2. eMERGE is a prospective cohort study expecting to enroll approximately 25,000 participants over two years.
      1. The primary research question is: Does receiving a High Risk Report for common diseases influence the adoption of recommendations and clinical outcomes?
      2. The primary outcomes for the study at the Network level are process outcomes (actions by providers such as orders for labs, imaging, or referrals).
      3. Secondary outcomes are phenotype-specific and include both clinical and intermediate outcomes (such as new diagnoses or lifestyle changes, respectively). The Outcomes group is in the process of meeting with the phenotype leads to develop plans for analysis of the secondary outcomes.
      4. All primary and secondary outcomes are feasible to collect during a 6-month window after return of results (RoR) to the participant. Outcomes data will be collected from the EHR whenever possible (such as for labs, new diagnoses, etc.), though some outcomes data will come from the post-RoR survey (such as lifestyle changes).
   3. eMERGE has been registered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/NCT05277116?id=NCT05277116&draw=2&rank=1&load=cart).
   4. The Network will decide in the future whether it will be feasible to return results in person to a random subset of non-high risk individuals. Primary limitations for this include time, personnel, and budgetary constraints.
   5. The Network plans to account for the background rate of the various process outcomes in the analysis, and will consider accounting for the time between enrollment and the RoR as a confounder in the statistical analysis as the study design is refined.
3. **EHRI and CDS progress: Provider notifications and report integration | Bob Freimuth (Mayo), Luke Rasmussen (NU), Eta Berner (UAB) and Emma Perez (MGB)**
   1. The GIRA report is a synthesis of four other inputs coming together within the R4 system.
      1. The GIRA is generated as two separate artifacts for each patient, one is a PDF and one is an abbreviated structured version that captures the discrete logic used to generate GIRA text.
   2. The EHRI workgroup has worked with the network to define elements of the structured data and how to place it in the EHR.
   3. The EHRI has examined the retrieval mechanisms for the GIRA reports to go into the EHR. Most sites are using an API, some sites are using a manual process, and some sites are planning to use an HL7 interface to receive the Invitae results in a structured format.
   4. The workgroup has discussed where the reports will land in the EHR. All sites are planning to make PDFs available in the EHR, but not all sites are planning on importing the structured data elements.
      1. Sites using Cerner will use the “M-Page” to hold the GIRA PDF.
      2. Some sites are looking at bringing in the GIRA, Invitae report, and Broad report PDFs into the lab results page.
      3. Some sites are looking at placing the Invitae and Broad reports in the lab results page, and the GIRA PDF in the media page.
   5. The workgroup is currently discussing how the structured data elements will be imported to the sites.
      1. Sites are considering using EPIC Smart Data Elements, which are custom data elements that can be defined by an individual site within their EHR.
         1. Sites can create smart data elements to create elements that are of interest from the Broad or GIRA reports.
      2. There is also the Genomic Module within the EPIC EHR. Sites are considering placing structured data from the Broad and Invitae reports into this.
      3. As these decisions are made, the workgroup will be able to provide examples.
   6. The CDS workgroup began meeting at the end of 2021.
      1. If the network outcomes are dependent on provider outcomes, it is important to consider how the provider is notified of the results.
      2. The goals of this group are to discuss how each returning institution is using CDS and see if harmonization can occur, and to document any differences to consider downstream.
      3. A return template diagram was circulated to the returning institutions.
         1. Many sites are still working with their coordinators and EHR integration teams to determine what is possible to implement.
         2. Nine of the eleven returning institutions are planning to place the GIRA in the EHR when it is ready in R4.
         3. Ten of the eleven returning institutions are planning to notify the provider once a high risk report is placed in the EHR. The patient may have access to the EHR so it is important for the provider to be aware.
            1. The one returning institution that was not planning on notifying will speak with their team in order to harmonize this across all returning institutions.
         4. Five of the eleven returning institutions are planning to notify providers when not high risk reports are placed in the EHR.
         5. Nine of the eleven returning institutions are planning to contact the high risk participant’s provider following a meeting with eMERGE study staff.
            1. All participants with a high risk GIRA are asked to meet with the study team, which includes a genetic counselor, to discuss the results and are encouraged to speak with their doctor regarding their results.
            2. This includes cc’ing the provider on a note or adding other CDS.
            3. This could mean up to two contacts with a provider, if they are notified when the report is first placed in the EHR and after the participant meets with the study team.
