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TITLE: Risk of Hepatocellular Cancer After Virological Cure with Direct Acting Antiviral Agents in Individuals with Hepatitis C

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Purpose: The overarching goal of this project is to reduce HCC-related morbidity and mortality in persons with chronic hepatitis C (CHC) who have been virologically cured by direct acting antivirals (DAAs).
Aims: 1) Examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC; 2) Conduct a virtual clinical trial using a mathematical model of the natural history of HCC to evaluate benefits vs harms of HCC surveillance; 3) Develop an online HCC Simulator.
Design: Using cause-specific Cox proportional hazard models for competing risks, we will identify risk factors in a retrospective cohort study of >100,000 patients with DAA-induced SVR. For dynamic risk prediction of HCC, we will use the landmark Cox model. We will use a mathematical model to simulate a virtual trial comparing long-term effectiveness of no surveillance vs routine surveillance. Finally, we will develop an interactive decision support tool.
Progress: The project is in final stages of completing the HCC Simulator on-line tool. Target completion date 09/30/2023.
Findings: We identified a range of predictors for HCC in virologically cured patients with CHC. Risk factors for HCC were different in patients with and without cirrhosis and some also evolved during follow-up. These factors can help with risk stratification and HCC surveillance decisions in patients with cured HCV. These findings were reported in a manuscript accepted for publication in Am J Gastroenterology. The AUCs for the models in patients with and without cirrhosis were 0.72 (95% CI, 0.70-0.74) and 0.68 (95% CI, 0.66-0.70), respectively.
A Mathematical model of the natural history of HCC in DAA-cured CHC patients was developed that led the team to conclude that the burden of HCC will shift from viremic to virologically cured CHC patients, and to older populations in the next decade. These findings are reported in a meeting abstract that will be presented during the Liver Meeting 2021 and a manuscript that was accepted by JAMA Network Open.

15. SUBJECT TERMS: Hepatocellular carcinoma; Chronic hepatitis C (CHC); Direct-acting antivirals (DAAs); Sustained viral response (SVR); Risk stratification; Protective factors; Risk factors; Risk prediction models; Benefits and harms; Decision support tool; Simulator tool; Cancer surveillance

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1.INTRODUCTION: Hepatocellular carcinoma (HCC) is the fastest growing cause of cancer deaths in Americans. HCC incidence has increased 3-fold between 1975–2009 and the trend is still upwards. Despite moderate advances in treatment, most HCC patients present with advanced stage and have low survival (5-year <15%). Chronic hepatitis C (CHC) infection is the leading cause of HCC. The direct-acting antiviral (DAA) treatments offer cure from chronic infection. However, the subsequent risk of HCC persists in patients with CHC after virological cure. In fact, virologically-cured CHC is one of the most important emerging risk factors for HCC. While patients with advanced HCC have a median survival of less than 1 year, patients with early HCC who receive potentially curative therapy achieve 5-year survival rates near 70%. Early diagnosis, therefore, is critical to improved survival. However, the long-term harms and benefits of routine HCC surveillance in virologically cured CHC patients have not been evaluated. Furthermore, instead of using a one-size-fits-all approach, surveillance recommendations based on individualized risk factors could be more efficient — such an approach could detect HCC in early stages in high-risk patients and spare many non-HCC patients who do not need surveillance. The goals of this study are to: (1) identify the most salient protective and risk factors, and combine these factors in predictive models that differentiate high from low risk patients; (2) provide data on long-term benefits and harms of HCC surveillance tailored to individualized risk factors; and (3) develop a first publicly available decision support tool, HCC Simulator, for individualized surveillance recommendations.

2.KEYWORDS:

Hepatocellular carcinoma

Chronic hepatitis C

Direct-acting antivirals

Sustained viral response

Risk stratification

Protective factors

Risk factors

Risk prediction models

Benefits and harms

Decision support tool

Simulator tool

Cancer surveillance

3.ACCOMPLISHMENTS:

◦**What were the major goals of the project?**

The Statement of Work includes the following major goals:

Specific Aim 1 (Kanwal Lead): To examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients

Major Task 1: Examine determinants of HCC in patients virologically cured with direct acting antiviral (DAA) agents

Subtask 1: Data acquisition from VA Corporate Data Warehouse, data cleaning, variable creation, and cohort identification (Target date 2/28/2020) – 100% complete.

Subtask 2: EMR chart abstractions to confirm HCC (Target date 2/28/2020) – 100% complete.

Subtask 3: Data analysis of HCC predictors (Target date 4/30/2020) – 100% complete.

Major Task 2: Develop & optimize HCC risk prediction model

Subtask 1: Model fitting/Variable selection (Target date 06/30/20) – 100% complete.

Subtask 2: Risk stratification (Target date 07/31/20) – 100% complete.

Subtask 3: Subgroup sensitivity analysis (Target date 08/31/20) – 100% complete.

Specific Aim 2 (Chhatwal Lead, Kanwal Team Participating): To evaluate the benefits vs harms of HCC surveillance in virologically cured patients

Major Task 3: Develop a mathematical model simulating the natural history of HCC that incorporates risk estimates and key factors identified in Aim 1

Subtask 1: Model description – Develop a simulation model (individual-level state-transition model) of the natural history of HCC in virologically cured hepatitis C patients (Target date 08/31/20) – 100% complete.

Subtask 2: Add modules to the simulation model: surveillance and diagnosis, treatment options based on the BCLC stage at diagnosis (Target date 11/30/2020) – 100% complete.

Subtask 3: Liver transplantation - Extend simLT module to simulate the life course of HCC patients on the UNOS waiting list and after the transplant; we will also incorporate HCC recurrence (Target date 11/30/2020) – 100% complete.

Subtask 4: Costs and quality of life – Using published studies, estimate costs associated with the mathematical model's (simHCC's) states (Target date 12/31/2020) – 100% complete.

Major Task 4: Use simHCC to compare long-term effectiveness of no surveillance versus routine surveillance

Subtask 1: Generate a set of outcomes for surveillance vs no surveillance strategies for each risk group (Target date 01/31/21) – 100% complete.

Subtask 2: Conduct probabilistic sensitivity analysis (Target date 02/28/21) – 100% complete.

Subtask 3: Conduct value of information analysis (Target date 04/30/21) – 100% complete.

Specific Aim 3 (Chhatwal Lead, Kanwal Team Participating): To develop HCC Simulator, an online interactive tool for physicians and patients that provides the short- and long-term value of HCC surveillance in different risk groups

Major Task 5: Create a large dataset of hypothetical virologically cured patients

Subtask 1: Using simHCC model, simulate the life course of 1 million patients having different profiles (Target date 05/31/21) – 100% complete.

Subtask 2: Generate a set of graphical outcomes for each patient profile with and without HCC surveillance (Target date 06/30/21) – 100% complete.

Major Task 6: Create an online tool, HCC Simulator

Subtask 1: Create an online platform using RShiny (Target date 09/30/21) – 100% complete.

Subtask 2: Create a homepage for HCC Simulator (Target date 10/31/21) – 100% complete.

Subtask 3: Make the HCC Simulator available on the internet (Target date 11/30/21) – 100% complete.

Major Task 7: Conduct a feasibility to assess the usability of the HCC Simulator in a clinical setting

Subtask 1 (Chhatwal & Kanwal Teams Combined): Develop focus group and patient interview guides (Target date 12/31/21) – 100% complete.

Subtask 2: Provider and patient recruitment for focus groups and individual patient interviews (Kanwal Team); Conduct focus groups and individual patient interviews (Chhatwal Team Lead; Kanwal Team Supporting) (target date 03/31/22) – Delayed. 0% complete. Target date 03/31/2023.

Team A (Fasiha Kanwal Team): Dr. Kanwal's team will recruit all providers and patients for focus group sessions and individual patient interviews and will record the sessions and interviews.

Recruit, consent, and enroll 30 patients/human subjects for participating in 6 focus groups

Recruit, consent and enroll 20 providers for individual interviews

Team B (Chhatwal Team): Dr. Chhatwal's team will conduct the focus groups and individual patient interviews

Subtask 3 (Kanwal Team): Transcription services (Target date 04/30/22) – Delayed. 0% complete. Target date 04/30/2023.

Subtask 4: Coding and analysis of transcripts (Target date 05/31/22) – Delayed. 0% complete. Target date 05/31/2023.

Team A (Kanwal Team): Dr. Kanwal's team will review coding and analysis results

Team B (Chhatwal Team): Dr. Chhatwal's team will code and analyze transcripts

Major Task 8: Incorporate results from focus group and individual patient feedback into the HCC Simulator

Subtask 1: Re-design relevant components of the HCC Simulator based on the feedback (Target date 07/31/22) – Delayed. 0% complete. Target date 06/30/2023.

Team A (Kanwal Team): Dr. Kanwal's team will review results

Team B (Chhatwal Team): Dr. Chhatwal's team will modify the HCC Simulator

Subtask 2: Launch the HCC Simulator (Target date 08/31/22) – Delayed. 0% complete. Target date 06/30/2023.

Team A (Kanwal Team): Dr. Kanwal's team will serve as in a supporting/consulting role

Team B (Chhatwal Team): Dr. Chhatwal's team will launch the HCC Simulator

Major Task 9: Manuscripts and dissemination of results

Subtask 1: Organize a Webinar on use of the HCC Simulator (Target date 08/31/22) – Delayed. 0% complete. Target date 08/31/23.

Team A (Kanwal Team): Dr. Kanwal's team will participate in the development of the Webinar contents

Team B (Chhatwal Team): Dr. Chhatwal's team take the lead to organize a Webinar on its use

Subtask 2: Report project results through manuscripts in peer-reviewed journals (Target date 09/30/22) – Delayed. 70% complete. Target date 08/31/23.

1. Predictors of HCC in CHC patients with virologically induced cure – article accepted for publication – Kramer JR, Cao Y, Li L, Smith D, Chhatwal J, El-Serag HB, Kanwal F. Longitudinal associations of risk factors and hepatocellular cancer in patients with cured hepatitis C virus infection. In Press. Am J Gastroenterol.

2. Risk prediction model to identify patients at high risk for HCC after DAA induced virological cure – manuscript in progress
3. Cost-effectiveness of personalized HCC surveillance in virologically cured CHC patients – published – Mueller PP, Chen Q, Ayer T, et al. Duration and cost-effectiveness of hepatocellular carcinoma surveillance in hepatitis C patients after viral eradication. J Hepatol. 2022;77(1):55-62. doi:10.1016/j.jhep.2022.01.027
4. When to stop HCC surveillance after virological cure with CHC – published – included in above article (doi:10.1016/j.jhep.2022.01.027)
5. What's the HCC incidence risk threshold above which surveillance is cost-effective? – manuscript in preparation (expected submission Oct 2022)
6. A brief report on HCC Simulator

Both Team A and Team B will participate collaboratively and equally in manuscript writing

◦**What was accomplished under these goals?** The following was accomplished under these goals:

Specific Aim 1: To examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients.

Study Cohort. We included patients ≥18 years who achieved SVR with DAA in any of the 130 VA hospitals. We defined DAA treatment as ≥1 filled prescription of DAA (appendix 1) between 1/1/2014 and 12/31/2018. We used 3 months after the date of DAA completion as the index date for start of follow up to consider time needed to determine SVR. We classified patients as SVR if all HCV RNA tests were negative after the end of DAA treatment, with ≥1 HCV RNA test recorded at least 12 weeks after completion. If no test was available after 12-weeks we used a negative test from 4-12 weeks as SVR (6.9% of cohort). We excluded patients who failed to achieve SVR, who had HCC or liver transplant before or within 3 months of DAA treatment, had prior evidence of cancers with a high likelihood of liver metastases (esophageal, stomach, pancreatic, lung, kidney, breast cancer, and melanoma), and patients did not have evidence of ≥1 visit in the VA following end of treatment.

The study **outcome** was new cases of HCC after the date of completing DAA. HCC was defined based on 2 or more instances of ICD-9 (155.0) or ICD-10 codes (C22.0, C22.8, C22.9, D01.5) in CDW or any instance of HCC recorded in the CCR. We also reviewed electronic medical records of cases that had ICD codes but not included in CCR. We followed patients to the development of HCC, liver transplant, death, or last VA visit before December 31, 2021, whichever was earlier.

Predictor variables. These include age, sex, race/ethnicity, marital status, place of residence (rural vs. urban), HCV genotype, previous HCV treatment status, diabetes, hypertension, dyslipidemia, body mass index (BMI), active alcohol use disorder, smoking, and other medical and mental health comorbidity. . We also derived laboratory variables including values of bilirubin, AST, ALT, international normalized ratio, platelet tests, hemoglobin, creatinine, and sodium values. We also used FIB-4 to identify patients with cirrhosis/fibrosis at baseline (FIB-4 >3.25) and used serial changes in FIB-4 to examine the decline or increase in fibrosis. All variables were longitudinal and time updating over time.

Statistical analysis. We used cause-specific Cox proportional hazard models for competing risks12 constructed at three landmark times13, 14 (baseline, and 12- and 24-months after index) to examine the associations between risk factors measured at these landmark times and subsequent HCC risk, stratified by cirrhosis status at baseline.

We constructed six separate models (at three separate landmark times for patients with and without cirrhosis). The outcome was the time from the landmark to HCC. At each landmark, the data only included the at-risk patients at that time (e.g., those who are alive without HCC).

The predictor variables included time-independent and time-dependent defined at each landmark time. For continuous measures, we assessed both categorical and continuous values to determine the best performing measure. The predictors also incorporated longitudinal information of a patient up to the landmark time, including change in FIB-4 [defined as remained stable at low risk (≤3.25), increased from low (≤3.25) to high risk (>3.25), declined from high (>3.25) to low risk (≤3.25), or remained stable at high risk (>3.25)] as well as changes in serum albumin, sodium, bilirubin, INR, creatinine, and hemoglobin between baseline and each landmark time. Log-transformation was used for variables with a skewed distribution. For model

interpretability, we only considered two-way interactions that are frequently observed in the cohort or suggested by literature.

