Overview

The National Human Genome Research Institute (NHGRI) Ethical, Legal and Social Implications (ELSI) Research Program frequently receives requests for examples of funded grant applications. Several investigators and their organizations agreed to let excerpts of their ELSI grant applications be posted online.

Acknowledgement

We are grateful to the investigators and their institutions for allowing us to provide this important resource to the community. To maintain confidentiality, we have redacted some information from these documents (e.g., budgets, social security numbers, home addresses, introduction to revised application), where applicable. We do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., budgets, biographical sketches, letters of recommendation or letters of support). NIH grant formats or rules may have changed since these applications were prepared; therefore, applicants should always follow the application format instructions included in the funding announcement.

Copyright Information

The text of the grant applications is copyrighted. Text from these applications can only be used for nonprofit, educational purposes. When using text from these applications for nonprofit, educational purposes, the text cannot be changed and the respective Principal Investigator, institution, and NHGRI must be appropriately cited and credited.

PI: **Korngiebel, Diane**	Title: Using Ethics and User-Centered Design to Create Templates for EHR-Mediated Return of Genetic Test Results	
Received: 11/13/2017	FOA: PA17-446	Council: 05/2018
Competition ID: FORMS-D	FOA Title: Ethical, Legal, and Social Implications (ELSI) of Genomics Exploratory/Developmental Research Grant Program (R21)	
1 R21 HG009958-01A1	Dual: CA	Accession Number: 4111893
IPF: 9087701	Organization: UNIVERSITY OF WASHINGTON	
Former Number:	Department:	
IRG/SRG: ZRG1 SEIR-B (80)	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 125,000 Year 2: 150,000	Animals: N Humans: Y Clinical Trial: N Current HS Code: Evaluative Info HESC: N	New Investigator: Early Stage Investigator:
Senior/Key Personnel:	*Organization:*	*Role Category:*
Diane Korngiebel	UNIVERSITY OF WASHINGTON	PD/PI
Stephanie Fullerton	University of Washington	Co-Investigator
LYNNE ROBINS	University of Washington	Co-Investigator

Appendices

Appendix_Data_Collection_Instruments_FINAL

Additions for Review

Unpublished

OMB Number: 4040-0001
Expiration Date: 10/31/2019

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier
HG009958

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number
GRANT12519536

5. APPLICANT INFORMATION **Organizational DUNS*:** 6057994690000

Legal Name*: UNIVERSITY OF WASHINGTON
Department:
Division:
Street1*: Office of Sponsored Programs
Street2: 4333 Brooklyn Ave NE
City*: SEATTLE
County:
State*: WA: Washington
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 981959472

Person to be contacted on matters involving this application
Prefix: First Name*: Carol Middle Name: Last Name*: Rhodes Suffix:
Position/Title: Director, Office of Sponsored Programs
Street1*: 4333 Brookly Ave NE
Street2: Box 359472
City*: Seattle
County: King
State*: WA: Washington
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 98195-9472
Phone Number*: 206-543-4043 Fax Number: 206-685-1732 Email: osp@uw.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 91-6001537

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

❍ New ● Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Using Ethics and User-Centered Design to Create Templates for EHR-Mediated Return of Genetic Test Results

12. PROPOSED PROJECT
Start Date* Ending Date*
07/01/2018 06/30/2020

13. CONGRESSIONAL DISTRICTS OF APPLICANT
WA-007

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Diane Middle Name: Last Name*: Korngiebel Suffix:
Position/Title: Assistant Professor
Organization Name*: UNIVERSITY OF WASHINGTON
Department:
Division:
Street1*: Health Sciences Bldg 1959 NE Pacific St
Street2: Box 357240
City*: Seattle
County:
State*: WA: Washington
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 981950000
Phone Number*: 206-616-8126 Fax Number: Email*: dianemk@u.washington.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$417,664.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$417,664.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Carol Middle Name: Last Name*: Rhodes Suffix:
Position/Title*: Director
Organization Name*: University of Washington
Department: Office of Sponsored Programs
Division:
Street1*: 4333 Brooklyn Ave. NE
Street2: Box 359472
City*: Seattle
County: King
State*: WA: Washington
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 98195-9472
Phone Number*: 206-543-4043 Fax Number: 206-685-1732 Email*: osp@uw.edu

Signature of Authorized Representative*
Lester Villaflor

Date Signed*
11/13/2017

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:

424 R&R and PHS-398 Specific
Table Of Contents

OMB Number: 4040-0010
Expiration Date: 10/31/2019

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	UNIVERSITY OF WASHINGTON
Duns Number:	6057994690000
Street1*:	4333 Brooklyn Ave NE
Street2:	Box 359472
City*:	SEATTLE
County:	King
State*:	WA: Washington
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	981959472
Project/Performance Site Congressional District*:	WA-007

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Washington
DUNS Number:	6057994690000
Street1*:	1959 NE Pacific St
Street2:	
City*:	Seattle
County:	WA - Washington
State*:	WA: Washington
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	98195-7240
Project/Performance Site Congressional District*:	WA-007

Funding Opportunity Number: PA-17-446. Received Date: 2017-11-13T15:53:47.000-05:00

Project/Performance Site Location 2

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Washington
DUNS Number:	6057994690000
Street1*:	850 Republican St, Bldg C
Street2:	
City*:	Seattle
County:	WA - Washington
State*:	WA: Washington
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	98109-0000
Project/Performance Site Congressional District*:	WA-007

Additional Location(s) File Name:

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00006878

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Project_Summary.pdf
8. Project Narrative*	Project_Narrative.pdf
9. Bibliography & References Cited	References_FINAL.pdf
10.Facilities & Other Resources	Facilities_and_Other_Resources.pdf
11.Equipment	

Funding Opportunity Number: PA-17-446. Received Date: 2017-11-13T15:53:47.000-05:00

PROJECT SUMMARY/ABSTRACT

Patient engagement is critical for implementation of the genomic component of precision medicine—with care taken to include the perspectives and needs of patients. Yet many patients may experience significant barriers to understanding genetic information and/or using the electronic patient portals that many health systems are using to meet the terms of meaningful use related to the return of laboratory and test results. Although the return of genetic results and patient portal use have each received considerable attention, there have been few studies concerning the return of genetic test results via patient portals—even as more test results are made available to patients electronically. The success of precision medicine relies not only on algorithms behind clinical decision support and “Big Data” analytics but also on the activated patient: the patient who receives health-related information and is motivated and supported to act upon it. Prospective attention to practical and ethical concerns will help to ensure that patient perspectives are taken into account as developing technology is prepared for clinical deployment. The goal of the project is to define patient and key stakeholder needs, including those of patients from underrepresented populations, concerning the acceptability of receiving genetic test results electronically via a patient portal. The study will take place in the University of Washington Medicine (UW Medicine) system, which provides care for a diverse patient population in western Washington State through its network of hospital- and neighborhood-based clinics and uses Epic software’s Electronic Health Record patient portal module. Specifically, the proposed investigation will: (1) explore with patients who have received genetic test results and non-genetic test results electronically their experience receiving those results and their views on their electronic return and how genetic results return differs, or does not differ, from non-genetic results; (2) expand the understanding of return of results thresholds by exploring with patient portal users who have received genetic test results how electronic return affects return thresholds and the nuances and challenges of presenting information for positive and negative results; and (3) following User-Centered Design principles, conduct cognitive interviews with portal users and non-users about the acceptability and ease of use of electronic return of results prototypes created using data from (1) and (2) with template options supporting use within and without the UW Medicine system. The proposed R21 exploratory research will provide preliminary data on patient perspectives across diverse populations on the use of patient portals to return genetic results electronically, including important work around thresholds for determining results that are appropriate for electronic delivery and developing report templates whose content is readily comprehensible and supports patient empowerment and enhances their engagement in their own health.

PROJECT NARRATIVE (PUBLIC HEALTH RELEVANCE)

The proposed research would provide preliminary, much-needed, timely data on patient perspectives across diverse populations on the use of patient portals to return genetic test results, including thresholds for determining results that are appropriate for electronic delivery and the content and presentation elements that diverse patients may require in order to benefit from genetic information delivered electronically. Research on patient values, needs, and preferences must be represented early—while issues are being explored and potential solutions identified—to ensure that the deployment of genomic medicine supports patient empowerment, enhances engagement, and does not contribute to healthcare delivery inequities.

