PRECISION MEDICINE STRATEGY SESSION
MAY 20, 2019

Facilitated by the Strategy and Innovation Office
**EXECUTIVE SUMMARY**

**Primary Objective of the Precision Medicine Strategy Session:**
Develop a formal plan to integrate, operationalize, and scale clinical genomics and develop one entry point for all germline and somatic risk prediction, assessment, and service line referral.

**Scope of Work/End-Product Audience:** VUMC clinicians

**Timeframe for work:** Incremental over the next two years

The Precision Medicine Strategy Session, held May 20, 2019, brought together a variety of subject matter experts to work through a straw model of a proposed operational model.

Participants were given three situational clinician/patient personas and asked to approach the problem from those points of view. The personas were:

- Specialist trying to diagnose a patient with a rare condition
- A cancer patient trying to navigate options including clinical research, NGS testing, and treatment
- A generalist who believes a patient would benefit from genetic testing but is not clear on the next steps

The personas highlighted key concerns for clinicians such as the risk of duplicate testing, use of informatics, adequately interpreting results, and uncertainty about next steps.

An overview was given of the current state of the PREDICT program, cancer genomics, and clinical genomics at VUMC. All three address aspects of precision medicine, but because of various issues – such as inability to scale, difficulty in managing knowledge assets, or complex cascading requirements for every change – none can serve as a solution (table 1, in the agenda portion of this report, shows how each of these efforts map to the needs of precision medicine, along with some identified successes, gaps, and opportunities).

The participants were then presented with the step-by-step process straw model for a precision medicine operational platform (figure 1, below; detail images in appendix). The top of the model (green process squares and red decision diamonds) shows clinician actions related to the patient and the EHR. The lower half of the model shows the algorithms working within the EHR at each clinical step. The ideal state for this operational system has the clinician working through

![Figure 1: Precision Medicine Operational Platform Straw Model](image)
traditional diagnostic steps in the EHR with seamless prompts when the system’s algorithms recognize a potential testing/treatment opportunity. In cases where results are inconclusive, and the clinician feels like a consult makes sense, there is an easy way for them to get the appropriate help. In cases where the algorithm cannot identify appropriate testing/treatment options, the system routinely checks for potential solutions as new literature, data, or tests become available, and automatically notifies the clinician/patient.

There was a discussion following the presentation of the model. Key concerns raised during the discussion included:

- The current PREDICT infrastructure is largely manual and has many fragile components. There is a plan in place to “harden” this infrastructure, which should be a priority.
- Future contact with patients when the system’s interpretation changes based on new information
  - Decision: park the idea of re-contacting patients about new findings; the issue should be handled separately, although there is still interest in contacting the clinician when new information is available.

The participants were then divided into three groups – two focused on clinician workflow in Dermatology and OBGYN as it relates to the model, the third focused on required building blocks for the system – and asked to review the straw model to identify:

- Possible issues
- Model iterations
- Next steps
- Technology/infrastructure requirements
- Policy requirements

**Recommendations from the Dermatology and OBGYN Break Out Groups**

1. Establish genomics counseling core
2. Collect patient-reported, clinical, and genetic information prior to the patient visit for Phenome Risk Score (PRS) and Best Practice Alerts (BPAs)
3. Begin work as soon decisions can be made
   a. When referral records arrive, trigger an immediate review for recommendations/orders
   b. An automatic trigger of PRS and BPAs for clinician
   c. Possible testing options that could be considered based on PRS and BPAs before in person appointment
   d. Begin pre-test counseling upon record arrival (telemedicine one possible mode)
4. Explore consented sharing of data among family members’ medical records
5. Pilot with Diagnostic Management Team (to facilitate the work) and a locally embedded specialist (to determine which diagnostic elements can be automated and which will require human input)
6. Provide computer-driven differential diagnosis support
7. Identify Clinical Champions/Power Users to provide first response to inquiries for specific phenotype sets
8. Build risk-benefit considerations into the results
9. Ensure there is pilot education

**Recommendations from the Building Blocks Break Out Group**

The building blocks group suggested a data and system framework that allows providers to make informed decisions about testing and treatment (not a fully automated process).

This framework requires the creation of:

- A common data platform to integrate different data types
- A service to assist in the ordering process

For the data platform, the group suggested several key categories of information:
• Known patient clinical data
  o Patients’ prior tests/results
  o Family history
  o Current patient treatments (e.g., allergy)
• Patient pre-visit responses to targeted, patient-specific questions generated by the system when it recognizes potential tests for the patient but requires more information before making a final determination
• Derivatives of clinical data (e.g., phenotype risk score)
• External data sources (e.g., EPIC Library)
• Current location in the care process (e.g., cardiology patient vs. primary care)

To manage the results and/or interpretations, the group suggested a data storage system that pulls in and integrates data from internal and external sources, Diagnostic Management Team support, and a dynamic differential diagnosis process.

The third primary block would focus on developing/implementing revised treatment plans based on new test data. This process would require facilitated consultation to succeed.

