

A. OVERALL COVER PAGE

Project Title: Hepatitis C virus infection in WTC responders	
Grant Number: 5U01OH011307-02	Project/Grant Period: 09/01/2016 - 08/31/2018
Reporting Period: 09/01/2017 - 08/31/2018	Requested Budget Period: 09/01/2017 - 08/31/2018
Report Term Frequency: Annual	Date Submitted: 12/04/2020
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Human Subjects: NA	Vertebrate Animals: NA
hESC: No	Inventions/Patents: No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The majority of persons in the World Trade Center (WTC) occupationally-exposed study cohort followed at the Icahn School of Medicine at Mount Sinai (WTC Health Program, WTCHP) were born during 1945-1965. According to CDC, persons born during this period are at high risk for chronic hepatitis C virus (HCV) infection and are likely to be unaware of their infection. Chronic HCV infection places infected persons at risk for liver cirrhosis, hepatocellular carcinoma (HCC), and extrahepatic complications, including non-Hodgkin lymphoma. With the development of new therapies that can halt disease progression and provide a virologic cure, CDC has advocated for one-time targeted testing to members of this cohort and linkage to care for those found to have HCV infection.¹ Provision of one time HCV testing with to the WTCHP occupationally-exposed study cohort at the study site where they are annually assessed will reach the targeted group, may identify additional risk factors for HCV infection, and may clarify identify characteristics associated with successful linkage to care among those infected.

At least 20% of patients with chronic HCV infection do not have a known risk factor for HCV infection suggesting that there is more to learn about the epidemiology of the disease. The currently known risk factors for disease include history of injection drug use, selected medical conditions (e.g., person who received clotting factors concentrates produced before 1987), recipients of transfusions or organ transplants, and person with recognized exposures, including health care, emergency medical and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood, and children born to HCV-positive women. The risk of exposure to human remains, blood and bodily fluid in the context of recovery work, like that done at the WTC site, has not been studied previously.

The overarching goals of the proposed research are to determine if the WTCHP cohort is at increased risk of HCV infection, determine if human exposure to human remains, blood, and/or bodily fluids during the WTC recover activities is associated with an increased risk of HCV infection, and to determine if referral to a co-located site for HCV care is associated with improved linkage to HCV care in the members of the WTCHP born during 1945 through 1965.

The Specific Aims of the proposed research are:

Specific Aim 1 – To estimate the prevalence of HCV infection in the WTCHP cohort and compare it to the birth cohort in the general population, and to assess the contribution of known risk factors. We will measure HCV infection status in 3900 WTCHP members to test the hypothesis that WTCHP members have an increased risk of HCV infection, with relative risk of 1.25 or greater.

Specific Aim 2 – To determine if exposure to human remains, blood, and/or bodily fluids during the WTC recovery activities is associated with an increased risk of HCV infection. We will test the hypothesis of a correlation between exposure to human remains, blood, and/or bodily fluid and risk of HCV infection, while adjusting for type of activity during work at the WTC site and use of personal protective equipment.

Specific Aim 3 – To determine if referral to the co-located Mount Sinai Liver Medicine Practice for WTCHP cohort members infected with HCV is associated with improved linkage to HCV care, compared to referral to other sites, and compared to rates of linkage to care in other studies. We will test the hypothesis of a correlation between referral for HCV infection care to the co-located Mount Sinai Liver Medicine Practice, and successful linkage to care, measured by adherence to an initial clinical evaluation by a liver specialist and initiation of treatment for HCV infection, if indicated.

The project will provide one time HCV testing to a high-risk group that has provided much service to this country and may be at increased risk of morbidity and mortality due to chronic HCV infection. Those identified as having HCV infection will be informed and referred for further evaluation and treatment. Those who choose to will be referred to the co-located Mount Sinai Liver Medicine Practice. The Mount Sinai Liver Medicine Practice is 2 blocks away from the WHTCHP annual assessment site and is a leading treatment center for liver disease which accepts multiple insurance plans and operates on a sliding scale for indigent and Medicaid patients. This project may provide additional epidemiologic data about a life-threatening infection including identification of characteristics associated with increased risk of infection and characteristics associated with successful linkage to care.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

Accomplishments

Activities

A total of 3935 World Trade Center General Responder Cohort (WTCGRC) members were enrolled in the study. Of those, 64 persons were excluded (18 born outside the birth cohort, 21 missing laboratory data, 15 with “indeterminate” hepatitis C virus (HCV) antibody results with negative HCV RNA PCR testing, and 10 withdrawals). Of the remaining 3871, 109 (2.8%) had HCV infection defined as having antibodies against HCV.