FACILITIES AND OTHER RESOURCES

Computer and Technical Support: The University of Washington (UW) leads the region in providing state-of-the-art access to networked information and innovative, cost-effective computing tools for a wide variety of applications. It includes access to the Internet, email, and the World Wide Web at no cost to the proposed project. Many library resources are on-line and readily accessible, and access to on-line bibliographic searches is available to the project at no cost. The UW Center for Social Science Computation and Research provides training and on-site consultations on statistical, word-processing, and graphical software packages that are readily accessible at no cost to the project. In addition, the UW School of Medicine provides expert consultation on hardware and software, as well as quarterly workshops that are available to faculty, staff, and students in the school at no charge.

Office: The Department of Biomedical Informatics and Medical Education provides Dr. Korngiebel with office space in the School of Medicine Health Sciences Building. This includes a telephone, Ethernet access, printers, and fax and mailing services. Dr. Korngiebel will also have access to support staff, a conference room, and technical support.

Other:

The University of Washington (UW) is one of the leading research universities in the nation and one of the largest institutions of higher education in the West. It is recognized regionally and nationally for the excellence of its academic programs, research contributions, and public service, and many of the approximately 3,900 teaching and research faculty are known nationally and internationally for their accomplishments. In fiscal year 2016, the University of Washington received about $1.37 billion in public and private grant and contract support for research and training. Since 1969, the University has ranked among the top five institutions in the nation in receipt of federal awards. Since 1974, UW has led the nation's public universities in competing for federal research and training grants. The UW is both a top-ranked scientific research institution and a leader in the training of physicians, nurses, and other health professionals. The six UW Health Sciences Schools are each ranked among the best in the nation. Nearly half of all extramural research funding at the UW comes from the US Department of Health and Human Services, testifying to the size and breadth of UW's health research program. UW is the third-largest employer in Washington State, following Boeing and Microsoft, and is one of the unique places in the nation to support a research environment to conduct interdisciplinary work linking bioethics with consumer health informatics. **The School of Medicine** is ranked among the top medical schools nationally and has an outstanding reputation for the quality and quantity of its research. Its programs enjoy an excellent reputation nationally that enables it to compete successfully for the top candidates applying to doctoral programs in the U.S. The School of Medicine has been ranked No. 1 in the nation in primary-care training for more than 20 years by *U.S. News & World Report*. It is also second in the nation in total federal research grants and contracts with $727.5 million in total revenue (fiscal year 2015) according to the Association of American Medical Colleges.

UW Medicine provides outstanding care to patients from around the globe, educates the next generation of physicians and scientists, and supports one of the world's largest and most comprehensive medical research programs. UW Medicine's four hospitals – Harborview Medical Center, Northwest Hospital & Medical Center, University of Washington Medical Center and Valley Medical Center – admit more than 63,000 patients each year. UW Medicine provides outpatient care for more than 1.3 million patients each year at its 12 UW Neighborhood Clinics and its many other primary and specialty care clinics. UW Medicine also includes Airlift Northwest and the UW Physicians practice group, the largest physician practice plan in the region. UW Medicine shares in the ownership and governance of the Seattle Cancer Care Alliance with Fred Hutchinson Cancer Research Center and Seattle Children's and also shares in the ownership of Children's University Medical Group with Seattle Children's. UW Medicine advances its mission through partnerships with other healthcare organizations in the region and through strong affiliations with Seattle Children's Hospital, Fred Hutchinson Cancer Research Center, VA Puget Sound Health Care System and Boise VA Medical Center.

UW Medicine eCare is a free, secure and convenient way for patients to access their health information online. Patients can use eCare to see, manage, and receive the health records from their clinic visits or hospital stays anywhere in the UW Medicine health system, including Harborview Medical Center, Northwest Hospital & Medical Center, UW Medical Center, Valley Medical Center, the UW

Neighborhood Clinics and other UW Medicine-affiliated clinics. UW Medicine eCare allows patients to view many different types of personal health information in their inpatient or outpatient medical records. This information may include:

- Current medicines
- Allergies
- Immunizations (vaccines)
- Medical history
- Test results
- Details of your previous clinic visits
- Hospital discharge instructions
- Questionnaires

The Family Medicine Clinic at Harborview (FMC) provides patients and their families with high quality, comprehensive health care. FMC medical staff emphasize prevention to help patients stay healthy. FMC healthcare professionals are board-certified in family medicine and provide personalized health care by taking the time to answer patient questions and address their concerns. FMC is a safety-net hospital-based clinic whose services include:

- Evaluation and treatment of acute and chronic illnesses
- Preventive health care
- Behavioral health care
- Hearing and vision screening
- Well-child exams and immunizations
- Pregnancy tests, prenatal care and family planning

The Department of Biomedical Informatics and Medical Education (BIME) is engaged in training, research, and the practice of biomedical informatics and medical education across the breadth of health sciences and healthcare. BIME consists of 32 core faculty and 57 extended faculty who work closely with 15 staff. Our core and extended faculty have appointments in 24 schools and departments across UW, including Nursing, Global Health, clinical departments, and Engineering. BIME has a very active research program with faculty and students involved in about 100 research grants that cross a broad range of disciplines in many departments and schools, focusing on using biomedical information to improve health and education. BIME faculty, graduate students, and postdoctoral fellows have opportunities for collaboration with almost every discipline. Faculty and student research interests range from foundational to applied, and some faculty take their applied work and put it into practice via tight collaborations with our clinical computing and research computing environments. Foundational research in the department includes: data modeling, data management, data visualization, data security/privacy, data integration, knowledge representation and ontologies, computable knowledge resources, information design, inference, machine learning, data mining, modeling uncertainty in data and knowledge, information workflow, people and organizational issues, observational/fieldwork methodologies, natural language processing, and text mining. Application areas range from translational bioinformatics to clinical research and applied informatics, including consumer health informatics and population or public health informatics. The department’s vision to unleash the potential for electronic biomedical information to improve biomedicine, clinician education, and patient health aligns well with the proposed research.

The Department of Human Centered Design & Engineering (HCDE) is one of ten departments in the College of Engineering, with Bachelor's, Master's, and PhD degree programs. Its mission is to "research, design, and engineer interactions between humans and technology, putting people first." HCDE research (1) considers the role of communication and technology in human activity; (2) prioritizes the needs, desires, and behaviors of people and communities who interact with technical systems; and (3) addresses the specifics of design by working with interdisciplinary communities of researchers to build innovative technological solutions. HCDE has user research labs available to students and faculty. Many faculty members also serve as consultants to large technology companies, such as Microsoft and Amazon. HCDE students regularly engage in user-centered design and usability research as part of their coursework; frequently they have faculty and industry partners engaged in these activities.

The Health Sciences Libraries (HSL) provides all University of Washington faculty, students, and staff access to biomedical information, regardless of their physical location, to accommodate education, research, and clinical programs that encompass Washington, Alaska, Montana, Idaho, and Wyoming. The HSL contracts with the National Library of Medicine to lead the Pacific Northwest Region of the national Network of Libraries of Medicine, connecting health professions across the region to information services. HSL collections focus on dentistry, medicine, nursing, pharmacy, public health, social work, and related disciplines. Each health sciences department or program has an assigned liaison who is responsible for coordination services to that program area, including development and presentation of targeted instructional sessions, individual information management consultation, collection development, and web page linkages. HSL focuses on digital provision of information and is particularly strong in clinical reference (e.g., drug information, evidence-based sources, textbooks, specialty databases, and journals). Linkage to the online article is standard in core databases such as MEDLINE. HSL knowledge resources include: 1500 current print journal subscriptions (1865 online titles), 136,000 book titles, 465 video titles, and 100 databases available via the web. The HealthLinks database includes links to an additional array of filtered resources available at no charge. Documents not available online may be requested for fast delivery, and HSL is a national leader in the delivery of documents via the web. Health sciences resources and the extensive collection of the entire University in relevant areas such as computing, engineering, public policy, technology, and business are available. In addition, all resources across disciplines are backed by the statewide network of state university libraries.

