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TITLE: Improving Diagnosis and Clinical Management of Familial Hypercholesterolemia Through Integrated Machine Learning, Implementation Science, and Behavioral Economics

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CONTRACTING ORGANIZATION: University of Pennsylvania

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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Fort Detrick, Maryland 21702-5012

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14. ABSTRACT

The overarching goal of the proposed project is to increase diagnosis and effective treatment of persons with Familial Hypercholesterolemia (FH). The proposed project aims to improve FH diagnosis by (1) using a validated machine learning tool in a large healthcare system (Penn Medicine) to flag individuals at high risk of having FH; (2) employing effective interventions based on implementation science (IS) and behavioral economics (BE) to engage the healthcare system, clinicians, and patients to ensure that the diagnosis of FH is appropriately made; and (3) to improve the uptake of, and adherence to, evidence-based practices (EBP) for these patients, resulting in a reduction in LDL-C and ultimately improved CV outcomes. The project initiated on July 1, 2021 and multiple work streams have been initiated to achieve specific goals of Aim 1 and Aim 2.

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NONE LISTED

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1. INTRODUCTION:

The overarching goal of the proposed project is to increase diagnosis and effective treatment of persons with Familial Hypercholesterolemia (FH). The proposed project aims to improve FH diagnosis by (1) using a validated machine learning tool in a large healthcare system (Penn Medicine) to flag individuals at high risk of having FH; (2) employing effective interventions based on implementation science (IS) and behavioral economics (BE) to engage the healthcare system, clinicians, and patients to ensure that the diagnosis of FH is appropriately made; and (3) to improve the uptake of, and adherence to, evidence-based practices (EBP) for these patients, resulting in a reduction in LDL-C and ultimately improved CV outcomes.

2. KEYWORDS:

Familial hypercholesterolemia, Machine Learning, Implementation Science, Behavioral Economics

3. ACCOMPLISHMENTS:

In the last year of the grant period (8/1/22 - 7/31/23) multiple sub-teams worked to achieve the subtasks/milestones set for Aims 1 and Aims 2.

Meetings:

- Regular meetings between stakeholders at the University of Pennsylvania and the Family Heart Foundation continued to provide an opportunity for high level discussion and decision making.
- The following sub-teams continued to meet in Year 2 of the grant:
    - Data Informatics Sub-team which was established to work on refining the FIND FH© algorithm tool that will be applied to Penn Medicine patients at the Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center (HUP/PPMC) for the identification of patients with potential FH for the pilot testing phase (Aim 1) continued to meet on an ad-hoc basis in Year 2.

      The data team at the Family Heart Foundation transferred the data for the first 399 patients within the Penn Population that were flagged by the FIND FH© algorithm as having probable FH to the Penn data team. The data team at Penn re-identified the 399 flagged patients and conducted preliminary analyses to get an understanding of the patient population. The Penn data team conducted analyses to understand how many of the flagged patients had a primary care physician on their patient chart, and how many had PCPs within the Penn Health System, in addition to other analyses to help inform the development of the decision support tools for the pilots.

      After the initial 399 patient list was delivered to the Penn data team, the Family Heart Foundation data team worked on refining their algorithm tool. The output of the FIND FH© algorithm tool required a manual curation process to ensure that the algorithm tool was applied correctly and that it was sufficiently picking up people who were flagged for potentially having FH at significant thresholds. The goal of the manual curation process was to significantly reduce the number of “false positives” that were flagged by the FIND FH© algorithm. In the last year,

the Family Heart Foundation data team refined and automated the manual curation process to have more confidence in their output.

Once the manual curation process was automated and finalized, the Family Heart Foundation data team transferred the data for the remaining 1164 patients to the Penn data team. The data team at Penn re-identified the 1164 flagged patients and started preliminary analyses to get an understanding of the patient population. The Penn data team is in the process of data reconciliation to identify the flagged patients across the entire Penn Health System who are actively seen by a Primary Care Provider (PCP) and those that are not.