There was a small amount of missing data. We used multiple imputation generated from the fully conditional specification method of SAS PROC MI to create five imputed datasets and then combined the results using multiple imputation. Each imputed dataset went through a model building process with stepwise selection (entry p-value ≤0.10; retaining p-value ≤0.05). The final model included all predictors selected from at least one dataset. For each landmark time, we forced baseline variable/s in the model if the final model/s included the corresponding change variable. Model fit with imputed datasets was checked using usual model checking procedures and no assumptions were violated.

We conducted 3 sensitivity analyses. We refined our cirrhosis definition by including only patients with a diagnosis of cirrhosis or its complications and excluding those with a FIB-4<1.45; we tested the robustness of our HCC definition by including patients with only 1 ICD code for HCC; and we examined the effect of BMI after excluding HCCs diagnosed in the first 12-months.**Specific objectives:** Our specific objectives were to acquire data from VA Corporate Data Warehouse and complete data cleaning, variable creation, and cohort identification; abstract EMR to confirm HCC; analyze data to identify predictors of HCC risk; develop and optimize HCC prediction models and perform subgroup analyses. We have completed these objectives.

Significant results: In total, 113,563 patients received DAA treatment between January 1, 2014, and December 31, 2018. We excluded 9112 without known SVR status, 1919 with prior HCC and 5034 with prior other cancers, 912 who received liver transplant, and 4019 who did not achieve SVR. Hence, our study cohort included 92,567 patients with SVR without prevalent HCC. The mean age of the overall cohort at baseline was 61.5 years (SD=7.55 year), 96.4% were men, 51.0% were white, and 38.7% were African American. A total of 26.5% had cirrhosis diagnosed at baseline and an additional 5.5% had a FIB-4 value greater than 3.25, 36.7% had diabetes, 83.1% had hypertension, 51.2% dyslipidemia, and 14.1% had an active alcohol use disorder. At baseline, 43.5% of patients with cirrhosis had diabetes; it increased to 46.4% at 24-month landmark time. Similarly, the proportion of patients with hypertension increased from 86.6% to 89.7% and dyslipidemia increased from 52.1% to 55.6% between baseline and 24-month landmark time. We found similar trends in patients without cirrhosis.

When examining changes in FIB-4 values from baseline to 24-months in patients with FIB-4 available at both time periods, 18.6% of patients with cirrhosis remained stable at high risk. In addition, 16.4% of patients had a high-risk FIB-4 at baseline that declined over time. FIB-4 values for few patients (3.5%) were low-risk at baseline but increased to high-risk. Approximately 61% with cirrhosis had low-risk FIB-4 values both at baseline and 24-months. In patients without cirrhosis where everyone had low FIB-4 at baseline, 97.8% remained stable at low-risk and 2.2% increased from low to high risk at 24-months.

There were 3,247 incident cases of HCC diagnosed during mean 2.51 (SD=1.66) years of follow-up (maximum 7.11 years); 74.0% (n=2,404) were diagnosed in patients with cirrhosis at baseline. In 29,398 patients with cirrhosis, cumulative incidence of HCC was 2.0%, 3.8%, and 5.4% at 1, 2 and 3 years, respectively. In contrast, HCC risk was considerably lower in 63,169 patients without cirrhosis in whom 843 were diagnosed with HCC (0.2%, 0.5%, and 0.8%, respectively) (p-value <0.0001).

In the baseline model, in patients with cirrhosis, the risk of HCC was higher in men (adjusted hazard ratio (HR) =1.89, 95% confidence interval (CI)=1.37-2.59) and lower in African American patients (HR=0.78, 95%CI=0.71-0.86). Patients with genotype 3 had a higher risk of HCC (HR=1.47, 95%CI=1.27-1.71) than those with other genotypes. Patients with a longer duration since cirrhosis diagnosis had higher risk (≥5 years vs. <1 year, HR=1.71, 95%CI=1.46-2.00). Serum bilirubin, albumin, presence of varices, and higher FIB-4 were associated with HCC risk. Specifically, HCC risk was 2.5-fold higher (95%CI, 2.11-2.94) in cirrhosis patients who also had FIB-4 >3.25 than those with FIB-4 values <1.45. Patients who were current smokers had an increased risk for HCC than non-smokers (HR=1.32, 95%CI=1.16-1.51). None of the pre-specified interaction terms were significant in the adjusted model at baseline.

Most of the associations observed at baseline persisted in direction and magnitude at 12- and 24-month landmark times, with few notable exceptions. Presence of ascites was associated with an increased risk for HCC at both 12- and 24-months. Changes in serum albumin, bilirubin, and FIB-4 between baseline and landmark times were strongly associated with subsequent risk of HCC. For example, one unit increase in serum bilirubin between baseline and 24-month landmark time was associated with a 22% increase in HCC risk. Compared with patients with persistently low FIB-4 at baseline and 24-months, the risk of HCC was almost 2-fold higher in patients who had persistently high FIB-4 at the time of virological cure and at 24-months (HR=1.70, 95%CI, 1.45-2.00) and 81% higher in patients who were at low risk (FIB-4≤3.25) but increased to

high risk (FIB-4>3.25) at 24-months (HR = 1.81, 95% CI = 1.37-2.38). Results were similar in the sensitivity analyses excluding cirrhosis patients with FIB-4<1.45 and including patients with 1 ICD code for HCC.

In patients without cirrhosis, patients with hypertension and diabetes had a 1.5-fold higher risk of HCC than their counterparts. After controlling for diabetes and hypertension, there was no difference in the risk of HCC between patients with BMI higher than 30 compared with BMI 25-30. Risk of HCC was higher in patients with BMI <25, with the highest risk in patients with BMI <18.5 compared with BMI 25-<30, (HR=1.93, 95%CI=1.20-3.12). The risk of HCC for BMI <18.5 was slightly attenuated after excluding patients with HCC in 12-months after index date. Baseline serum albumin and FIB-4 were associated with HCC risk. Patients with baseline FIB-4 between 1.45 and 3.25 had 2.3-fold higher risk of HCC than those with low FIB-4 <1.45 (HR=2.27, 95%CI=1.96-2.63). Prior failure of HCV treatment, HCV genotype 3, and current smoking were also associated with HCC risk in patients without cirrhosis.

Only metabolic traits (diabetes, hypertension) and change in FIB-4 remained associated with HCC risk at all landmark times. At 24-month landmark time, patients with hypertension and diabetes had 1.7 to 1.5-fold higher risk of HCC than their counterparts. Patients who had an increase from FIB-4 of low risk at baseline to high risk at 24-month landmark time had 3-fold increase in HCC risk (HR=3.12, 95%CI, 2.12-4.60).

Following the 24-month landmark time, the 3-year cumulative incidence of HCC varied from 3.4% (95%CI, 3.1%-3.7%) in patients who had persistently low FIB-4 value to 9.2% (95%CI, 8.3%-10.2%) in patients with persistently high FIB-4. Risk of HCC was low in all subgroups without cirrhosis, with few notable exceptions. In patients who increased from low to high risk, the 2- and 3-year cumulative incidence of HCC was 2.4% (95%CI, 1.6%-3.6%) and 3.0% (95%CI, 2.1%-4.4%), respectively. Cumulative 1, 2- and 3-year risk of HCC in 419 patients without cirrhosis who had hypertension, diabetes and who experienced an increase from low to high risk between baseline and 24-month landmark was 3.1%, 5.7%, and 7.2%, respectively.

The AUCs for the models in patients with and without cirrhosis were 0.72 (95% CI, 0.70-0.74) and .0.68 (95% CI, 0.66-0.70), respectively.

Specific Aim 2: To evaluate the benefits vs harms of HCC surveillance in virologically cured patients

For Specific Aim 2, **the major activities** undertaken by the Chhatwal Team, with participation from the Kanwal Team, in Year 2 included developing a mathematical model simulating the natural history of HCC to evaluate the benefits and harms of routine HCC screening in virologically cured patients. We included the following new modules in year 2: surveillance and diagnosis; treatment options based on the BCLC stage at diagnosis; costs associated with HCC surveillance, hepatitis C sequelae, liver transplant and other HCC treatments. We also extracted quality of life associated with all health states in the model. Using this extended model, we conducted three studies.

Study 1

We evaluated the cost effectiveness of HCC surveillance in hepatitis C cured patients. Primary outcomes included life expectancy, quality-adjusted life years (QALYs), total costs, and incremental cost-effectiveness ratio (ICER) of each of the simulated surveillance strategies.

Preliminary results: In virologically-cured patients with cirrhosis, the ICER of biannual surveillance remained below $100,000/QALY (range: $85,000-$98,100) when surveillance was stopped at age 65, rising above $100,000 if surveillance continued beyond 65. For every 1000 patients, surveillance detected 260 HCCs in ‘very early’/early stage, and 120 in intermediate/advanced stage. In contrast, no surveillance detected 92 HCCs in ‘very early’/early stage, and 274 in intermediate/advanced stage. Compared to no surveillance, HCC surveillance provided QALY gains of 47 per 1000 patients. In virologically-cured patients with advanced fibrosis, the ICER of biannual surveillance remained above $100,000 irrespective of the stopping age.

Conclusion: Biannual surveillance for HCC in virologically-cured hepatitis C patients with cirrhosis is cost-effective until the age of 65.

Study 2

The AASLD guidance recommends biannual surveillance for hepatocellular carcinoma (HCC) in hepatitis C virus (HCV) infected individuals with cirrhosis if HCC incidence is above 1.5 per 100 person-years (PY). However, the incidence threshold for surveillance in cirrhosis individuals who achieved virological cure with direct-acting antivirals is unknown. Using our microsimulation model, we estimated the HCC incidence above which routine HCC surveillance is cost-effective in this growing population of individuals with virologically cured HCV.

We developed a Markov-based microsimulation model of the natural history of HCC in individuals with hepatitis C who achieved virological cure with oral direct-acting antivirals. We used published data on the natural history of hepatitis C, competing risk post virological cure, HCC tumor progression, real-world HCC surveillance adherence, contemporary HCC treatment options and associated costs, and utilities of different health states. We estimated the HCC incidence above which biannual HCC surveillance using ultrasound and alpha-fetoprotein would be cost-effective.

In virologically cured hepatitis C individuals with cirrhosis and advanced fibrosis, HCC surveillance is cost-effective if HCC incidence exceeds 0.7 per 100-PY using $100,000 per quality-adjusted life-year (QALY) willingness-to-pay. At this HCC incidence, routine HCC surveillance would result in 2,650 and 5,700 additional life-years per 100,000 cirrhosis and advanced fibrosis persons, respectively, compared to no surveillance. At $150,000 willingness-to-pay, surveillance is cost-effective if HCC incidence exceeds 0.4 per 100-PY. Sensitivity analysis showed that the threshold mostly remained below 1.5 per 100-PY.

Conclusion. Our study suggests that for patients with virologically cured hepatitis C, routine surveillance is warranted above the HCC incidence threshold of 0.7 per 100-PY, which is lower than the previous 1.5% incidence value used to guide HCC surveillance decisions. Updating clinical guidelines could improve the early diagnosis of HCC. Use of this revised threshold could increase HCC surveillance for hepatitis C patients, providing an opportunity for earlier diagnosis and treatment.

Study 3

We also conducted probabilistic sensitivity analysis and value of information analysis to evaluate the impact of uncertainty of HCC surveillance recommendations. Preliminary results are being analyzed and will be finalized in soon for submission to a journal.

Specific Aim 3: To develop HCC Simulator, an online interactive tool for physicians and patients that provides the short- and long-term value of HCC surveillance in different risk groups

For Specific Aim 3, the **major activities** undertaken by the Chhatwal Team, with participation from the Kanwal Team, in Year 3 included the following.

Using the mathematical model, we simulated the life course of hypothetical patients with different risk profiles and stored them in a database. The dataset included cause of death (liver-related, or non-liver-related), development of HCC overtime, and likelihood of detection of HCC with or without surveillance.

We used the above database to create an online, interactive framework, which allows users to enter specific patient profiles and generate model-predicted long-term outcomes in graphical format. We use RShiny, an R package to develop an interactive online interface of the HCC Simulator. Figure shows the screenshots of Liver Cancer Simulator.

Liver Cancer Simulator

About Liver Cancer | Team | About The Simulator | Simulator

Choose Risk Factors

Current Age:

40 75

40 44 48 52 56 60 64 68 72 75

Sex:

- (•) Male
- ( ) Female

Race

- (•) Black
- ( ) Hispanic
- ( ) Other

Fibrosis Stage

- ( ) Advanced Fibrosis
- (•) Cirrhosis

Additional Risk Factors:

- [ ] Diabetes Diagnosis
- [ ] Hypertension Diagnosis
- [ ] Alcohol Use

Run Simulator

Tool Introduction and Description

Simulator Purpose:

The Liver Cancer Simulator is an interactive tool that allows patients and physicians to simulate the potential health outcomes for a specific patient with their unique demographic profile. This tool can be used to evaluate the risk of developing liver cancer and to identify the benefits of regular screening for a particular individual.

Tool Overview:

To use the simulator, please input the patient's personal risk factors in the panel to the right. Once your selections have been made, please click the 'run simulator' button to generate the results.

Key Terms:

- *Surveillance* - This refers to a patient undergoing screening with a medical professional. The aim of surveillance is to detect any cancer at the earliest stage possible.
- *Risk Factors* - Any personal characteristic that may impact the occurrence or progression of liver cancer is considered a risk factor in this simulator.
- *Liver Cancer* - Liver cancer is a type of cancer that starts in the liver. Hepatocellular carcinoma (HCC) is the most common type of liver cancer.
- *Liver Cirrhosis* - Cirrhosis is a permanent and end-stage liver disease that occurs due to the accumulation of scar tissue in the liver. Causes of liver cirrhosis include chronic alcohol abuse and hepatitis among others.

