Study Type and Performance Site Information

Type of study:
[**x**] **Standard or Expedited**
[ ] Exempt
[ ] .118 Determination
[ ] Non-Human Subject Determination
[ ] Quality Improvement/Non-Research Determination
[ ] Request review by another IRB
[ ] Coordinating Center ONLY

Please indicate which Committee is most appropriate to review your project:
[ ] Social and Behavioral Sciences
[**x**] **Health Sciences**

Are there any international sites involved in this study in which the PI is responsible?
[ ] Yes
[**x**] **No**

Is this project cancer-related?
[ ] Yes
[**x**] **No**

Study Purpose and Description

Provide a brief abstract of the study in lay language. The IRB Committees are comprised of scientists with varied backgrounds, non-scientists, and community members.
This study will implement a prognostic model which calculates the probability of hospital-acquired venous thromboembolism (HA-VTE) among hospitalized adults at Vanderbilt Adult Hospital and evaluate its performance in preventing HA-VTE by facilitating appropriate and timely initiation of preventative treatment. We will conduct a pragmatic randomized trial of the prognostic model plus clinical decision-support (CDS) tools for prophylaxis compared with usual care for the prevention of VTE among hospitalized adults.

The model calculates the probability of HA-VTE, updates as the clinical scenario evolves, discriminates well between high- and low-risk patients, and exhibits superior prediction performance compared with extant risk-stratification tools. The risk score calculation will not require clinician input and will show for patients who have been randomized to the intervention as part of the clinical team's workflow in the electronic health record. The score will be dynamic, updating daily using real-time patient data to reflect the patient's current risk.

Through an adaptive platform trial, we will evaluate on a prospective basis the effectiveness of model-guided CDS to reduce HA-VTE, both overall and among key patient subgroups, and study through randomization the implementation strategies that work best for clinicians and improve patient outcomes. In a complementary implementation evaluation, we will assess acceptability, appropriateness, and feasibility of the intervention; identify barriers and facilitators to its implementation; and measure its uptake by providers in daily clinical practice.

Expected duration of the study.
18 months

The IRB needs to understand how this study adds to the knowledge on this topic in order to be able to judge the risks and benefits to the research participants.
There is a critical need for a modern and innovative approach to personalized risk assessment for venous thromboembolism (VTE) among hospitalized adults. VTEs are a significant cause of morbidity and mortality that can be prevented with appropriate and timely initiation of thromboprophylaxis. The annual incidence of VTE is 1–2 per 1000, or 300,000–600,000 events in the United States annually. The VTE attack rate is much higher among currently or recently hospitalized patients compared with those in the general community: 330 versus 8 per 100,000 person-years, respectively. Hospital-acquired VTE (HA-VTE) includes deep vein thrombosis (DVT) and those that travel to the lungs and result in acute pulmonary emboli (PE), which are the most common cause of preventable deaths in the hospital. Despite widespread recognition of the problem and implementation strategies to prevent it, the incidence of VTE has not changed substantially in the last 30 years. The reasons for this lack of progress are complex and not only include the increasing prevalence of contributing factors such as obesity and cancer, but also reflect a significant gap in current risk-stratification and prevention strategies.

Acknowledging the increased risk of VTE among hospitalized adults, efforts have focused on VTE prevention during hospitalization. Universal mechanical or pharmacologic prophylaxis increases cost and the potential for harm from the overtreatment of patients at low risk. Numerous prognostic models have therefore been developed to identify those patients with elevated risk of HA-VTE for whom prophylaxis should be considered. A recent systematic review identified several available models and summarized their operational characteristics. Generally, these models are limited to specific patient subpopulations (e.g., patients requiring medical care not in the intensive care unit, patients undergoing surgery), provide overly coarse categories for predicted risk based on dichotomized values for continuous risk factors (e.g., age, body mass index), and are difficult to automate in electronic health record (EHR) systems for use in real time.Unfortunately, most of these models have exhibited modest prediction accuracy in derivation and validation cohorts, resulting in insufficient evidence to recommend the use of any specific model to guide clinical decision making. While clinical practice

guidelines recommend some form of risk assessment, many clinicians continue to rely solely on clinical gestalt. The lack of an accurate, flexible, and universal prognostic tool results in variable practice patterns among clinical groups in the same facility and even among practicing partners in the same subspecialty.

