Protocol Details

Basic Info

Confirmation Number:	**cbjecjbd**
Protocol Number:	**825821**
Created By:	**HERMAN, DANIEL S**
Principal Investigator:	**HERMAN, DANIEL S**
Protocol Title:	**Development of computational strategies for diagnosis, prognosis, and management of cardiovascular disease**
Short Title:	**Prediction of cardiovascular disease**
Protocol Description:	**This proposal is to collect clinical data to develop new methods for the predication of cardiovascular disease. This study will be observational, using clinical data collected as part of standard practice. We will not be directly recruiting patients or collecting biospecimens.**
Submission Type:	**Biomedical Research**

Resubmission*
Yes

Study Personnel

Principal Investigator

Name:	**HERMAN, DANIEL S**
Dept / School / Div:	**4521 - PA-Pathology & Laboratory Medicine**
Campus Address Mail Code	**6082**
Address:	**PATH&LAB MED - M163 JM** **3620 HAMILTON WALK**
City State Zip:	**PHILADELPHIA PA 19104-6082**
Phone:	
Fax:	
Pager:	
Email:	**Daniel.Herman2@uphs.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	**08/04/2017**
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**

Study Contacts

None

Other Investigator

None

Responsible Org (Department/School/Division):

4521 - PA-Pathology & Laboratory Medicine

Key Study Personnel

None

Disclosure of Significant Financial Interests*
Does any person who is responsible for the design, conduct, or reporting of this research protocol have a **FINANCIAL INTEREST**?
No

Certification
I have reviewed the *Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials* and the *Financial Disclosure Policy for Research and Sponsored Projects* with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

Biomedical Research

Investigator Initiated Trial
Is this an investigator-initiated trial?
No

Drugs or Devices*
Does this research study involve Drugs or Devices?
No

IND Exemption

For studies that fall under an IND exemption, please provide the number below

For studies including IND or IDE's, please provide the number(s) below

IDE Review*
NOTE: For research involving investigational devices, you are required to review the guidance on Managing Research Device Inventory. Consult the Penn Manual for Clinical Research: https://somapps.med.upenn.edu/pennmanual/secure/pm/investigational-product-management Please check the box Yes if you have reviewed the guidance.
No

Research Device Management*
Please indicate how research device(s) will be managed.
Not Applicable (no investigational devices)

Drug, Herbal Product or Other Chemical Element Management *
Please indicate how drugs, herbal products or other chemical entities will be managed.
Not Applicable (no drugs, herbal products or other chemical entities)

Radiation Exposure*
Are research subjects receiving any radiation exposure (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.) that they would not receive if they were not enrolled in this protocol?
No

Gene Transfer*
Does this research involve gene transfer (including all vectors) to human subjects?
No

Human Source Material*
Does this research include collection or use of human source material (i.e., human blood, blood

products, tissues or body fluids)?
No

CACTIS and CT Studies*
Does the research involve Center for Advanced Computed Tomography Imaging Services (CACTIS) and CT studies that research subjects would not receive if they were not part of this protocol?
No

CAMRIS and MRI Studies*
Does the research involve Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS) and MRI studies that research subjects would not receive if they were not part of this protocol?
No

Investigational Agent or Device within the Operating Room*
Does the research project involve the use of an investigational agent or device within the Operating Room?
No

Cancer Related research not being conducted by an NCI cooperative group*
Does this protocol involve cancer-related studies in any of the following categories?
No

Processing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

In-House Manufacturing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

Medical Information Disclosure*
Does the research proposal involve the use and disclosure of research subject's medical information for research purposes?
Yes

If the answer is YES, indicate which items is is provided with this submission:

Request for HIPAA Waiver of Authorization

CTRC Resources*
Does the research involve CTRC resources?
No

Pathology and Laboratory Medicine Resources*
Will samples be collected by hospital phlebotomy and/or processed or analyzed by any of the clinical laboratories of the University of Pennsylvania Health System?
No

Research Involves Apheresis, Cell Collection, and/or Blood Product Collection*
Does this research involve collection of blood products in the Penn Donor Center and/or the use of apheresis for treatment or collection of cells or other blood components?
No

Research involving blood transfusion or drug infusions*
Will your research involve blood transfusion or infusion of study drug in 3 Ravdin Apheresis Unit for research purposes?
No

Trial in Radiation Oncology
Is this research a prospective trial being done in Radiation Oncology, and if so, has this protocol been approved by the Radiation Oncology Protocol committee?