Finally, the Building blocks group identified four cross-cutting concerns for the system:

• Appropriate graphic user interface
• Ensuring evaluation and discovery iteration
• Governance to ensure compliance
• Knowledge curation

Additional building blocks were suggested during the discussion following the group’s report out:

• Combine all known algorithms (internal and external) to ensure the most appropriate algorithms are being used for the right patients
• Outcomes capture module to refine algorithms/system
• Iteration module for the future reinterpretation of patient information based on new data
Agenda (or... The Challenge)

Part 01: Spin Up, Persona Stories, and Current State

01A: Spin-Up

Dr. Jeff Balser, CEO for VUMC and Dean of VUSM

Dr. Balser welcomed the participants and gave an overview of the purpose of the day’s work. Balser explained that VUMC is at an inflection point with an opportunity to lead what genomic medicine will look like. The goal is to embed genomic decision making to personalize treatment.

The future includes the design of a genomics framework that is part of “The Vanderbilt Inventory” vision. This inventory, built to scale, will provide the best decision support for our clinicians who directly interact with our patients.

The future includes resources that are readily available, easy for clinicians to use, and understand. The future will align with VUMC’s distinctive strengths and systems approach to care.

Examples of future tools:

- Mypharmacogenome – a guide for clinicians to select the right drug based on the genome for all drugs
- Mydiseaseeriskgenome – an analog of Predict including phenome risk scoring

The goal is to build a decision support system that enables all clinicians at VUMC (and ultimately VHAN) to have the ability to counsel, and/or refer their patients regarding germline or somatic risk and drug selection. This will not only provide data tools but a comprehensive clinic resource with a hybrid combination of centralized resources to support clinical genomic medicine.

Very few of the 3,000 VUMC clinicians are equipped to know what to do, or what to say to their patients. Vanderbilt should have the best decision support for genomic therapy and genomic disease risk and build on that foundation.

Figure 3 Model of Vanderbilt Precision Medicine current and future state
01B: Persona Stories

Patient personas, along with clinician responses, give insight into the magnitude of the challenges in personalizing solutions.

The baseline clinician/patient personas:

1. **The Specialist Workflow**  
   *Dr. Hamid Rizwan, Director, Pediatric Medical Genetics and Genomic Medicine*  
   A patient with a history of recurrent fevers who has been seen by multiple specialists. The new specialist suggests testing for Familial Mediterranean Fever. However, the patient points out that this has already been done by one of the specialist’s partner. The physician tells the patient that at this time, he does not have anything else to offer. Several weeks later, the physician discusses the case with a rare disease specialist. The rare disease specialist uses informatics algorithms to offer additional ideas about conditions and appropriate testing. The physician does the tests with negative results. Specialist discusses the results with the Genomic Specialist. Their analysis shows that the results are positive. The patient is started on gene-specific therapy with resolution of symptoms.

2. **Cancer Patient**  
   *Dr. Ben Ho Park, Associate Director for Translational Research, Director of Precision Oncology*  
   A 57-year-old woman with metastatic colon cancer living in a small rural community. She was diagnosed three years ago and underwent standard of care treatment, but recently had a recurrence in her lungs and liver. Her oncologist has put her on chemotherapy and referred her to a specialist at a local academic medical center where a doctor and research team evaluated her. She was disappointed to find out she was not eligible for any of their trials. She went home and began to contemplate when and how she would die. She then sees a commercial regarding immunotherapies and cancer. After researching on the internet, she asks her oncologist about this and genetic testing. Her oncologist looks puzzled but states that colon cancer is generally not responsive to immunotherapies, so he would not recommend it and that she does not have a family history so there is no need for genetic testing. He also points out that they did test for KRAS mutations on the tumor, which was negative, and she had already received chemotherapy based on that, so there was nothing more to do.

3. **Clinician Generalist**  
   *Dr. Kevin Johnson, Chair, Department of Biomedical Informatics*  
   A male patient presented with rheumatologic symptoms, including Raynaud’s and a hyperpigmented patchy skin rash, and now intermittent large and small joint arthralgias. Internist’s basic workup is non-specific. However, the patient’s family history is remarkable for two deaths in younger relatives due to arthritis, and a mother and maternal grandfather with similar symptoms by history. The internist is sure this is a clue but cannot find anything in the literature. He confers with colleagues whose differential for the patient are unhelpful and decides to refer the patient to a genetics doctor for evaluation. He looks in the directory but cannot be sure which genetics approach to take. Should he test, and if so, for what? Should he refer for testing and advice?  
   - Patient or family brings information into Vanderbilt from Ancestry.com or 23andme that shows important info and/or elevated risk. Patient do not know how to interpret risk. PCP Asks three questions:  
     - How do I get this into the EHR?  
     - What do I do with this increased risk of CHD?  
     - Does this mean I have to test the kids? HELP!
## PARTICIPANTS

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Appendix

Precision Medicine Operational Platform Straw Model Detail Images

Figure 4 Precision Medicine Operational Platform Straw Model Detail Image One (of Three)

Figure 5 Precision Medicine Operational Platform Straw Model Detail Image Two (of Three)
Figure 6 Precision Medicine Operational Platform Straw Model Detail Image Three (of Three)