We challenge the current paradigm that accurate risk assessment for HA-VTE requires the development and implementation of distinct prognostic models among different patient populations. Although the constellation of predisposing risk factors differs across these patient populations, there is no biological rationale for considering VTE as a different clinical entity among these patient groups. Such a fragmented approach results in models with poor prediction performance and hinders the integration of automated risk assessment into routine clinical practice. Our approach to individualized risk assessment is to develop a single prognostic model in a general patient population and tailor it to individual patients based on their unique combination of risk factors; the model should then be improved and refined over time. Our team has successfully developed an initial model for HA-VTE among all adults admitted to Vanderbilt University Medical Center (VUMC) (A.2.1). Our model provides granular risk stratification by calculating the predicted probability of HA-VTE for each patient,12 maximizes the use of available data by avoiding the arbitrary categorization of continuous variables,13,14 and can be automated in EHR systems for use in real time. The model's prediction accuracy is excellent (C statistic: 0.892) and superior to all extant models for HA-VTE.

We acknowledge that, on its own, providing the predicted probability of HA-VTE for each patient will not improve outcomes. User-friendly, understandable, and shareable clinical decision support (CDS) tools are necessary to change provider behaviors and clinical practice. The CDS tool currently in use at VUMC—a best practice advisory (BPA)—is meant to help clinicians order appropriate thromboprophylaxis, but several barriers exist: there is a disconnect between the number of times the BPA 'fires' and the level of harm for HA-VTE; instead of helping clinicians, the BPA is a cognitive interruption in their workflow; and the BPA fires inappropriately at times because it does not take into consideration the full clinical scenario. These barriers provide a ripe environment within which to improve upon and test CDS tools that can lower rates of HA-VTE.

While accurate prognostic models and useful CDS tools can be developed within an individual organization, the ability to generalize to other organizations is a major barrier to disseminating prognostic modes and improving patient outcomes. Precisely representing the knowledge underlying model development and implementation in a semantically interoperable way is key to effective dissemination. We will represent all clinical concepts referenced by the prognostic model using current terminology standards and adopt knowledge management best practices: standards-based semantic models to represent concepts and relationships; and versioning of data elements that map to clinical concepts. Thus, we will enhance sustainability of the prognostic model by precisely defining the clinical concepts that underpin model derivation and validation and by accommodating the evolving nature of data. We will implement the model using the native build capabilities of VUMC's Epic EHR system; Epic is the most-commonly implemented EHR system nationwide. We will overcome barriers to dissemination by developing universal CDS tools and sharing an implementation manual with best practices.

Research, Activities, Procedures, and Schedule of Events for Study Participants

Please check all that apply to your study and describe each below.
[ ] Behavioral Observation
[**x**] **Randomization**
[ ] Blinding
[ ] Surveys, Interviews, Questionnaires
[ ] Document and Artifact Collection
[ ] Deception, Withholding or Postponing Medications/Treatments, or Imposing other Restrictions
[ ] Audio/Video Recording
[ ] Sham Procedure
[**x**] **Specimen/Data Collection and/or Storage**

DATA COLLECTION, STORAGE OF DATA/SPECIMENS, AND/OR ISSUES OF CONFIDENTIALITY - Describe the procedures that will be utilized to protect the privacy of the research participant. Include who will have access to the research information (for example, video/audio recordings, discovering information about the participant that could be harmful if released such as mental illness, genetic information, sexual preference, drug abuse, etc.) and where it will be stored.
Data collection will be acquired directly from EHR and stored securely in the VUMC Data Center on lab-owned servers for analysis. Data to be collected includes the VTE risk score, the predictors for the risk score including lab values, central line status, history of vte, demographics (age, sex), admission type. We will collect data on the usage statistics of the clinical decision support tool. We will also collect data on the incidence of venous thromboembolism using diagnostic codes to identify events.

Only approved VUMC staff and faculty will have access to study data. All staff who has access to data will have up to date IRB training and PII/PHI training. These data will only exist on VUMC systems behind VUMC firewalls.