         6. The CDS group is working with the Outcomes workgroup to determine if this could impact outcomes.
   7. Will there be tracking in the EHR to know if the reports were opened?
      1. There will be data in the post-return survey asking if the participant met with their provider to discuss results.
      2. There are a number of sites examining linking active decision support to the notification.
         1. For example, if a report is placed in the EHR, an inbasket message is sent to the provider including a link to the report. The site EHRs have the capability to track if the report was accessed via that CDS link.
         2. It is unknown if there is tracking at the level to see if an individual provider looked at the report within a certain timeframe.
      3. In provider education, providers are being made aware that positive results will be returned by a genetic counselor/study staff, with a note cc’ing the provider. Knowing this, providers may not open a GIRA unless they see the note from the genetic counselor/study staff.
      4. Based on how sites are notifying providers, there will be different ways to learn their report viewing.
      5. This will be easier to track for high risk results than not high risk results.
   8. How would the differences in approach of notifying the provider (high risk and not high risk) be resolved for outcomes? What kind of considerations are being kept in mind going forward?
      1. If providers are notified at all levels of risk, they may not open the report until receiving a note from a genetic counselor or study staff.
         1. Providers may also be overwhelmed by result notifications.
      2. Documentation of what sites are doing as a baseline and monitoring progress and any changes is important. The actions can change as the study progresses.
      3. If providers are overwhelmed by receiving notifications for all GIRA results, sites may change notifications to be only for high risk GIRAs.
      4. There are constraints that affect how sites can act, including legal, site-specific policy, and staffing.
      5. The workgroup is trying to be consistent and harmonize where they can, and document any differences.
   9. Do these elements impact the IRB and approach to the consent?
      1. The main consent uses ‘may,’ for example “the report may go into your EHR” and “we may contact your provider.”
      2. The part two consents also use similar language.
      3. The IRB is open enough to allow for this.
   10. The EHR and CDS workgroups are aiming to provide specific examples at the next ESP meeting of future progress and decisions made.
4. **Input and feedback from the ESP**
   1. Most recruitment will occur via Epic messaging and using an online consent process.
   2. The network is working to harmonize the return of results and how physicians are alerted of high risk results. Return of results has been budgeted to 25% of the cohort. If patients recruited are older, there may be a high rate of return and the network is recruiting 75% minority and it is anticipated that 25% will be high risk but it could be more.
      1. If genetic counselors are going to return results, their time is more limited than a trained coordinator.
      2. Recognizing the budgetary limitations, the ESP feels harmonizing the return of results is an important factor.
   3. The ESP is not totally clear whether any of the actions that occur in the high risk group count toward the primary endpoint or only if it is an action that is directly related to what they are high risk for. For example, if a lipid panel is drawn on someone who is at high risk for breast cancer, would that count or not?
      1. For the overall analysis, there is a preset list of outcomes directly related to recommendations that include lipid panels so the composite of outcomes in everyone with a high risk result will be measured and compared to those with high risk versus not high risk. In that case, it would count. The outcomes co-chairs will discuss this further with the network and clarify the overall analysis plan.
      2. For the phenotype analysis, a lipid profile will be done in patients at high risk for hypercholesterolemia. For the common tests like lipid profiles and blood glucose, analysis could potentially be collapsed to increase power, examining an interim analysis or other data would be a good idea.
   4. If there is a high frequency of unjustified interventions, it is worth trying to keep track of because there is an interest in an overall increase in follow up services and risk related recommendations.
   5. The ESP recommends generating EHR real world data on the frequencies of all these things discussed and model what the aggregate primary endpoint is going to look like.
      1. For example, if someone is at high risk for hypercholesterolemia then the lipid profile ordered needs to be connected, an outcome like a breast MRI would not be related to the high risk return.
   6. The network is thinking very carefully about how to assess providers’ perceptions and attitudes toward receiving information and how helpful it is to them. Interviews and small surveys are being considered.
   7. If a high risk participant has multiple actions as a result, it is important to note if those are counted individuals and independently toward the overall aggregate primary endpoint. For example, if an individual has 10 different orders all completed over 6 months and another has one test done, the person who received a high risk intervention is only counted once. Number of interventions will be tracked.
   8. The timeframe individuals are under for the implementation continues to be compressed which presents challenges with what can actually be put into place. Initial integration of discrete data into the EHRs will happen in very pragmatic ways that will be less reliant on formalized standard based approaches.