University of Washington Institute of Translational Health Sciences (ITHS) (www.iths.org) is one of more than 60 Clinical and Translational Science Awards (CTSAs) funded by NIH's National Center for Advancing Translational Sciences to facilitate the translation of advances in biomedical research into beneficial health applications. The goal of ITHS is to improve the health of people throughout Washington, Wyoming, Alaska, Montana, and Idaho (the WWAMI region). Local institutional partners include the Fred Hutchinson Cancer Research Center, Seattle Children's Hospital, and the Group Health Research Institute. ITHS also provides research infrastructure to the WWAMI region through partnerships with regional collaborators including universities, research institutes, and Tribal and other community organizations. ITHS provides expert consultation, training, clinical and administrative support services, equipment access, and pilot funding to facilitate translational research. All UW investigators have access to Institute resources and services, including clinical research and support services; study and data management services; access to Core facilities and technological resources; regulatory support; and assistance with research design and implementation.

The ITHS Biomedical Informatics team (BMI) extracts useful data from electronic medical records to assist with patient cohort identification, trial recruitment, feasibility determination, study design, and more. BMI has access to more than 50 clinical data sources from UW Medicine as well as a network of primary care community clinics. The UW Medicine Clinical Data Repository alone contains more than 10 billion facts from 20 years of data on five million patient lives.
The Biomedical Informatics team assists investigators with:

- Custom electronic medical record screening to identify potential study participants and determine study feasibility
- Identification of patient cohorts for study planning and retrospective review

The ITHS Research Coordination Center (RCC) is a multidisciplinary team of research coordinators, regulatory specialists, research nurses, and study monitors who can support the design and conduct of clinical and translational research. RCC provides expert consultation and staffing solutions to propel projects forward with the requisite knowledge to conduct observational and experimental research designs in both biomedical and behavioral disciplines.

This study will leverage the ITHS research coordinator services as a cost-effective way to provide study support. ITHS Biomedical Informatics working with UW Medicine's eCare (patient portal) team will provide cohort identification support through Amalga.

The Department of Bioethics and Humanities (BH), located in the School of Medicine, provides academic education and professional training in bioethics and humanities through an MA in Bioethics; an undergraduate Minor in Bioethics and Humanities; curricula in clinical ethics and professionalism for medical students, residents, and fellows; and sponsored continuing education activities for practicing health care professionals.

BH faculty represent diverse scholarly disciplines, including medicine, genetics, philosophy, health services, religious studies, education, pathology, history, and other areas. BH collaborates with faculty from the schools of medicine, law, nursing, pharmacy, public health, social work, and the college of arts and sciences. Faculty publications explore a wide range of areas, including the ethical, legal, and social implications of genetics and genomic research; community-based participatory research; social justice and access to health care; social inequalities in health and health disparities; medical error; and palliative and end of life care.

The Division of Medical Genetics in the Department of Medicine in the School of Medicine is a leader in genetics research, training, and clinical care. Members of the Medical Genetics faculty conduct research in most areas of human and medical genetics and modern molecular biology. They work in a wide range of settings within the University of Washington, the Veterans Affairs Puget Sound Health Care System, and the Fred Hutchinson Cancer Research Center. Over 40 UW scientists work in conjunction with the Division of Medical Genetics, conducting research related to medical genetics. Faculty and affiliates include one Nobel laureate, fifteen diplomates of the American Board of Medical Genetics, six members of the National Academy of Sciences, and two members of the Institute of Medicine.

The Department of Laboratory Medicine was established in the School of Medicine at the University of Washington in July 1969 to integrate the clinical laboratories at the University Hospital (now the University of Washington Medical Center) and Harborview Medical Center. The department now employs 800 people who work at the University of Washington Medical Center, Harborview Medical Center, and many other clinical and research facilities in the area. The primary purpose of the Department of Laboratory Medicine is to serve as a regional resource for clinical laboratory services required for patient care and for educational programs in Laboratory Medicine. The Department strives to minimize the cost of delivering its high-quality diagnostic services. The Department also emphasizes education and research and actively facilitates interdisciplinary studies.

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 10/31/2018

1. Human Subjects Section

Clinical Trial? ○ Yes ● No

*Agency-Defined Phase III Clinical Trial? ○ Yes ○ No

2. Vertebrate Animals Section

Are vertebrate animals euthanized? ○ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

○ Yes ○ No

If "No" to AVMA guidelines, describe method and proved scientific justification

3. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

PHS 398 Cover Page Supplement

4. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

5. Inventions and Patents Section (RENEWAL)

*Inventions and Patents: ○ Yes ● No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

6. Change of Investigator / Change of Institution Section

❑ Change of Project Director / Principal Investigator

Name of former Project Director / Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

Personnel Justification for "Using Ethics and User-Centered Design to Create Templates for EHR-Mediated Return of Genetic Test Results"

Diane M. Korngiebel, DPhil, Principal Investigator (Year 1: EFFORT months; Year 2: EFFORT months)

Dr. Korngiebel is an Assistant Professor in the Department of Biomedical Informatics and Medical Education and an Adjunct Assistant Professor in the Department of Bioethics and Humanities in the School of Medicine at the University of Washington. She is the recipient of a K01 Mentored Career Development Award from NHGRI (2014-2019) focused on the implementation of screening for Lynch Syndrome, an inherited cancer syndrome. The current proposal addresses issues complementary to the research undertaken with the K01 funding. Dr. Korngiebel has expertise in qualitative analysis techniques with a focus on the ethical issues surrounding the clinical implementation of genomic medicine and the use of technology in delivering care. She is certified in User-Centered Design. She is active in the University of Washington Biomedical Research Integrity Program, the Precision Medicine Informatics Group, and the Center for Leadership and Innovation in Medical Education. As the Principal Investigator, Dr. Korngiebel will lead all generative data collection and analysis activities in Year 1 and will lead design, program, evaluation (including formal data collection and analysis on patient feedback) and prototype revision activities in Year 2 when she will also have the help of a graduate research assistant. She will direct all administrative-related activities necessary for achieving the aims of the study.

Lynne Robins, PhD, Co-Investigator (Year 1: EFFORT months)

Dr. Robins is a Professor in the Department of Biomedical Informatics and Medical Education, with a joint appointment in the Department of Anesthesiology and Pain Medicine and adjunct appointments in the Departments of Family Medicine and Pediatric Dentistry in the Schools of Medicine and Dentistry at the University of Washington. She has doctoral training in anthropology and linguistics and over 25 years of experience applying qualitative research methods to inform the design, implementation, and evaluation of community-based health interventions, curricula, and performance assessments. Dr. Robins has been a Principal Investigator or Co-Investigator on University of Washington grants funded by the Agency for Healthcare Research and Quality, the Health Resources and Services Administration, and the NIH on projects examining the effects of a variety of communication-based interventions targeting health professionals on patient health outcomes, patient safety, interprofessional practice, litigation rates, relationship development, trust, and satisfaction. She is the Director of the University of Washington's Teaching Scholars Program as well as the Center for Leadership and Innovation in Medical Education. Dr. Robins will assist Dr. Korngiebel in qualitative data collection and analysis in Year 1.

Stephanie Malia Fullerton, DPhil, Co-Investigator (Years 1-2: EFFORT months)

Dr. Fullerton is an Associate Professor in the Department of Bioethics and Humanities in the School of Medicine at the University of Washington. She is a bioethicist with doctoral training in human genetics and her research focuses on the ethical and social implications of genetic and genomic investigation, including the use of genetic information in patient care. She is active in the University of Washington Biomedical Research Integrity Program and the Electronic Medical Record and Genomics (eMERGE) Network. Dr. Fullerton will be responsible for reviewing study materials, particularly report prototype content, for accuracy and comprehensibility and will provide expert advice throughout both years of the study, including assisting Drs. Korngiebel and Robins in data analysis and the review of qualitative results and in prototype development activities.

Laura Amendola, MS, CGC, Licensed Genetic Counselor (Years 1-2: EFFORT months)

Ms. Amendola is a board-certified genetic counselor based in the Division of Medical Genetics in the School of Medicine at the University of Washington. Ms. Amendola has both clinical and research expertise in issues surrounding the return of genetic test results to patients. Ms. Amendola will be responsible for reviewing study materials, including report prototype content, for accuracy and comprehensibility, and will provide expert advice throughout the project. Dr. Korngiebel will supervise this position.

All salary calculations are based on an estimate of 3.00% annual escalation.

