Introduction
The objectives of the Genomics in Health and Wellness Meeting were to determine employers’ interest in a genomic medicine ‘formulary’ and charge a group to develop it, determine employers’ interest in a genomic medicine employee health program, explore the potential for developing a consensus around the role of genomics in employee health systems and disseminating recommendations, and explore collaborative opportunities and potential projects to deploy genetic tests and a formulary-based program within employer populations and measure and publish the clinical and health economic impact.

Tipping the scales to choose from amongst ‘equal’ treatment options – Howard McLeod

Howard McLeod, Medical Director of the DeBartolo Family Personalized Medicine Institute at the Moffitt Cancer Center, gave a brief talk about the ways that genomics can help doctors choose amongst medications that seem effectively equal. Often, doctors use general population-based recommendations when prescribing medications. Genomic information offers a method to tailor a patient’s medication to their unique metabolism, or reduce the risk for developing an adverse reaction. Reducing the incidence of ineffective treatment and adverse events can result in improved health for employees while reducing health care cost and increasing productivity.

Background & Objectives

This meeting was inspired by a session at Genomic Medicine XI, where panelists suggested that NHGRI should interact with employers who are often the real “payers” of their employees’ healthcare. It was added that an evidence-based “formulary” that reviews guidelines on which tests to offer to employees might be helpful to employers. There was also discussion of the potential value of an employer network that could identify a framework for genomic testing in employee health, implement genomic interventions, and evaluate outcomes to help generate evidence for genomic medicine implementation.

Prior to the meeting, Vanderbilt participants surveyed attending employers about the use of genomics in their employee health programs. 19 employers filled out the survey, representing 16 organizations, including one healthcare organization, one insurer, one genetic testing company, one retirement system, one university, two large multi-national corporations, four biotechnology companies, and five hospital systems. Currently, about 31% are offering genomic testing as part of their wellness programs, with the main motivations being to reduce costs and improve employee health. Employers listed ELSI issues, reliance on insurers, and concerns about the cost of testing as major reasons for not offering genomic testing. Survey results showed that employee uptake of genomic testing has been relatively low (less than 25% participation). Employers also indicated interest in collaborative projects with other employers and papers that investigate the role of genetic testing in employee health.

Discussion
The group discussed perceived differences between pre-emptive genomics in wellness plans and genomic testing for those who are already ill. Larry Wu from North Carolina Blue Cross Blue Shield responded that generally, insurance companies think about coverage in several stages: 1) treatments that are not covered; 2) treatments that are covered, but are not promoted or encouraged; 3) treatments that are promoted to physicians; and 4) treatments that are mandated. It was also noted that the term ‘payer’ is a misnomer, and a better term might be “risk manager.” The people that pay the cost are employees and the employer.

Some employers noted that coverage policy for insurers is not typically constructed around what is most helpful for a particular population. For example, Quest’s insurer does not conduct a clinical or health economic analysis for their health plan. Disease genetics demands a strong understanding of what is clinically and economically valuable, as the clinical and economic value can vary depending on the length of the employer-employee relationship. The group noted that Intermountain, Gundersen, Geisinger, and the Health Transformation Alliance all have an average employee-employer relationship of 12 years, while an insurance company usually has a relationship of about 18 months and thus maintains a much shorter-term view.

In cases of large self-insured employers like IBM, the employer is the payer and decides what to cover based on available evidence. An employer network would be useful if it generated evidence that suggested employers should be offering something different from what they currently cover. Employer-driven research is also an opportunity to understand how employees make informed decisions about testing and how they follow up on results.

**Overview of pre-emptive genomics in employee wellness**

Currently, physicians practice intuitive medicine through empiric “trial and error” based on population-based evidence, expert opinion, and guidelines, while observing an individual’s responses to determine therapy efficacy. In many cases, the treatment does not work for a percentage of the population, but its efficacy is difficult to predict on a case-by-case basis. The field is shifting towards precision medicine, in which prevention is emphasized and diseases are treated with rules-based therapies that are predicted to be effective. Genomic medicine, which includes testing for single-gene disorders, genome-wide analyses, and detailed family histories, is expected to play a key role in precision medicine.