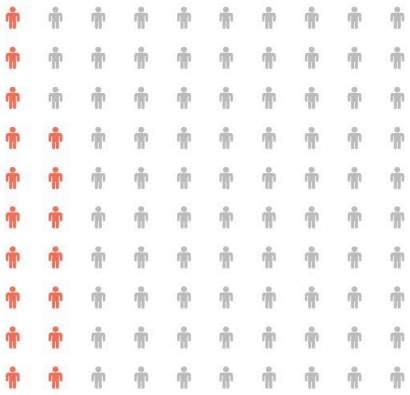
Intro

W My Chance of Getting Liver Cancer?

Why is this important?

Your 10-Year Chance of Developing Liver Cancer:

18 out of 100 People Like You



What Are My Chances of Surviving Liver Cancer?

5-Year Survival by Cancer Stage at Diagnosis

Why is this important?

Early	Intermediate	Late
56%	24%	5%

Survival after 5 years is highly related to the stage of the liver cancer at diagnosis. On average, individuals diagnosed at an early stage have the highest 5-year survival rate with treatment.

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

Two student analysts got an opportunity to gain knowledge of the natural history of HCC in hepatitis C cured patients. This knowledge was transferred in the development of Liver Cancer Simulator, which is intended to be used by patients to understand the risk factors of HCC and importance of early detection of HCC to improve patients survival.

◦**How were the results disseminated to communities of interest?**

The results were disseminated via meeting presentations and manuscripts.

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

We received approval for a no cost extension through 08/31/2023 and expect to complete Major Tasks 7, 8 and 9 during this timeframe.

Major Task 7 (conduct a usability study of the on-line simulator) – Both teams will work together to conduct user-centered design assessments of the Liver Cancer Simulator with patients and feasibility testing with patients and providers to assess usability of the simulator in clinical settings. As part of a user-centered design process, we will initially elicit patients' perceptions on the design and understandability of the simulator as a decision support tool using focus groups. Themes arising from the focus groups will inform the design of a live prototype of the Liver Cancer Simulator. The team will then conduct individual, Think-Aloud interviews with patient and providers to elicit usability of the simulator. Themes from patient and provider interviews will inform refinements to the final design as needed, before wide-spread dissemination. The team has built this tool with the goal of expanding the use of the program beyond specialists (e.g., hepatologists and gastroenterologists) and patients at risk of developing liver cancer.

Kanwal Team – The Kanwal team will recruit participants, record interviews and coordinate transcription.

Chhatwal Team – The Chhatwal team will conduct the interviews (via video-teleconference), analyze transcript data, and summarize usability feedback.

Major Task 8 – The Chhatwal team will complete Major Task 8 to modify the on-line liver cancer simulator.

Major Task 9 (manuscripts and dissemination of results) – Both teams will work together to organize a Webinar on the use of the Liver Cancer Simulator. Both teams will work together to finalize the manuscript publications that are now in process. Target date 08/31/23.

4.IMPACT: Our study provides evidence from a well characterized cohort of virologically cured patients with HCV but free of cirrhosis that monitoring changes in FIB-4 might have clinical utility, especially in patients with co-existing diabetes and hypertension. In patients with cirrhosis, evolution of FIB-4 and other select markers of liver disease severity could refine risk stratification. We believe risk assessment based on repeat measurements at 2 years is practical and can improve shared decision-making between patients and their physicians by providing a quantifiable personalized HCC risk assessment, including how it changes over time. These findings may guide clinical practice guidelines about management of patients with virologically cured HCV.

5.CHANGES/PROBLEMS:

◦**Changes in approach and reasons for change**

Nothing to Report.

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

Both teams experienced delays related to the IRB approval process at both sites involving changes required for the MGH team qualitative expert to conduct interviews with provider and patient participants at the Houston site. A SMART IRB agreement had to be established and protocols at both locations needed to be amended. First, MGH IRB reviewed and approved the changes on 06/30/2022. Then, the Houston IRB began its review and is in the final stages of approval. After Houston IRB approval is received, the teams will seek HRPO approval. The IRB approval process delays have caused a delay in the team's ability to begin Major Task 7 – To conduct a feasibility study to assess the usability of the HCC Simulator in a clinical setting and Major Task 8 – Incorporate results from focus group and individual patient feedback into the HCC Simulator. We received approval of a no cost extension through 08/31/2023 and expect to complete Major Tasks 7, 8 and 9 during this timeframe.

◦**Changes that had a significant impact on expenditures**

Chhatwal Team – Nothing to report. No change in the scope of work is planned.

Kanwal Team – Nothing to report. No change in the scope of work is planned.

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

Nothing to Report.

6.PRODUCTS:

◦**Publications, conference papers, and presentations**

Mueller PP, Chen Q, Ayer T, Nemutlu G, Bethea ED, Peters MLB, Lee B, Nanjua NZ, Kanwal F, Chhatwal J. Duration and cost-effectiveness of hepatocellular carcinoma surveillance in hepatitis C patients after viral eradication. J Hepatol. 2022;77(1):55-62. doi:10.1016/j.jhep.2022.01.027 Epub 2022 Feb 12. PMID: 35157959. Acknowledgement of Federal support reported.

Kramer JR, Cao Y, Li L, Smith D, Chhatwal J, El-Serag HB, Kanwal F. Longitudinal associations of risk factors and hepatocellular cancer in patients with cured hepatitis C virus infection. In Press. Am J Gastroenterol. Acknowledgement of Federal support reported.

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

Nothing to report.

▪Other publications, conference papers, and presentations.

Kramer JR, Cao Y, Li L, Smith D, Chhatwal J, El-Serag HB, Kanwal F. Longitudinal associations between risk factors and subsequent risk of hepatocellular cancer in patients with hepatitis C virus infection and virological cure. 2021 AASLD The Liver Meeting, November 12-15th. Anaheim, CA.

Chhatwal J, Hajjar A, Mueller PP, Nemutlu G, Peters MLB, Kanwal F. Hepatocellular Carcinoma Incidence Threshold for Routine Surveillance is Much Lower in Hepatitis C Cirrhosis Individuals Who Achieve Virological Cure. 2021 AASLD The Liver Meeting, November 12-15th. Anaheim, CA. Also accepted for inclusion in the Best of The Liver Meeting's summary slide deck in the Health Services and Public Health Research category.

Nemutlu G, Mueller PP, Qiushi Chen, Turgay Ayer, Naveed Janjua, Kanwal F, Chhatwal J. Liver Cancer Surveillance in the Era of New Hepatitis C Antiviral Treatments: A Value of Information Analysis. 2021 INFORMS Annual Meeting, October 27-27th 2021. Anaheim, CA.

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

https://analytics-tools.shinyapps.io/HCC_Simulator_2/

The Liver Cancer Simulator is an interactive tool that allows patients and physicians to simulate the potential health outcomes for a specific patient with their unique demographic profile. This tool can be used to evaluate the risk of developing liver cancer and to identify the benefits of regular screening for a particular individual.

◦**Technologies or techniques**

Nothing to report.

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

Nothing to report.

◦**Other Products**

Nothing to report.

7.PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

◦**What individuals have worked on the project?**

Name: Fasiha Kanwal, MD, MSHS
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0001-6715-3966
Nearest person month worked: 2.4
Contribution to Project: As the Principal Investigator, Dr. Kanwal oversees all aspects of the project and has primary responsibility for supervising Aim 1 activities: 1) Data acquisition, data cleaning, variable creation, cohort identification, 2) EMR chart abstractions to confirm HCC, 3) data analysis of HCC predictors, 4) develop and optimize HCC risk prediction model.
Funding Support:

Name: Jennifer R. Kramer, PhD
Project Role: co-Investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0003-2953-4949

Nearest person month worked: 2
Contribution to Project: Dr. Kramer is leading the Data Analysis Team based at the VA (Aim 1 to examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients). She works closely with the PI, the biostatistician, and the data analyst on data acquisition, and operationalizing study variables. She supervises chart abstractors, oversees data analysis, and interprets results.
Funding Support:

Name: Roxanne Desiderio, BS
Project Role: Research Assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6
Contribution to Project: Ms. Desiderio conducted electronic medical record (EMR) chart reviews and assisted with administrative tasks, such as meeting scheduling, reporting, and maintaining regulatory documentation.
Funding Support:

Name: Yumei Cao, MS
Project Role: Data Analyst
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6
Contribution to Project: Ms. Cao is the data analyst for Aim 1 of the project, responsible for the build and upkeep of the study databases, quality control measures, and conducting statistical analyses with the guidance of Drs. Kramer, Richardson, and Kanwal. She performed the programming required to identify the cohort, define the study variables, and construct analytic datasets. Ms. Cao provided weekly summary reports on the state of data analysis at the weekly project meeting headed by Dr. Kanwal (PI).
Funding Support:

Name: Donna Smith, MEd
Project Role: Project Coordinator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0003-1906-666X
Nearest person month worked: 3
Contribution to Project: Ms. Smith is responsible for all administrative and regulatory tasks of the project, including IRB protocol approvals, renewals, and amendments; organizing project team meetings; maintaining study binders; and managing the budget. She coordinates data acquisition requests and data use agreement renewal updates. She will work closely with the core research investigators to coordinate writing and editing of progress reports and will assist with the development and publication of dissemination products.
Funding Support:

Name: Chris Williams, BS
Project Role: IT Manager
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Mr. Williams is responsible for performing computer server maintenance and upgrades. He provides support and training for study personnel on project-related software programs. He ensures that data privacy standards are maintained and processes Data Use Agreements and PKI for study personnel. These functions are critical part of our data-management security plan to ensure compliance and the safety of all encrypted veteran data.
Funding Support:

Name: Jagpreet Chhatwal, PhD
Project Role: Principal investigator
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0001-8741-4430
Nearest person month worked: 2

Contribution to Project: As the Principal Investigator, Dr. Chhatwal has primary responsibility for supervising Aim 2 activities: development of the mathematical model to simulate the natural history of HCC in hepatitis C cured patients, literature review, validation and analysis of the proposed model.
Funding Support:

Name: Ali Hjaar, PhD
Project Role: Postdoc
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6
Contribution to Project: Dr. Hjaar is a postdoctoral fellow who developed the natural history model of hepatitis C and HCC using a programming language. He also assisted with estimation model inputs and analysis of outcomes.
Funding Support:

Name: Neeti Kulkarni,
Project Role: Analyst
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6
Contribution to Project: Ms. Kulkarni is a research analyst responsible for conducting literature review of model parameters to evaluate the cost effectiveness of HCC screening in hepatitis C cured persons.
Funding Support:

Name: Alec Aaron,
Project Role: Programmer Analyst
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3
Contribution to Project: Mr. Aaron is a programmer analyst responsible for developing an online tool to inform HCC screening for patients and providers. He developed the interface of the Liver Cancer Simulator and downloadable reports.
Funding Support:

Name: Mary Ann Ladd, BS
Project Role: Data Manager
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Ms. Ladd is the Systems Manager of the MGH Institute for Technology Assessment. She was responsible for overseeing the integration and day-to-day management of computer systems at the Institute for Technology Assessment, and for facilitating electronic communications among collaborators. She worked with the other team members to facilitate data extraction and storage, and ensure that all study data are secure, adequately stored and backed up.
Funding Support:

Name: Peter Mueller, PhD
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3
Contribution to Project: Dr. Mueller is a research scientist who assisted with the development of the natural history model of hepatitis C and HCC using a programming language, setup of the computer server for computational runs for the model. He also assisted with the analysis of outcomes.
Funding Support:

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

PREVIOUS, CURRENT, AND PENDING SUPPORT (PCPS)

KANWAL, FASIHA

PREVIOUS

Title: HSR&D Project # IIR 16-075 (Application # 1 I01 HX002204-01A2) Patient Centered Care for Individuals with Advanced Liver Disease
Role on project: MPI
AIMS: 1) To develop risk stratification models of advanced liver disease (AdvLD) prognosis; 2) To describe patients' experiences and goals of AdvLD care; 3) To identify clinicians' perceptions of opportunities and barriers to patient-centered AdvLD care.
Time Commitment (Level of Effort): 0 calendar months
Supporting Agency: VA HSR&D
Name and address of funding agency's Grant's Officer:
Cathie Plouzek, PhD, PMP
Health Services Research and Development (10P9H)
Office of Research and Development, VA Central Office
Department of Veterans Affairs
810 Vermont Avenue NW
Washington, DC 20420
E-mail: cathie.plouzek@va.gov
Performance Period: 05/2018-04/2021 (NCE 05/2021-04/2022)
Level of funding:
Brief description of project's goals: The main goal of the project is to develop a patient-centered care model for advanced liver disease, including risk-prediction models and clinician-patient collaborative treatment planning guides that focus on addressing patient unmet needs and expectations about illness course and care preferences for curative, supportive, and palliative care. The study findings will have direct impacts on current advanced liver disease care, as well as provide evidence for developing innovative care models for other serious chronic illnesses.
% Overlap: None

CURRENT

Title: NIDDK P30 DK 56338-10/15 Center for Gastrointestinal Development, Infection and Injury
Role on project: Co-director (Overall PI: El-Serag)
AIMS: 1) To serve clinical and basic science investigators in digestive diseases with comprehensive study design consultation and support; 2) To assist DDC investigators in all aspects of the acquisition of clinical specimens required for their research in digestive diseases; 3) To support comprehensive data analyses and interpretation of basic, translation, clinical and epidemiological studies.
Time Commitment (Level of Effort): 0.6 calendar months
Supporting Agency: NIH/National Institute of Diabetes and Digestive and Kidney Diseases
Name and address of funding agency's Grant's Officer:
Peter J Perrin
Program Official
Division of Digestive Diseases and Nutrition, NIDDK, NIH
6707 Democracy Blvd., Room 6015
Bethesda, MD 20892-5450
Email: Peter.Perrin@nih.hhs.gov
Performance Period: 12/1999-02/2023
Level of funding:
Brief description of project's goals: This Center supports four scientific cores, conferences and a pilot project program to facilitate on-going Digestive Disease research of center members, promote interactions and translational research between basic and clinical areas, develop new projects, nurture new investigators, and provide GI educational activities.
% Overlap: None