N/A

Study in Radiation Oncology
Is this research a retrospective study being done in Radiation Oncology, and if so, has this project been reviewed by the Radiation Oncology Clinical Research Group?
N/A

Use of UPHS services*
Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures*, whether considered routine care or strictly for research purposes?
No

Primary Focus*
Research on human data sets (e.g. medical records, clinical registries, existing research data sets, medical administrative data, etc.)

Protocol Interventions

	Sociobehavioral (i.e. cognitive or behavioral therapy)
	Drug
	Device - therapeutic
	Device - diagnostic (assessing a device for sensitivity or specificity in disease diagnosis)
	Surgical
	Diagnostic test/procedure (research-related diagnostic test or procedure)
	Obtaining human tissue for basic research or biospecimen bank
	Survey instrument
x	**None of the above**

The following documents are currently attached to this item:

HIPAA Waiver of Authorization (irbrequestforwaiverofhipaaauthorization-forrelease_0.docx)

Department budget code

None

Multi-Site Research

Other Sites

No other sites

Management of Information for Multi-Center Research

The following documents are currently attached to this item:

There are no documents attached for this item.

Protocol

Abstract
The goal of this study is to leverage standard clinical data to identify new computational strategies to improve the prediction and diagnosis of cardiovascular disease. All patients in UPHS will be eligible. No subjects will be contacted directly. Identified algorithms will be used to benefit future patients.

Objectives

Overall objectives
Develop new computational algorithms to improve the diagnosis and prediction of cardiovascular disease.

Primary outcome variable(s)
Diagnosis with cardiovascular disease, including primary acute myocardial infarction and acute heart failure.

Secondary outcome variable(s)
Intermediate variables will include risk factors, such as hypertension and hyperlipidemia.

Background
Current approaches to predict primary cardiovascular disease enable reasonable risk stratification using scores such as the ASCVD risk equations (C-scores ~ 0.7). These methods are much better than clinical gestalt alone and are reasonable on a population level, but are very poor for the individual patient. Moreover, they do not predict well on shorter time-scales, such as 30-days. There is a wealth of clinical information being collected and more complex strategies to analyze this day should yield better prediction.

Study Design

Phase*
Not applicable

Design
Observational. Both prospective and retrospective. Cohort and case-control designs.

Study duration
Estimate that data will be collected for 3 years. This may be extended by amendment if initial data is promising. Individual subjects will studied throughout the study period, but never be contacted directly.

Resources necessary for human research protection
Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Please allow adequate time for the researchers to conduct and complete the research. Please confirm that there are adequate facilities for the research.
Human subject protection relates to subject confidentiality because there is no direct patient contact for this study. All study personal have received the appropriate CITI training and are experiences in the conduct of research with human subjects. Appropriate computer security measures are in place; all data that has PHI identifiers will be kept behind PHI firewall or on encrypted, password protected computers or digital media.

Characteristics of the Study Population

Target population
Adult patients at risk of cardiovascular disease

Subjects enrolled by Penn Researchers
10000

Subjects enrolled by Collaborating Researchers
0

Accrual
N/A

Key inclusion criteria
18 - 110, any gender/sex.

Key exclusion criteria
Age less than 18.

Vulnerable Populations

	Children Form
	Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form
	Fetuses and/or Neonates Form
	Prisoners Form
	Other
x	**None of the above populations are included in the research study**

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
N/A

Subject recruitment
N/A

Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

N/A

Study Procedures

Suicidal Ideation and Behavior
Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)?
No

Procedures
Clinical data will be collected from CERNER Laboratory information system, laboratory middleware systems, and Penn Data Store by ODBC connections or related APIs. All locally stored data will be protected by remaining within UPHS network and by using physical protections (locked, restricted access rooms). Data will be verified and follow-up by focused chart review in Epic, Sunrise, and CERNER, as appropriate.

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception?
No

Analysis Plan
Data will be modeled using a variety of statistical and machine learning approaches to identify patterns and associations. Any findings will be validated in independent populations or the significance will be assessed by simulation and permutation.

The following documents are currently attached to this item:

There are no documents attached for this item.