There are many approaches to genetic testing, including diagnostic testing, somatic testing, polygenic risk scores, pharmacogenomic (PGx) testing, and population screening. The group spent some time discussing whether these categories provide an adequate description of the types of genetic testing. The group acknowledged that these categories are not rigid and can depend on the specific context of testing. For example, prenatal genetic testing could be either diagnostic or part of a population screening effort. The group also noted that the number of available tests and their complexity can make it difficult for insurance companies to decide what to cover. It would be helpful to solidify testing classifications, to ensure that employers and employees are consistently talking about the same tests.

At Geisinger, MyCode analyzes participants’ genomes and returns screening results for familial hypercholesterolemia (FH), hereditary breast and ovarian cancer (HBOC), Lynch syndrome, and a number of other conditions. It is estimated that 1% of their population has a pathogenic or likely pathogenic variant for one of these conditions. Results have been returned to 1,061 patients, and by mid-year over 150,000 patients will have been sequenced through MyCode. A recent MyCode paper investigated the impacts of this screening on individuals with BRCA1/2 variants, and found that a
significant number of patients who meet the criteria for BRCA1/2 testing are not being tested, and that the criteria that define eligibility are insensitive. 50% of the BRCA1/2 carriers in the Geisinger cohort did not meet existing criteria for HBOC testing, which represents multiple lost opportunities for prevention.

From an employer perspective, the value of services depends on the relationship between outcomes and cost of care. Outcomes can include medical and service outcomes, but can also involve other outcomes such as employee productivity that are difficult to value economically. Ideally, however, services would decrease cost of care while improving outcomes. According to an Optum White Paper published in 2015, 91% of 275 employers said that they offered wellness programs to their employees for reasons beyond medical cost savings, including reduced employee health risks, reduced healthcare costs, and improved employee productivity.

Discussion

That half the BRCA1/2 carriers in the Geisinger cohort did not meet criteria for HBOC testing suggests that current screening criteria are insensitive for identifying at-risk individuals. These results have been repeated in other studies, and may be due to family history being so poorly captured in clinical care. Employers agreed that showing insurers the percentage of cases missed even when good family history data are available would be important. Additionally, while family history is valuable, BRCA1/2 results can also inform physicians about a number of other cancers and impact cascade testing, so they have potentially significant added value. However, one potential barrier to implementation is that employers and consultants prefer to follow evidence-based guidelines where available. An employer network could investigate how changing from targeted to universal screening affects the value of tests.

The group emphasized that simply providing accredited tests is not enough; it is necessary to develop the downstream clinical infrastructure that translates these results into the best patient care. Geisinger carefully measures outcomes to ensure recommendations are being followed. They also invest in navigator systems that help patients make follow-up appointments and evaluate whether the patient received and understood the message. It is also necessary to provide a mechanism by which employees can opt-in and receive services, even if their primary care provider (PCP) may not initiate testing. Simply instructing employees to request genetic testing from their PCPs has not been historically successful, even if the test is covered by their insurance. Both employees and physicians need increased support.

Multi-national companies like IBM need to think about employee health not just based on U.S. guidelines, but on a global basis. Additionally, though many employers support cancer testing, offering other initiatives becomes more difficult as employers need to consider whether they are able to offer robust downstream follow-up. Alicia Zhou added that Color works with over 100 employers to implement genomic testing, and much of the downstream delivery infrastructure is not available to employers in non-healthcare settings. Color’s staff spends 15% of their time talking with physicians. While genetic counseling can help fill this gap, employers need to ensure that PCPs can appropriately handle the results of testing. In the case of PGx, clinical pharmacy staff need to be engaged as well.

An optimal delivery system will be necessary to demonstrate return on investment (ROI) to benefits managers. However, the group agreed that promoting interventions solely based on ROI would be a mistake. Employers should also consider benefits to employee health and the opportunity to distinguish themselves as innovative organizations.