Describe how the confidentiality of participants' data will be assured. Include a description of any issues specific to the study that might increase the risk of breach of confidentiality. Describe how codes will be generated if codes are used to protect identities, and who will have access to such codes. If a certificate of confidentiality will be provided, include the name of the person holding the certificate. Describe the final disposition of research data when the study is concluded (e.g., will information be destroyed, will the PI maintain the information indefinitely, etc.).
All efforts will be made to keep personal information and research records completely confidential throughout the study. Study records, data, and any documents pertaining to the study will be kept in a HIPPA compliant, secure, and password protected database on servers secured in the VUH data center.

All patients will be assigned a unique study ID. Only key study personnel will have access to PHI for the purpose of data analysis. The information from the research study will be reported in aggregate and no individual subject will be identified in publication. Records will be maintained in accordance with IRB, institutional, and sponsor policies. Upon conclusion of the study, closeout will occur 12 months after all data analysis is complete. All data will be stored securely at VUH after study conclusion. Raw data will be kept for 7 years after study conclusion. After 7 years, raw data will be destroyed and a de-identified copy of the data will remain stored securely on VUH servers.

The study holds a certificate of confidentiality through the NIH.

RANDOMIZATION - Describe the randomization process (who will randomize, how will randomization be determined, etc.)
Randomization will occur through a built-in functionality in Epic EHR at the patient level. The clinical decision regarding randomization between the two treatment arms will be arbitrary, meaning randomization will not be based on clinical factors. Patients randomized to receive the intervention will have visualization of HA-VTE risk score to clinical team in their EPIC workflow, and patients randomized to the control will receive standard care without intervention. Patients under observation status will not be subject to randomization unless transitioned to inpatient status.

SPECIMEN COLLECTION - Describe all procedures used for specimen collection.
Data collection will be performed by the VUMC Vanderbilt Clinical Informatics Center (VCLIC) core. Data will be collected directly from EHR and stored securely on VUMC managed servers using Microsoft OneDrive/Teams for later analysis. Statistical analyses will be performed using the most recent version of R statistical software. No data will be stored on non-VUMC managed servers. Data to be collected includes: VTE risk score, the predictors for that probability including central line status, demographics, admission type, history of VTE, coagulopathy factors, history of cancer, and mobility. We will also collect data on the usage of clinical decision support tools. We will collect data on venous thromboembolism incidence using diagnostic (ICD) codes to identify events. Additionally, we will collect data on visits to VUH up to 90 days post-discharge, major bleeding complications during hospitalization (identified using ICD codes, orders for transfusion, and lab values for drop in hemoglobin), and prophylactic treatments ordered and administered (pharmacological and non-pharmacological).

Data collected from observations and interviews as part of a related IRB study (#240579) is stored securely on VUMC managed servers on OneDrive. Deidentified data from these observations and interviews may be accessed throughout the course of this study. Data that will be accessed includes qualitative data analysis of VTE risk assessment process as recorded in observations as well as participant perceptions and recommendations of CDS tools. This data will be considered when creating and implementing CDS tools and processes.

Will you be performing a blood draw(s)?
[ ] Yes
[**x**] **No**

Will specimens be obtained for genetic testing?
[ ] Yes
[**x**] **No**

Will the PI create a repository at VU/VUMC with any of the specimens and/or data for future use?
[ ] Yes
[**x**] **No**

Please indicate all procedures and activities performed for research purposes only and the frequency at which they occur in the study (e.g., skin biopsy, 3 times).

Procedure/Activity	Frequency
Randomization of patient	Once
VTE risk score visualization	daily during hospitalization until day of discharge
Automated calculation of risk score	daily during hospitalization until day of discharge
EHR record access	daily during hospitalization until day of discharge
EHR record access	90 days post discharge

If all of your study is minimal risk, please indicate the categories that it fits 45 CFR 46.110 or 21 CFR 56.110:

[**x**] **N/A: Study is greater than minimal risk or Standard**
[ ] (F)(1) Drugs or devices where no IND/IDE is required
[ ] (F)(2) Collection of blood by stick or venipuncture
[ ] (F)(3) Prospective collection of specimens by non invasive means
[ ] (F)(4) Collection of noninvasive data through routine clinical practice
[ ] (F)(5) Research on materials that have been collected for non research
[ ] (F)(6) Collection of data from voice, video, digital or image recordings
[ ] (F)(7) Research on individual or group characteristics (surveys)

Data and Safety

Describe how the risks to participants are minimized (e.g., screening to assure appropriate selection of participants, identify standard of care procedures, sound research design, safety monitoring and reporting).