Title: 1 U01 CA230997-01 Risk Stratification for and Early Detection of Liver Cancer
Role on project: PI
AIMS: 1) Develop and test novel personalized risk stratification indices for predicting future HCC development in cirrhosis from diverse etiologies; 2) Develop and evaluate an algorithm combining existing HCC blood based

biomarkers (AFP, AFPL3, DCP), their longitudinal changes and host features (e.g., cirrhosis etiology) to improve early HCC detection; 3) Evaluate novel plasma-based methylation markers for cell-free DNA (MDMs) as an independent surveillance biomarker for early HCC detection. Using the PRoBE design, we will test 12 individuals MDMs identified in Phase 2 study.
Time Commitment (Level of Effort): 1.8 calendar months
Supporting Agency: NIH Consortium on Translational Research in Early Detection of Liver Cancer: Translational Research Centers (U01)
Name and address of funding agency's Grant's Officer:
Viviana Knowles
National Cancer Institute
Office of Grants Administration
9609 Medical Center Drive
West Tower, 2nd floor
Rockville MD 20850
viviana.knowles@nih.gov
Performance Period: 09/2018-08/2023
Level of funding:
Brief description of project's goals: The overarching goal of our Translational Research Center (TRC) is to reduce the mortality of hepatocellular cancer (HCC) by developing personalized indices that combine novel and existing biomarkers with clinical, behavioral and genetic data to improve clinical risk stratification and increase early detection of HCC.
% Overlap: None

Title: PR181562 Risk of hepatocellular cancer after virological cure with direct acting antiviral agents in individuals with hepatitis C (subject grant)
Role on project: MPI
AIMS: 1) To examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients; 2) To evaluate benefits versus harms of HCC surveillance in virologically cured patients; 3) To develop HCC Simulator, an online interactive tool for physicians and patients that provides the short- and long-term value of HCC surveillance in different risk groups.
Time Commitment (Level of Effort): 0.05 calendar months
Supporting Agency: Department of Defense Office of Congressionally Directed medical Research Programs (CDMRP)
Name and address of funding agency's Grant's Officer:
Claudio Ortiz, Ph.D.
Science Officer, Goldbelt Frontier
Congressionally Directed Medical Research Programs (CDMRP)
US Army Medical Research Materiel Command (USAMRMC)
1077 Patchel Street
Fort. Detrick, MD 21702-5024
Email: claudio.d.ortiz.ctr@mail.mil
Performance Period: 09/2019-08/2022; 09/2022-08/2023 (NCE)
Level of funding:
Brief description of project's goals: The goal of this study is to examine the risk and determinants of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C (CHC) virologically cured with new direct acting antiviral agent (DAA) regimens and to identify cost-effective strategies for early detection of HCC in those patients.
% Overlap: None

Title: Cirrhosis Quality Collaborative
Role on project: co-PI (Corresponding co-PI: Volk)
AIMS: Phase 1: Design phase and network development. Aim 1a: Design a collaborative chronic care network that involves stakeholders at all levels in the design process. Aim 1b: Engage clinician, patient and policy stakeholders to refine a parsimonious set of quality measures – including patient-reported outcomes (PRO's). Phase 2: Software build and network pilot. Aim 2a: Work with ArborMetrix to build the data registry. Aim 2b: Prospectively collect data on the set of quality measures across 10 sites, to identify variation in process,

outcome, and patient reported measures of cirrhosis care. Aim 2c: Pilot test a rapid-cycle quality improvement project on a single focused target.
Time Commitment (Level of Effort): 0.05 calendar months
Supporting Agency: American Association for the Study of Liver Diseases
Name and address of funding agency's Grant's Officer:
Julie Deal
Interim CEO, American Association for the Study of Liver Diseases
1001 N. Fairfax Street, #400
Alexandria, VA 22314
Phone:
Performance Period: 09/2018-08/2023
Level of funding:
Brief description of project's goals: This is the first large-scale quality improvement project targeting patients with advanced and chronic liver diseases. It will pilot test a collaborative chronic care network, including necessary technology infrastructure.
% Overlap: None

Title: The Texas Collaborative Center for Hepatocellular Cancer
Role on project: co-Investigator
AIMS: Aim 1/Year 1: Support and enhance research collaborations among CAP researchers by providing multiple levels of connectivity and necessary research support. Aim 2/Year 2: To set up the framework to educate healthcare providers, researchers, and the public on best practices and to engage private and public entities in policy considerations. Aim 3/Year 2: To engage all stakeholders and solicit strategies to improve HCC-related prevention and care and best disseminate those improvements. Aim 4/Years 3-5: To begin disseminating results on best practices and new opportunities that will impact HCC burden in Texas.
Time Commitment (Level of Effort): 0.6 calendar months
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Name and address of funding agency's Grant's Officer:
General CPRIT Contact Information:
Email: cprit@cprit.state.tx.us
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue, Suite 6-127
Austin, TX 78701
Performance Period: 08/2019-02/2024
Level of funding:
Brief description of project's goals: The Collaborative Action Program (CAP) goal is reducing liver cancer mortality in Texas. To maximize the impact of CAP awards, we propose the creation of the Texas Collaborative Center for Hepatocellular Cancer (TeCH), which will have a robust Administrative Core and an External Advisory Committee and house infrastructure to facilitate CAP research activities, foster cross-project collaboration, and disseminate emerging findings.
% Overlap: None

Title: CPRIT RP200633 Reducing Disparities in the Risk of Hepatocellular Cancer
Role on project: MPI
AIMS: 1) Examine the role of individual, inter-personal and community level factors in explaining racial/ethnic disparities in cirrhosis progression to HCC (prevention); 2) Examine the role of individual, inter-personal and community level factors in explaining racial/ethnic disparities in HCC tumor stage at diagnosis (early detection); 3) Identify specific targets for future interventions to reduce racial/ethnic HCC disparities.
Time Commitment (Level of Effort): 1.5 calendar months
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Name and address of funding agency's Grant's Officer:
General CPRIT Contact Information:
Email: cprit@cprit.state.tx.us
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue, Suite 6-127
Austin, TX 78701

Phone:
Performance Period: 08/2020-08/2025
Level of funding:
Brief description of project's goals: The primary objective of this study is to identify in a large racial/ethnically and socioeconomically diverse cohort of patients with cirrhosis the multi-level factors that explain racial and ethnic disparities in HCC risk/incidence and tumor stage at diagnosis, as well as a set of potentially actionable (identifiable, preventable or treatable) determinants of HCC disparities in Texas.
% Overlap: None

Title: 1R01CA256977 Multi-level Evaluation of Racial/Ethnic Disparities in Liver Disease Outcomes
Role on project: MPI
AIMS: 1) Examine the contribution of individual-, interpersonal-, and community-level factors to racial/ethnic and socioeconomic disparities in cirrhosis progression to hepatic decompensation, including HCC; 2) Identify individual-, interpersonal-, and community-level determinants of racial/ethnic and socioeconomic disparities in liver-related hospitalization; 3) Characterize the contribution of individual-, interpersonal-, and community-level factors to racial/ethnic and socioeconomic disparities in overall survival of patients with cirrhosis.
Time Commitment (Level of Effort): 1.8 calendar months
Supporting Agency: National Institutes of Health
Name and address of funding agency's Grant's Officer:
Rina Das, PhD
National Institute on Minority Health and Health Disparities (NIMHD (https://www.nimhd.nih.gov/))
Telephone:
Email: dasr2@mail.nih.gov (mailto:dasr2@mail.nih.gov)
Performance Period: 03/2021-02/2026
Level of funding:
Brief description of project's goals: To conduct a comprehensive evaluation of multilevel factors hypothesized to play important roles in causing racial/ethnic and SES disparities in three key measures of cirrhosis prognosis: a) hepatic decompensation, including HCC, b) liver-related hospitalization, and c) overall survival.
% Overlap: None

Title: RP200554 A Novel Risk Stratification and Early Detection Strategy to Reduce Liver Cancer Mortality (New)
Role on project: co-Investigator
AIMS: 1) Develop and validate risk stratification models using EMR data to risk stratify cirrhosis patients for developing HCC; 1b) Compare the performance of risk stratification models using EMR data alone to one incorporating EMR data, patient factors and a serum-based molecular signature panel; 2) Characterize the performance of the Glycotest Panel for early HCC detection, in a phase III surveillance biomarker study among patients with cirrhosis.
Time Commitment (Level of Effort): 1.2 calendar months
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Name and address of funding agency's Grant's Officer:
General CPRIT Contact Information:
Email: cprit@cprit.state.tx.us
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue, Suite 6-127
Austin, TX 78701
Phone:
Performance Period: 08/2021-08/2025
Level of funding:
Brief description of project's goals: To improve the approach to risk assessment and early detection of liver cancer as two high priority targets to reducing liver cancer mortality.
% Overlap: None

Title: 1P01CA263025-01A1 Prevention of Hepatocellular Carcinoma Related to Metabolic Syndrome, Project 2 (new)

Role on project: Project Lead, Project #2
AIMS: 1) To examine the chemopreventive effects for each of metformin, statins, and glitazones in reducing the risk of incident HCC among individuals with MAFLD; 2) To measure potential harms of metformin, statins and glitazones in individuals with MAFLD; 3) To examine the modifying effects of genetic markers on chemopreventive benefits of metformin and statins in a high-risk group of patients with MAFLD cirrhosis.
Time Commitment (Level of Effort): 0.36 calendar months
Supporting Agency: National Cancer Institute Division of Cancer Prevention
Name and address of funding agency's Grant's Officer:
Umar Asad, DVM, PhD
National Cancer Institute
Gastrointestinal & Other Cancers Research Group
Division of Cancer Prevention National Cancer Institute
9609 Medical Center Drive
MSC 9782
Room: 5E226
Bethesda, MD 20892-9782

umara@mail.nih.gov
Fax: (240)276-7848
Performance Period: 07/2022-06/2027
Level of funding:
Brief description of project's goals: The overarching goal of this project is to reduce the burden of hepatocellular carcinoma (HCC)-related mortality through better understanding of contemporary risk factors and protective factors of HCC related to metabolic (dysfunction) fatty liver disease (MAFLD).
% Overlap: None

Title: 1U01CA271887-01 Clinical Validation Center for Hepatocellular Carcinoma
Role on project: MPI
AIMS: 1) Facilitate efficient validation of blood and imaging biomarkers for risk stratification and early detection of HCC by expanding contemporary blood and radiology biorepositories of patients with and without HCC; 2a) Evaluate the performance of a risk stratification model to stratify patients with indeterminate liver nodules (ILNs) into low- and high-risk of developing HCC; 2b) Evaluate the performance of a serum biomarker panel, GALAD (including AFP, AFP-L3, and DCP) for early HCC detection in patients with indeterminate liver nodules (ILNs)
Time Commitment (Level of Effort): 1.2 calendar months
Supporting Agency: National Cancer Institute
Name and address of funding agency's Grant's Officer:
Sharmistha Ghosh-Janjigian, PhD
Program Director, Cancer Biomarkers Research Group
Phone:
Room: 5E134
Division of Cancer Prevention
National Cancer Institute
9609 Medical Center Drive
Bethesda, MD 20892
Email: ghoshjanjigias@mail.nih.gov
Performance Period: 08/2022 – 07/2027
Level of funding: Brief description of project's goals: The proposed project will leverage existing infrastructure across five health systems to create two novel resources not offered by the current sample sets including (1) a biorepository with both blood and imaging data from patients, with and without HCC, representing contemporary etiologies of liver disease for Phase I-II biomarker studies and (2) a prospective cohort of patients with indeterminate liver nodules to evaluate HCC risk stratification and early detection biomarkers to conduct Phase III biomarker studies using a prospective- specimen-collection, retrospective-blinded-evaluation (PRoBE) design. Overall, the CVC-HCC will lead to significant advances in phase I-III validation of novel biomarkers for HCC risk stratification and early detection, areas of need that will facilitate

development of well-designed phase IV clinical utility trials with high potential for a long-lasting impact on liver cancer mortality.
% Overlap: None

PENDING

Title: 1 I01HX003541-01A1 Integrated, Veteran-Centered Care for Advanced Liver Disease (I-VCALD)
Role on project: MPI
AIMS: 1) Conduct a formative assessment of I-VCALD implementation for Veterans with advanced liver disease; 2) Evaluate the effectiveness of I-VCALD in a randomized controlled study at four VA centers; 3) Conduct a summative assessment of implementation outcomes of I-VCALD.
Time Commitment (Level of Effort): 3.0 calendar months
Supporting Agency: Department of Veterans Affairs Health Services Research & Development (HSR&D)
Name and address of funding agency's Grant's Officer:
Cathie Plouzek, PhD, PMP
Health Services Research and Development (10P9H)
Office of Research and Development, VA Central Office
Department of Veterans Affairs
810 Vermont Avenue NW
Washington, DC 20420
Phone
E-mail: cathie.plouzek@va.gov
Performance Period: 01/2023 – 12/2026 (JIT)
Level of funding:
Brief description of project's goals: The proposed project employs a whole person, Veteran-centered approach that identifies Veterans with advanced liver disease using a population-based health management system, and integrates curative and early supportive care using a virtual outreach nurse care counselor based at a liver transplant center to (1) discuss patient's understanding of illness severity and prognosis, (2) identify priorities and care preferences and (3) align curative and supportive care options to achieve patient priorities.
% Overlap: None

OVERLAP
There is no overlap between current projects and this application.

The study supported by the NIH/NCI grant (1 R01 CA256977-01; MPI: Kanwal; Singal) will conduct a comprehensive evaluation of multilevel factors hypothesized to play important roles in causing racial/ethnic and socioeconomic disparities in three key measures of cirrhosis prognosis: a) hepatic decompensation, b) liver-related hospitalization, and c) overall survival. The study supported by this grant is complementary but non overlapping with the study supported by the CPRIT grant (RP200633, PI: Kanwal), which focuses on disparities in only liver cancer. Although liver cancer is included in the larger composite outcome for Aim 1 of the R01, the scientific overlap is minimal because liver cancer is relatively rare compared to the other disparate complications of cirrhosis (progression to ascites, hepatic encephalopathy, gastrointestinal bleeding, hospitalizations) that are the main focus on the R01. Aims 2 and 3 of both grants are distinct with no overlap.

