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ARTICLE

Returning actionable genetic results to participants in the biobank at the Colorado Center for Personalized Medicine and UCHealth

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ABSTRACT

Purpose: To describe our process for returning genetic results to participants in the Colorado Center for Personalized Medicine biobank.

Methods: Enrollment in the biobank is open to all adult UCHealth patients. Participants who provided a sample that was genotyped and signed the proper consent were eligible to receive results. Genetic data were generated using a custom genotyping array and confirmed via Sanger sequencing. We used 2 models for returning results and conducted interviews with participants to assess satisfaction with our process, follow-up care, and family communication.

Results: As of July 2022, 73,313 participants had provided a sample and proper consent. Of these, 10,489 samples were genotyped, 137 (1.3%) had initial results, and 62 were confirmed and eligible for return. We returned results to 51 participants, 33% for cardiac risk, 31% cancer, 15% familial hypercholesterolemia, and 21% for other conditions (11 participants refused or did not respond). Less than half of participants had a relevant family history. The majority of participants were glad to receive results and satisfied with our process.

Conclusion: Although array-based genotyping has known limitations that reduce its accuracy, we were able to identify persons with underlying genetic risk who were previously unaware. It is important to establish a process for returning results that follows clinical guidelines, protects participant autonomy, and is amenable to all participants.

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Introduction

Biobanks play an important and emerging role in supporting both basic and translational research. In particular, biobanks that are able to combine participants' clinical history with genomic data represent a valuable resource for a broad range of research topics. Additionally, incidental discovery of secondary findings, genetic variations that predispose participants to diseases for which there are reasonable measures to prevent or mitigate the course of disease, provides an opportunity for biobanks to return these findings to participants and thus impact their future care and health outcomes. Although not mandated, there is consensus that biobanks should return results to research participants if they are able to do so.[1-3] In 2012, a working group of experts assembled by the National Institutes of Health suggested that biobanks have a duty to manage secondary findings. They recommend that biobanks clarify criteria for evaluating findings, analyze results for clinical relevance, and offer return of clinically actionable findings to participants when possible.[1]

In 2013, the American College of Medical Genetics (ACMG) released recommendations for reporting secondary findings discovered from clinical exome and genome sequencing.[4] Although these recommendations are intended to support clinicians who order genetic tests in clinical settings, several research biobanks use these to guide them in determining which results discovered through genetic sequencing for research purposes they should return to their participants.[3,5,6] There are no comparable recommendations on how to return results generated from research biobanks. The process will vary depending on the biobank's infrastructure, consenting process, results generated, and available resources.

The Biobank Clinical Research study at the Colorado Center for Personalized Medicine (CCPM biobank) was launched in 2015 as a partnership between the University of Colorado and UCHealth, a large, regional health care network comprising 12 acute care hospitals and >150 clinics covering >2.7 million patients for a total of >7.3 million encounters per year. The CCPM biobank was established with 2 primary goals: (1) to integrate genomic and real-world clinical data from participants' electronic health records (EHR) to support personalized medicine research and discovery and (2) to impact clinical care and health outcomes by returning clinically actionable genetic results to participants and their providers.[7] Genomic data were generated using a genotyping array platform that produced a high volume of genetic variants to support both research and clinical initiatives. The CCPM biobank reports clinical results, including pharmacogenomics (PGx) and results that predict risk for certain cancers, cardiac conditions, and rare genetic diseases (secondary findings), through our Clinical Laboratory Improvement Amendments (CLIA)-certified, College of American Pathologists (CAP)-accredited laboratory. Our process for returning PGx results for select genes has been described previously.[8] Herein, we describe our process for returning secondary findings to eligible participants and early results.