**Economic implications of including genomics in employee wellness programs**
Due to the high cost of clinical trials, health economists often use modeling techniques to determine which tests to use. Economic evaluations compare the value of testing to the current standard of care. Multiple factors need to be considered while weighing the costs and benefits of an intervention like genomic testing. On the cost side, employers are interested in the cost of the test, along with additional costs likely to be incurred after the intervention, such as healthcare costs and impaired productivity. Benefits include health outcomes like disease prevention and increased life expectancy, but also work outcomes like enhanced team work, performance, and concentration.

A common misperception is that prevention efforts will be cost-saving but they often are not. They can, however, be cost-effective, with benefits that outweigh the costs. If an intervention is applied to a large population, very few people are likely to have an actionable finding, but for them that finding can be life-changing. Thus, value of the test depends on the population being tested, the cost and accuracy of the test, and the cost and effectiveness of available follow-up interventions. Simulation models can also be modified at multiple steps to reflect different assumptions about populations, test results, and changes in cost of testing over time.

Ideally, such models would include published data that combine lab data, claims data, and employer data such as number of lost days of work. Current published data are limited and mainly focus on specific patient populations; there is thus an opportunity for an employer group to help fill the data gap. A model would also focus on cost-effectiveness, which can be measured in terms of cost per quality of adjusted life year gained (QALY). The U.S. threshold for cost effectiveness is $100,000 per QALY. The QALY standard allows health economists to compare genetic testing to other cost-effective interventions.

Discussion

The group noted that there is no “magic threshold” for what insurance companies use to determine what is cost effective, though QALY measurements can be helpful in informing recommendations. However, QALY metrics may not be the most useful to employers, as their employees are not likely to die during the course of their employment. Data on avoidance of health episodes, shortening of episodes, and reduction of costs within episodes would be helpful. Pilot studies in well populations that show the value of early interventions could also help sway employers, who often have limited funds to spend on employee health programs and need to rely on health economic analyses.

The data required to make decisions on implementation vary greatly depending on if the employer is looking at regular insurance benefits or at a wellness plan. Regular insurance benefits are analyzed in the context of data related to cost avoidance and episode costs, while wellness program considerations may rely less on health economic modeling and on more holistic considerations.

There is great heterogeneity in employer decisions so the available data are not uniform or standardized and economic models take into account different levels of uncertainty in their parameters. However, working with heterogenous data can also help economists identify which data elements are the most important to have correct. Economic models also need to incorporate family-based data, including information on cascade testing and the “family spillover effect,” in which the poor health of a family member can adversely affect the employee. Finally, the group agreed that it will be important to investigate the perspectives of employees themselves to determine what they think is most valuable.
Healthcare employer experience: Challenges within employee health programs

Jeff Thompson presented his experience with employee health programs as CEO of Gundersen Health System. Gundersen focuses on a holistic view of the health system and building a supportive system of care. In their experience, a healthcare system operates best if it considers the roles of all stakeholders. By engaging and encouraging doctors, nurses, and other health care team members to champion a new intervention, Gundersen was able to implement advance care plans for 95% of its seniors, with 98% of these plans being honored in the last two years of life. In genetics, many physicians are overwhelmed by the variety of testing options. Therefore, clinical decision support and a pathway for follow-up could support genetic implementation in a dynamically changing test environment.

Numerous stakeholders are involved in deciding whether a test will be included in an employee plan, and different organizations rely on different combinations of these stakeholders to make decisions. However, there are also communication barriers between these multiple stakeholders, which include representatives of employee assistance programs, human resources, sustainability, nutrition, employee health, preventive services, and the employees themselves. The amount of available money for testing also differs substantially based on employer size. Larger organizations may have larger margins that enable more robust genetic testing budgets.

Employers have a responsibility to and a long-term vested interest in the communities they serve. They thus aim to make healthcare decisions that are in the best interest of the community not just now, but in the future. Clear and open communications and careful measures of healthcare outcomes will help to build credibility within the health system and within their employee community.