If the pending projects receive funding, Dr. Kanwal will adjust her effort on other projects after consultation with and approval from each affected funding agency program officer.

PREVIOUS, CURRENT, AND PENDING SUPPORT (PCPS)

KRAMER, JENNIFER R., MPH, PhD

Title: VA IIR 16-025 Less is More: Improving Antimicrobial Stewardship for Asymptomatic Bacteriuria
Role on project: Co-Investigator
AIMS: 1) Conduct formative assessments of context, barriers and facilitators at each of the four VA medical sites to inform intervention implementation; 2) Evaluate implementation of a scalable version of the Kicking CAUTI intervention in four geographically distinct VA medical centers, including acute and long-term care

settings, with four contemporaneous controls; 3) Assess the financial implications of the intervention through a budget impact analysis
Time Commitment (Level of Effort): 0.6 calendar months
Supporting Agency: VA HSR&D
Name and address of funding agency's Grant Officer:
Cathie Plouzek, PhD, PMP
Health Services Research and Development (10P9H)
Office of Research and Development, VA Central Office
Department of Veterans Affairs
810 Vermont Avenue NW
Washington, DC 20420
Phone:
E-mail: cathie.plouzek@va.gov
Performance Period: 02/2018-09/2021
Level of funding;
Brief description of project's goals: The main goal of this project is to implement the Kicking UTI intervention across four VA sites nationally. Kicking UTI is an intervention to improve management of Asymptomatic Bacteriuria in Veterans in hospitals and long-term care, to protect Veterans from the harms of unnecessary antibiotic use. It was designed and validated in a previous study.
% Overlap: None

Title: HSR&D Project # IIR 16-075 (Application # 1 I01 HX002204-01A2) Patient Centered Care for Individuals with Advanced Liver Disease
Role on project: Co-Investigator
AIMS: 1) To develop risk stratification models of advanced liver disease (AdvLD) prognosis; 2) To describe patients' experiences and goals of AdvLD care; 3) To identify clinicians' perceptions of opportunities and barriers to patient-centered AdvLD care.
Time Commitment (Level of Effort): 0.6 calendar months
Supporting Agency: VA HSR&D
Name and address of funding agency's Grant Officer:
Cathie Plouzek, PhD, PMP
Health Services Research and Development (10P9H)
Office of Research and Development, VA Central Office
Department of Veterans Affairs
810 Vermont Avenue NW
Washington, DC 20420
Phone:
E-mail: cathie.plouzek@va.gov
Performance Period: 05/2018-04/2021 (NCE 05/2021-04/2022)
Level of funding;
Brief description of project's goals: The main goal of the project is to develop a patient-centered care model for advanced liver disease, including risk-prediction models and clinician-patient collaborative treatment planning guides that focus on addressing patient unmet needs and expectations about illness course and care preferences for curative, supportive, and palliative care. The study findings will have direct impacts on current advanced liver disease care, as well as provide evidence for developing innovative care models for other serious chronic illnesses.
% Overlap: None

Title: 5R01CA212008-02 Harms of Hepatocellular Carcinoma Screening in Patients with Cirrhosis
Role on project: Co-Investigator
AIMS: 1) Assess the effect of HCC screening on a) physical harms due to follow-up tests, b) financial harms, and c) overdiagnosis in patients with severe liver dysfunction or comorbid illness, through electronic medical record data, manual chart review, and validated survey measures; 2) Assess the effect of HCC screening on screening-related psychosocial harms, e.g. cancer-specific worry, situational anxiety, mood disturbances, and decisional regret, through longitudinal validated measures and qualitative interviews; 3) Create and

disseminate a balance sheet of benefits and harms to inform patients, nurses, providers, healthcare organizations, payers, and policymakers about the value of HCC screening in patients with cirrhosis.
Time Commitment (Level of Effort): 0.6 calendar months
Supporting Agency: National Cancer Institute
Name and address of funding agency's Grant Officer:
Crystal Wolfrey
Chief Grants Management Officer
National Cancer Institute
Office of Grants Administration
9609 Medical Center Drive
West Tower, 2nd floor
Rockville MD 20850
wolfreyc@mail.nih.gov,
Tel.
Performance Period: 08/2017-07/2022
Level of funding;
Brief description of project's goals: The purpose of this study is to investigate the harms that may be associated with screening for HCC in patients with cirrhosis recruited from 4 medical centers in Texas.
% Overlap: None

CURRENT

Title: VA HSR&D IIR 19-365 Enhancing the Efficiency of Data Collection for Surgical Quality Improvement (new)
Role on project: Co-Investigator
AIMS: Specific Aim 1: Evaluate whether analyzing all VASQIP eligible non-cardiac surgical cases, relative to current systematic case sampling, improves negative predictive value (i.e.: decreases false negative rates) for identifying VA hospitals with outlier performance; Specific Aim 2: Compare the use of hybrid CDW and clinical registry data, relative to clinical registry alone, for evaluating risk-adjusted surgical performance at VA hospitals; *Specific Aim 3: Conduct semi-structured interviews with SQNs to understand and inform how more efficient VASQIP data collection could affect and potentially enhance local QI efforts.*
Time Commitment (Level of Effort): 1.2 calendar months
Supporting Agency: Department of Veterans Affairs Health Service Research and Development
Name and address of funding agency's Grant's Officer:
Cathie Plouzek, PhD, PMP
Health Services Research and Development (14RD)
Office of Research and Development, VA Central Office
Department of Veterans Affairs
810 Vermont Avenue NW
Washington, DC 20420
Phone:
E-mail: cathie.plouzek@va.gov
Performance Period: 05/01/2021-04/30/2025
Level of funding:
Brief description of project's goals: This mixed-methods proposal will evaluate the reliability of VASQIP's current case sampling strategy for identifying outlier VA hospitals, explore the use of hybrid data as a means of enhancing data collection efficiency, and will identify how more efficient data collection could enhance local QI through semi-structured interviews with Surgical Quality Nurses.
% Overlap: None

Title: 1P01CA263025-01A1 Prevention of Hepatocellular Carcinoma Related to Metabolic Syndrome, Project 2 (new)
Role on project: co-I
AIMS: 1) To examine the chemopreventive effects for each of metformin, statins, and glitazones in reducing the risk of incident HCC among individuals with MAFLD; 2) To measure potential harms of metformin, statins

and glitazones in individuals with MAFLD; 3) To examine the modifying effects of genetic markers on chemopreventive benefits of metformin and statins in a high-risk group of patients with MAFLD cirrhosis.
Time Commitment (Level of Effort): 1.2 calendar months
Supporting Agency: National Cancer Institute Division of Cancer Prevention
Name and address of funding agency's Grant's Officer:
Umar Asad, DVM, PhD
National Cancer Institute
Gastrointestinal & Other Cancers Research Group
Division of Cancer Prevention National Cancer Institute
9609 Medical Center Drive
MSC 9782
Room: 5E226
Bethesda, MD 20892-9782
Phone
umara@mail.nih.gov
Fax:
Performance Period: 07/2022-06/2027
Level of funding:
Brief description of project's goals: The overarching goal of this project is to reduce the burden of hepatocellular carcinoma (HCC)-related mortality through better understanding of contemporary risk factors and protective factors of HCC related to metabolic (dysfunction) fatty liver disease (MAFLD).
% Overlap: None

Title: 1 U01 CA230997-01 Risk Stratification for and Early Detection of Liver Cancer (new)
Role on project: co-I
AIMS: 1) Develop and test novel personalized risk stratification indices for predicting future HCC development in cirrhosis from diverse etiologies; 2) Develop and evaluate an algorithm combining existing HCC blood based biomarkers (AFP, AFPL3, DCP), their longitudinal changes and host features (e.g., cirrhosis etiology) to improve early HCC detection; 3) Evaluate novel plasma-based methylation markers for cell-free DNA (MDMs) as an independent surveillance biomarker for early HCC detection. Using the PRoBE design, we will test 12 individuals MDMs identified in Phase 2 study.
Time Commitment (Level of Effort): 0.48 calendar months
Supporting Agency: NIH Consortium on Translational Research in Early Detection of Liver Cancer: Translational Research Centers (U01)
Name and address of funding agency's Grant's Officer:
Viviana Knowles
National Cancer Institute
Office of Grants Administration
9609 Medical Center Drive
West Tower, 2nd floor
Rockville MD 20850
Phone
viviana.knowles@nih.gov
Tel.
Performance Period: 09/2018-08/2023
Level of funding:
Brief description of project's goals: The overarching goal of our Translational Research Center (TRC) is to reduce the mortality of hepatocellular cancer (HCC) by developing personalized indices that combine novel and existing biomarkers with clinical, behavioral and genetic data to improve clinical risk stratification and increase early detection of HCC.
% Overlap: None

Title: 1R01CA260689-01 (PQ3) Addressing Cancer Treatment Disparities for Persons with HIV
Role on project: Co-Investigator

Aims: Aim 1: To evaluate differences in the timing of cancer treatment initiation between PWH and matched uninfected patients, and risk factors for delayed treatment in PWH. Aim 2: To evaluate disparities in short-term SAEs and cancer treatment.
Time Commitment (Level of Effort): 1.4 calendar months
Supporting Agency: NIH/NCI
Name and address of funding agency's Grant Officer:
Geraldina Dominguez
National Cancer Institute
National Institutes of Health
31 Center Drive, Room 3A33
Bethesda, MD, USA 20852-2440
Telephone:
Email: domingug@mail.nih.gov
Performance Period: 06/15/2021 – 05/31/2026
Level of Funding: (subcontract total DC)
Brief Description of project's goals: This project will address critical knowledge gaps for the four most common NADCs in PWH treated with CRT/RT (anal, head and neck, lung, or prostate cancer).
% Overlap: None

Title: PR181562 Risk of hepatocellular cancer after virological cure with direct acting antiviral agents in individuals with hepatitis C (subject grant)
Role on project: Co-Investigator
AIMS: 1) To examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients; 2) To evaluate benefits versus harms of HCC surveillance in virologically cured patients; 3) To develop HCC Simulator, an online interactive tool for physicians and patients that provides the short- and long-term value of HCC surveillance in different risk groups.
Time Commitment (Level of Effort): 2 calendar months
Supporting Agency: Department of Defense Office of Congressionally Directed medical Research Programs (CDMRP)
Name and address of funding agency's Grant's Officer:
Claudio Ortiz, Ph.D.
Science Officer, Goldbelt Frontier
Congressionally Directed Medical Research Programs (CDMRP)
US Army Medical Research Materiel Command (USAMRMC)
1077 Patchel Street
Fort. Detrick, MD 21702-5024
PH:
Email: claudio.d.ortiz.ctr@mail.mil
Performance Period: 07/2019-06/2022
Level of funding;
Brief description of project's goals: The goal of this study is to examine the risk and determinants of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C (CHC) virologically cured with new direct acting antiviral agent (DAA) regimens and to identify cost-effective strategies for early detection of HCC in those patients.
% Overlap: None

Title: CPRIT RP200633 Reducing disparities in the risk of hepatocellular cancer
Role on project: co-Investigator
AIMS: 1) Examine the role of individual, inter-personal and community level factors in explaining racial/ethnic disparities in cirrhosis progression to HCC (prevention); 2) Examine the role of individual, inter-personal and community level factors in explaining racial/ethnic disparities in HCC tumor stage at diagnosis (early detection); 3) Identify specific targets for future interventions to reduce racial/ethnic HCC disparities.
Time Commitment (Level of Effort): 1.9 calendar months
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Name and address of funding agency's Grant's Officer:
General CPRIT Contact Information:

Email: cprit@cprit.state.tx.us
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue, Suite 6-127
Austin, TX 78701
Phone:
Fax:
Performance Period: 08/2020-08/2025
Level of funding:
Brief description of project's goals: The primary objective of this study is to identify in a large racial/ethnically and socioeconomically diverse cohort of patients with cirrhosis the multi-level factors that explain racial and ethnic disparities in HCC risk/incidence and tumor stage at diagnosis, as well as a set of potentially actionable (identifiable, preventable or treatable) determinants of HCC disparities in Texas.
% Overlap: None

Title: 1R01CA256977 Multi-level Evaluation of Racial/Ethnic and Socioeconomic Disparities in Liver Disease Outcomes
Role on project: co-Investigator
AIMS: 1) Examine the contribution of individual-, interpersonal-, and community-level factors to racial/ethnic and socioeconomic disparities in cirrhosis progression to hepatic decompensation, including HCC; 2) Identify individual-, interpersonal-, and community-level determinants of racial/ethnic and socioeconomic disparities in liver-related hospitalization; 3) Characterize the contribution of individual-, interpersonal-, and community-level factors to racial/ethnic and socioeconomic disparities in overall survival of patients with cirrhosis.
Time Commitment (Level of Effort): 1.9 calendar months
Supporting Agency: National Institutes of Health
Name and address of funding agency's Grant's Officer:
Rina Das, PhD
National Institute on Minority Health and Health Disparities (NIMHD (https://www.nimhd.nih.gov/))
Telephone:
Email: dasr2@mail.nih.gov (mailto:dasr2@mail.nih.gov)
Performance Period: 03/2021-02/2026
Level of funding:
Brief description of project's goals: To conduct a comprehensive evaluation of multilevel factors hypothesized to play important roles in causing racial/ethnic and SES disparities in three key measures of cirrhosis prognosis: a) hepatic decompensation, including HCC, b) liver-related hospitalization, and c) overall survival.
% Overlap: None

PENDING

OVERLAP
None

PREVIOUS/ CURRENT/ PENDING SUPPORT

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PREVIOUS

PREVIOUS

Title/Grant Number:	Media-rich mobile dissemination of a dysphagia prevention program for head and neck cancer patients during radiation / PP150077
Effort:	0.24 Calendar Months, 2% Effort (all years of participation)
Supporting Agency:	Cancer Prevention & Research Institute of Texas (CPRIT)
Grants Officer:	Patricia Moore, , cprit@cprit.state.tx.us
Performance Period:	6/1/2015-5/30/2020

Funding Amount:
Project Goals: To provide evidence-based speech pathology functional swallow evaluation. PID600053 (Completed 12/31/2019)
Specific Aims: 1) Pre- and post-treatment and targeted swallowing exercises to head and neck cancer patients during radiation.

