INSTRUCTIONS:

- *You may use a different format, order, outline or template provided the necessary information is included.*
- *Remove italicized instructions and subheadings prior to submission.*
- *Depending on the nature of what you are doing, some sections may not be applicable to your research. If so mark as "NA" or delete.*
- ***For any items described in the sponsor's protocol, grant, contract, or other documents submitted with the application, include the appropriate text within this template.***
- *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*

1) Protocol Title

a) The Effect of an Electronic Medical Record (EMR) Alert on Hepatitis B Screening: A Randomized Controlled Trial.

b) May 15, 2019

2) **Author of Protocol:** Eric Chak MD, MPH (UC Davis Researcher)

3) IRB Review History: Not Applicable.

4) Objectives: The purpose of this study is to determine the effect of an EMR alert released through the UC Davis EMR on Hepatitis B screening.

5) Background

Chronic hepatitis B is a significant public health problem, which affects Asian American/Pacific Islander (API) Americans disproportionately. Of the CHB-positive foreign born persons living in the United States in 2009, 58% migrated from Asia (Kowdley et al. Hepatology 2012). Not only are foreign born APIs disproportionately infected with HBV, but they also have the highest incidence rates of hepatocellular carcinoma (HCC) and HCC-related mortality. According to analysis of the Surveillance Epidemiology and End Results (SEER) database, APIs had the highest age-adjusted HCC incidence rates consistently from 1992-2002. Hispanics had the second highest HCC incidence rates, but these were 40% lower than that of the APIs (El Serag et al. Arch Intern Med 2007). In the same study, APIs were also found to have the highest mortality associated with HCC of all groups studied with a relative risk of 3.6 compared to whites.

Despite this, the diagnosis of CHB remains low and only 20-30% of high risk individuals are aware of their infection (Cohen et al. J Viral Hepat 2011, Institute of Medicine, 2010). In 2014, the US Preventive Services Task Force placed a Grade B

recommendation on screening for Hepatitis B particularly among persons born in countries and regions with high prevalence of HBV infection (≥2%) or US born persons not vaccinated as infants whose parents were born in very high prevalence areas such as sub-Saharan Africa or central and Southeast Asia (LeFevre et al. Annals of Internal Medicine, 2014).

This study is part of a larger CDC-funded collaboration to increase screening and linkage to care for CHB (Sacramento Collaborative to Advance Testing and Care of Hepatitis B-SCrATCH B). Data from the Thousand Asian American Study at UC Davis suggests that the HBV prevalence in Sacramento County is 6%. Thus, we aim to increase HBV screening further with introduction of this EMR alert and to measure its effect in a randomized fashion.

6) Inclusion and Exclusion Criteria

Inclusion:

- Outpatients enrolled in the UC Davis EMR system aged 18 years and older with Chinese, Vietnamese, Japanese, Korean, or Indian surnames as determined by a peer reviewed listing of the 50 most common surnames within each ethnicity (Lauderdale et al. Population Research and Policy Review, 2000)
- Outpatients who have established in the UC Davis Primary Care Network
- No Hepatitis B surface Antigen (HBsAg) test previously
- No history of vaccination for HBV previously
- Primary care physicians (PCP) within the UCD network entities

Exclusion:

- Patients outside of this age range
- Pregnant patients
- Prisoners

7) Number of Subjects: We expect that 50% of intervention (EMR alert) patients will be tested for hepatitis B and that 20% in the control will be tested. Therefore, to achieve 80% power at the 0.05 significance level (2-sided), 45 patients in each group will be needed (90 total). While 90 is the minimum number of patients required to show a difference between control and EMR groups, the patient database has the potential to randomize 4,000 patients (2,000patients in each arm). This could increase the validity of the alert. In addition, 10,000 more patients (5,000 in each arm) will be randomized to account patients with Medicare. In sum, 14,000 patients will be in the study. The inclusion of additional patients can help to increase the validity of such implementation. Physicians of the patients will be part of the study, in which they will be informed about the EMR alert study at the end. The number of PCPs involved in the study will be determined after the computer randomization of the study patients.