Discussion

Gundersen is a system that has a lot of control over and influence on its providers, but employers in non-self-contained organizations have less control over the healthcare their patients receive. This presents a limitation to other employers who are interested in ensuring employees get appropriate testing follow-up. Though it won’t be possible to create numerous Geisinger-like systems due to market heterogeneity, there are provider leaders who are trying to move in the right direction.

In states with more of a “cottage industry” healthcare system like North Carolina, insurance companies focus on paying for value. Accountable Care Organizations (ACOs) like Duke decide whether they want to implement an intervention such as genomic screening and reap both the savings and the costs depending on the success of the intervention. Sharing risks and benefits between insurance companies and ACOs is one way to help create a sustainable business model. Money gained from a successful intervention can then be reinvested to investigate whether the model can be successfully repeated.

The group agreed that trust in the healthcare system is extremely important and can be affected by population demographics like age and race. Employees need to be able to trust that their employers are not accessing their genetic testing data. Therefore, the tone set by the organization is very important. One potential solution is to make benefits available through a wellness initiative that is external to the company itself. This would allow the employee to use money for testing through an independent system. Employers would also prefer to narrow available healthcare networks, to guide employee healthcare choices and guarantee they are providing high quality care. However, this is difficult when there are multiple available healthcare networks that do not communicate with each other. Additionally, narrowing choices often results in pushback from employees.
Non-healthcare employer offering genetic testing

The Teachers’ Retirement System (TRS) of Kentucky is a defined benefit group retirement plan. TRS retirees are 72% female and 28% male and have an average annual pension of $36,000/year. TRS does not employ clinicians, and staff work as a concierge service to help retirees maneuver Medicare.

The TRS plan is self-funded and is working to obtain funding for the next 30 years. In Kentucky, a pension is a guaranteed benefit for teachers, but new revenue is required to keep the plan running. Therefore, TRS has a strong incentive to save costs. In late 2017, they began working on a PGx pilot with Coriell Life Sciences (CLS). They found that 84% of TRS retirees were on medications that are influenced by genetics, and TRS retirees have an average of 15 prescriptions. Using de-identified claims information, CLS provided TRS with an in-depth analysis of the potential ROI with the program.

The resulting PGx pilot project was a partnership between TRS, CLS, and the Know Your Rx coalition, a purchasing/member services coalition for public sector and non-profit entities. The team focused on communication pieces that had clear branding to emphasize transparency and build retiree trust. Retirees received an explanatory letter from the executive director of the retirement system, inviting them to participate and making it clear that the system would not have access to their test results. Upon enrollment, DNA collection kits were sent to TRS members’ homes. Over 35,000 invitations were sent out, and 7,000 enrolled; of these, 5,000 completed the kit and sent it back. Medication Therapy Management (MTM) was provided by the Know Your Rx coalition for 3,300 members and communicated directly to the retiree’s primary care physician. The pharmacist delivered two copies of a medication action plan. One copy was intended for personal use, and one copy was sent to the primary care physician. The goal was to empower retirees to have informed conversations with their providers, but steer them away from addressing their medical concerns on their own. As a result, 64% of testing resulted in medication change recommendations, and 94% of the recommendations were accepted by prescribers. TRS also analyzed the claims data of 2,200 members who participated in the program and 2,200 members who did not participate in the program. Overall, there was a 17% reduction per participant in cost-to-plan spending after 6 months.

It is especially important to remember that DNA testing alone is not sufficient to achieve these results. Healthcare providers were empowered with answers rather than research materials. Real-time modeling via CLS’ GeneDose decision support tool allows pharmacists and doctors to see the results of medication changes before they implement them in their patients. The goal is to integrate genetic testing results into a universal medical record and allow this information to be carried along with a retired teacher to each pharmacy and doctor they see in the future.