The study coordinator, with MPI (multiple principal investigators) oversight, is responsible for ensuring protocol compliance, data integrity, and participant safety. This protocol presents minimal risks to participants and adverse events or other problems are not anticipated. In the unlikely event that such events occur, unanticipated problems involving risks to subjects or others will be reported immediately to the MPI and responsible IRBs, and in writing within 7 days to the IRB and any appropriate funding and regulatory agencies. The MPI will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular study meetings. Annual reports will be submitted to the responsible IRBs summarizing study progress, adverse events, complaints about the research or withdrawals, and any protocol violations.

To ensure appropriate selection of participants, participant screening will be performed using our pre-specified eligibility criteria applied to data contained within the electronic health record (EHR). Eligible patients will be identified through an EHR-based query. The proposed intervention will provide clinicians with additional context regarding patient risk for VTE and prompt another opportunity to order VTE Prophylaxis when appropriate. All patients admitted to the inpatient setting at Vanderbilt Adult Hospital are assessed for VTE risk on admission as part of standard care. as such, providers are already being prompted to order prophylaxis or enter a contraindication for all admitted inpatients. Clinicians will continue to use standard of care procedures when assessing risk, with the addition of the information (risk score) provided by the model. To ensure transparency, the CDS tool containing the risk score will also include a link for clinicians to click-in and explore details about the prognostic model and its risk score calculation, such as contributing factors to the risk score, the logistic regression equation used to calculate the score, how the logistic regression converts to a % risk, the criteria % risk categories for low, elevated , and critically high risk, and a link to a journal publication on the model’s development and validation. The model does not override standard of care but rather provides additional context and tools for current standard of care procedures surrounding VTE risk assessment.

Describe how the risks to participants are reasonable in relation to anticipated benefits (e.g., includes benefits to the individual as well as to human kind, indicate how the risks are justified in this population).
All patients will receive standard of care throughout this study. The intervention will not interfere with or replace clinical judgment; rather, it will be an additional tool for clinicians to review in their decision-making process. All decisions regarding treatment and management of the patient will be at the discretion of the treating provider and will not be restricted or altered in any way by the study. This study does not involve an investigational intervention given or administered directly to patients.

This protocol presents no more than minimal risk to patients and healthcare providers. Adverse events include potential increased bleeding risk if prophylaxis is ordered based on the model output that may have otherwise not been ordered. The model is not intended to dictate care of the patient and the medical team may ignore the risk score and proceed with prophylaxis as they see fit.

There are risks associated with standard clinical care inherent to VTE prophylaxis, including:
• Risk of bleeding inherent to VTE prophylaxis
• Discomfort with administration of prophylaxis (adherence to treatment)

The benefits include:
- possible HA VTE prevention in patients that did not receive prophylaxis without the intervention
- providing clinicians with more context and information regarding their patients' risk.
- better understanding how CDS tools can be used to improve care delivery while minimizing burden on clinicians.
- directly contribute to development of accessible resources and CDS tools for implementation across other sites, if effective.

Is there a data safety monitor or board/committee to review this study for safety and adherence to the study protocol?
[**x**] **Yes**
[ ] No

Describe the composition of the committee and their qualifications.
Membership will consist of persons independent of the investigators who have no conflict of interest with the trial. The DSMB includes experts in or representatives of the fields of Biostatistics, Hematology, and Internal Medicine. The following individuals have agreed to serve on the DSMB:

1) John VanBuren, Ph.D., Associate Professor, University of Utah Data Coordinating Center
2) Colin G. Walsh, MD, MA, Associate Professor of Biomedical Informatics, Vanderbilt University Medical Center
3) Lisa B. Kreuziger, MD, MS, Associate Medical Director at Versiti Blood Center of Wisconsin and Assistant Professor at Medical College of Wisconsin

Provide a general description of the data and safety monitoring plan.
All project staff will complete training in the conduct of human subjects research. Any protocol deviation resulting in a breach of confidentiality will be reported to IRB
promptly.

Subject identification numbers will be assigned to each study participant. Research subjects' identities will be kept confidential at all times. Subject identifiers will never be revealed in publication, presentation, or other scientific purpose. Participant identities will be available as needed to the investigators and research staff. All data will be collected for research purposes only. All study subjects will be assigned a unique study identification number for use in secure computer database and analytic work. Linkage of patient study IDs to patient identifiers will be maintained by the PIs and Project Coordinator only, with username/password protected access. All electronic data will be kept in password-protected computer files on secured VUH servers.