Materials and Methods

Biobank enrollment and sample collection

Enrollment in the CCPM biobank is open to all active UCHealth patients who are ≥18 years old and can provide consent for themselves in English. For the first 3.5 years of the study (January 2015-July 2018), we implemented a paper-based consent process at select UCHealth clinics at the Anschutz Medical Campus. In August of 2018, we transitioned to an electronic self-consent model using My Health Connection, the patient portal for UCHealth. On the portal, patients can view the consent form and a brief video (https://www.youtube.com/watch?v=8ij-qNLYUFU) and visit our program website before deciding whether to participate (https://medschool.cuanschutz.edu/cobiobank/). By moving to an online process, we are able to offer enrollment to patients across the entire UCHealth system. The Biobank Clinical Research study was approved by the Colorado Institutional Research Board (Protocol #15-0461)

Consenting participants agree to provide biological samples that may be processed to generate genetic data and to allow linkage with their EHR at UCHealth. Upon providing consent, an order is automatically triggered within the EHR to collect a dedicated blood sample (4 mL EDTA) at the patient's next scheduled clinical blood draw at a UCHealth facility. Participant samples are collected and transported to the biobank laboratory where DNA is extracted and stored.

Participant eligibility to receive results

Early versions of the CCPM biobank consent form did not contain language about the possibility of having clinical genetic results returned. As clinical results became available, we offered enrolled participants who had signed an early consent and whose samples had been genotyped (n = 2000) the opportunity to sign a secondary consent to receive clinical test results. In October 2019, we revised our consent document, now called the unified consent, to include collection of samples for research and the return of clinical genetic results.

Genotyping via Multi-Ethnic Genotyping Array (MEGA)

The biobank laboratory performed genotyping on the first 33,864 samples collected using a customized version of the Illumina MEGA.[9] This array tests for the presence of nearly 2.1 million genetic variants, primarily single-nucleotide polymorphisms and some small insertion/deletion polymorphisms from various ethnicities, making it highly suitable for diverse and admixed populations.[10] The biobank's custom version of the MEGA contains over 17,000 additional variants chosen for clinical genetic and PGx

utility.[7,11] Coverage of known pathogenic or likely pathogenic variants in the genes recommended for return is presented in Supplemental Figure 1 and ranged from 0 to 100%, with the majority being 50% or less. However, it is notable that for many genes, including the 16 genes for which results were detected and returned (and described below), the variants covered represent a greater percentage of possible results based on population allele frequency (Supplemental Figure 2).

Confirmation of results

As a CLIA-certified, CAP-accredited laboratory, the CCPM biobank returns genetic results from its validated, laboratory-developed tests. Common population variants (eg, *HFE* p.C282Y, and PGx variants) were individually validated on the MEGA. Individually validating the thousands of rare variants that represent the potential secondary findings was cost-prohibitive, and Illumina microarray genotyping technology is inappropriate for platform- or methods-based validation. A Sanger sequencing method was validated as an orthogonal confirmatory laboratory-developed test for secondary findings. Secondary findings eligible for clinical Sanger confirmation and potential return to participants included variants classified by the 2015 ACMG/Association for Molecular Pathology guidelines for interpretation of sequence variants as pathogenic or likely pathogenic for any of the gene-disorder pairs in version 3.1 of the ACMG secondary findings lists according to inheritance pattern (eg, carrier results for autosomal recessive disorders were ineligible).[12,13] In addition, the participant's EHR was reviewed to confirm that the patient was alive with no evidence of an allogeneic bone marrow transplant before sample collection date, consent for return of results was current, and the variant was not already documented from prior clinical testing. Eligible findings were subject to Sanger confirmation of a second DNA extraction performed at the time of testing from the participant's original EDTA blood tube, which is stored indefinitely at −70°C. Variants that could not be confirmed were deemed ineligible for return.

Process for returning results

Given the more sensitive nature and significant impact of secondary findings for participants, we developed a model for returning these results that differed from that used to return PGx results.[8] To guide us in this process, we established the Return of Results Roadmap Committee (RRR) that comprised CCPM leadership, primary care and specialty care providers, clinical and laboratory geneticists, clinical pharmacologists, genetic counselors, medical ethicists, patient representatives, legal experts, and regulatory and compliance specialists. The RRR made several recommendations that became our guiding principles (Figure 1). We used 2 models using first an in-person approach and subsequently a telephone-based approach to return secondary findings to participants.