Discussion

In this example, it was not possible to determine if the 17% reduction in costs was due to increased MTM regardless of genomic results. However, the group noted that genetics can be a great incentive for better adherence to medications, so it may not matter whether the cost reduction was due to genomics or MTM. This PGx pilot had two features that helped to make it successful. The first was branding; TRS took a lot of care in how the program was presented to retirees. There are many testimonials from TRS members proclaiming their support for the program. The second feature was physician education. Physicians were provided with just-in-time information that was shared with employees, which allowed for collaboration between physicians, pharmacists, and retirees.
Genomic Medicine WG Formulary: Choosing the right test

At Genomic Medicine XI, it was recommended that the Genomic Medicine Working Group (GMWG) review current guidelines to develop a list of tests that are ready for implementation. Currently there are mixed guidelines and opinions on what should be provided in genomics. However, despite current gaps in testing availability, it is estimated that 26 million people in the United States have had direct to consumer genetic testing. Thus, the general population has significant interest in genetic testing.

A preliminary formulary was created using established guidelines, such as CDC Tier 1 conditions, that review genetic testing. If one of the guidelines recommended the test, recommendations were compared across all guidelines. GMWG members’ expertise was used to identify conditions that have readily available screening and are backed by evidence that this screening improves outcomes. Key criteria included the prevalence and penetrance of the variants, the risk associated with the intervention, the actionability of test results, and the feasibility of test implementation. This formulary may offer a first step towards test implementation and action plans for this group.

Discussion

The group agreed that the title of “formulary” may be misleading to clinicians. They also proposed that GMWG add information to the formulary about who might benefit the most from each test and the resources needed to implement each specific test. Test implementation will depend heavily on the population being tested, the follow-up management required for each test, the education required for employers and employees, and the estimated time required to achieve benefits. This information could be captured in the form of a toolkit or implementation guide that includes a suite of implementation materials and is guided by developed principles that allow new tests to become integrated as they become available. Ideally, this implementation guide would be routinely updated and web-based, so that employers could “plug in” their population’s characteristics in order to examine the best possible implementation strategy based on their unique situation. This guide would also need to account for ELSI and policy considerations and would require investigating the endpoints that matter most to employees. Partnerships with labor unions could be one way to strengthen employee input.

If information about time required to achieve benefits is included, employers might be interested in immediately implementing the easiest and quickest tests first. Hypothetically, a group of companies could try out different interventions tailored to the needs of their individual populations and recruiting strategies and compare the efficacies of these different interventions. Employers also suggested that it would be helpful to include references along with the tests that suggest systems of care for managing positive results. However, NHGRI and GMWG do not have the resources to do a comprehensive evidence review. This could potentially be supported by natural language processing. Additionally, evidence may be a less important limiting factor than cost.

The group noted that some employers may need clinicians to help translate the results of the formulary if it becomes too technical. It may also be helpful to look into engaging consulting organizations that provide benefits advice to companies.

Panel: Employer priorities & gaps in understanding of genomics in employee wellness
The group agreed that a sufficiently large set of employers could create a “tipping point” to influence insurance companies’ decisions if they are backed up by aggregated data. Thus, data sharing among groups needs to be prioritized. The formulary could potentially take the form of a standing committee with employers, insurance companies, and other advisors. This would also require a sustainability model to help guide how to keep the formulary running and updated, especially as the original list was created by volunteers. The group also agreed that it is necessary to clarify employers’ goals with regard to the separate considerations of wellness and healthcare. In certain markets, wellness benefits can be particularly valuable in recruiting the best and brightest employees.

There is also a strong need to engage employees. Jefferson is attempting to survey employees who have and have not undergone genetic testing to assess their thoughts on information received about genetic testing. Color has also been interested in doing a study of employers who have opted to do testing to assess their satisfaction and their feedback.

**Exploring future collaborations in genomics & employee wellness**

Employers have the power to improve care and lower cost through aggressive population health and cost management programs. However, they need help understanding which tests to offer and how to offer them. Quest has implemented an aggressive employee health program that offers genomics and provides high quality healthcare to employees. They also implemented a chronic kidney disease program that focused on finding a group of employees at high risk for kidney disease. These patients were offered a telemedicine interaction to get re-testing and a nephrologist referral if needed. 70% engaged in the program as a free benefit, and were provided support for making appointments and follow-up. This follow-up support is crucial to ensure employee uptake.