Describe plans for monitoring the progress of trials and the safety of participants (e.g., timing of DSM reviews and reports, planned interim analysis, etc.).
We will convene the DSMB biannually to review interim analysis of primary outcomes as well as safety outcomes.

For interim analyses, we will use a quality outcome: model-indicated prescription of HA-VTE prophylaxis (i.e., implementation among high-risk patients but not among low-risk patients). A readily defined, proximal binary outcome will facilitate timely within-trial adaptations. Use of an intermediate outcome is appropriate given the strong association between the intermediate outcome (e.g., HA-VTE prophylaxis) and the primary outcome (e.g., HA-VTE). At each interim analysis, we will calculate an odds ratio comparing the odds of model-indicated prescription of HA-VTE prophylaxis between the intervention and control groups. If the posterior probability that the odds is positive (e.g., >1.05) is high (e.g., >95%), we will accept the current implementation of the intervention as effective and adopt it for the duration of the trial. If the posterior probability that the odds ratio is positive (e.g., >1.05) is small (e.g., <20%, we will abandon the current implementation of the intervention due to futility and subsequently adopt a new implementation of the intervention. We anticipate that interim analyses will occur every 3 months, subject to sufficient enrollment to support interim analyses.

Additionally we will review out safety outcomes data with the DSMB biannually. This includes reviewing any major bleeding complications that occur throughout the course of the trial to ensure the continued safety of participants.

Describe plans for assuring compliance with requirements regarding the reporting of adverse events (AEs), including plans for reporting of AEs to the IRB and appropriate regulatory agencies.
The multiple principle investigators (MPI) are responsible for monitoring study data, assuring protocol compliance, and conducting safety reviews. Adverse events or other problems are not anticipated. In the unlikely event that such events occur, unanticipated problems involving risks to subjects or others will be reported immediately to the MPI and responsible IRBs, and in writing within 7 days to the IRB and any appropriate funding and regulatory agencies. The MPI will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular study meetings. Annual reports will be submitted to the responsible IRBs summarizing study progress, adverse events, complaints about the research or withdrawals, and any protocol violations.

We will follow the VHRPP guidelines that require investigators to promptly notify the IRB within 7 days of the occurrence when unexpected AEs occur. These are events that could possibly be related to the intervention, or occur more frequently or are more severe than anticipated. VHRPP requires that any AE that is unexpected and related or possibly related to the research be reported. Risks that are described in the protocol do not have to be reported as Study Adverse Events (SAEs), unless the expected SAE occurs more frequently or is more serious than expected. One exception to this rule is in the case of a death. All deaths must be reported, whether or not the death was related to the research.

Describe plans for assuring that any action resulting in a temporary or permanent suspension of a federally funded research project is reported to the grant program director responsible for the grant.
This study presents minimal risk; as such, we do not anticipate patient safety concerns arising. In the event that there is significant concern about patient safety as a result of the trial, we will consult with the Data Safety Monitoring Board and notify our sponsor program officer at NHLBI.

Describe plans for assuring data accuracy and protocol compliance.
The MPI will work closely with the study coordinator to oversee all aspects of study conduct and ensure data accuracy and protocol compliance.

Is Vanderbilt going to be the Coordinating Center?
[ ] Yes
[**x**] **No**

Please select the phase of study.
[ ] Phase I
[ ] Phase I/II combined
[ ] Phase II
[ ] Phase III,
[ ] Phase IV
[**x**] **N/A**

Does this study require registration with clinicaltrials.gov?
[**x**] **Yes**
[ ] No

Subject Population(s)

Is this a study in which you will have interaction with individuals? NOTE: Please check "yes" if you need to report accrual goals for participant engagement.
[**x**] **Yes**
[ ] No

Accrual Goal: What is your total accrual goal at Vanderbilt?
65000

Does this study target one gender or specific social/ethnic group(s)?
[ ] Yes
[**x**] **No**

Is the population being enrolled in this study at high risk for incarceration?
[ ] Yes
[**x**] **No**

Check all that apply (*Complete the appropriate supplemental information as applicable):
[**x**] **N/A**
[ ] Children/minors*
[ ] Cognitively impaired - comatose/traumatized*
[ ] Pregnant women/fetal tissue/placenta*
[ ] Prisoners*