Model 1: In-person approach

Our first attempt to return secondary findings was through an in-person model. At that time (summer 2018), the initial consent form did not include returning clinical genetic test results. For this pilot, participants with confirmed research results were contacted by a genetic counselor, informed that there was a research genetic result available, and invited to come in for a clinical visit. At the visit, participants were offered the opportunity to sign the secondary consent to receive secondary findings and the confirmatory genetic test was ordered in the EHR by a medical geneticist. Clinical results were then returned in-person by a genetic counselor and a medical geneticist.

Major challenges to this model were cost and availability of clinical space and staff. This model was also a substantial time commitment for both the providers and the participants. For these reasons, we explored an alternative model that was more sustainable and scalable because we sought to increase the number of secondary findings we could return. We consulted with several other biobanks who already had or who were planning to return secondary findings to their participants and as result, we developed an alternative model using a telehealth approach.

Model 2: Telephone-based approach

In contrast to our in-person model, only participants who previously consented to receive clinical results were eligible to receive secondary findings (Figure 2). Eligible participants were contacted by phone and via their UCHealth patient portal to inform them of an available result and to confirm the participant's consent to receive results. We added this last step because of the significant lag time between providing consent and identification of a secondary finding, which could be a year or longer. During this initial discussion, genetic counselors also discussed the risks, benefits, and limitations of receipt of these genetic results, including review of issues related to Genetic Information Nondiscrimination Act and purchase of certain insurances.

Three attempts to contact participants were made by a genetic counselor (by MyHealth Connection and/or phone). If contact was made and the participant affirmed consent, a clinical order was placed in the EHR, the result was confirmed, and the participant was scheduled for a telephone appointment with a genetic counselor, optimally within 7 to 10 days. If a participant declined to affirm consent, no order was placed, no result was returned, and the participant was withdrawn from the biobank. If no contact was made, and the participant had signed the unified consent, no test order was placed, and the finding remained preliminary.

1. For secondary findings, patient should have the opportunity to talk with a genetic counselor or other trained specialist/provider to inform them of their results at **no cost** to patient.
2. For PGx and secondary findings, we need to establish a service to answer both physician questions and participant questions. This could be a genetic counselor, trained specialist, pharmacist or physician.
3. Patients should have an opportunity to 'opt-out' and 'opt-in' of getting genetic results.
4. RoR consent and process must be vetted with patient advisory group and other key stakeholders.
5. There should be a **reasonable** wait time for patients who are referred for a clinical visit with genetic counselor or other specialty provider at UCHealth following return of results. These visits are billed to patient.
6. Model (and second/unified consent) should establish clear lines of what CCPM pays for vs. patient/insurance.
7. We must evaluate and refine our processes on a regular basis, setting key performance indicators, metrics, milestones and timelines.

Figure 1 Guiding principles for returning secondary findings to biobank participants.

Telephone appointment

Before implementing our phone-based model, we created scripts for the disclosure of results for each gene by the genetic counselor, as well as laboratory report templates and pre-written templates for documenting the results and telephone appointment in the EHR. We also met with specialty providers in oncology, cardiology, and the adult genetics clinic to discuss a process for referring biobank participants for follow-up care.