- The Implementation Science Sub-team was established to develop interview materials and conduct interviews with both providers and patients (Aim 2). The team consisted of members of the Family Heart Foundation as well as a qualitative expert from the University of Pennsylvania, Dr. Tamar Klaiman, and Co-Investigator, Dr. Rinad Beidas at Northwestern University.

  The Implementation Science Sub-team worked in conjunction with the Qualitative Interview Coding sub-team to code the interviews and identify the core themes that arose from the provider and patient interviews. Once the interviews were fully coded, the Implementation Science Sub-team discussed the preliminary findings of the interviews and conducted their preliminary analyses. They also finalized the construction of the behavioral roadmap to inform the pilot development and pilot implementation strategies. Once the data analysis and development of the behavioral roadmap was completed, the Implementation Science Sub-team prepared a manuscript for publication to disseminate findings from the qualitative interviews with patients and providers. The manuscript is almost completed, and the Implementation Science Sub-team aims to submit the manuscript by the end of the September.

- The Pilot Development Sub-Team continued to meet to design and discuss operational logistics for developing the pilots that will be tested and implemented in the Penn Medicine health system. The team consists of members of the Family Heart Foundation as well as study team leadership at the University of Pennsylvania. During the current development phase, the pilot development sub-team meets on a bi-weekly basis to refine processes, develop specific protocols, and build and refine decision support tools in the Electronic Health Record to help clinicians diagnose and treat patients who are flagged by the FIND FH© algorithm tool and have probable FH.

  In Year 3, after reviewing the initial list of flagged patients, the Pilot Development Sub-Team will test two different pilots based on whether flagged patients have a PCP within the Penn Medicine health system.

  For patients with a Penn PCP, we will test out the centralized referral model with Penn PCPs using clinical decision support tools that will be built in Epic to nudge PCPs to sign off on a referral for their flagged patients to see a lipid specialist. Once patients have been referred to a lipid specialist, we will test two different outreach methods – Penn health system vs Family Heart Foundation mediated outreach to schedule patient appointments.

  For patients without a Penn PCP, we will skip the centralized referral approach and proceed straight to testing the direct outreach methods to patients outlined above.

  Since the centralized referral model for the pilot for patients with a Penn PCP involves building clinical decision tools on Epic, the group is currently still in the process of obtaining approvals

and sign off from multiple stakeholders at Penn. The Pilot Development Sub-Team presented the proposed decision support tools for the centralized referral model for clinicians to key governance groups at Penn. Within the UPHS health system, changes or additions in Epic and the clinician workflow require approval by multiple governance groups to both get permission and have Epic Analyst resources assigned to build and implement these tools. The team presented the initial prototypes for this and the proposed clinical decision support workflow to the three key governance groups involved in this project in continue to address feedback and concerns. The Pilot Development Sub-team submitted a ticket with the Penn Epic application analysts to start the preliminary build of the clinical decision tools.

Now that the entire dataset of flagged patients within the Penn Health System has been delivered, we are moving actively forward. Based on the insights we gained from looking at the distribution of patients with a PCP at Penn, we are working to identify specific clinics that would be good candidates for the PCP pilot. Once these specific clinics are confirmed (due to having sufficient volume of patients to test the centralized referral mechanism in their clinic), the Pilot Development Sub-Team will work with these clinics to socialize the study and map out strategies that work best for the clinic's workflow to allow for the successful testing of the centralized referral mechanism among the practice's PCPs. Working specifically with a handful of clinics will allow for more feasible implementation of either option because it would be easier to get buy in and support versus trying to implement this on a health systems level before we have established proof of concept.

In the meantime, the Pilot Development Sub-Team submitted a ticket with the Penn Epic application analysts to start the preliminary build of the clinical decision tools. We will continue to engage with these governance groups to address any concerns and to encourage them to dedicate Penn Epic application analyst support to this project so we can continue to make progress in Year 3.