Are you conducting research outside of the United States?
No

Data confidentiality

	Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.
x	**Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**
	Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.
x	**Wherever feasible, identifiers will be removed from study-related information.**
	A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.
	A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)
	Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.
	Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

Subject Confidentiality
All study personal have received the appropriate CITI training and are experienced in the conduct of research with human subjects and issues relating to subject confidentiality. No PHI containing materials will be distributed to non-study personnel. Minimal datasets will be used with only PHI necessary for the conduct of the study. Chart review will only be performed to study personnel. All PHI extracted from health system will be stored digitally on computers within the UPHS firewall. The data will therefore be protected by UPHS credentials. No data will be stored on laptop computers. In addition, access will be restricted by file permissions to only study personnel. PHI will not be disclosed. If PHI will need to be stored on digital media or transferred outside of UPHS firewall, it will be encrypted and password protected.

Sensitive Research Information*
Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record?
No

Subject Privacy
Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).
There is no active enrollment directly into this study and no direct subject contact.

Data Disclosure
Will the data be disclosed to anyone who is not listed under Personnel?
The data may be disclosed to other investigators within the University of Pennsylvania Health system, but will only be distributed in completely de-identified data sets. Such data sets will not contain any codes or other HIPAA identifiers.

*Data Protection**

- x **Name**
- x **Street address, city, county, precinct, zip code, and equivalent geocodes**
- x **All elements of dates (except year) for dates directly related to an individual and all ages over 89**
- **Telephone and fax number**
- **Electronic mail addresses**
- **Social security numbers**
- x **Medical record numbers**
- **Health plan ID numbers**
- **Account numbers**
- **Certificate/license numbers**
- **Vehicle identifiers and serial numbers, including license plate numbers**
- **Device identifiers/serial numbers**
- **Web addresses (URLs)**
- **Internet IP addresses**
- **Biometric identifiers, incl. finger and voice prints**
- **Full face photographic images and any comparable images**
- **Any other unique identifying number, characteristic, or code**
- **None**

Does your research request both a waiver of HIPAA authorization for collection of patient information and involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
No

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
No

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
No

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not applicable.

Consent

1. Consent Process

Overview
N/A

Children and Adolescents
N/A

Adult Subjects Not Competent to Give Consent
N/A

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
Waiver or alteration of required elements of consent

Minimal Risk*
The only risk associated with this research is if confidentiality is breached and PHI and associated clinical information is released. This risk is low because all study personnel have received appropriate CITI training and are experienced in the conduct of research with human subjects and issues related to subject confidentiality. No PHI containing materials will be distributed to non-study personnel. Minimal datasets will be used with only PHI necessary for the conduct of the study. Chart review will only be performed to study personnel. All PHI extracted from health system will be stored digitally on computers within the UPHS firewall. The data will therefore be protected by UPHS credentials. No data will be stored on laptop computers. In addition, access will be restricted by file permissions to only study personnel. PHI will not be disclosed. If PHI will need to be stored on digital media or transferred outside of UPHS firewall, it will be encrypted and password protected.

Impact on Subject Rights and Welfare*
There is no return of information, so we reasonably do not expect any impact on subject rights and welfare.

Waiver Essential to Research*
There will be no direct contact with subjects. Training computational algorithms will require very large numbers of patients, so directly consenting each subject would make the study cost-prohibitive.

Additional Information to Subjects
There will be no return of information to participants.

Written Statement of Research*
No

If no written statement will be provided, please provide justificiation

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit

Potential Study Risks
Risk to patients from this study derive from any breach in confidentiality or privacy protections that could result in the release of PHI and associated data. No protections (passwords, coding) are perfect, but the storing of coded data on a secure, password-protected computer should provide very reasonable protection against any security breach.

Potential Study Benefits
There are no direct benefits to individual subjects, as information will not be returned. However, the future application of study findings has the potential to improve clinical diagnosis, prognostication, and management for future patients.

Alternatives to Participation (optional)

Data and Safety Monitoring
The Principal Investigator will be ultimately responsible for assuring the security of all data to minimize risk to participants.

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit Assessment
This study offers no direct benefit and only minimal risk to the subjects. There is significant societal benefit, however, as a better ability to predict and diagnosis cardiovascular disease will ultimately lead to early intervention to prevent morbidity and mortality. As such, the minimal risk to the subjects is outweighed by the potential societal benefit.

General Attachments

The following documents are currently attached to this item:

Additional forms (825821.resubmission.docx)