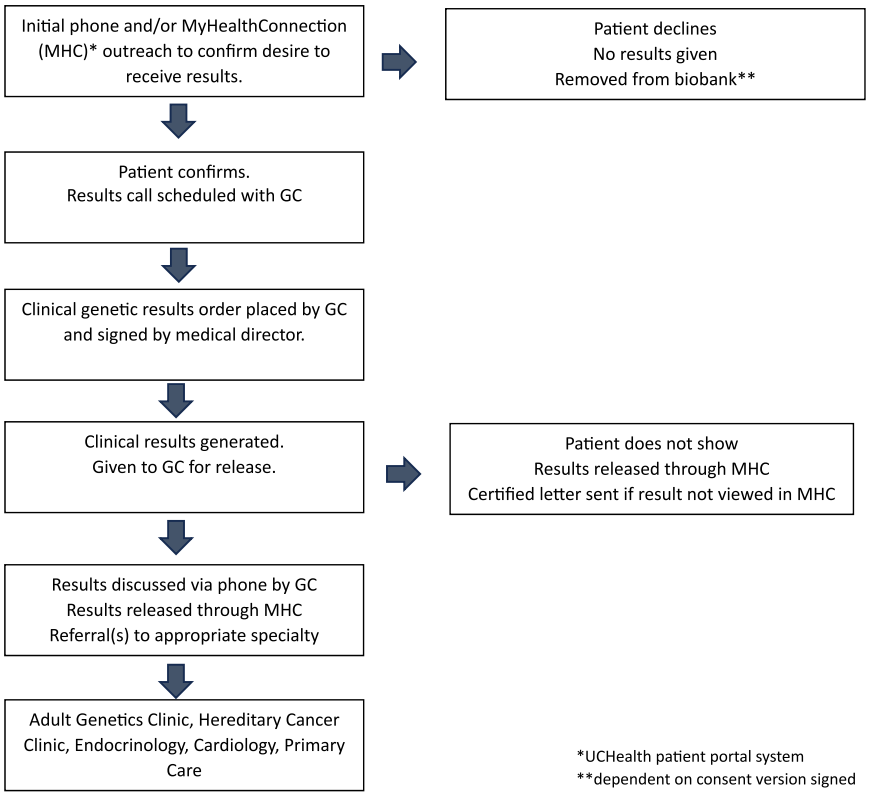

Figure 2 Process for return of results with telephone-based model.

Before the telephone appointment, the genetic counselor placed an order for the biobank confirmatory genetic test in the EHR, which was then signed by a medical provider. During the telephone visit, the genetic counselor provided general information to participants about the condition related to their genetic result, the implications of their result (eg, increased risk for certain types of cancer, cardiac conditions, and risk to family members), and general recommendations for follow-up. The genetic counselor did not collect any additional information about the participant's personal medical or family history during the call. Results were placed in the participant's medical record and, if desired by the participant, referrals to specialty providers for clinical follow-up were made. Participants are able view their results in their UCHealth patient portal and download a letter describing the results that they can share with their provider(s) and family members. Test results and the clinical documentation of the return of results encounter are documented in the EHR.

Follow-up

Within 3 to 8 weeks of returning results, we contacted participants by phone to complete a brief interview regarding their experience and thoughts about getting results from the CCPM biobank, whether they have sought follow-up care with a specialty or primary care provider, and whether they have shared results with family members. We also asked participants what, if any, additional resources we could provide to support them and their families.

Participant education and support

To support our CCPM biobank participants, we created educational content on our program website (https://medschool.cuanschutz.edu/cobiobank), which provides general information and a list of resources regarding genetic results we are returning and their associated conditions. We send out regular newsletters to inform and educate participants on associated research projects, the return of results process, and general information about personalized medicine initiatives.

Clinician education and support

Provider engagement and education are essential to support the utilization of secondary findings in clinical care because clinicians may be unaware that a patient has received a result through their biobank participation. Low levels of genomic knowledge among nongenetics professionals further hinder the use of these results to inform clinical decision making.[14-17] The RRR, described above, created a forum to engage with representative stakeholders from various provider groups to ensure that our return of results process supported clinicians. Before the return of secondary findings through the telehealth model, we conducted a survey of local primary care providers to explore their preferences for the return of actionable genomic results generated by our biobank.[18]

Our initial educational efforts for providers involved both in-person and virtual lectures and the development of quick reference materials. Lectures were given during departmental grand rounds or faculty meetings to all relevant provider groups. To assist clinicians in the use of secondary findings in clinical care, written materials were developed and reviewed by relevant practitioners. These materials are housed on our program website and undergo at least annual evaluation. Program updates are communicated through email distribution lists to affected provider groups and through in-person education.