Graduate Student Research Assistant

We request support for a 50.00% appointment for a graduate research assistant from an appropriate department, such as the University of Washington Department of Human-Centered Design and Engineering, for three academic quarters in Year 2. The student will assist Dr. Korngiebel on Aim 3 in graphic design and high-fidelity prototype programming, evaluation, and iterative improvements. (Note that under the terms of the union contract with United Auto Workers 4121, graduate students are entitled to resident, in-state tuition during academic quarters in which a student holds an appointment of 50.00% or more, i.e., a “full-time” graduate student. Therefore, we also request tuition support for this student as described under “Tuition.”) Dr. Korngiebel, who has experience mentoring graduate research assistants (including one who recently completed a PhD in Public Health Genetics while supported by Dr. Korngiebel’s K01 Award), will supervise this position.

Fringe Benefit Rates

Fringe benefit calculations include workmen’s compensation, unemployment compensation, health plans, retirement plans, social security, and Medicare.

Employee Type	Benefit Rate
Faculty	24.9%
Professional Staff	32.5%
Graduate Student Appointments	18.4%

Facilities and Administrative Costs

The rate for recovery of facilities and administrative costs is set at 55.5% of modified total direct costs (MTDC) per the negotiated rate agreement signed 7-21-2017. (Under the terms of the agreement, equipment, capital expenditures, charges for patient care and tuition remission, rental costs, scholarships, and fellowships as well as the portion of each subcontract in excess of $25,000 are excluded from modified total direct costs.)

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 10/31/2018

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Tracking Number: GRANT12519791
Funding Opportunity Number: PA-17-446, Received Date: 2017-11-13T15:53:47.000-05:00

2. SPECIFIC AIMS

Health care systems must provide timely electronic access to genetic test results within the terms of HIPAA regulations to meet meaningful use requirements.[1] Genetic test results provided in-person by a genetics professional allow appropriate counseling and prompt clinical management decisions; however, health systems are responding to meaningful use requirements by delivering test results via patient portals linked to electronic health records (EHR). According to the U.S. government's Regional Extension Program, 73% of providers had EHRs in 2015.[2] The expansion of applications of genetic testing and the increased role of Health Information Technology raise questions for medical genetics about how to respect the information needs and preferences of diverse patients and address key content and process challenges: Should some (or all) genetic test results be posted only after the patient has received results in person; and if so, is a delay in availability of some (or all) results acceptable to patients? What information, how much, and in what format would support patient decision-making and improve patient engagement with their health information and, ultimately, improve patient health and wellness? **To ensure a patient-centered approach, patient input is needed to guide electronic reporting practices and templates.** Currently, patient input has not been solicited and their views and concerns explored.

The goal of this R21 is to define patient needs for delivery of genetic test results via patient portals. We will develop genetic test report prototypes leveraging User-Centered Design methodologies and that recognize patient needs may be different for positive results and negative results and may also vary depending on the severity of the condition. This exploratory project will be based at University of Washington Medicine (UW Medicine), a large geographically dispersed health care system that serves a diverse patient population in western Washington State. In 2006, UW Medicine implemented eCare, Epic software's patient portal module; over 260,000 patients are enrolled in eCare. Epic EHR software is used by 19 of the 20 top-ranked U.S. hospitals,[3] 190 million patients have health records in Epic,[4] and Epic's patient portal is the most used patient portal smartphone app.[5] Within this setting and context, we will explore patient views concerning the acceptability of receiving genetic test results via a patient portal. What characteristics might make genetic results different from other test results? What threshold elements should inform which results are appropriate for electronic delivery in lieu of in-person return? Which elements require in-person delivery? To accommodate a range of portal deployment options, we will create "blue sky," visionary report templates alongside Epic-friendly ones, and to gather diverse patient views, we will use stratified sampling methods to recruit from underrepresented groups.

Therefore, the **Specific Aims** are to:

Aim 1: ***Explore the views of 40 eCare users who have received via eCare both genetic results and non-genetic results concerning electronic return of results.*** Hour-long audio-recorded interviews will be conducted with UW Medicine patients to identify similarities and differences in the electronic return of genetic and non-genetic results. Each participant will have received via eCare at least one genetic result and non-genetic result to support questions exploring comparisons. To garner diverse opinions, eligible eCare users will be identified by CTSA informatics working with the UW eCare team and using stratified sampling.

Aim 2: ***Explore with 40 patients who have received genetic results via eCare their experience receiving those results and their views on their electronic return (10 patients each with positive results for pharmacogenomic findings, hereditary hemochromatosis, and colon cancer risk, and 10 with negative results).*** Data collection will comprise hour-long audio-recorded interviews focused on identifying severity thresholds and information and support needs for electronic return for each result group. UW eCare, Laboratory Medicine, and Medical Genetics will identify participants retrospectively.

Aim 3: ***Following User-Centered Design principles, conduct cognitive interviews with 42 eCare users and 42 non-users about the acceptability and ease of use of preliminary electronic prototypes of patient portal materials reporting genetic results.*** Prototype content will be based on findings from Aims 1 and 2, and comprise reports for examples participants defined as less concerning, more concerning, and very concerning as well as a negative finding report. Prototypes will be created using design software. Cognitive interviews using the prototypes will be administered in-person using a laptop. Patients will be identified by CTSA informatics with additional recruitment via the Family Medicine Clinic at Harborview Medical Center (where one-third of patients are minorities) to ensure the collection of diverse patient perspectives.

The proposed R21 will provide preliminary, timely **data on patient perspectives across diverse populations on the use of patient portals to return genetic results electronically** and will develop and evaluate prototype content starting with patient end users. Early evaluation of patient needs and preferences will help ensure that the deployment of genomic medicine addresses those needs and does not contribute to healthcare inequities.

3. RESEARCH STRATEGY

SIGNIFICANCE

As more genetic tests are used clinically, health systems will need to ensure that electronic return of results is appropriate, taking into account both meaningful use requirements and patient information needs and preferences for receipt and presentation of that information. Although there is a robust discussion on the return of genetic results,[6-8] including results of carrier screening,[9, 10] for research participants,[11-13] or of incidental findings,[14] and a growing literature studying patient portal usage,[15-17] there have been few studies concerning the return of genetic testing or screening results via patient portals.[18] With the national promotion of EHRs and an emphasis on their meaningful use, many test results are available through the portal within 2-4 days.[19] However, genetic results can be sensitive and difficult for patients to understand. Often results need to be interpreted carefully in terms of the patient's medical and family history; a negative result, for example, may have a different meaning depending on how strongly the patient's family history suggests the presence of an inherited disorder.[20] In addressing this challenge, patient views and preferences must be taken into account. In one study done as part of the Coriell Personalized Medicine Collaborative, Sweet and colleagues documented recipients' interest in a participant-driven approach that considers how results are delivered.[21]

Ensuring that portals are tailored to meet patient needs has the potential not only to ensure appropriate delivery of results but also to enable the use of patient portals to encourage appropriate follow-up.[22] For example, some studies demonstrate that patients respond to electronic reminders, sent through the portal, to schedule screenings and other preventive services.[23] While more research is needed, it is evident that some patient populations may require additional support to use portals[24, 25] and understand genetic test results.[26] In particular, patients from minority groups[27] and those with limited health literacy may need engagement methods that assist them in effective portal and information use.[26, 28-30] Patient preferences for the return of negative test results generally exhibit more openness to "impersonal" return (e.g., via secure messaging) than for results that are not normal; however, patient preferences vary greatly and as noted above, negative genetic results may have nuanced implications.[31, 32] This exploratory project will use an innovative multi-step approach to assess patient views about electronic return of genetic results and, using that data, create prototype templates for results return.

INNOVATION

Most technological interventions that seek to address ethical issues do not use an ethical framework or seek to develop one. Our innovative approach considers the ethical issues that might accompany the electronic return of genetic (and other) test results. The study team will iteratively develop a "Points to Consider" framework (see Figure 1) that will be refined throughout the project's data collection activities.