As mentioned above, data from multiple employers could help increase the likelihood that insurance companies add genetic testing to their plans. With a formulary that incorporates clear guidelines, employers can engage around the implementation science. It’s also important that employers outside the healthcare field engage in these programs to broaden the programs’ applicability.

**Discussion**

Geoff Ginsburg, Director of the Duke Center for Applied Genomics and Precision Medicine, polled the group to get a sense of the employers’ perspectives. The group agreed that a set of testing recommendations from a trusted source would be valuable. They also agreed that a web-based implementation guide would be useful. About half of the employers said they would be motivated to collect clinical, employee, and economic data, with appropriate consent and privacy protections, to study the impact of genetic testing. Employers may be able to pool aggregated data and data summaries independently, but employees would need to be appropriately consented and consulted about individual-level data sharing. This will require clear language that explains what the data will be used for. Data sharing would also require funding, and there are challenges with the perceived proprietary use of data. Some employers may need to ask for permission from insurance companies to share claims data.

Any efforts to create a dataset will need to consider the diversity of employee populations, to avoid exacerbating socioeconomic or racial disparities, so it will be important to engage employers representing multiple types of populations. A “buy-up” wellness plan should be avoided, as this might discourage diverse populations from participating.
One potential opportunity for implementation could be to add a genetic component to an existing wellness program that already focuses on a specific disease paradigm. This is already being done in some settings with cancer treatment. It will be important to create a sustainable business model with clear information about who is structuring and extracting data.

**Summary & next steps**

Teri Manolio, Division Director for Genomic Medicine at NHGRI, reviewed the main takeaways from the meeting. In addition to creating a meeting summary, there is interest amongst employer groups in preparing a publication from this meeting and potentially submitting it to a journal like *Genetics in Medicine*. The group is also interested in creating a dynamic, web-based, and regularly updated implementation guide that helps employers contextualize implementations within their systems and is supported beyond volunteer efforts. A specific proposal that can be shared with health systems would be most useful, especially in specific use cases like PGx.

The group decided that for near-term work, there is adequate representation from employers. However, once a specific project is identified, it will be necessary to engage other employers. An emphasis needs to be made on diversity in size, geographic distribution, business focus, and employee population. The group should also consider the interactions they will be having with vendors in the future. Perhaps this will include involving fully insured employers and their insurers in implementation pilots. It would be helpful to canvas employers and employees that have already implemented genomics to get a sense of what already works. Very little data on these efforts have been published, so on-site surveys may be necessary. Data from more pilots like the TRS PGx program would be invaluable to provide information on perspectives and also to help motivate employers to share de-identified implementation data.

Finally, the group had questions about legislation that might protect individual privacy in genetics and genomics. Some states, such as Massachusetts and California, have this sort of legislation. Though this is a short-term solution, it was offered that employers could buy products from insurers in states that follow those legislative guidelines, thus helping to ensure these protections for employees.

Moving forward, NHGRI will create a summary of this meeting and share slides from the presentations (action). NHGRI will also propose working groups and invite employer participation (action). Participants will finalize and rename the formulary (action). They will also work to develop both an implementation guide and protocol for pilot studies on cancer and PGx (action). A policy review will be needed on data sharing, privacy, and national and state laws. For this review, it will be necessary to consider that self-insured employers are not governed by state laws, but by the national Employee Retirement Income Security Act (ERISA) laws. Eventually, this group could perform outreach to other employers and develop communication and sustainability strategies for engaging with the larger employer community.

Please refer to the Executive Summary for a summary of meeting recommendations.

**Summary of Action Items:**

- NHGRI will create a summary of this meeting and share slides from the presentations.
- NHGRI will propose working groups for future work and ask for employer participation. *(complete)*
- WG members will finalize and rename the formulary.
- WG members will develop an implementation guide and protocol for pilot studies on cancer and PGx.