Results

Biobank participants

As of July 2022, 205,590 individuals had enrolled in the CCPM biobank, 117,718 had provided a sample, and of these, 73,313 had signed a consent to receive results (Table 1). The discrepancy between the number of consents and samples reflects the delay inherent in our protocol to collect a sample at the participants' next clinical visit when a blood draw is ordered. About 60% of biobank participants are female, 50% are age 50 or older, 83% are White, and 9% are Hispanic. The demographic breakdown of biobank participants reflects the patient population at UCHealth in terms of sex and age, although it slightly underrepresents Hispanic and Black patients. Older participants (age 50+) were slightly more likely to have provided a sample compared with younger adults.

Results from MEGA and Sanger confirmation

Of the 73,313 samples from participants who had signed consent to receive results, 10,489 were evaluated on the MEGA. After initial evaluation, 137 samples (1.3%) were found to have results for consideration to return to study participants based on recommendations.[4] Of these 137 results, 114 met additional eligible criteria and underwent Sanger sequencing; 48 failed confirmation and 66 were confirmed via Sanger sequencing. Of these, 62 results were deemed eligible for return (Figure 3).

Participant recontact and result disclosure

We attempted to recontact all 62 participants with eligible results and were able to return results to 51 participants: 9 confirmed consent and received results in a clinical setting as part of Model 1, 39 consented and received results over the phone. Another 3 participants did not respond to outreach, and because they had signed the secondary

Table 1 Characteristics of biobank participants with sample and consent to receive results (reflects enrollment as of July 2022)

Demographic	Total Enrolled $N = 205,590$	Sample Collected $N = 117,718$	Sample Collected With Consent to Receive Results $N = 73,313$
Gender			
Male	83,483 (40.6)	45,913 (39.0)	28,790 (39.3)
Female	122,092 (59.4)	71,803 (61.0)	44,521 (60.7)
Unknown	15	2	2
Age group			
18-29	23,413 (11.3)	10,461 (8.9)	7365 (10.0)
30-49	79,711 (38.8)	42,880 (36.4)	26,299 (35.9)
50-69	68,574 (33.4)	41,914 (35.6)	26,507 (35.2)
70+	33,892 (16.5)	22,463 (19.1)	13,142 (17.9)
Race			
White	170,671 (83.0)	99,228 (84.3)	63,175 (86.2)
Black	8160 (4.0)	4658 (4.0)	2221 (3.0)
Asian	59 (<1)	39 (<1)	20 (<1)
Native American	763 (<1)	455 (<1)	277 (<1)
Pacific Islander	232 (<1)	121 (<1)	47 (<1)
Multiple race	6,247 (3.0)	3446 (2.9)	2181 (3.0)
Other	10,726 (5.2)	5844 (5.0)	3337 (4.6)
Unknown	8732 (4.2)	3927 (3.3)	2055 (2.8)
Ethnicity			
Hispanic	18,373 (8.9)	10,410 (8.8)	6340 (8.6)
Non-Hispanic	173,196 (84.2)	101,631 (86.3)	62,767 (85.6)
Unknown	14,021 (6.8)	5677 (4.8)	4206 (5.7)

consent, we were obligated to return their results to their EHR. Four participants declined to receive results resulting in withdrawal from the CCPM biobank study, and 7 did not respond to outreach.

The 51 results returned represented variants detected in 16 genes (Table 2). Of the 51 results returned, most were related to cardiac disease risk (33%) or cancer risk (31%). The remainder of results were related to risk for familial hypercholesterolemia (15%), hereditary transthyretin amyloidosis (10%) and susceptibility to malignant hyperthermia (10%). Information on specific variants detected in these genes is provided in the Supplemental Table 1.