In the last year, the Pilot Development Sub-team has worked on mapping out and refining the workflow for the pilot for patients without a Penn PCP. This pilot skips the centralized referral model since these patients do not have a primary care clinician at Penn and will go straight to direct mediated outreach. In skipping the centralized referral model, we can bypass the need for governance approvals for developing new centralized referral mechanisms in Epic and this will start off as a manual process by the research team.

The Pilot Development Sub-Team developed outreach materials for the Penn vs Family Heart mediated outreach. The Pilot Development Sub-Team worked with the Family Heart Foundation's Living with FH group to get feedback from individuals living with FH on the outreach. Based on their feedback, the Pilot Development sub-team is continuing to refine and develop additional outreach materials that are informative and action provoking while not causing undue alarm to patients when they have yet to receive a formal diagnosis. On the back end, the Pilot Development Sub-Team is working with the Penn Health System to develop the organizational structures on Epic that would allow for the scheduling of research visits with the lipid specialist involved with this study.

The Pilot Development Sub-Team submitted three IRB modifications to the original Penn IRB protocol to incorporate the other phases of the study (including the Phase 2 rapid cycle pilots and the Phase 3 large scale pragmatic trial). IRB modifications were also submitted to get approval for changes to personnel and approval for the outreach materials what were developed for the direct to patient pilot.

Upon receiving IRB approval, the lipid specialist has started to conduct preliminary chart review and screen patients who had been flagged by the FIND FH© algorithm using the Study Team Validity Check which was developed in Year 1. This work is being conducted in batches and is currently focused on patients without a PCP within the Penn Medicine Health System to enable the Pilot Development Sub-Team to select the first sample of 40 patients for the direct to patient pilot and get closer to launching this pilot.

The overall research staffing shortages and hiring freezes due to Covid-19 that initially presented obstacles to hiring staff continue to impact the timeline. In the last year, we finalized the subcontract with Northwestern University so that Dr. Rinad Beidas could continue to work on the implementation science piece of this study. We also hired a Clinical Research Coordinator in the last year as we get closer to launching the pilots.

- Initiating and Partnering PIs (Drs. Rader and Volpp) meet with the Project Director bi-weekly to review overall progress.

Regulatory Accomplishments:

- The subcontract between the University of Pennsylvania and Northwestern University was initiated and executed.
- UPenn IRB modification approval for adding the new pilots and additional phases of the study to the IRB protocol was obtained on February 7, 2023.
- UPenn IRB modification approval for adding new personnel to the study to work with patient data was obtained on February 22, 2023.

Personnel:

- Dr. Sameh Saleh, a clinical informaticist and physician builder, joined the team through his clinical informatics fellowship at Penn and helped us develop the centralized referral mechanisms with his expertise in data informatics and machine learning, and familiarity with the Penn Medicine electronic health record.
- Dr. Deepak Vedamurthy, a lipid specialist, joined the team through his cardiology fellowship at Penn and is serving as the lipid specialist that patients will have an appointment with for the pilots for the evaluation and diagnosis of FH. He has also been conducting preliminary chart review using the Study Team Validity Check.
- A temporary Clinical Research Coordinator, Rebecca Connelly, was brought on as art of the Qualitative Interview Coding Sub-Team where she worked under the supervision of Tamar Klaiman to code the qualitative interviews using ATLAS.ti and drafted the manuscript of the learnings from the qualitative interviews.
- Maeve Moran, a Clinical Research Coordinator at Penn left the University on September 16, 2022. A Clinical Research Coordinator, Emily Kim, was hired and started work on this project in March 2023. Emily has been involved in taking meeting minutes, coordinating upcoming piloting activities, and developing data tracking systems for the pilots.

What were the major goals of the project?