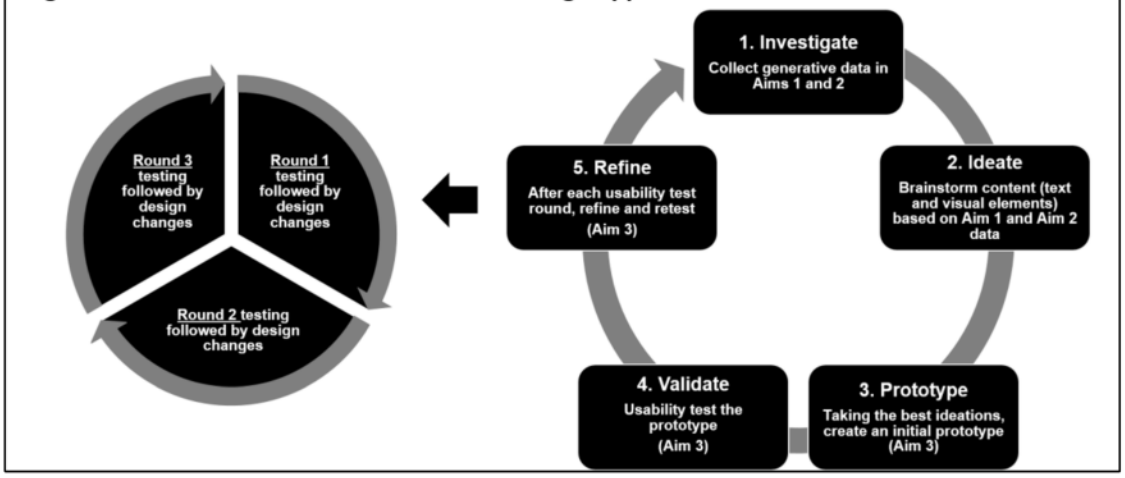
Figure 1. Points to consider for returning genetic results electronically (initial framework)

Beneficence and non-maleficence	Respect for autonomy	Justice and equity
• Are results likely to cause worry? • What are the implications for family members? • Is a particular mode of return, content, or presentation likely to benefit the patient more? • Is a particular mode of return, content, or presentation likely to harm the patient more? • Does the mode of return support (or undermine) the clinician-patient relationship?	• What is the patient's preferred mode of return? • Does the mode of return and content support informed decision making? • Can results be returned in a culturally sensitive manner? • Does the mode of return enable or support appropriate family communication?	• Can accommodation be made for patients with low Information Technology literacy and/or limited electronic access? • Can results be conveyed in ways that accommodate different levels of health literacy? • Do some modes of return require additional support to avoid healthcare delivery inequity? • How should use of limited resources be considered?

In addition, taking lessons from successful software creation and implementation in industry, this project follows the process and methods of User-Centered Design (see Figure 2). Our User-Centered Design (UCD) approach engages patient end users through formal generative and formative data collection and analysis (Aims 1 and 2) before the interventions (represented by the prototypes) are even created, and we continue to leverage patient expertise and input through iterative prototype design and formal evaluation (Aim 3). This level of early-stage participatory research with patients is rarely invoked in biomedical research in the Health Information Technology (HIT) space. This project will demonstrate how a UCD approach can be tailored in a healthcare delivery context, while maintaining the high levels of rigor desired in biomedical research. We will collect qualitative, generative data from diverse patients to inform high-fidelity sample reports (i.e., electronic prototypes) that patients can then interact with to provide further feedback **before** time and resource investments are made, such as those needed for broader piloting to establish validity or, ultimately, to evaluate outcomes. Prototypes, a key element in UCD, support innovation in three areas. First, prototypes serve as data collection aids. When users can respond to a

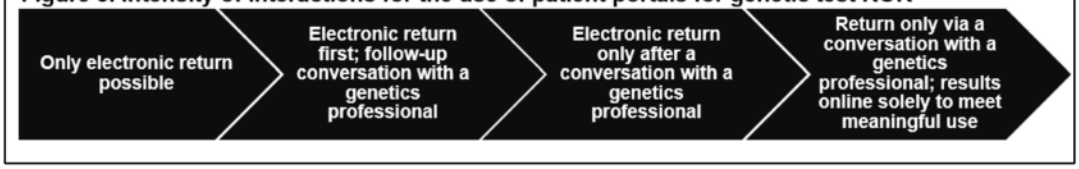
product in an early stage of development, one can gather more specific feedback across both content and presentation and make revisions at a development stage when it is less costly to do so. Second, prototypes help in disseminating results; they can inform HIT professionals and software developers in ways that a list of best practices cannot—because prototypes reify those best practices and provide blueprints for product creation. Third, prototypes provide a starting point of engagement and discussion for follow-up studies. For example, prototypes created during this project can be further refined with clinicians, including primary care providers, and HIT professionals as part of a larger follow-up project.

Figure 2. Process chart for User-Centered Design approach in Aims 1-3



Furthermore, **there has been little research conducted around patient views on the return of genetic results via an electronic patient portal**. Unlike other lab tests, genetic results are often considered inherently sensitive and unsuitable for electronic delivery as the primary means of return (versus displaying the results electronically after in-person delivery by a clinician). However, in practice, some genetic results are deemed more sensitive than others. Reflexive tumor testing to guide cancer treatment is done as a matter of course with minimal genetic counseling and results duly available among portal lab results. The same is also true of pharmacogenomic results, which are routinely entered into a patient's record and available for viewing. Starting from the patient perspectives, which are rarely considered in early health intervention design phases, this project will evaluate thresholds for what should or should not be returned electronically, patient preferences concerning what content is included when results are returned (including visual representation of data), what elements would engage patients and promote follow-up as needed, and how electronic materials could be crafted in ways that are broadly accessible and understandable to a diverse patient population. We will explore a range of interaction possibilities for electronic ROR (Figure 3). Taken together, this study employs a novel combination of the qualitative methods used in bioethical inquiry,[33, 34] an analytic clarification of emerging bioethical concerns in this new area,[35, 36] and the UCD methods used in industry for formative and user experience (UX) research in product development.[37, 38] These elements create an innovative and rigorous approach to developing methods for electronic delivery of genetic results to patients, an emerging and understudied problem that is of growing importance for healthcare systems.

Figure 3. Intensity of interactions for the use of patient portals for genetic test ROR



APPROACH

Overview. Traditional bioethical approaches have emphasized the importance of stakeholder perspectives in the development of innovative practice.[39-41] This project will seek the views of patients, who represent a key stakeholder group in the development of patient portal content, and will complement Dr. Korngiebel's current work on clinician stakeholder views on the implementation of genomic medicine (see Preliminary Results below). The project employs UCD, a method and a philosophy that places the user at the center of product or service creation.[38] The majority of patient portals are add-ons to commercial EHR software packages; often they are designed without patient or clinician input.[42, 43] In the era of precision medicine, HIT will become a crucial means to involve patients in managing their health information and engaging in their own healthcare.[44] Our UCD approach engages patient end users in creating and evaluating report templates to meet their information needs.

Multi-disciplinary investigative team and advisory board. The principal investigator, Dr. Korngiebel, is a social scientist and qualitative researcher with experience in bioethical inquiry in several domains, with a focus on the delivery of genomic medicine. She is the recipient of a K01 Mentored Career Development Award from

NHGRI for the project "Ethically responsible clinical decision support for Lynch Syndrome screening." The current proposal addresses issues complementary to her K01 research and draws upon its preliminary findings. In addition, Dr. Korngiebel is certified in User-Centered Design through the University of Washington's innovative Department of Human-Centered Design and Engineering. She is trained in formative data collection and analysis, creating low- and high-fidelity electronic prototypes using design software, and usability testing. Her co-investigators each bring complementary expertise to the project. **Dr. Lynne Robins has over 25 years of experience applying qualitative research methods** to inform the design, implementation, and evaluation of community-based health interventions, curricula, and performance assessments. **Dr. Malia Fullerton is a bioethicist with doctoral training in human genetics**; her research focuses on the ethical and social implications of genomic medicine and the use of genetic information in patient care. **Ms. Laura Amendola is an experienced board-certified genetic counselor** and has collaborated on many genomic research projects, including working with the Clinical Sequencing Exploratory Research (CSER) consortia. The study team will be supported by an advisory board to ensure accuracy of report prototypes and to assist in participant recruitment across all three aims. The advisory board will convene twice yearly to review findings and progress. Dr. Korngiebel will also consult with board members as needed and has engaged three outside experts to review prototypes developed as part of this study (see letters of support) to enhance generalizability outside of the UW Medicine system. Consultants represent both high and low portal use settings. Dr. Korngiebel will also have access to her K Mentoring Committee. **Of the 10 advisors to the project, 8 are clinicians** (Table 1). Patients will be represented throughout the process following UCD methods.