The age of participants who received results ranged from 27 to 87; 32 (63%) were female. Using information reported in the EHR, 78% were White, 8% were Black or African American, 2% were Hispanic, 8% reported "other or more than 1 race," and 4% were "unknown." In addition, 29% had

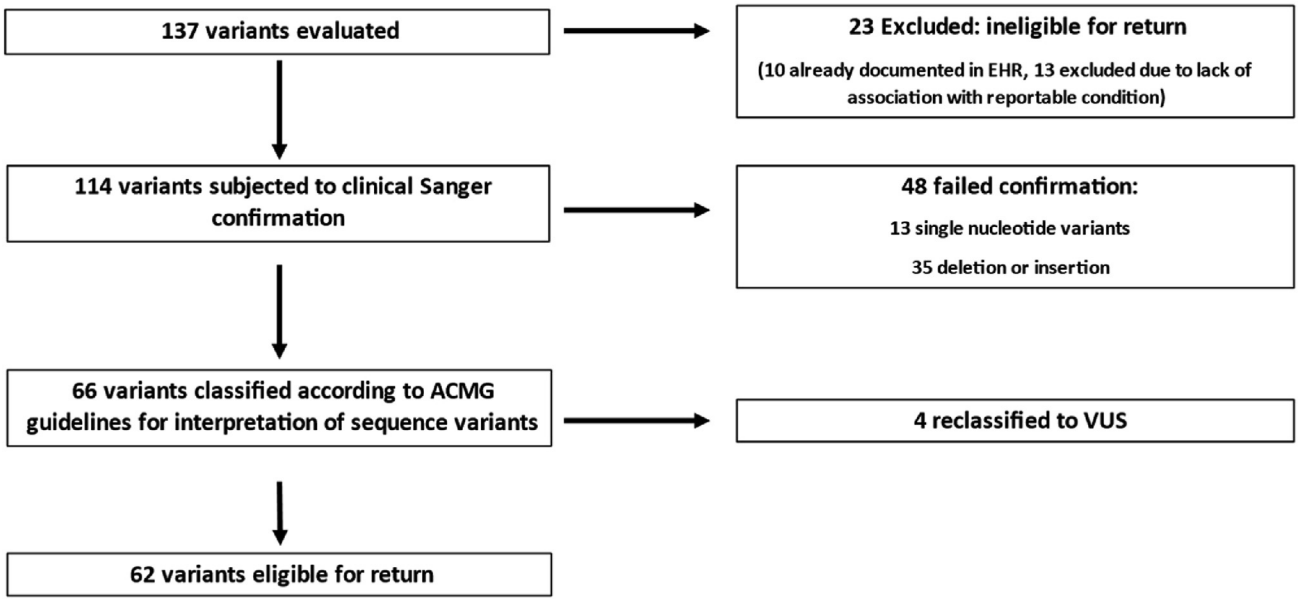

Figure 3 **Process for confirmation of results from Multi-Ethnic Genotyping Array**.

Table 2 Frequency of results returned by clinical indication

Condition/Phenotype	Total *N* (% of Total)	Genes (Number of Each Reported)
Cancer	16 (31%)	*BRCA1* (4) *BRCA2* (6) *MSH6* (1) *PALB2* (3) *SDHB* (1) *TMEM127* (1)
Cardiac	17 (33%)	*ACTC1* (1) *KCNQ1* (1) *MYBPC3* (6) *MYH7* (4) *SCN5A* (3) *TNNI3* (1) *TNNT2* (1)
Familial Hypercholesterolemia	8 (15%)	*LDLR* (8)
Hereditary Transthyretin Amyloidosis	5 (10%)	*TTR* (5)
Malignant Hyperthermia Susceptibility	5 (10%)	*RYR1* (5)
All	51	

a personal history of the disease or condition for which they have genetic susceptibility (eg, diagnosis or symptoms), and 43% reported possibly having a relevant family history. Half of the participants with cancer-related results met guidelines for referral for genetic counseling and testing based on the National Comprehensive Cancer Network (https://www.nccn.org/guidelines/nccn-guidelines).