Specific Aim 1: To apply a "big data" machine-learning strategy (the FIND FH© tool) to identify individuals at high risk of FH within UPHS EHR databases	**Timeline (Months)**	**Site 1 (Initiating PI)**	**Site 2 (Partnering PI)**	**Status**	**% Complete**
Major Task 1: *Adjust the precision and reach of the FIND FH© tool*	1-3	X		Completed	100%
Subtask 1: Work with Penn IT group to secure EHR Limited Dataset	1	X		Completed	100%
Subtask 2: Optimize and configure FIND FH© model to work on unrestricted Penn Population	1-3	X		Completed	100%
Subtask 3: Evaluate performance statistics and make adjustments	2-3	X		Completed	100%
Major Task 2: *Identify and prioritize undiagnosed probable FH cases*	4-5	X		Completed	100%
Subtask 1: Apply updated FIND FH© model to Penn Population	4	X		Completed	100%
Subtask 2: Assess and ensure quality of model application	4-5	X		Completed	100%
Subtask 3: Identify probable FH cases and apply triage rules to prioritize the patients for care	4-5	X		Completed	100%
Milestone: *Probable FH Individuals flagged and prioritized*	5	X		Completed	100%
Major Task 3: *Analyze factors associated diagnosis and insufficient treatment for hypercholesterolemia*	6	X		In Progress	65%
Subtask 1: Compare model scores with prior FIND FH© implementations to assess, improve, and compare scores over time	6	X		Completed	100%
Subtask 2: Identify specific factors and characteristics of missed opportunities: - 'False Negative' patient population – i.e. those training individuals known to have FH that the model scored very low - 'False Positive' patient population – i.e. those training individuals known to NOT have FH but that the model scored very high	6	X		In Progress	10%

Specific Aim 2: Apply principles of implementation science and behavioral economics, many of which were pioneered by members of the research team, to design and implement a novel approach in which flagged individuals are reliably evaluated for diagnosis of FH and appropriately treated	**Timeline (Months)**	**Site 1 (Initiating PI)**	**Site 2 (Partnering PI)**	**Status**	**% Complete**
Major Task 1: Qualitative interviews	1-6		X	Completed	100%
Subtask 1: Prepare launch of qualitative interviews (Penn IRB submission and approval, HRPO submission and approval, onboard any new staff)	1-3		X	Completed	100%
Subtask 2: Conduct key informant interviews with four stakeholder groups (clinicians and patients from HUP/PPMC and from LGH) to explore barriers and facilitators in diagnosing FH and initiating or intensifying therapy for individuals with FH or taking lipid-lowering therapies	3-4		X	Completed	100%
Subtask 3: Code and analyze interviews with two stakeholder groups	4-5		X	Completed	100%
Subtask 4: Construction of a behavioral roadmap with guidelines used to refine implementation strategies proposed in the pilots	6		X	Completed	100%
Milestone: Interviews completed and evaluated	5		X	Completed	100%
Milestone: Behavioral roadmap completed	6		X	Completed	100%
Major Task 2: Innovation pilot testing					
Subtask 1: Design, launch and evaluate pilot 1 for opt out and active choice for ordering lipid testing (50 patients) QI approval process Implement EPIC integrations for provider intervention behavior modification strategies	7-13			In Progress	25%
Subtask 2: Design, launch and evaluate pilot 2 with three approaches to respond to flag for probable FH (50 patients) QI approval process Implement EPIC integrations for provider intervention behavior modification strategies	13-15			In Progress	15%
Subtask 3: Design, launch and evaluate pilot 3a that will use defaults and active choice from pilot 1 to prompt clinician to run FH Diagnosis Care Protocol (50	15-17			In Progress	10%