Table 1. Project advisors

Advisory Board Members	
Frederick M. Chen, MD	Director, Family Medicine Clinic, Harborview Medical Center
Jane Fellner, MD	Director, Ambulatory IT Services, UW Medicine
Gail Jarvik, MD, PhD	Professor and Head, Division of Medical Genetics
Brian Shirts, MD, PhD	Director, Informatics, Genetics, Solid Tumor Divisions, Laboratory Medicine
Electronic Prototype Consultants	
Josh F. Peterson, MD, MPH	Assoc. Prof., Biomedical Informatics, Vanderbilt University School of Medicine
Brandon Welch, PhD	Asst. Prof., Public Health Sciences, Medical University of South Carolina
Marc S. Williams, MD	Director, Genomic Medicine Institute, Geisinger Health
K Mentoring Committee	
Wylie Burke, MD, PhD	Professor, Bioethics & Humanities
Peter Tarczy-Hornoch, MD	Chair & Professor, Biomedical Informatics and Medical Education
Jan Carline, PhD	Professor, Biomedical Informatics and Medical Education

Consideration of relevant biological variables.

We will use stratified sampling to address age, gender, and race and ethnicity across all aims (Table 2) to enable qualitative exploration of differences in responses.

Table 2. Participant distribution by age, gender, and race and ethnicity

	Aim 1 participants	Aim 2 participants	Aim 3 participants
Age	6 aged 18-30 years; 17 each age range: 31-50 and > 50	6 aged 18-30 years; 17 each age range: 31-50 and > 50	20 aged 18-30 years; 32 each age range: 31-50 and > 50
Gender	20 male; 20 female	20 male; 20 female	42 male; 42 female
Race	≥ 13 non-White or Hispanic	≥ 13 non-White or Hispanic	≥ 28 non-White or Hispanic

PRELIMINARY STUDIES

As part of her K01, Dr. Korngiebel asked clinicians (medical geneticists, genetic counselors, oncologists, gastroenterologists, pathologists, and primary care providers) for their views on returning Lynch Syndrome screening results via a patient portal and their recommendations for content. Most felt that sensitive test results need a personal return and should not initially be returned electronically, but there was no consensus on which genetic results should be considered sensitive.[22] Dr. Korngiebel also participated in a CSER project (PI Goddard) that developed categories (rather than individual conditions) to guide returning genetic results for reproductive planning, exploring the views of ethicists, clinicians, and patients.[10] Conditions were defined by attributes that resonated with patients: whether a condition was controllable, predictable, visible, severe, or adult onset.[9] This project and Dr. Korngiebel's own data provide the framework for the results categories explored in Aim 2.

RESEARCH DESIGN: AIM 1 Explore the views of 40 eCare users who have received via eCare both genetic results and non-genetic results concerning electronic return of results.

Aim 1 focuses on understanding **how diverse patients would want to receive genetic test results electronically** and explores **what elements make genetic results different** from non-genetic test results.

Participants. To ensure the prototypes are useful to a broad range of potential patient end users who can speak from direct experience on their use of portals to receive test results, we will recruit eCare users using stratified sampling across gender, age, and race and ethnicity (see Table 2). To achieve a diverse patient interview cohort, participants will be recruited using the informatics services of the University of Washington's Clinical and

Translational Science Award (CTSA) institute with assistance from the UW Medicine eCare team. Each participant must have received via eCare at least one genetic result and one non-genetic result to support questions exploring comparisons. Other eligibility criteria for this exploratory R21 will include that participants must be English-speaking (eCare is in English currently), have been patients in the UW Medicine system for at least the last 24 months, have had a patient visit within the last 12 months, and are enrolled in eCare and have used at least one of its functions (e.g., viewing test results) in the last 12 months. Currently, 39% of patients seen in the last 12 months use eCare and of those 35% have logged in over the last 3 months; over 262,600 patients are enrolled overall. Potential participants will be contacted via email, telephone, or postal mail based on their preferences. We expect to recruit up to 40 participants for hour-long interviews. This is a large number of participants for a qualitative aim that focuses on a single major theme, genetic vs. non-genetic test results and their electronic return; however, we feel it is justified to collect diverse views, explore similarities and differences in depth, and gather information sufficient to guide the study team in refining the Points to Consider framework. Interviews will cease when diversity recruitment goals have been met and the research team judges that idea saturation concerning major differences has been achieved (i.e., no new content is being suggested). Participants will receive a $50 incentive following usability guidelines for compensation for non-professionals.[38]

Data collection. Hour-long audio-recorded interviews will be conducted with UW Medicine patients to identify similarities and differences in the electronic return of genetic and non-genetic results. Interviews will be conducted using a semi-structured protocol[34] (either in person or via telephone per patient preference) developed by the study team and reviewed by the Advisory Board. Participants will be asked questions concerning their experience receiving genetic and non-genetic results, their use of eCare, their ideas concerning genetic results thresholds for electronic return, and their thoughts on what would make electronic results more usable and accessible. (See Appendix section 16.A for potential domains and some potential questions for data collection interviews; this table is not intended to be final or exhaustive as final data collection instruments will be determined by the study team, advisory board, and insights from pilot interviews.) Individual interviews will allow issues to be explored confidentially while enabling the interviewer to adjust the interview to explore new issues. Pilot interviews will ensure the protocol captures the data required. Interviews will be audio-recorded, transcribed, de-identified, and the transcripts checked for accuracy.

Data analysis. We will use inductive and deductive analysis methods leveraging *a priori* coding categories informed by preliminary work around thresholds[9, 10] while accommodating new themes that arise from the data.[45] Coded data will be analyzed via directed content analysis,[46] in which two coders will code all transcripts and will periodically review and clarify all coding. Both coders will perform thematic analysis to capture themes across coding categories and discordant interpretation will be resolved by consensus.[47] Qualitative analysis software, Atlas.ti, will be used to assist in the organization of themes, codebook creation, and the coding of transcripts. Drs. Korngiebel and Robins, both experienced qualitative researchers, will perform the data analysis. The study team and Advisory Board will review findings. Data analysis will identify the elements most crucial in determining severity thresholds, including in the context of comparing genetic electronic results return with non-genetic results. The study team will refine the initial Points to Consider framework (Figure 1) based on these insights.

RESEARCH DESIGN: AIM 2 Explore with 40 patients who have received genetic results via eCare their experience receiving those results and their views on their electronic return (10 patients each with positive results for pharmacogenomic findings, hereditary hemochromatosis, and colon cancer risk, and 10 with negative results).

Aim 2 focuses on the experiences of **patients who have received genetic test results electronically** and will explore results that range from negative to very concerning (see Figure 4) and what elements an electronic report should address for nuanced or complex results—or even whether a portal can adequately return such results.

Figure 4. Rationale for Aim 2 results categories (adapted and modified from Leo, et al.)[9]

Mild: PGx and negative results	Moderate: Hemochromatosis	Serious: Colorectal cancer risk
PGx: Improve medications or targeted drug therapies Negative: Results are "good" but nuanced	Usually begins in middle age Treatable with regular, well-established, low-risk intervention	Many factors at play including consequences for patient and family with potential impacts on physical and psychosocial wellness

Participants. To maximize the range of viewpoints, the study team will recruit participants with four types of genetic test results (negative results, and positive results that range from mild to moderate to high concern, represented by pharmacogenomics (PGx) results, a hemochromatosis diagnosis, and identification of inherited colon cancer risk, respectively). This initial categorization draws upon a taxonomy of testing categories validated

in a previous CSER study involving preconception carrier screening.[9] It will be refined based on Aim 2 findings. The study team will recruit up to 40 participants, ten for each result category, and will use stratified sampling to address biological variables (see Table 2). PGx test results will be used as the least concerning example because they are consistent with normal health and used to improve use of medications. Hereditary hemochromatosis was chosen to represent the mid-range of concern because although life-altering, it has a readily available safe and effective treatment (i.e., regular phlebotomies); it also introduces the complexities of identifying potential at-risk family members.[48, 49] Colon cancer risk was chosen as a very concerning result because it has substantial implications for patients and their at-risk family members.[50] Finally, negative genetic results (for any heritable risk-related genetic test) are included to explore possible misinterpretations[51] as such results are nuanced, often taking into account personal and family health history. Due to the limited resources of an exploratory R21, eligible participants must be English-speaking (eCare is only available in English), and have received genetic test results within the last 12 months; they will be identified retrospectively by the UW eCare team, Laboratory Medicine, and Medical Genetics with assistance from Drs. Fellner, Jarvik, and Shirts. Participants will each receive a $50 incentive. Aim 2 participants will not overlap with Aim 1 participants.