Follow-up interviews

We completed follow-up interviews with 32 participants who received results (63%). When asked how they felt about being recontacted by the biobank about the availability of results, the majority indicated that they were happy to have received results, and all participants reported that they were satisfied with our process. Among participants who received results in-person ($n = 9$), all expressed a preference for a face-to-face visit (vs via telephone). In contrast, all participants who received results via telephone and were interviewed ($n = 23$) expressed a preference for phone vs an in-person visit. Some of the reasons given by participants who preferred to receive results by phone included the convenience of not having to drive, and the flexibility around scheduling a 30-minute phone appointment vs an in person visit.

Several participants who were contacted by phone to inform them of availability of results and affirm consent were grateful to have had a choice to accept or decline results. Many had forgotten they had enrolled in the CCPM biobank and appreciated the reminder. All participants preferred speaking with someone about their results vs receiving a written result via mail or through their patient portal. Over a third of participants ($n = 18$) sought follow-up care with their primary care providers and/or 1 or more specialists after receiving their results: genetic counselor (12), oncology (8), cardiology (13), or endocrinology (2). All participants said that they felt supported by CCPM and UCHealth in this process, and when asked about how the biobank could support them further, many asked for credible resources (eg, websites) that they could use and share with family members.

At least 18 of the participants had shared their results with their family members at the time of our interview. Many opted to download the results letter placed in their medical record to share with family members and with their primary care provider. Others expressed interest in having a letter template that they could use to introduce and share their genetic results with family members.

Discussion

Overall, our experience in returning results from the CCPM biobank has been positive. We successfully returned results to 51 participants who were unaware of their genetic predisposition and the associated risks for themselves and their family members. It is notable that less than half of participants who received results had record of any relevant family history in their medical record that might have prompted genetic testing (eg, for cancer or cardiac conditions). This exemplifies the potential for population-based screening afforded by biobanks to identify persons with genetic risks who might otherwise be missed. To optimize the reach and benefit of this model, it is important to assure equal access and support for all persons to participate.

We found that our process for returning results was well received by participants. We also learned that some participants do not want to receive results, which is consistent with reports from other biobanks.[3,19] This finding supports having a return process that allows participants to opt-out. Our telephone-based model has proven to be both amenable and beneficial for participants. It is encouraging that participants were equally agreeable to receive results by phone (vs in person) because this creates an opportunity to expand our reach across the UCHealth system and reduces barriers to care related to transportation, work schedules, and childcare commitments. A telephone-based model also reduces costs and space requirements associated with in-person clinical visits.

Several key components of the CCPM biobank have afforded us the ability to return results to our participants. The opportunity to create a custom MEGA (to include variants to support both research and clinical use) and the capacity of our lab to process and evaluate these results enabled us to identify high-risk, actionable variants that we can return for clinical decision making. Further, because the CCPM biobank is CLIA-approved and CAP accredited, we can return these clinical results directly to participants

without external verification, thereby streamlining the return process and further reducing costs. In addition, having access to participant records via the EHR at UCHealth allowed us to determine whether participants had undergone genetic testing previously so that we could avoid unnecessary confirmatory testing and notification of participants with results that they already knew. We are also able to place results directly into the health record after disclosure so that participants and providers can access this information at will for use in clinical decision making. The involvement of genetic counselors to return results has been invaluable to our process and to our participants and is consistent with how some other biobanks return results.[3] Lastly, having an infrastructure, including advisory committees and platforms, for providing education and resources to participants and clinicians is essential for ensuring that these groups are protected and supported in this process.