8) Recruitment Methods

As mentioned, patients will be identified by EMR search based on their surname, previous HBsAg testing status, and previous HBV vaccination status. If they meet criteria for the study, the EMR alert will be released to their chart for their primary care provider to view. No in person recruitment will be done. PCPs will be informed at completion of the study about the EMR alert study. We will request for a HIPAA waiver of authorization as below:

HIPAA Authorization for Research (check all that apply):

Do you want to request a waiver of authorization?

☒Yes ☐ No

If you require a waiver of authorization, the IRB must make determinations to approve this waiver. Does the use or disclosure of PHI involve no more than a minimal risk to the privacy of the individual based on at least the presence of the following:

☒ I confirm that only authorized persons will be granted access to the identifiers; identifiers stored on a computers, electronic notebooks, mobile devices, data-storage devices will be encrypted and password protected; identifiers maintained in paper format will be kept in a locked area with access limited to only research staff who require access to conduct the study.

☒ I confirm that I will 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 as otherwise required by law.

Date or event for when the identifiers will be destroyed: *October 31, 2024*

☒ I confirm that protected health information from this research will not be reused or disclosed to another person or entity, except as required by law, for authorized oversight of the research study, or other research for which the use or disclosure of PHI would be permitted.

Why will this waiver not adversely affect the privacy rights of the individual?

Identification of the subjects or their responses will not place them at risk of criminal or civil liability or be damaging to the their financial standing, employability, insurability, reputation, or be stigmatizing, as appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal risk.

Why do you need this waiver to conduct this research?

Patients will be identified as previously aforementioned. The only identifying information will be patient MRNs. There will be minimal risks for those identified who meet inclusion criteria. We will be activating the alert system-wide in a great number of patients. For these reasons, obtaining HIPAA authorization from subjects would not be feasible. Appropriate precautions will be taken to ensure that the privacy rights of those identified will be maintained.

9) Compensation to the Subjects

Patients will not be compensated.

10) Study Timelines

We anticipate that we will be able to recruit all 14,000 subjects for the study within 12 months. Once the EMR alert is released to a patient's chart, we will perform quarterly EMR data searches to determine if the primary care physician has ordered the HBsAg on those patients. Once a HBsAg test is ordered, the result will be recorded and the patient's participation in the study will end. If no HBsAg test is ordered, we will continue our quarterly EMR data searches to determine if the primary care physician orders the HBsAg at subsequent visits. The post-EMR release observation period may last up to 2 years. If no HBsAg test is ordered at the end of 2 year observation, the patient's participation in the study will end. The study will end on October 31, 2024 due to additional participants to allow time for data collection, analysis, and manuscript writing.

11) Study Endpoints

The study end points will be measurement of an HBsAg level after the EMR alert is release to each patients chart. As mentioned, certain proportion of patients will not reach this end point and this will be recorded.

12) Procedures Involved

- A list of patients meeting the eligibility requirements stated above will be obtained by searching the UC Davis EMR. At a given time, computerized 1:1 randomization of these patients will occur placing them in the intervention or control group. After randomization, the EMR alert will be released in the patients' charts notifying primary care doctors that these patients should be screened for hepatitis B with a HBsAg test. Control group patients will not have the EMR alert released in their chart and will undergo "usual care." As mentioned above (see Study Timelines), we will perform quarterly

EMR searches to determine if a HBsAg test was ordered by the patient's primary care physician in response to the EMR alert. We will continue to perform quarterly EMR searches to determine if HBsAg tests are ordered at subsequent visits up to 2 years after the index visit.

- The data points that will be collected are MRN, age, sex, number of office visits, primary language, insurance type (private, medi-cal, or medicare), hepatitis B antigen test result, and date of the hepatitis B antigen test. All data points will strip off identifiable information. Study ID will be assigned and codes created are the only links to identifiable information.
- Patients who are randomly chosen for this study will be number coded. The only link to the patient identifiers will be through a separate key code which will be kept on a secure, password-protected computer. Anypaper copies of such information will be kept in a locked filing cabinet in the division office accessible only to the PI and co-PI. The key code will be destroyed once it is confirmed that the data collection is complete.

13) Data and/or Specimen Management and Confidentiality

Will data be banked for future use?
☐ Yes ☒ No

If yes, will the data that are banked be identifiable?

☐ Yes, the data will be identifiable:
☐ No, the data will be completely anonymous.

☐ No, the data will be stripped of identifiers and coded. The link to the individual's identity will not be accessible by the research team.

Where will the data be stored?