2)To administer an effective adherence program via a mobile health technology application (GuideVue) to head and neck cancer patients during radiation.

3) To lay the groundwork for future dissemination of this prevention program.

Overlap: None

Title/Grant Number: The Texas Hepatocellular Carcinoma Consortium (THCCC) Core 2: (SCC) / RP150587
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: Subaward from Baylor College of Medicine pass through from CPRIT
Grants Officer: Patricia Moore, , cprit@cprit.state.tx.us
Performance Period: 6/1/2015-5/31/2020
Funding Amount:
Project Goals: Provide critical statistical, data management, and multi-center study coordination and support for all projects in the consortium. PID600060
Specific Aims: 1) Use Texas VA datasets to assemble the largest NAFLD-to-HCC study to date (including over 45,000 NAFLD patients in Texas) to determine the number of patients to develop HCC and to identify factors that increase patients' risk for HCC.
2) Develop risk stratification algorithms based on demographic, clinical, molecular and epidemiological risk factors to identify cirrhosis patients who might benefit from prevention or intensive surveillance.

3) Identify pathways for chemoprevention related to the role of circadian rhythm and bile acids in AFLD, metabolic syndrome, and HCC.

4) Identify and validate novel blood markers (tests) for early HCC detection.

5) Comparative effectiveness randomized controlled trial of strategies to increase HCC surveillance.

Overlap: None

Title/Grant Number: Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer: Coordinating and Data Management Center (CSCPDPC-CDMC)/ 5U01DK108328-05
Effort: 2.4 Calendar Months, 20% Effort (all years of participation)
Supporting Agency: NIH/NIDDK
Grants Officer: Aynur Unalp-Arida, , aynur.unalp-arida@nih.gov
Performance Period: 9/28/2015-8/31/2020
Funding Amount:
Project Goals: Coordinate the research efforts and will manage and analyze the data for the Consortium under the direction of the Consortium Steering Committee (SC). PID3496
Specific Aims: 1) Provide coordination of the Consortium in order to enhance communication and collaboration among Consortium investigators and with the larger scientific communities.

2) provide scientific and statistical leadership for the Consortium in research

strategy, study design approaches, and statistical and computational methods

3) coordinate Consortium collaborative studies.

Overlap: None

Title/Grant Number: Using game mechanics to improve among stem cell transplant/ 2R42CA168107-03
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: Radiant Creative Group, LLC
Grants Officer: Patricia A Weber; weberpa@mail.nih.gov
Performance Period: 12/1/2015-11/30/2018
Funding Amount:
Project Goals: To develop an innovative interactive online intervention that utilizes novel social game mechanics to promote improved self-management behaviors among patients who have undergone hematopoietic stem cell transplantation for treatment of leukemia and lymphoma. PID4024
Specific Aims: To determine the impact of the intervention during the post-HSCT phase, and to evaluate changes and trends in the psychosocial and behavioral outcomes during the immediate post-HSCT recovery phase. The proposed study will advance scientific knowledge on the impact of game mechanics and social networking on patient behavior, and will provide insights, evidence, and guidance on how to build practical online social intervention systems to support behavioral change in AYAs.
Overlap: None

Title/Grant Number: Visualizing T-cell Trafficking/ RP160013
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Grants Officer: Patricia Moore, , cprit@cprit.state.tx.us
Performance Period: 3/1/2016-2/28/2020
Funding Amount:
Project Goals: To develop SSTR2-based methods for marking T-cells in vitro and following T-cells in vivo. PID600080
Specific Aims: 1) Test the hypothesis that human somatostatin receptor type 2 (SSTR2)-based reporters can be created that are deficient in signaling and do not interfere with T-cell function in vitro.
2) Test the hypothesis that non-invasive signaling deficient SSTR2-based reporter imaging can be used to localize T-cells in tumors and assess their expansion at the tumor site.
3) Test the hypothesis that imaging T-cells expressing signaling deficient SSTR2-based reporters can be used to predict tumor response.
4) Test the hypothesis that T-cells expressing signaling deficient SSTR2-based reporters persist against a subsequent tumor challenge. Thus, this proposal uses innovative methods to address significant unmet needs required to advance T-cell therapy.
Overlap: None

Title/Grant Number: Multi-Site Development & Evaluation of a Quantitative 3D Hyperpolarized C-13 MRI Clinical Prostate Cancer Exam / 5R01CA211150-05
Effort: 0.24 Calendar Months, 2% Effort (all years of participation)
Supporting Agency: NIH/NCI
Grants Officer: Huiming Zhang, zhanghui@mail.nih.gov,
Performance Period: 03/1/2017-02/28/2023
Funding Amount:

Project Goals:	Demonstrating new and improved imaging methods that enhance image quality, and consequently, improve sensitivity and specificity of minimally invasive metabolic imaging strategies. (Effort ended effective 9/1/22) PID5247
Specific Aims:	1) Establish a method for external validation of HP MRI measurements. 2) Implement highly optimized preclinical dynamic HP MRS and MRI protocols and a robust constrained reconstruction algorithm for quantifying tumor metabolism using HP [1-13C]-pyruvate. 3) Develop a data-driven HP MRI protocol and establish imaging characteristics in patients with head and neck cancers.
Overlap:	None

Title/Grant Number:	Socioeconomic status, stress, and smoking cessation / 5R01CA190329-06
Effort:	0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency:	NIH/NCI Subaward via University of Utah
Grants Officer:	Xinzhi Zhang, zhangx12@mail.nih.gov
Performance Period:	7/1/2017-06/30/2022
Funding Amount:	
Project Goals:	To examine the influence of socioeconomic status and social history, contextual and environmental influences, bio-behavioral/psychosocial predispositions, and acute momentary precipitants on stress, smoking lapse, and abstinence PID5135 (under NCE)
Specific Aims:	1) Delineates the key hypothesized pathway linking SES to stress to smoking lapse/abstinence. 2) Delineates the key hypothesized links of environment/context and bio-behavioral/psychosocial predispositions with SES, smoking lapse/abstinence, and stress. 3) Examines the dynamic relationships of acute precipitants and stress, and their influence on lapse/abstinence.
Overlap:	None

Title/Grant Number:	Using hunger training to enhance weight loss and modulate cancer-related biomarkers in women at high risk for breast cancer; a pilot study/ 1R21CA215415-01A1
Effort:	0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency:	NIH/NCI
Grants Officer:	Agurs-Collins, Tanya, , collinsta@mail.nih.gov
Performance Period:	8/11/2017-7/31/2019
Funding Amount:	
Project Goals:	To pilot test the synergistic effect of adding Hunger Training to a highly-disseminated, evidence-based lifestyle intervention. PID6143 (Effort completed as of 5/31/2019)
Specific Aims:	1) Determine the feasibility of adding Hunger Training to the DPP using the following criteria: accrual rates >50%, attrition rates <20% and, in the DPP-plus-HT group, training protocol adherence rates >75%. 2) Estimate the magnitude of effect sizes and variation in outcome variables for the DPP-only and DPPplus-HT interventions on changes in weight; in metabolic and breast cancer risk biomarkers (e.g., fasting insulin and BG levels, levels of glycosylated hemoglobin, insulin resistance, adiponectin, interleukin-6, and Creactive protein); and in proposed behavioral mediators (e.g., reduction in total energy intake, overall eating frequency, percent of eating events occurring at or below the average fasting blood BG level).
Overlap:	None

Title/Grant Number:	Using hunger training to enhance weight loss and modulate cancer-related biomarkers in women at high risk for breast cancer; a pilot study/ 1R21CA215415-01A1
Effort:	0.24 Calendar Months, 2% Effort (all years of participation)
Supporting Agency:	NIH/NCI
Grants Officer:	Agurs-Collins, Tanya, collinsta@mail.nih.gov
Performance Period:	8/11/2017-7/31/2019
Funding Amount:	
Project Goals:	To pilot test the synergistic effect of adding Hunger Training to a highly-disseminated, evidence-based lifestyle intervention (Diabetes Prevention Program; DPP) on weight loss outcomes and on metabolic and breast cancer risk biomarkers in a sample of obese postmenopausal women. PID6143. (Effort completed as of 6/1/2018; PI left institution.)
Specific Aims:	1) Determine the feasibility of adding Hunger Training to the DPP using the following criteria: accrual rates >50%, attrition rates <20% and, in the DPP-plus-HT group, training protocol adherence rates >75%. 2) Estimate the magnitude of effect sizes and variation in outcome variables for the DPP-only and DPPplus-HT interventions on changes in weight; in metabolic and breast cancer risk biomarkers (e.g., fasting insulin and BG levels, levels of glycosylated hemoglobin, insulin resistance, adiponectin, interleukin-6, and Creactive protein); and in proposed behavioral mediators (e.g., reduction in total energy intake, overall eating frequency, percent of eating events occurring at or below the average fasting blood BG level).
Overlap:	None

Title/Grant Number:	Eliminating tobacco-related disparities among African Americans/5R01MD010362-04
Effort:	1.32 Calendar Months, 11% Effort (all years of participation)
Supporting Agency:	NIH/NHMD Subaward via Utah University
Grants Officer:	Xinzhi Zhang, zhangx12@mail.nih.gov
Performance Period:	8/28/2017-1/31/2021
Funding Amount:	
Project Goals:	To examine the influence of demographics and social history, bio-behavioral and psychosocial predispositions, contextual and environmental factors, and acute individual and contextual precipitants on smoking lapse and abstinence. PID5129 (Effort complete as of 1/31/2019)
Specific Aims:	1) Influence of demographics and social history, bio-behavioral/psychosocial predispositions, contextual and environmental influences, and acute precipitants on smoking lapses among AA smokers. 2. Influence of demographics and social history, bio-behavioral/psychosocial predispositions, contextual and environmental influences, and acute precipitants on early and long-term abstinence from smoking among AA smoker.
Overlap:	None

Title/Grant Number:	Affective science and smoking cessation: Real time real world assessment/ 1R01CA224537-01
Effort:	0.48 Calendar Months, 4% Effort (all years of participation)
Supporting Agency:	NIH via subaward from University of Utah
Grants Officer:	Rebecca Ferrrer, ferrerra@mail.nih.gov
Performance Period:	01/1/2018-12/31/2022
Funding Amount:	
Project Goals:	To create a more detailed and comprehensive conceptual model of the role of distinct emotions in self-regulation. PID6397 (Effort complete as of 12/31/2018)

Specific Aims: 1) Models the impact of distinct emotions on SRC and smoking lapse, both in the moment and as trajectories over time. Aim 1 will also examine how the impact of specific emotions may differ based on the levels of other emotions (e.g., “blended” emotional states).
2) Investigates whether the associations of affective experience with SRC and lapse are modified by contextual factors.
Overlap: None

Title/Grant Number: Multimodal Imaging and Therapy of Ovarian Cancer / 1R01CA255753-01A1
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: NIH/NCI
Grants Officer: Christopher Hatch, Ch29v@nih.gov
Performance Period: 7/1/2021-6/30/2026
Funding Amount:
Project Goals: To create a new paradigm for approaching ovarian cancer that enables presurgical planning, surgical resection, and tumor photodestruction after a single nanoparticle injection. FP00010097_Res1 (PI left institution prior to project starting, award to be transferred to new institution)
Specific Aims: 1) Test the hypothesis that ovarian tumor deliver can be augmented by targeting DM-Dual-Gd to proven targets or novel imaging target CDCP1.
2) Test the hypothesis that ovarian tumor detection can be improved using the NIR II window compared to the NIR I window.
3) Test the hypothesis that DM-Dual-Gd-based nanoparticles enable photodestruction of ovarian tumors.
4) Test the hypothesis that pre-surgical NIR imaging employing DM-Dual-Gd can improve survival of models of intraperitoneal ovarian cancer.

Overlap: None

Title/Grant Number: Comparative Effectiveness Research on Cancer in Texas (CERCIT) 2.0: Data Core / RP160674
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: Cancer Prevention & Research Institute of Texas Subaward via UTMB
Grants Officer: Patricia Moore, , cprit@cprit.state.tx.us
Performance Period: 6/1/2016-8/30/2022
Funding Amount:
Project Goals: To create a statewide resource for outcomes and comparative effectiveness research in cancer for Texas. PID4721 (No Cost Extension)
Specific Aims: 1) Create Data Resource of linked cancer and claims data for Texas residents.
2) Use data resource to examine the entire trajectory of cancer care in Texas.
3) Train the next generation of cancer outcomes and comparative effectiveness investigators in Texas.
4) Disseminate Findings.
Overlap: None

CURRENT

Title/Grant Number: Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer: Coordinating and Data Management Center (CSCPDPC-CDMC)/5U01DK108328-08
Effort: 2.4 Calendar Months, 20% Effort (all years of participation)
Supporting Agency: NIH/NIDDK
Grants Officer: Aynur Unalp-Arida, Phone: 301-594-8897, aynur.unalp-arida@nih.gov
Performance Period: 9/28/2015-6/30/2025
Funding Amount:
Project Goals: To provide network coordination and collaborative activities, will provide scientific

leadership in study design, statistical support, and computational analyses, and will provide data management and protocol development and execution. PID11706

Specific Aims: 1) Support Operation and Coordination of CPDPC
2) Continue the Accrual and Follow up of Patients in CPDPC-approved Studies
3) Support the Infrastructure for Biomarker Development, Prevention Studies, and Therapeutic Trials
4) Design and Support New Studies as Selected by the Steering Committee.