Data Collection. Hour-long interviews will be conducted (in person or via telephone per patient preference) using a semi-structured protocol developed by the study team and reviewed by the Advisory Board. Participants will be asked about their use of eCare, their experience receiving genetic results, and their thoughts on what makes results appropriate or inappropriate for electronic return, and when it is acceptable or unacceptable to provide results without accompanying in-person counseling. Piloting will ensure the protocol captures the data required. (See Appendix 16.B for sample domains. Note these are not final or exhaustive. Final instruments will be determined by the study team and advisory board and informed by Aim 1 data and pilot interviews.) Interviews will be audio-recorded, transcribed, de-identified, and the transcripts checked for accuracy.

Data Analysis. Drs. Korngiebel and Robins will lead the data analysis, following the methods outlined above for Aim 1. The data analysis report will identify the appropriate role of electronic return of genetic results and will explore elements most crucial in determining ROR concern thresholds, based on patient reports of their direct experience. As part of the data analysis, and combined with Aim 1 findings, the study team will further refine the Points to Consider framework (Figure 1). All data will inform Aim 3 prototype development.

RESEARCH DESIGN: AIM 3 Following User-Centered Design principles, conduct cognitive interviews with 42 eCare users and 42 non-users about the acceptability and ease of use of preliminary electronic prototypes of patient portal materials reporting genetic results.

This aim's focus is on evaluating and iteratively improving electronic prototypes for returning genetic test results. The study team will **create two prototype exemplars, one Epic-style and one "blue sky," for the results categories** for a total of 6-8 prototypes. The choice of Epic-style prototypes reflects the software's high use among healthcare systems; including prototypes without software-determined constraints (blue sky) will support adaptation to non-Epic healthcare systems. Prototype content will be based on findings from Aims 1 and 2 and study team guidance and will be revised following UCD data collection and analysis approaches. Prototypes are expected to contain textual and graphic information concerning test results and their interpretation, next steps, and direction to quality online resources (e.g., the American Society of Clinical Oncology's Cancer.net).[52]

Participants. Participants will be recruited using stratified sampling across biological variables (see Table 2). Usability experts recommend focusing on key areas of known or anticipated diversity;[38] therefore, non-users of eCare are included for valuable feedback in two areas: 1. They will not have been primed for genetic test results before "receiving" a prototype report; this will allow the study team to explore whether the portal can function as a substitute for in-person return or if—and when—a supplementation role is more appropriate and 2. Non-users will provide insights on usability as completely novice portal users. Usability industry standards recommend testing with 5 users, preferably across at least three iterative phases based on average problem discovery rates.[53] To increase discovery rates, we will recruit 28 users for each of three iterative testing phases (**total n=84**) with each user reviewing 3-4 prototypes; this raises the minimum discovery rate to over 98% (mean 99.6%)[54] for each participant type, eCare user or eCare non-user. Each prototype will be reviewed by the same number of participants, half eCare users and half non-users. There will be no repeat participants across testing rounds to avoid priming, and the order in which the prototypes are presented to each participant will vary to counter-balance participant learning prototype functions and information presentation.[37] Dr. Korngiebel will leverage the Family Medicine Clinic at Harborview Medical Center, a hospital-based safety net clinic with low eCare enrollment where over one-third of patients comprise minority groups. Additional participants will be identified by CTSA informatics and UW Medicine eCare. Each participant will receive a $50 incentive for an hour-long session.

Data collection and analysis. UCD usability research methods draw upon ethnography and cognitive science and include interviews, think-aloud studies (e.g., cognitive interviews), and the use of mental models (e.g., the process of decision-making).[55] A 2011 report by the Institute of Medicine (IOM) recognizes the validity of usability testing methods as an evidence-based approach to HIT evaluation.[56] Following IOM recommendations and UCD methods, we will use "think aloud" cognitive in-person interviews[57] to collect data from diverse patient users using interactive prototypes. This research will include a focus on user experience (UX), so that "issues" identified go beyond does-it-not-break to explore whether the templates provide the experience that the user expects, desires, and values. Interviews will include tasks for users to perform using the prototypes via a laptop computer, e.g., "Based on this report, identify what next steps are recommended for you." (See Appendix 16.C for potential domains and sample questions for Aim 3 interviews. These are not final or exhaustive. Final instruments will be determined by the study team and advisory board and informed by Aim 1 and 2 data.) Data analysis and subsequent refinements will occur between interview rounds. Because of this iterative approach, questions may evolve from round to round. The protocol for the first round of interviews will be piloted and piloted before each round if it changes significantly. After each round, Dr. Korngiebel will analyze the data following UCD usability guidelines (including standards for quantitative analysis of small sample sizes) to determine redesign priorities.[37] The study team will review proposed changes each round to ensure accuracy and to achieve consensus in cases of disparate feedback. After this process, Dr. Korngiebel and her graduate assistant will revise the prototypes. After Round 2 testing and revisions, external consultants (see Table 1 and letters of support) will conduct heuristic expert walkthroughs and review the prototypes with revisions based on their feedback made before Round 3 testing. The Points to Consider framework will be revised to reflect Aim 3 findings.

EXPECTED OUTCOMES

The main outcomes are: 1. **Electronic patient-centered prototypes** to return genetic test results to patients will have been created. Prototypes serve as starting points and engagement aids for follow-up studies with clinicians, including PCPs, HIT professionals, and EHR designers to further refine and tailor the results templates to meet clinical and health setting requirements and needs. 2. **A bioethics "points to consider" model** for returning genetic results electronically will have been developed and disseminated. 3. **Publications on how patients use, and would want to use, patient portals in the context of genomic medicine** to improve their and their families' health. This data can inform patient engagement for genetic and non-genetic electronic ROR. Prototypes and the framework would be available for download on Dr. Korngiebel's department website.

TIMELINE

Activity		Quarters	1	2	3	4	1	2	3	4
Aim 1:	Collect patient views of ROR for genetic vs. non-genetic tests									
	Analysis of patient data of ROR for genetic vs. non-genetic tests									
Aim 2:	Collect patient views re: genetic test results received electronically									
	Analysis of data from patients re: their electronic ROR									
Aim 3:	Creation and Round 1 testing of initial ROR prototypes									
	Revision of prototypes, Round 2 testing, consultant review									
	Revision of prototypes and Round 3 testing									

POTENTIAL PROBLEMS AND ALTERNATIVE APPROACHES

It is possible that underrepresented groups will tend to be non-users of eCare. This, in itself, would be an important finding and would point to follow-up research to explore and address issues related to equitable access to genetic test results delivered electronically. To ensure that the views of these groups are represented in the data, the study team has several recruitment strategies, such as in-person recruitment and same-day data collection and prioritizing underrepresented groups in CTSA, eCare, and clinic data pulls to identify participants. For Epic compatibility, Dr. Fellner and her team will review Epic prototypes, and to support generalizability beyond UW Medicine, both Epic-similar and blue sky prototypes will be reviewed by external consultants (see Table 1 and letters of support). We may discover that portal return for certain results (e.g., those in the serious category) should only be supplemental; our final ethical framework and prototypes would reflect this finding.

FUTURE DIRECTIONS

The future of the return of many genetic test results will be via electronic means. The next iteration of the prototypes would use UCD co-production methods for revisions informed by clinicians, HIT professionals, and other key stakeholders. Patient customization preferences can be explored. In a larger study, refined prototypes can be converted into fully functioning reports—with report sets created with and for non-English speakers—and tested among diverse patients. Investigations can include institutions and clinics where portal use is high and where it is low to explore engagement strategies and create a deployment and evaluation plan informed by implementation science. Reports could be piloted with diverse patients and multiple sites to investigate if UCD-created genetic reports improve patient engagement, and ultimately, the health of patients and their families.

5. PROTECTION OF HUMAN SUBJECTS

5.1 RISKS TO HUMAN SUBJECTS

Human Subjects Involvement, Characteristics, and Design

The subject population will comprise patients of the UW Medicine network. We anticipate conducting qualitative interviews with up to 180 patients ranging in age from 18-75. (This number includes interviews to pilot data collection instruments.) Health status will not be a recruitment criterion; however, receipt of particular test results will be, as described in the research strategy. These results may be indicative of a health status (e.g., high cholesterol), but health status itself is not a criterion for recruitment. We are planning on conducting some recruiting in clinic waiting rooms before or after appointments, particularly for Aim 3. Participants will be recruited based on their use (Aims 1, 2, and 3) or non-use (Aim 3) of UW's patient portal, eCare, in keeping with collecting data from portal users and non-users as indicated in the research strategy.