How long will the data be stored?

Who will have access to the data?

Describe the procedures to release data, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

14) Data and/or Specimen Banking: Not applicable.

15) Provisions to Monitor the Data to Ensure the Safety of Subjects:
All data will be stored in a password protected Excel file on a secure server and uploaded to REDCap, which is a secure web application, used to build and manage online databases specifically for research, supported by the CTSC. Only those directly involved in research design, data gathering analysis will have access to the database.

16) Withdrawal of Subjects: A patient will be withdrawn from the study by our staff if they fail to make at least one clinic appointment after release of EMR alert during the observation period. This may be due to change or insurance, being lost to follow up, or death.

17) Risks to Subjects
This record/data review poses the risk of loss of confidentiality. This risk will be minimized by coding of patients' data and protection of private health information. This study will abide by all regulations in place governing the protection of human subjects and protected health information.

18) Potential Benefits to Subjects
The direct benefit to subjects is that they may have an increased chance of screening for hepatitis B since the EMR alert will be reminding their primary care doctors to do so.

19) Vulnerable Populations: Not applicable.

20) Multi-Site Research: Not applicable.

21) Community-Based Participatory Research: Not applicable.

22) Sharing of Results with Subjects
The results will not be shared with the subjects.

23) Setting: This project will be conducted solely among UC Davis primary care network clinic sites.

24) Resources Available

Eric Chak, MD, MPH is an Assistant Professor of Internal Medicine in the Division of Gastroenterology and Hepatology. He is primarily interested in

outcomes research in viral hepatitis resulting in several first author publications in the field. Since coming to UC Davis, he has been involved in several projects including SCrATCH B and the R21 Biologic Basis of Disparities in Liver Cancer Survival Among Asian Americans Study. He will the Principal Investigator of this Study and coordinate the randomization of subjects, EMR data searches, and statistical analysis.

Dr. Bowlus is a Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, UC Davis School of Medicine and the Fellowship Director supervising the training of gastroenterologists and hepatologists at UC Davis. Dr. Bowlus serves as the primary hepatologist treating patients with hepatitis B in the UC Davis Health System. He is the Principle Investigator for SCrATCH B and the R21 Biologic Basis of Disparities in Liver Cancer Survival Among Asian Americans Study and will serve as a mentor to Dr. Chak during this study.

Dr. Susan Stewart is an Associate Adjunct Professor in the Division of Biostatistics, Department of Public Health Sciences at the University of California, Davis School of Medicine as well as the Program Evaluator for AANCART and the Director, Biostatistics Core for "Liver Cancer Control Interventions for Asian Americans". Dr. Stewart is a seasoned cancer biostatistician having directed a NCI-funded Biostatistics Core in four program projects. She has more than 19 years of experience in being responsible for the statistical aspects for numerous cancer epidemiology and control studies. Her role includes providing advice on study design, data analyses, methods for analyzing genetic and lifestyle factors, including analyses to assess factors associated with the survival of patients with hepatocellular carcinoma. She directed the biostatistical work and analyses of three interventions to promote hepatitis B testing among Vietnamese, Hmong, and Korean Americans. Her role is to provide biostatistical counsel and to contribute to data analyses and manuscripts based on this study.

25) Prior Approvals: Not applicable.

26) Provisions to Protect the Privacy Interests of Subjects: Not applicable.

27) Compensation for Research-Related Injury: Not applicable.

28) Consent Process:

- We are requesting a waiver of informed consent for this study for the following reasons:
  i) The EMR alert is distributed to primary care units across the Sacramento area. Thus it is not practical to be present at every or any visit to consent the patients.
  ii) Consenting patients to participate in the study prior to EMR alert randomization would create bias if the subjects are informed that they are selected because they are at risk of hepatitis B. The consent process would cause patients to more likely if they are informed and/or they request to be tested.
  iii) Patient's right and welfare will not be violated. They will not be informed of the EMR alert study at all. This study will not affect clinical decisions made on the subjects.
- This study is specifically for UCD network clinics and the data will not be disclosed to outside of UCD entities
- This alert is also for clinical purposes and improve their treatment care
- The PCPs of the selected study subjects will be informed at end of the study about the EMR alert. No information will be collected on the PCPs

29) Process to Document Consent in Writing: Not applicable.

30) Drugs or Devices: Not applicable.