We have experienced several challenges in using the microarray technology. Although it was cost-effective to add custom loci to the MEGA to identify candidate secondary findings, known limitations of the technology reduced its performance in the detection of rare variants. In the setting of tri-allelic single-nucleotide polymorphisms, the inability of the base array chemistry to distinguish variant adenosine from thymine or cytosine from guanine contributed to the high false-positive rate. For rare variants, the validation data set had no representation of heterozygous or homozygous alternative alleles on which to establish accurate clustering for variant calling, further reducing accuracy. Other variants were not amenable to detection by this technology; therefore, probes could not be designed for them. Finally, the MEGA array cannot interrogate novel or private variants. Together, these limitations reduced the sensitivity and specificity of our array-based screening, leading to a positivity rate of 1.3% and a false-positive rate of 42%. These values are similar to previously published estimates for array-based genotyping.[3]

Challenges specific to our return of results process were similar to those reported by other biobanks.[3,5,19] A major obstacle has been reconsenting early participants who signed a research-only consent and for whom clinical results are now available. Despite multiple attempts to recontact these individuals via the UCHealth patient portal and targeted emails to invite them to update their consent, only about 20% have opted to do so. Other biobanks that intend to return clinical results to participants might consider implementing a consent form that includes corresponding language from the outset. Nevertheless, we have found it somewhat challenging to reach even those individuals who have signed the proper consent and confirm their desire to receive results. Our standard procedure is to attempt contact both by phone and via the portal 3 times. We suspect that nonresponse may in part be due to the participant's lack of contact with the health system over time or to migration outside the state. In these cases, we do not finalize these results or return them to the chart.

After results were disclosed, we discovered through follow-up interviews that some participants encounter long wait times to get an appointment with a specialty provider. We have also found that some do not seek follow-up care (eg, with genetics or specialty providers) and thus we do not know to what extent the potential health impacts of results is understood by participants or shared with at-risk family members. Lastly, although we would like to offer cascade testing for at-risk family members to expand the impact of our program, we have not yet found a way to provide this service to family members who may not have insurance, ability to pay, or who may live out of state.

Although the custom MEGA enabled us to identify results with clinical relevance, it was primarily developed to support research. Accordingly, the MEGA coverage for even highly penetrant genes is not 100%. Thus, a challenge when using microarray technology is conveying to participants that "no news does not necessarily mean good news" because we are only able to interrogate results available on the MEGA. We have created educational materials on our website to explain this to participants and providers. CCPM has now added exome sequencing in addition to the Illumina Genetic Diversity Array to preserve interrogation of results for research and PGx return and to expand the scope of clinically actionable results we can return. As mentioned above, another challenge in using the MEGA was that it could not discriminate between variant A or T nucleotides or variant C or G nucleotides such that it would, for example, erroneously flag a C>T benign variant for confirmation if the probe was designed to detect a pathogenic C>A variant at that locus. Thus, by using the MEGA as an initial screen for secondary findings, we had to evaluate a number of results that did not confirm via Sanger sequencing because of the lack of discrimination on the MEGA between exact nucleotides. The move to exome sequencing as an initial screen will help to mitigate this issue.

We have not yet returned enough results to conduct a thorough outcomes analysis to evaluate the impact of receiving results on medical management and health outcomes, such as enhanced screening and/or surveillance, prophylactic surgery, and disease onset or progression. As we continue to return a wider spectrum of results with higher throughput, we will be able to assess these and other outcomes of interest, including the impact on family members.

Conclusion

Biobanks are uniquely poised to facilitate research on a broad scale and to offer participants the opportunity to receive genetic results that they may not have access to otherwise because of cost and/or lack of predisposing factors to warrant testing. Because certain results may

dramatically affect participants' future health needs and outcomes, it is imperative to establish a process of return that follows recommendations and clinical guidelines, protects participant autonomy, and importantly, is accessible and amenable to all participants. Having key components in place to support the return of results, and guidance from key stakeholders has been critical for optimizing the benefit to our participants.

Data Availability

Data for Multi-Ethnic Genotyping Array results on eligible participants and for participants who received results (deidentified) can be made available upon request. Dr Kristy Crooks can be contacted for any data requests at kristy.crooks@cuanschutz.edu.

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Ethics Declaration

The Colorado Center for Personalized Medicine Biobank Clinical Research Study was approved by the Colorado Multiple Institutional Review Board (Protocol #15-0461).

Conflict of Interest

The authors declare no conflicts of interest.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gimo.2024.101852) contains supplemental material, which is available to authorized users.

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