Recruitment

Describe the specific steps to be used to identify and/or contact prospective participants. (If applicable, also describe how you have access to lists of potential participants.) Note: When recruiting VUMC patients, please confirm if your outreach is limited to patients marked as OK to Contact in eStar. If not, describe who will be contacting patients marked as Do Not Contact.
Participant screening will be performed using predefined eligibility criteria applied to data contained within the electronic health record (EHR). Eligible patients will be identified through an EHR-based data query developed and maintained by the Vanderbilt Clinical Informatics Center (VCLIC) core team. All adult patients receiving routine inpatient care at VUH will be eligible for inclusion in this trial (standard of care dictates that all admitted patient encounters include DVT/VTE prophylaxis set as part of admitting orders). There will be no active recruitment for the trial. Randomization will occur through a built-in functionality in Epic EHR at the patient level. Patients will appear in study sites for routine care at health system scale. As such, it is not practicable or feasible to actively recruit and consent patients in this dynamic real-world setting.

Identify the criteria for inclusion and exclusion and explain the procedures that will be used to determine eligibility. If psychiatric/psychological assessments will be conducted (e.g., depression or suicidal ideation screenings), state who will administer, his/her experience, and how risks will be managed.
Inclusion:
• 18 years of age or older
• Admitted to an inpatient setting at VUH within study period

Exclusion Criteria:
• less than 18 years of age

Patients under observation status are eligible but will not be subject to randomization unless transitioned to inpatient status. Participation in the trial will end in the case a patient dies during hospitalization or is converted to hospice care at Vanderbilt Adult Hospital.

Describe how the selection of participants is equitable in relation to the research purpose and setting.
This study will apply to all adult patients receiving inpatient care at VUH; thus, no group will be targeted or excluded based on any demographic. Furthermore, patients not randomized to intervention will continue to receive standard of care at Vanderbilt Health and their care will not be impacted by the study.

Please indicate whether you plan to enroll any of the populations indicated below:
[ ] VU Medical Students/trainees
[ ] Students
[**x**] **Elderly/Aged - targeted**
[ ] Subordinates/Employees - VUMC Employees may only be recruited through general announcements or advertisements, rather than individual solicitations.
[**x**] **Females of childbearing potential**
[ ] Terminally ill participants
[ ] Healthy Volunteers
[**x**] **Other**
[**x**] **Minorities**

Please specify 'Other' populations:
Any adult (18+ years) admitted to an inpatient setting at VUH within study period including, but not limited to, the populations checked off above.

Please identify ALL applicable recruitment methods:
[ ] N/A
[ ] Flyers
[ ] Internet
[ ] Letter
[ ] Departmental Research Boards,
[ ] Mass E-mail Solicitation/Research Notifications Email Distribution List
[ ] Newspaper
[ ] Posters
[ ] ResearchMatch (IRB 090207)
[ ] Radio
[ ] Telephone
[ ] Television
[ ] Social Media
[x] **EHR-Based Recruitment**
[ ] EMR Recruitment - Existing provider relationship
[ ] Other

Will the study provide compensation to research participants? Please be advised, any resident of a country subject to U.S. comprehensive territorial sanctions or any person designated on the U.S. Treasury Department's Office of Foreign Assets Control's Specially Designated Nationals list of prohibited individuals related to national security or foreign policy cannot accept any compensation for participation.
[ ] Yes
[x] **No**

Does this study include a certificate of confidentiality or sensitive research information that must be hidden in the medical record?
[x] **Yes**
[ ] No

Please indicate any protections in place:
[x] **this study holds a Certificate of Confidentiality through NIH**
[ ] this study does not hold a certificate of confidentiality however participants could be put at risk if participation was discovered/disclosed
[ ] other

Radiation Procedures and Radioactive Drugs

Does this study involve any radiation ionizing procedures for research?
[ ] Yes
[**x**] **No**

Drugs, Devices, Biologics

Please check all that apply:
[ ] N/A
[ ] Drug(s)/Biologic(s) or Placebo (inactive substance) Used for Research that HAVE an IND
[ ] Drug(s)/Biologic(s) or Placebo (inactive substance) used for Research that DO NOT have an IND
[ ] IBC Review for Live, Recombinant, and/or Attenuated Microorganisms for Vaccination, Gene Transfer or Botox
[**x**] **Device(s) Used for Research (devices may also include computer software, in vitro diagnostics, etc.)**