patients from pilot 2) QI approval process Revise EPIC integrations for provider intervention behavior modification strategies					
Subtask 4: Design, launch and evaluate pilot 3b to test communication of FH diagnosis to patients with active and passive resources (50 patients from pilot 2) QI approval process Develop discussion guide Develop patient navigation resources	17-19			In Progress	10%
Subtask 5: Design, launch and evaluate pilot 4 with clinician opt out or active choice of prescribing daily atorvastatin (50 patients from pilot 2) QI approval process Revise EPIC integrations for provider intervention behavior modification strategies	19-21			Not Started	0%
Subtask 6: Design, launch and evaluate pilot 5 to test approaches to increasing medication adherence in patients using social accountability and gamification (100 patients total) QI approval process Build Way to Health platform for testing of social accountability and gamification	21-23			In Progress	5%
Milestone: Iterative Innovation pilot phase complete	23			Not Started	0%
Milestone: Iterative Innovation pilot phase evaluated	24			Not Started	0%

Specific Aim 3: Evaluate whether the approach is a viable solution to the current under-diagnosis and under-treatment of FH across a variety of health systems	**Timeline (Months)**	**Site 1**	**Site 2**	**Site 3**	**Status**	**% Complete**
Major Task 1: Design QI intervention						
Subtask 1: Design combined provider and patient intervention with behavior modification strategies for roughly half of remaining patients identified by FIND FH algorithm (1000 patients)	24-26	X	X	X	Not Started	0%
Subtask 2: Implement changes to EPIC integration for provider behavior	24-26		X		Not Started	0%

modification strategies						
Subtask 3: Implement changes to Way to Health platform for patient behavior modification strategies	24-26		X		Not Started	0%
Milestone: Design completed for combined provider and patient intervention	26	X	X	X	Not Started	0%
Milestone: Completed EPIC integration for provider nudges and completed Way to Health platform for patient intervention	26		X		Not Started	0%
Major Task 2: Implement QI intervention						
Subtask 1: Launch and run multi-strategy QI intervention	27-39		X		Not Started	0%
Subtask 2: Analysis and evaluation QI intervention	40-48	X	X	X	Not Started	0%
Milestone: QI intervention launched	27	X	X	X	Not Started	0%
Milestone: QI intervention analysis complete	42	X	X	X	Not Started	0%
Major Task 3: Share findings						
Subtask 1: Prepare abstract(s) for presentations, conferences	42-48	X	X	X	Not Started	0%
Subtask 2: Prepare manuscripts	42-48	X	X	X	In Progress	20%

What was accomplished under these goals?

Over year 2 of the grant period, multiple sub-teams worked to achieve the subtasks/milestones set for Aims 1 and 2. Regular monthly meetings between all stakeholders at the University of Pennsylvania and the Family Heart Foundation provided an opportunity for high level discussion and decision making. These meetings also provided a forum for sub-teams to report on and receive input from the larger group. The Data Informatics sub-team and the Implementation Science Sub-Team continued to meet on a reoccurring basis to refine the FIND FH© algorithm tool (Aim 1) and to code and analyze the qualitative interviews that would inform the implementation of the pilot phase (Aim 2).

In the last year, the Aim 1 Data Informatics Sub-team met as needed to refine the FIND FH© algorithm tool and to refine and automate the manual curation process. In this last year, the Family Heart Foundation team continued to refine the manual curation process after delivering the initial list of patients. After making subsequent edits to their processes and automating the manual curation process, the Family Heart Foundation team shared the rest of the data for the patients flagged at Penn by the algorithm tool has potentially having FH. The Data Informatics Sub-team re-identified all flagged individuals and is conducting preliminary descriptive analyses to understand the flagged patient population, and determine which patients have PCPs within the Penn Health System and which do not. This work is ongoing.

In the last year, the Implementation Science Sub-team in partnership with the Qualitative Coding Sub-team reviewed the interview transcripts and conducted thematic analysis of the interviews under the guidance of the qualitative expert at Penn. All coding of interviews and thematic analysis of the interviews was completed this year. Together, the Implementation Science Sub-team and Qualitative Coding Sub-teams developed the behavioral roadmap to develop implementation strategies to address barriers and challenges for the diagnosis and treatment of patients with FH based on learnings from the qual interviews. Both teams worked together to also write a manuscript to disseminate the research findings from the interviews, which will be submitted for publication at the end of the summer.