Overlap: None

Title/Grant Number: Estimating the Cost Trajectories and Projecting the Cost of Cancer Care in the United States: Methodology and Application / 5R01CA225646-05

Effort: 2.28 Calendar Months, 19% Effort (all years of participation)

Supporting Agency: NIH/NCI

Grants Officer: Martinson Owusu, , owusumo@mail.nih.gov

Performance Period: 7/5/2018-6/30/2022

Funding Amount:

Project Goals: To develop novel methodology and apply the methodology to estimate and project the future cost of cancer care in the US. PID6729

Specific Aims: 1) To develop new statistical methods to model the longitudinal incident costs of cancer patients.
2) To improve the net costing approach by developing innovative propensity score methods for the selection of non-cancer controls.
3) To project the cancer care costs in the United States for the next 10 years.
4) To facilitate the reproducibility and application of the methods developed from this project by developing and disseminating user-friendly software programs.

Overlap: None

Title/Grant Number: Magnetic resonance Imaging as a Non-Invasive Method for Assessment of Pancreatic fibrosis (MINIMAP): a pilot study / 5R01DK116963-03

Effort: 0.12 Calendar Months, 1% Effort (all years of participation)

Supporting Agency: NIH/NIDDK via subaward from Indiana University

Grants Officer: Chelsie Bousum, cbousum@iu.edu

Performance Period: 09/20/2018-06/30/2023

Funding Amount:

Project Goals: To evaluate non-invasive methods to detect and quantify pancreatic fibrosis. PID7394. FP00004518 (Under no cost extension)

Specific Aims: 1). The objective of this protocol is to perform statistical analysis of de-identified data for the MINIMAP study.

Overlap: None

Title/Grant Number: Dynamic Prediction of Renal Failure Using Longitudinal Prognostic Information among Patients with Chronic Kidney Disease and Kidney Transplant / 5R01DK118079-04

Effort: 2.28 Calendar Months, 19% Effort (all years of participation)

Supporting Agency: NIH/NIDDK

Grants Officer: Kevin C. Abbott, , Kevin.abbott@nih.gov

Performance Period: 04/1/2019-03/31/2023

Funding Amount:

Project Goals: To develop novel DP methods for kidney/graft failure with adjustment for the competing risk by death, external validation and re-calibration, and creating software for routine use in clinical practice. PID7824

Specific Aims: 1) Develop novel statistical methodology for dynamic prediction;
2) Develop and externally validate dynamic kidney failure prediction models for (a)

patients with CKD and (b) KTx recipients;
3) Develop and disseminate web-based dynamic prediction model software for clinical practice.

Overlap: None

Title/Grant Number: Phase 1/2 Trial of Indomethacin in Chronic Pancreatitis (The PAIR Trial) / 5R21DK117212-03
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: NIH/NIDDK Subaward via May Clinic-Rochester
Grants Officer: Jose Serrano, serranoj@extra.niddk.nih.gov
Performance Period: 7/12/2019-3/31/2023
Funding Amount: To investigate the pancreatic effects of IN in humans, and to correlate changes in a
Project Goals: pancreatitis biomarker with changes in clinical symptoms of CP. PID11646 / FP00005110 (Under no cost extension)
1) the primary analysis will be a linear random intercept model that incorporates PJ
Specific Aims: PGE2 data from both baseline and day 28 from all randomized patients.
2) we will use multivariate analysis of variance model (MANOVA) with repeated measures. The multivariate outcomes include patient-related outcomes (BPI and PROMIS-10 scores) and PJ PGE2 concentrations between baseline and day 28.
None
Overlap:

Title/Grant Number: Risk Of Hepatocellular Cancer After Virological Cure With Direct Acting Anitviral Agents In Individuals With Hepatitis C/W81XWH-19-1-0689
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: DOD via subaward Baylor College of Medicine
Grants Officer: Baylor College of Medicine, subaward@bcm.edu
Performance Period: 9/1/2019-8/31/2023
Funding Amount:
Project Goals: To examine the determinants of hepatocellular carcinoma (HCC) in patients diagnosed with chronic hepatitis C (CHC) who have been virologically cured with the new direct acting antiviral (DAA) regimens. PID11158 / FP00008073
Specific Aims: 1) To examine determinants of HCC in virologically cured patients and develop a risk prediction model for HCC in these patients.
2) To evaluate benefits versus harms of HCC surveillance in virologically cured patients.
3) To develop an HCC Simulator, an online interactive tool for physicians and patients that provides the short- and long-term value of HCC surveillance in different risk groups.
Overlap: None

Title/Grant Number: A novel natural history study of medullary thyroid carcinoma: Incorporating the patient perspective to inform advanced disease management /5R01FD006650-04
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: NIH/FDA
Grants Officer: Daniel Lukash, daniel.lukash@fda.hhs.gov,
Performance Period: 9/1/2019-7/31/2023
Funding Amount:
Project Goals: To understand the pathway to progressive disease, integrating for the first time patients perspectives. PID8226
Specific Aims: 1) To fully characterize the disease longitudinally from both the clinical and patient perspectives to understand the significance of each in association with outcome.
2) To derive a treatment algorithm (decision aid) for utilization of MTC drug therapy in which the patient's unique set of values are considered.

3) To determine if current and novel biomarkers can be used to enhance decision making in the treatment of advanced disease.

Overlap: None

Title/Grant Number: Improving Risk Prediction for Li-Fraumeni Syndrome: A Practical Tool for Clinical Health Care Providers / RP200383
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: Cancer Prevention & Research Institute of Texas (CPRIT)
Grants Officer: Patricia Moore, cprit@cprit.state.tx.us
Performance Period: 8/31/2020- 8/30/2023
Funding Amount:
Project Goals: Improving the clinical management of individuals with a family history of early-onset cancers by developing a user friendly genetic counseling application to assess carrier probability and lifetime risk of developing cancers in individuals with TP53 mutations. PID11859
Specific Aims: 1) Validation of TP53 prediction (carrier status and cancer occurrence) using family data from MDACC Clinical Cancer Genetics Program.
2) LFSPRO dissemination into clinical genetic counseling practice.

Overlap: None

Title/Grant Number: Mechanism-based Approach to Pain in Chronic Pancreatitis (MAP-CP) / 5R21DK122293-02
Effort: 0.12 Calendar Months, 1% Effort (all years of participation)
Supporting Agency: NIH/NIDDK subaward via University Of Pittsburgh
Grants Officer: Jose Serrano, serranoj@extra.niddk.nih.gov
Performance Period: 9/14/2020-5/31/2023
Funding Amount:
Project Goals: To use data and serum collected by the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer as part of the PROCEED study to investigate the subtypes of pain in Chronic Pancreatitis and identify potential biomarkers. (Under NCE) FP00006539_Res1 PID12612
Specific Aims: This study is designed to test the hypothesis that patient-derived information can be used to identify pain phenotypes that inform management of chronic pancreatitis-related pain.

1) is to determine if distinct biomarker profiles can discriminate pain phenotypes. We will measure expression of selected targets in sera and compare across chronic pancreatitis patients stratified by pain characteristic (intensity, temporality, and interference) as well as pain mechanism (nociceptive versus neuropathic).

2) is designed to evaluate whether temporal changes in pain phenotype are associated with the natural course of disease and/or treatment such as opioid use.

Overlap: None

Title/Grant Number: Data Management and Analysis Core for Comparative Effectiveness Research on Cancer in Texas / RP210130
Effort: 1.2 Calendar Months, 10% Effort (all years of participation)
Supporting Agency: Cancer Prevention & Research Institute of Texas Subaward via UTMB
Grants Officer: Patty Moore, Phone:, Email: research@cprit.texas.gov
Performance Period: 8/31/2021-8/30/2026
Funding Amount:

Project Goals: The Data Management and Analysis Core will become the hub for cancer comparative effectiveness research in Texas. PID13370

Specific Aims: 1) Support data management and analysis.

2) Expand our TCR linkage to nationally representative survey data.

3) Recruit and train new CER investigators from at least 8 Texas academic and research institutions with a large number of underrepresented investigators.

Overlap: None

PENDING

Title/Grant Number: A Pilot Clinical Trial of Paricalcitol for Chronic Pancreatitis /1R01DK132631-01
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: NIH/NIDDK subaward via Cedars-Sinai Medical Center
Grants Officer: Not available for this submission
Performance Period: 4/1/2022-3/31/2025
Funding Amount:
Project Goals: The objective of the study is to examine the feasibility of testing the effect of a potent vitamin D analogue, paricalcitol, on health-related quality of life (HRQoL) and potentially delay disease progression in patients with Chronic Pancreatitis (CP). FP00014083 **(JIT Pending as of 9/14/22)**

Specific Aims: 1) Conduct a randomized double-blind, placebo-controlled pilot trial of paricalcitol to evaluate the feasibility of performing subsequent efficacy focused trials. Feasibility will be met if the of patients who enroll and complete the 12-month study is ≥75% of planned. There will be a 21-month recruitment period and a one-year treatment period.
2) Monitor health-related quality of life (HRQoL) measures; and imaging biomarkers and liquid biomarkers to identify measures/biomarkers that have the potential to measure responses to the treatment in subsequent efficacy focused trials.

Overlap: There is budgetary and scientific overlap under this application and the resubmission (1R01DK132631-01A1). If this submission is awarded, the resubmission will be withdrawn by the PD/PI. Alternatively, if the resubmission is funded, this submission will be withdrawn by the PD/PI.

Title/Grant Number: Coordinating and Data Management Center for Translational and Basic Science Research in Early Lesions/1U24CA274212-01
Effort: 1.8 Calendar Months, 15% Effort (all years of participation)
Supporting Agency: NIH/NCI
Grants Officer: Christos Patriotis, Phone: patriotisc@mail.nih.gov
Performance Period: 9/16/2022-8/31/2027
Funding Amount:
Project Goals: We propose to establish a Coordinating and Data Management Center (CDMC) for the Program on the Translational and Basic Science Research in Early Lesions (TBEL), which is being established to undertake various translational and basic science studies to provide fundamental knowledge on the mechanisms driving or restraining early cancers. **(Pending award setup as of 9/19/22 – 15% effort effective 10/1/22)** FP00015239

Specific Aims: 1) Statistical and computational support.
2) Data management, study protocol development and implementation.

3) Our team of experts include information technology specialists who have been supporting and developing innovative software tools for numerous basic and translation cancer studies, experienced research coordinators who have worked on both NIH- and industry-funded multicenter studies, and faculty statisticians and

bioinformaticians who have led CDMC work for large NIH consortiums and are well-known experts in biostatistics and bioinformatics methodological research areas closely related to biomarker development, risk prediction, single cell analysis, image analysis, machine learning, and clinical trials.

Overlap: None

Title/Grant Number: Prevention of Hepatocellular Carcinoma Related to Metabolic Syndrome/ 1P01CA263025-01A1
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: NIH/NCI subaward via Baylor College of Medicine
Grants Officer: Yujing Liu, Ph.D. Deputy Director, Division of Receipt and Referral Center for Scientific Review National Institutes of Health, 6700B Rockledge Dr. Room 4518 Bethesda, MD 20892, E-Mail:liuyujin@mail.nih.gov
Performance Period: 7/1/2022-6/30/2027
Funding Amount:
Project Goals: To prevent HCC among people with MAFLD by investigating the role of chemoprevention, surveillance, and risk scores in 3 highly synergistic scientific projects that are supported by 2 shared cores for data and samples collection and analysis. **(Pending receipt of subaward agreement from Baylor as of 9/19/22)** FP00012063_Res1
Specific Aims: 1) To develop HCC risk stratification models based on phenotypic, metabolic, radiomic and genetic markers of metabolic dysfunction among patients with cirrhosis. We propose the analysis of data and biospecimens from the prospective THCCC cohort of >5000 patients with cirrhosis (and 350-400 incident HCC) to develop a suite of risk score algorithms) for predicting the risk of HCC among patients with cirrhosis.
2) To evaluate the chemopreventive effects and potential harms of metformin, statins or glitazones in reducing the risk of HCC in individuals with MAFLD. We propose a retrospective cohort study using national VA datasets of >580,000 patients with MAFLD. We will also examine the effect of genetic markers on the chemopreventive effects of these medications in patients with MAFLD cirrhosis in THCCC.
3) To examine comparative cost-effectiveness of prevention strategies in MAFLD.
Overlap: None

Title/Grant Number: A Pilot Clinical Trial of Paricalcitol for Chronic Pancreatitis/ 1R01DK132631-01A1
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: NIH/NIDDK subaward via Cedars-Sinai Medical Center
Grants Officer: Not available for this submission
Performance Period: 9/1/2022-8/31/2025
Funding Amount:
Project Goals: The objective of the study is to examine the feasibility of testing the effect of a potent vitamin D analogue, paricalcitol, on health-related quality of life (HRQoL) and potentially delay disease progression in patients with Chronic Pancreatitis (CP). **(Funding status pending as of 9/14/22)** FP14083_Res1
Specific Aims: 1) Conduct a randomized double-blind, placebo-controlled pilot trial of paricalcitol to evaluate the feasibility of performing subsequent efficacy focused trials. Feasibility will be met if the of patients who enroll and complete the 12-month study is ≥75% of planned. There will be a 21-month recruitment period and a one-year treatment period.
2) Monitor health-related quality of life (HRQoL) measures; and imaging biomarkers and liquid biomarkers to identify measures/biomarkers that have the potential to measure responses to the treatment in subsequent efficacy focused trials.

Overlap: There is budgetary and scientific overlap under this application and the original submission that is pending JIT review (1R01DK132631-01). If this submission is awarded, the original submission will be withdrawn by the PD/PI. Alternatively, if the original submission is funded, this submission will be withdrawn by the PD/PI.