Please provide a description of each device:
The intervention uses a logistic regression model to to estimate a probability that hospital-acquired venous thromboembolism will occur for an individual. This model provides a risk score for each patient assigned to the intervention . To calculate the risk score, the model uses 17 factors selected from a candidate set of 105 predictors. Selected variables include: admission type, presence of a central line, Braden scores, vital signs (e.g., respiratory rate), laboratory values (e.g., lactate, fibrinogen), and ordered medications (e.g., glucocorticoids, immunoglobulins). The model also includes variables identified through clinician feedback including: history of VTE, active comorbidities (e.g., cancer, coagulopathy, blood loss, history of thrombosis) and demographic characteristics (e.g., age and sex). This risk score will be displayed for the patient's clinical care team to provide additional information on the patient's risk. To ensure transparency, the risk scoring tool will also include a link for clinicians to click-in and explore details about the prognostic model and its risk score calculation, such as contributing factors to the risk score, the logistic regression equation used to calculate the score, how the logistic regression converts to a % risk, the criteria % risk categories for low, elevated , and critically high risk, and a link to a journal publication on the model’s development and validation The model and the risk score is intended to help inform clinical decision-making by providing additional context; however, the model will not dictate patient care or replace clinical judgment. Providers may choose not to act on the model's recommendations at any time.

Please provide an explanation for each determination of non-significant risk.
This model is not a device and does not replace or dictate clinical judgment. Furthermore, this model does not replace standard of care. It is a tool to provide clinicians with more information on patient risk during the standard VTE risk assessment process. Below is the criteria, as defined by the FDA, for non-device CDS. Our model meets all four criteria and, thus, should not be considered a device. The device does not process or analyze any imaging, our data inputs do not include any continuous data streams, it will not replace or dictate clinical judgment, and data will be available for clinicians to review how the model arrived at the risk score. Please see the criteria below.

Criteria:
The statutory exclusion for Non-Device CDS is based on four criteria set out in section 520(o)(1)(E) of the Federal Food, Drug and Cosmetic Act. Each criterion addresses a different aspect of how the software operates and how it influences clinical decision-making.

The first criterion restricts the types of inputs the software may use. To qualify as Non Device CDS, the software must not acquire, process or analyse medical images or signals from in vitro diagnostic devices or from signal acquisition systems. This includes image analysis such as CT, MRI or pathology slides, physiological signal processing such as ECG waveforms or continuous glucose monitoring data and laboratory assay signal processing.

The second criterion defines what inputs are permitted. The software may display, analyse or print medical information about a patient or other medical information. This includes patient demographics, test results, discharge summaries, vital signs, clinical guidelines and peer-reviewed literature. However, the FDA draws a clear distinction between discrete medical information and continuous or time-sensitive data streams, which it considers signals or patterns rather than medical information.

The third criterion focuses on the nature of the recommendation. The software must support or inform a healthcare professional and must not direct or replace clinical judgment. Outputs should present options, considerations or contextual information rather than a single definitive diagnosis or treatment decision, particularly in time-critical situations.

The fourth criterion requires transparency. The software must enable the healthcare professional to independently review the basis for the recommendations. This means the clinician must be able to understand how the software arrived at its output without relying solely on the software itself. For our tool, clinicians will have the option to click-in to view more details about the prognostic model using an embedded link.

Additionally, the risk score provides additional information for an existing risk-assessment process. All patients in the inpatient setting are assessed for VTE as standard care. Thus, the model poses no more than minimal risk to patients.

Has any other IRB determined any of the device pose Significant Risk?
[ ] Yes
[**x**] **No**

Will a sham product and/or procedure be used in this study?
[ ] Yes
[**x**] **No**

Privacy

Will the VUMC IRB be acting as the Privacy Board for Research with respect to the review of Authorizations or Waiver of Authorizations?
[**x**] **Yes**
[ ] No

Are you requesting a Waiver of Authorization?
[**x**] **Yes**
[ ] No

Please explain why the research could not be practically conducted without the use of the HIPAA protected data:
Due to the nature of the study, it is not feasible to conduct research within the electronic health record without the potential access of identifiable information. No data will be analyzed outside of secure systems in VUH HealthIT clinical production or secured data servers in the VUH data center.