During this last year, the Pilot Development Sub-Team made significant progress to shape pilot design to evaluate and diagnose patients flagged for FH After evaluating the data of flagged patients, the Pilot Development Sub-Team will test two different types of pilots. The initial proposal was focused on only testing strategies for patients who have a PCP within the health system. After review, many flagged patients did not have a PCP within the health system and would therefore be unable to be evaluated. Therefore, the team decided to test two approaches, one focused on creating a centralized referral mechanism for patients with a Penn PCP centralized referral mechanism via the EMR (EPIC) and a second approach that skips the centralized referral mechanism and goes direct to patients.

A total of 1563 unique patients were flagged by the FIND FH algorithm as potentially having FH across Penn Medicine. We did preliminary data analysis to understand the flagged patient population. Of the 1563 flagged patients, 39 were no longer alive per their electronic health records, and another 97 already had a diagnosis of FH based on the ICD-10 code. The average age of the flagged patients is 62.9 years old, with 82% below 65 years old and 30% below the age of 45 years old. Additionally, most PCPs within Penn Medicine only had 1 patient that was flagged by the FIND FH algorithm. Due to the low number of flagged patients per PCP, we shifted to a centralized referral model in which PCPs are encouraged to refer the patient to see a lipid

specialist who would then evaluate the patient for FH before deciding whether or not to hand off the management of the patient's care as this seemed more likely to be successful than to try to change the behavior of hundreds of PCPs and teach them to diagnose and treat FH, given that each would have very small numbers of patients. Furthermore, out of the 1563 unique patients, only 814 patients have a PCP within the Penn Medicine health system. If we limited testing this quality improvement initiative with patients with a Penn PCP, we would be missing ~48% of the flagged patient population that could greatly benefit from further chart review and clinical evaluation for FH. The delivery of the final patient list and the final breakdown of the full patient list further emphasized the importance of creating two pilots; 1) the Direct to Patient pilot for anyone without a PCP at Penn that by-passes the need for a PCP in order to get clinical evaluation for FH, and 2) the Penn PCP pilot for all patients that have a PCP at Penn where Penn PCPs will be provided with a centralized referral model for their flagged patients.

For the PCP pilot, the Pilot Development Sub-Team worked on sketching out the centralized referral model. This centralized referral model involves building clinical decision tools on Epic. Anything that requires building clinical decision tools on Epic requires an extensive approval process and sign off from multiple stakeholders within the Penn Medicine Health System. The Pilot Development Sub-Team drafted and refined the proposed decision support tools for the centralized referral and presented these tools to key governance groups at Penn. The team presented the initial prototypes for these tools and laid out the proposed clinical decision support workflow to the three key governance groups involved in this project and refined the prototypes based on feedback received from the governance groups. After addressing the feedback and refining the prototypes further, the Pilot Development Sub-team submitted a ticket with the Penn Epic application analysts to start the preliminary build of the clinical decision tools, with the understanding that we would continue to work with the specific providers at whichever clinic to refine the workflow further in a way that would be manageable with the workflow at that specific practice.

For the direct to patient pilots, the Pilot Development Sub-Team finalized outreach materials for the Penn-mediated outreach vs Family Heart Foundation outreach and solicited feedback from patients with FH in order to make sure the information in the outreach felt relevant, and appropriate to them, and might encourage them to seek care. In addition to developing the outreach materials the sub-team has begun to develop the Standard Operating Procedures for this pilot and is working on coordinating the process for the handoff of patients between the Family Heart Foundation and Penn, for scheduling telehealth visits with the lipid specialist at Penn. The Pilot Development Sub-Team has been working with analysts at Penn Medicine to operationalize the telehealth appointments and ensure structures are in place to cover the costs of the telemedicine appointments in order to try to reduce barriers to care for patients. In addition, the lipid specialist has to conduct chart review to determine whether flagged patients pass the Study Validity Check (a screening tool developed in Year 1), ensuring exclusion of those patients who do not have FH.