Sources of Material

Data collected from participants will comprise audio-recorded interviews that are transcribed and de-identified. Whether participants are enrolled in eCare or not will be contained in their patient appointment notes; we will ask clinic front desk personnel to share this with us when we conduct waiting room recruitment. Information concerning eCare enrollment will also be available for patients recruited through the Institute of Translational Health Sciences (ITHS) Biomedical Informatics core's Amalga database. We will apply for a HIPAA waiver in order to access this data.

Potential Risks

Risks to participants will be minimal as interviews will be de-identified; however, there is the possibility that, for Aim 3, other people in the waiting room area may note that some patients are being approached while others are not. Participants may provide information that identifies someone (e.g., a family member) not enrolled in the study, which would breach third-party confidentiality and possibly pose a reputational risk; this risk is small. In addition, there may be sensitivity around discussing with patients their experience of receiving positive results for heritable colorectal cancer risk. Overall, the anticipated physical, psychological, social, or legal risks are minimal.

5.2 ADEQUACY OF PROTECTION AGAINST RISKS

Recruitment and Informed Consent

Participants will either be recruited waiting-room style or via letter, phone, or email (based on patient contact preferences) by a trained research coordinator. Informed consent will include conveying to participants the procedures for the study (i.e., interviews), the privacy measures that will be in place (i.e., interviews will be de-identified; the data will be kept in a secure place and destroyed at the close of the study; and only members of the research team will have access to the data), and the risks and benefits of the research. The information sheet used to recruit participants will also describe these methods and the risks and benefits. We will ask for Institutional Review Board approval to waive written documentation of consent as maintaining that connection to participants would present a risk of identifiability. Participants will be assured that they can stop participating in the project at any time. Key informant interview transcriptions and audio records will be carefully excised of any identifying data pertaining to participants or in the information they share.

Protections against Risk

Data collected from participants will comprise audio-recorded interviews that are transcribed and de-identified. Any identifying information (e.g., names collected for the purpose of disbursing and tracking modest thank-you incentives) will be stored securely and separately. Study data will be kept on a secure server or password-protected computer or in a locked cabinet, as appropriate, and only members of the research team will have access to this data. Interview questions should not cause discomfort; we will not be asking about anything more sensitive than opinions. However, there is always the risk of discomfort when discussing health-related issues, including heritable colon cancer risk, and some people may find being audio-recorded uncomfortable. If participants find any aspect of their involvement in the research study psychologically or otherwise uncomfortable, they will be encouraged to discontinue participation and directed to help should that be needed. To mitigate the risk posed by participants in identifying a third-party during interviews, participants will be reminded at the start of interviews not to provide identifying details. Should such details be shared, that information will be removed from the audio record and will not appear in the redacted transcription. We do not anticipate that there will be incidental findings uncovered as a result of this research.

5.3 POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO HUMAN SUBJECTS AND OTHERS

There is minimal risk to participants and the risk is reasonable in relation to the anticipated benefits: the identification of issues related to the return of genetic test results electronically via an Electronic Health Record's patient portal or other electronic portal (e.g., a link in the report to an external web site). None of the participants will benefit directly; this will be stated in the patient information sheet used for recruitment. We expect study results might inform how genomic medicine is delivered and how portals can better foster patient engagement with the ultimate goal of improving health.

5.4 IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

The expected knowledge will be in two complementary areas: exploring how to tailor genetic test reports for dissemination electronically via a patient portal and investigating ethical "points to consider" when returning genetic test results electronically—both among a diverse patient base. There is some evidence that use of patient portals could support improved health outcomes. Precision genomic medicine will have the most positive effect when patients are activated by their health knowledge, but we currently do not know how to best support this in an electronic return-of-results setting nor do we know how electronic return of potentially fraught results affects patient views on appropriate modes for results return.

7. INCLUSION OF WOMEN AND MINORITIES

In order to include a substantial exploration of gender, and race and ethnicity as study variables, we will make every effort to include women (half of all participants) and minorities (i.e., using stratified sampling to achieve 30% of participants from minority populations and underserved communities) when recruiting for Aims 1-3 data collection activities. We have increased the likelihood of recruiting women and underrepresented and underserved populations by using the services of the University of Washington's CTSA's biomedical informatics services (for Aims 1, 2, and 3) and by leveraging the Family Medicine Clinic at Harborview Medical Center (Aim 3) when conducting recruitment.

7.1 PLANNED ENROLLMENT DISTRIBUTION

Although a qualitative study with a relatively small *n* (up to 164 participants for non-piloting data collection) across all 3 aims, the planned enrollment distribution reflects an emphasis on recruiting women and those from underserved populations. We will recruit 50% women participants and approximately one-third of participants from non-white racial and ethnic categories as shown in the Planned Enrollment Tables in the PHS Inclusion Enrollment Report.

7.2 SUBJECT SELECTION CRITERIA

We are seeking input from a wide range of potential recipients of genetic test results and potential users of Electronic Health Record patient portals. We will collect racially and ethnically diverse input by recruiting approximately one-third of participants from non-white or Latino populations. There is no particular disease or condition under study, although Aim 1 focuses on those who have received genetic and non-genetic test results and Aim 2 focuses on those who have received genetic test results for specific conditions (pharmacogenomic, hereditary hemochromatosis, and colon cancer risk) or negative genetic results. Interviews will be about how test results were returned to them, not about the conditions themselves. This is generative research to inform the creation of templates to return genetic test results electronically via a patient portal.

7.3 RATIONALE FOR PROPOSED SAMPLE

We are not excluding any sex/gender or racial or ethnic group as potential participants. On the contrary, we are seeking to over-represent underrepresented participant groups. Because the portal (eCare) is only deployed in English currently, and because this is an exploratory R21, we will recruit English-speaking participants only. However, a larger follow-up study should also explore electronic return of results among non-English speaking population groups.

7.4 PROPOSED OUTREACH PROGRAMS FOR RECRUITING DIVERSE PARTICIPANTS

We have specifically chosen to use the services of the Institute of Translational Health Sciences Biomedical Informatics core to assist in identifying diverse participants (Aims 1, 2, and 3) and to partner with Harborview Medical Center's Family Medicine Clinic (which has a diverse patient population) to ensure we reach recruitment goals. Having consulted with Dr. Frederick Chen, the Director of the Harborview Family Medicine Clinic, the Biomedical Informatics core of the Institute of Translational Health Sciences, and Dr. Jane Fellner, Director of Ambulatory IT Services for UW Medicine, we do not anticipate difficulties meeting our planned recruitment (see letters of support).

PHS Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

OMB Number:0925-0001 and 0925-0002
Expiration Date: 10/31/2018

***Study Title:** Using Ethics and User-Centered Design to Create Templates for EHR-Mediated Return of Genetic Test Results

***Delayed Onset Study?** ❑ Yes ☑ No

If study is not delayed onset, the following selections are required:

Enrollment Type ☑ Planned ❑ Cumulative (Actual)

Using an Existing Dataset or Resource ❑ Yes ☑ No

Enrollment Location ☑ Domestic ❑ Foreign

Clinical Trial ❑ Yes ☑ No

NIH-Defined Phase III Clinical Trial ❑ Yes ☑ No

Comments: We will use stratified sampling to ensure that one-third of participants represent under-served ethnic or racial groups as these groups have been underrepresented in genetic studies and in research concerning the use of electronic patient portals.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	2	2		0	0					4
Asian	9	9		0	0					18
Native Hawaiian or Other Pacific Islander	2	2		0	0					4
Black or African American	7	7		0	0					14
White	54	54		8	8					124
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	74	74		8	8					164

Report 1 of 1

Funding Opportunity Number: PA-17-446. Received Date: 2017-11-13T15:53:47.000-05:00

8. INCLUSION OF CHILDREN

No children will participate in this study because children would not possess the experience needed to participate in the research topic to be studied, issues around receiving genetic research results electronically via a patient portal. Therefore, the exclusion criterion that the research topic to be studied is not relevant to children applies.

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