Please explain how the data will be protected
Only key study personnel will have access to study data. Data are secured on servers in the VUH data center or in HealthIT only. These systems are secured via personal, physical, and technical controls including their invisibility to networks outside the VUH firewall. User credentials are maintained by the VUH Active Directory and IT and are necessary to access any study data. Only those
credentialed and on an approved IRB will have permissions to access study data on these servers. No paper records will be generated nor recorded in this study - all data collection will be digital and will leverage operational clinical systems and EHRs in their generation. No new data collection mechanisms will be required and therefore no new vulnerabilities generated.

When will the data no longer be accessed?
Raw data will be deleted 7 years after conclusion of the study. We will keep a de-identified copy of data for our records.

Please describe the plan to protect the identifiers from improper use and disclosure.
Identifiers will never leave VUH clinical production systems or VUH data center secured servers. All analyses will be conducted on those same systems.

Please indicate the source of the PHI to be collected.
VUH EHR

Please describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.
All raw data will be destroyed 7 years following the conclusion of the study, except in the case IRB policy requires retention for an allotted amount of time.

Please verify that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research.
Protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research.

Does this research disclose Protected Health Information (PHI)?
[ ] Yes
[**x**] **No**

Consent

Please indicate what you plan to do with regard to consent (check all that apply):
[ ] Consent
[**x**] **Request Waiver or Alteration of Consent**
[ ] Consent was obtained in another study

Which type of waiver is being selected (check all that apply):
[ ] Waiver of Documentation
[ ] Alteration of Informed Consent Process
[**x**] **Waiver of Informed Consent Process**

Describe how the waiver or alteration of consent involves no more than minimal risk and will not adversely affect the rights and the welfare of the individual (also, discuss how the waiver will not adversely affect the privacy rights of an individual).
This study does not involve an investigational intervention given or administered to patients. The potential benefit of this study would be improving the incidence of VTE rates and standard of care surrounding VTE risk assessment and preventative treatment. The intervention for the trial will display a patient's estimated risk for the clinical team to consider alongside their clinical judgment when making a decision about whether or not to initiate prophylaxis. Thus, this intervention will provide additional context for clinicians while maintaining their agency in deciding on patient care - filling a potential quality gap. Waiver of consent will have no impact on privacy for patients or providers because the CDS tool will be applied in encounters already scheduled for unrelated reasons and no data from this study will exist outside of the individuals' EHR. We are seeking a waiver of consent because participation of patients in the trial will not affect their rights or welfare, as both arms will be receiving standard of care (i.e. current workflows for determining risk and ordering of prophylaxis) at minimum.

Explain why the research could not practicably be conducted without the waiver or alteration.
Patients will appear in study sites for routine care at health system scale. It is not practicable or feasible to consent patients or providers in this dynamic real-world setting.

Define the plan, where appropriate, to provide individuals with additional pertinent information after participation.
A participant notification sheet would be impracticable to provide to all inpatients. Patients will be unaware of which arm they are randomized to, as the risk score will be presented to the clinical team, and we are determining how the risk score affects their decision on VTE prophylaxis. There would be no advantage to the patient to be in the treatment arm vs the control arm, as both arms will receive standard of care. It would not be appropriate to provide patients which arm they are randomized to, as it would affect the integrity of study.

Are you requesting a waiver of consent to use identifiable information?
[**x**] **Yes**
[ ] No

Please explain why the research could not practicably be conducted without the use of identifiable information:
This pragmatic RCT in real-world settings necessitates the use of PHI to link CDS and outcome data to study participation. We will use real-world EHRs to track study outcomes and the model will calculate and update based on EHR data in real-time (although no PHI will be used in the calculation of the risk score).

Conflict of Interest Disclosure

Is there a potential conflict of interest for the Principal Investigator or key personnel? • The PI is responsible for assuring that no arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research and no arrangement has been entered into where the amount of compensation will be affected by the outcome of the research. • Assessment should include anyone listed as Principal Investigator, or other research personnel on page 1 of this application. Please note that ownership described below apply to the aggregate ownership of an individual investigator, his/her spouse, domestic partner and dependent children). Do not consider the combined ownership of all investigators.

[ ] Yes
[**x**] **No**