The lipid specialist has conducted chart review for 139 patients. Of the 139 patients, 29 patients did not pass the Study Validity Check. Based on chart review, the lipid specialist has identified the first 40 patients who are eligible for the direct to patient pilot which we aim to launch in September 2023. Once we receive IRB approvals and approvals on EPIC for scheduling purposes, we plan to launch the direct to patient pilot. We also continue to engage with primary care practices to implement the clinical nudge in order to launch the PCP pilot.

REGULATORY PROTOCOL AND ACTIVITY STATUS

In the last year, a subcontract between the University of Pennsylvania and Northwestern University were initiated and executed. The subcontract was established because Dr. Rinad Beidas switched institutions in Year 2 and left the University of Pennsylvania for a new position at Northwestern University. Her expertise in Implementation Science was critical for the ongoing success of the study and thus the subcontract was established.

The University of Pennsylvania submitted three modifications to the UPenn IRB to lay out the addition of the second pilot, and to include the phases of the study that follow the pilots to the Penn IRB protocol. The UPenn IRB modification approval for the addition of the pilot and other phases of the study was obtained on February 7, 2023. The HRPO IRB modification for this addition was submitted to HRPO IRB on February 10, 2023. HRPO IRB acknowledge the non-substantive amendment on March 14, 2023, and informed us that they did not meet OHRO's reporting requirements and did not require OHRO review and approval prior to implementation. The second Penn IRB modification which was solely to add personnel to the study was obtained on February 22, 2023. The third Penn IRB modification for the outreach materials is pending approval.

PROTOCOL (_1 of 1_ total):

Protocol [ACURO Assigned Number]: **PR201840P1**

Title: **Improving diagnosis and clinical management of familial hypercholesterolemia through integrated machine learning, implementation science, and behavioral economics**

Target required for statistical significance: **38 (21 patients and 17 providers)**

Target approved for statistical significance: **40 (20 patients and 20 providers)**

Total subjects to date: 38

SUBMITTED TO AND APPROVED BY:

Ms. Jill Graygo, MPH, MSED

STATUS:

40 patients without PCPs across Penn Medicine were identified as eligible for the direct to patient pilot after chart review was conducted to evaluate patients using the Study Validity Check.

The age range for the patients was 24-76, and the average age of the flagged patients is 53.7 years old. 80% of the patients were below 65 years old, and 20% are below the age of 45 years old. 62.5% of the patients are male and 37.5% of the patients are female. Per their electronic health records data, 70% of the patients were identified as white, 17.5% were identified as Black or African American, 2.5% of the patients identified as American Indian or Alaskan Native, and 10% of the patients identified as other or unknown.

			Enter information regarding number of subjects					
HRPO Protocol Number	Protocol PI Name	Organization (Site)	# Target	# Enrolled	# Completed	# Screened	# Recruited	Other
PR201840P1	Dr. Kevin Volpp	UPENN	40	38	38	38	53	

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?

The full project team and all sub-teams will continue to meet regularly to accomplish the goals set out in Aims 1 and 2. The Family Heart Foundation and Data Informatics sub-team will complete preliminary data reconciliation and demographic analysis of the full flagged patient population in Year 2 to inform any changes to the pilots and to tee up the pilot phase.

The manuscript for the qualitative interviews (Aim 2) will be submitted for publication at the beginning of fall. Additionally, regular meetings will continue to proceed with the Pilot Development Sub-team focused on the design and execution of the piloting phase. The Pilot Development Sub-team will continue to engage with external stakeholders to get input on the feasibility and practicality of potential decision support tools in Penn Medicine's electronic health record and the impact this will have on clinician workflow. The Pilot Development Sub-team will also focus their efforts on launching the direct to patient pilots in the interim to test out different outreach and scheduling methods and to refine the workflow and development of the standard operating procedures between the Family Heart Foundation team, the UPenn study team, and the UPenn lipid specialist. Sub-teams will continue to expedite work wherever possible to make up for time lost in this last year to Covid-19 related delays.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Nothing to Report.