Title/Grant Number: Assessment of Impact of blood pressure/phosphate-lowering Medication on CardioVascular Disease endpoints in Chronic Kidney Disease (AIM-CVD-CKD)/ #TBA
Effort: 1.8 Calendar Months, 15% Effort (all years of participation)
Supporting Agency: NIH/NCI subaward via Penn State University College of Medicine
Grants Officer: Not available for this submission
Performance Period: 4/1/2023-3/31/2028
Funding Amount:
Project Goals: Leveraging two epidemiological observational cohort studies, the Chronic Renal Insufficiency Cohort (CRIC) and the Assessment, Serial Evaluation, and Subsequent Sequelae in Acute Kidney Injury (ASSESS-AKI), we propose to develop advanced causal inference techniques for exploring these treatment effects in CKD patients. FP00016518
Specific Aims: 1) Develop a novel propensity score process for causal inference to evaluate medication effects on time-to-event outcomes by incorporating time-dependent treatment administration and covariates.
2) Extend statistical methods proposed in Aim 1 for comperting risk analysis to assess casual medication effects in the presence of death.
3) Conduct systematic evaluation of the proposed methods in Aims 1-2 through simulations and perform the analysis of the CRIC and ASSESS-AKI studies.
Overlap: None

Title/Grant Number: Biomarkers to stratify pain severity and type in pancreatic disease / #TBA
Effort: 1.2 Calendar Months, 10% Effort (all years of participation)
Supporting Agency: NIH/NIDDK subaward via Boston Children's Hospital
Grants Officer: Not available for this submission
Performance Period: 7/1/2023-6/30/2028
Funding Amount:
Project Goals: Based on the preliminary data from our labs and those of others, we hypothesize that CP has a unique objective set of blood- and/or urine-based biomarkers to stratify and grade CP-associated pain. In line with RFA-NS-22-050, we propose studies that will identify (UG3) and validate (UH3) biological biomarkers of CP pain. FP00017679
Specific Aims: 1) Map the plasma proteins, and cytokines/chemokines from a well-annotated CP cohort to identify pain biomarkers.
2) Map the urinary proteins, and cytokines/chemokines from a well-annotated CP cohort to identify pain biomarkers.
3) Validate all plasma biomarker candidates in an independent CP cohort.
4) Validate all urine biomarker candidates in an independent CP cohort.
Overlap: None

Title/Grant Number: Simvastatin Treatment to Improve Patient-Reported Outcomes in Patients with Chronic Pancreatitis/ #TBA
Effort: 0.6 Calendar Months, 5% Effort (all years of participation)
Supporting Agency: DOD subaward via Cedars-Sinai Medical Center
Grants Officer: Not available for this submission
Performance Period: 10/1/2023-9/30/2027
Funding Amount:
Project Goals: Our strategic goals within this topic area are to develop and test novel treatments

and develop technologies for tracking progress of associated diseases and conditions. Our overarching goal is to develop treatments that improve symptoms and other outcomes of chronic pancreatitis (CP); and tests that can be used to monitor the effectiveness of treatments. FP17344
1 & 2, 10% year 3 & 4)

Specific Aims: 1) Determine feasibility of oral simvastatin (40mg) in patients with painful suspected or definite CP.
2) Ancillary measurements will be made in blood products collected before and during the trial to identify biomarkers associated with pain and HRQoL measures.
3. To extend the therapeutic benefit of simvastatin, we will test the ability of modulators of inflammatory and fibrosis pathways to augment the beneficial effect of simvastatin using pre-clinical models of CP.

Overlap: None

In-Kind: None

Foreign Collaboration: None

OTHER SUPPORT

JAGPREET CHHATWAL

CURRENT SUPPORT

R01 (Samir) 03/01/2019 – 02/28/2023 0.24 calendar months
National Institutes of Health total costs
Development of a Machine Learning Model to Integrate Clinical, Laboratory, Sonographic, and Elastographic Data for Noninvasive Liver Tissue Characterization in NAFLD
Goals: We have developed a set of general-purpose shear wave elastography (SWE) liver image analysis algorithms, termed SWE-Assist. We propose (1) to customize and refine SWE-Assist to create a new high-risk NASH-specific SWE image diagnosis toolkit, termed hrNASH-Det, and (2) to integrate hrNASH-Det with clinical, and laboratory data to create an accurate, non-invasive hrNASH diagnostic tool.
Role: Co-Investigator
Overlap with proposed project: None.

R01 (Deshmukh) 03/01/2019 – 02/28/2023 0.39 calendar months
National Institutes of Health total costs
Optimizing Age-based Anal Cancer Screening among People Living with HIV using Decision Analytic Modeling
Goals: The goal of the proposed research is to identify optimal (effective and cost-effective) age-specific anal cancer screening algorithms considering HSIL management using a Simulation Model of Anal Cancer.
Role: Co-Investigator
Overlap with proposed project: None.

UM1DA049394 (Williams) 04/01/2019 – 03/31/2023 3.53 calendar months
National Institutes of Health total costs
HEALing Communities Study: Developing and Testing an Integrated Approach to Address the Opioid Crisis (Data Coordinating Center)
Goals: We aim to evaluate the cost-effectiveness and budget impact of interventions that can reduce opioid-related deaths in HEALing Communities Study and other jurisdictions.
Role: Co-Investigator
Overlap with proposed project: None.

R37 CA231957 (Lubitz) 08/01/2019 – 07/31/2024 1.38 calendar months
National Institutes of Health total costs
Thyroid Nodule Treatment Optimization: A Personalized Approach
Goals: The objective of this proposed research is to harness a comprehensive computer model to simulate individuals with benign and malignant nodules in the U.S. population to identify optimal personalized treatment approaches.
Role: Co-Investigator
Overlap with proposed project: None.

(THIS AWARD)
W81XWH1910690 (Chhatwal) 09/01/2019 – 08/31/2023 2.98 calendar months
Department of Defense total costs
Risk of hepatocellular cancer after virologic cure with direct acting antiviral agents in individuals with hepatitis C
Goals: The overall goal of this study is to examine the determinants of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C virologically cured with the new direct-acting antiviral regimens and to evaluate benefits versus harms of HCC surveillance in those patients.
Role: Co-Principal Investigator
Overlap with proposed project: None.

NSF 18-541 (Gopalappa) 01/01/2020 – 12/31/2023 0.81 calendar months
National Science Foundation total costs
Simulation and Decision-Analysis Algorithms for Integrated Modeling of Diseases: A healthy lives for all approach
Goals: The goal of the proposed research is to develop an integrated multi-disease modeling framework to inform public health strategy plans such as HealthPeople2020 that address social determinants, reduce disparities and aims for healthy lives for all.
Role: Principal Investigator
Overlap with proposed project: None.

Contract (Chhatwal) 03/01/2020 – 06/30/2023 (NCE) 0.84 calendar months
Task Force for Global Health total costs
Hepatitis C Elimination Simulator: An Interactive Global Analysis and Planning Tool for Hepatitis C Elimination
Goals: To help countries identify effective and affordable policies to diagnose and treat HCV, we are developing an interactive online tool, the Hep C Elimination Simulator that will provide country-level information on the HCV epidemic, model the impact of various diagnostic and treatment strategies on HCV disease burden, estimate the budget impact of different interventions, and track the treatment cascade and progress towards elimination.
Role: Principal Investigator
Overlap with proposed project: None.

(Loomba) 05/20/2020 – 04/30/2023 1.24 calendar months
University of California, San Diego total costs
Non-invasive screening of diabetics for advanced fibrosis due to NAFLD
Goals: This project will enable us to determine the circumstances under which NAFLD screening is efficient and cost-effective and identify optimal screening strategies for individuals based on age, sex, obesity, and other risk factors.
Role: Co-Investigator
Overlap with proposed project: None.

Completed Support

(Chhatwal) 01/01/2017 – 12/31/2018
Gilead Sciences, Inc.
Simulation of Patients Who Fail Treatment in the Era of DAAs in Europe
Goals: The overall goal is to estimate the burden of HCV in five European countries in the era of direct-acting antivirals (DAAs) who will fail to achieve sustained virologic response and will need some salvage treatment.
Role: Principal Investigator
Overlap with proposed project: None.

(Chhatwal) 5/10/2017 – 12/31/2018
Gilead Sciences, Inc.
Cost-effective strategies for elimination of Hepatitis C in Spain's prisons
Goals: The overall goal is to evaluate cost-effective strategies to scale-up HCV treatment in Spain's prisons that can lead to HCV elimination.
Role: Principal Investigator
Overlap with proposed project: None.

Merck (Chhatwal) 08/15/2017 – 06/30/2019
Merck Research Laboratories
Strategies for management of hepatitis C virus: A global optimization tool
Goals: We propose to develop a mathematical tool to inform optimal strategies for management of HCV in different countries that will lead to elimination of HCV by 2030.
Role: Principal Investigator
Overlap with proposed project: None.

AASLD Innovation Fund 01/01/2018 – 12/31/2019
American Association for the Study of Liver Diseases
NAFLD Simulator: An online tool for predicting long-term patient outcomes
Goals: We aim to develop an online, open-access tool, NAFLD Simulator, that will simulate the life course of patients with NAFLD and provide information on the long-term risks. This will serve as an educational tool in the clinical setting and aid in shared patient-physician decision-making.
Role: Principal Investigator
Overlap with proposed project: None.

Contractor Services Agreement 02/05/2018 – 03/31/2019
ChangeLab Solutions/CDC
Hepatitis C investment calculator: An online tool for state-level management of Hepatitis C burden
Goals: The objective of this project is to develop the Hepatitis C Investment Calculator, an interactive online tool that allows users to enter state-specific information (e.g. the price of DAAs, testing cost, treatment rates) and evaluate outcomes.
Role: Principal Investigator
Overlap with proposed project: None.

ENDED

(Chhatwal) 01/31/2018 – 12/31/2020
Foundation for Innovative New Diagnostics total costs
Cost-effective analysis of Simplified diagnostic algorithms for Hepatitis C
Goals: The objective is to evaluate the long-term effectiveness and cost-effectiveness of different HCV diagnostic algorithms that FIND will implement as part of the demonstration research projects in India, Georgia, Myanmar, Vietnam, Cameroon, and Malaysia.
Role: Principal Investigator
Overlap with proposed project: None.

ENDED

(Chhatwal) 07/01/2020 – 02/282021
Johns Hopkins University total costs
Informing State-level COVID-19 Testing and Contact Tracing using the COVID-19 Simulator
Goals: To address several time-sensitive policy decisions at the state and national level, we recently developed and launched an interactive COVID-19 policy simulation model. We propose to extend the COVID-19 Simulator to: (1) Estimate the underlying antibody prevalence of COVID-19 and active COVID-19 cases in each state, and (2)Evaluate minimum testing and contract tracing needed to mitigate the spread of COVID-19 at different phases of reopening in each state.
Role: Principal Investigator
Overlap with proposed project: None.

Research Scholar Grant (Chhatwal) 07/01/2017 – 06/30/2022
American Cancer Society total costs
A personalized surveillance program for hepatocellular carcinoma
Goals: The goal of this proposal is to reduce the burden of hepatocellular carcinoma by identifying effective surveillance programs that improve early detection.
Role: Principal Investigator
Overlap with proposed project: None.

NSF 16-601 (Chhatwal) 08/15/2017 – 07/31/2022
National Science Foundation total costs
Collaborative Research: Smart intervention strategies for Hepatitis C elimination
Goals: In this project, we will estimate the true disease burden of hepatitis C at the state and national level, identify effective control strategies using infectious disease modeling and optimal control theory, and develop decision support tools for practical use by stakeholders.
Role: Principal Investigator
Overlap with proposed project: None.

2035361 (Chhatwal) 07/01/2020 – 06/30/2022 (NCE) 0.00 calendar months
National Science Foundation total costs
Mitigation and Suppression of Coronavirus Pandemic with Data-driven RAPID Decisions Using COVID-19 Simulator
Goals: To evaluate and identify effective mitigation strategies using COVID-19 Simulator at the county level in the US by considering testing rates in the absence and presence of COVID-19 pharmaceutical interventions.
Role: Principal Investigator
Overlap with proposed project: None.

(Chhatwal) 04/05/2021 – 03/31/2022 0.00 calendar months
Johns Hopkins University total costs
Simulation modeling to end the COVID pandemic
Goals: (1) Estimate the timing of lifting of restrictions (by different phases) in each state considering different vaccine uptake rates. (2) Evaluate the effect of emerging SARS-CoV-2 variants on the timing of herd immunity in each state. (3) Improve general accessibility and user experience for COVID-19 Simulator by improving conducting user interface design research.
Role: Principal Investigator
Overlap with proposed project: None.

Pending Support

(Pandharipande) 09/01/2021 – 08/31/2026 0.60 calendar months

National Institutes of Health total costs

Improving Treatment Selection in Advanced Ovarian Cancer

Goals: Our goal is to improve treatment selection and survival in women diagnosed with advanced ovarian cancer.

Role: Principal Investigator

Overlap with proposed project: None.

(El-Serag) 07/01/2022 – 06/30/2023 2.4 calendar months

National Institutes of Health total costs

Prevention of Hepatocellular Carcinoma Related to Metabolic Syndrome

Goals: To examine the risk and determinants of hepatocellular cancer in patients with nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome.

Role: Project lead

Overlap with proposed project: None.

◦**What other organizations were involved as partners?**

MD Anderson Cancer Center (Houston, TX) provided the following types of support:

- In-kind support (partner makes software, computers, equipment, etc., available to project staff)
- Facilities (project staff use the partner's facilities for project activities)

University of Texas Health Science Center (Houston, TX) provided the following types of support:

- In-kind support (partner makes software, computers, equipment, etc., available to project staff)
- Facilities (project staff use the partner's facilities for project activities)

8.SPECIAL REPORTING REQUIREMENTS

◦**COLLABORATIVE AWARDS:**

The Initiating PI and the Collaborating/Partnering PI are submitting separate reports.

◦**QUAD CHARTS:**

Nothing to report.

9.APPENDICES:

Appendix I – Journal Publication – Duration and cost-effectiveness of hepatocellular carcinoma surveillance in hepatitis C patients after viral eradication

Appendix II – Abstracts Presented