5. **CHANGES/PROBLEMS:**

Changes in approach and reasons for change

Nothing to Report.

Actual or anticipated problems or delays and actions or plans to resolve them

There were delays in getting this study up and running due to Covid-19 related constraints in the last year, and our subtask and milestone completion dates are still behind schedule. However, we are more on track than before, and we plan to redouble our efforts to achieve our subtask and milestone completion dates whenever possible in the coming year as we move forward on the development and execution of the piloting phase.

Changes that had a significant impact on expenditures

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Nothing to Report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report. Not applicable for this protocol.

Significant changes in use of biohazards and/or select agents

Nothing to Report. Not applicable for this protocol.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Nothing to Report

Journal publications.

Nothing to Report

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers and presentations.

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name	Project Role	Researcher Identifier	% Effort	Contribution to Project:	Funding Support:
Daniel Rader, MD	Initiating PI		10%	Initiating PI, Oversight	Grant
Kevin Volpp, MD, PhD	Partnering PI		10%	Partnering PI, Oversight	Grant
Rinad Beidas, PhD	Co-Investigator		10%	Co-investigator - oversight of Implementation Science	Grant
Sameh Saleh	Informatics Fellow		10%	Advisory role – informatics and electronic health record build	Other
Tamar Klaiman, PhD	Sr. Qualitative Research Scientist		5%	Oversight of qualitative framework approach, Interview guide development for patients and providers	Grant
Laurie Norton	Project Director		20%	Project administration, budget oversight, grant reporting, support for Data Informatics sub-team	Grant
Jennifer Orr	Project Manager		50%	IRB, regulatory, support	Grant

				for Implementation Science sub-team, pilot planning	
Rebecca Connelly	Clinical Research Coordinator - Qualitative		25%	Qualitative interview coding, qualitative interview manuscript	Grant
Emily Kim	Clinical Research Coordinator		50%	Overall project support, support for Pilot Development sub-team	Grant
Maeve Moran	Clinical Research Coordinator		50%	Overall project support, support for Implementation Science sub-team, qualitative interviews	Grant

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Provide the following information for each partnership:

Organization Name: Family Heart Foundation
Location of Organization:680 E. Colorado Blvd. Suite 180, Pasadena, CA 91101
Partner's contribution to the project:
Collaborator: The Family Heart Foundation is a non-profit research and advocacy organization founded in 2011 to address gaps in healthcare that lead to misdiagnosis, delayed care, preventable heart attacks, the need for stents or coronary artery bypass graft surgery, and premature death for individuals with FH. The Family Heart Foundation collaborates closely with the UPenn group. This includes regular monthly leadership meetings between UPenn and Family Heart Foundation for high level discussion and decision making. In addition, the sub-teams are comprised of UPenn and Family Heart Foundation collaborators who are developing the qualitative interviews and focus groups to inform the Implementation Science approaches as well the Data Informatics sub-team, comprised of experts at both UPenn and the Family Heart Foundation who will refine and implement the FIND FH© algorithm tool.

Organization Name: Northwestern University
Location of Organization: 625 N. Michigan Avenue, 21st Floor, Illinois 60661
Partner's contribution to the project:
Collaborator: Rinad Beidas moved from the University of Pennsylvania for a new position at Northwestern University in Year 2 of the grant. Her expertise in implementation science is critical for the ongoing success of the study. She leads the Implementation Science Sub-Team meetings and provides extremely valuable insight in developing the pilots.

SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

A Quad chart is not applicable. A duplicative report will be submitted by both the Initiating PI (Dr. Rader) and the Collaborating PI (Dr. Volpp).

8. APPENDICES:

Nothing to Report