Of the 3871 participants, 544 persons were not included in further analysis (89 did not consent to share WTCGRC data, eight had data that were not yet integrated into the WTCGRC database, and 447 did not have complete data on at least one of the three main exposures – exposure to human remains, blood and/or bodily fluid, and sewage at the World Trade Center site), and 3277 were included in the analysis.

Specific objectives and significant results

Specific Aim 1. To estimate the prevalence of HCV infection in the WTCHP cohort and compare it to the birth cohort in the general population, and to assess the contribution of known risk factors.

The age-standardized point prevalence of HCV infection among the 3871 members of the WTC Cohort who were successfully tested was 2.98% [95% CI (2.39, 3.56)] and in the US population was 3.33% [95% CI (2.54, 4.11)]. These measures are not statistically different [% difference = 0.35%, 95% CI (- 0.31%, 1.01%), $P=0.47$].

Among the 3327 who consented to participate in research, only ten (11%) of HCV-infected persons reported exposure to a known HCV risk factor.

Specific Aim 2. To determine if exposure to human remains, blood, and/or bodily fluids during the WTC recovery activities is associated with an increased risk of HCV infection.

To adequately answer the intention of this Specific Aim, we used 3 exposures that were asked of all WTC GRC members at their enrolment visit. Study personnel asked members if they had “contact” with “human remains” “blood or bodily fluids,” and/or “sewage.”

The three exposures of interest were common among WTCGRC members with 1559 of 3243 (48%) reporting exposure to human remains, 996 of 3206 (31%) reporting exposure to blood and/or bodily fluid, and 1561 of 3217 (49%) reporting exposure to sewage. In the final multivariable logistic regression model with HCV infection as the outcome, and adjusting for age and recognized HCV risk factors, contact with sewage was associated with an increased risk of HCV infection [odds ratio (OR) = 1.74, 95% CI (1.01, 3.01)]. Contact with human remains and blood or bodily fluids were not associated with HCV infection in univariable or multivariable analysis (OR = 1.02, 95% CI (0.59, 1.75; OR = 1.37, 95% CI (0.78, 2.41), respectively).

Frequency of glove use may be an effect modifier in the relationship between contact with sewage and HCV infection. The point estimate for the OR for the relationship between sewage and HCV infection decreases as the frequency-weighted average glove use increases, from OR = 6.17 (95% CI 0.58, 316.06) among ‘sometimes’ users, to OR = 2.12 (95% CI 0.66, 7.91) in ‘most of the time’ users, to OR = 1.84 (95% CI 0.73, 5.04) among ‘always’ users.

However, none of these point estimates are statistically significant and among those who rarely or never used protective gloves, the OR for the sewage-HCV relationship is 0.35.

Specific Aim 3 – To determine if referral to the co-located Mount Sinai Liver Medicine Practice (MSLMP) for WTCHP cohort members infected with HCV is associated with improved linkage to HCV care, compared to referral to other sites, and compared to rates of linkage to care in other studies.

Of the 96 persons with HCV infection, 13 (14%) had current infection, 33 (34%) reported successful treatment for HCV infection in the past, 35 (36%) reported no history of treatment, and the remaining 15(9%) were not sure or did not answer the question. The rate of spontaneous clearance of HCV infection in this cohort is at least 36%. If the 15 persons who were unsure of past treatment or did not answer the question are assumed to have spontaneously cleared the infection, the spontaneous clearance rate in this population would be 52%.

Of the 13 persons with current infection, 12 accepted referral to the MSLMP. Of those 12, 10 (83%) were linked to care defined as presenting for at least 1 appointment. The single WTC member who do not accept referral the MSLMP had insurance from an outside state, was given a referral to a Federally-qualified health center near his home, and was linked to care. This is a much greater percentage than the percentage who are linked to care in emergency room and hospital-based screening programs which usually report between 20 and 40% linkage to care. This is similar to the linkage to care rate found in a study done among Kaiser Permanente patients who were tested by their regular primary care provider (81%).

Of the 10 persons who were linked to care, all were recommended to receive treatment, 9 have initiated treatment thus far, 9 completed treatment, and 9 have achieved a sustained virological response.

Key outcomes or other achievements

All of the objectives have been met. We have determined that the prevalence of HCV infection is similar to general US population.

This is the first well-designed epidemiology study to suggest an association between contact with sewage and HCV infection. This finding is biologically plausible as persons with HCV infection shed HCV in their stool.

The proportion of participants who were successfully linked to care is higher in than most studies. This study combined with other research suggests that screening programs for HCV which are collocated at HCV treatment sites have higher linkage to care.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Other	Boffetta B, Dieterich DT, Desai V, Crane M, Factor SH. Contact with sewage as a risk factor for hepatitis C virus infection. Poster presented at: Public health for the future of humanity: analysis, advocacy and action. 16th World Congress on Public Health; 2020 October 12-17; Rome, Italy.

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
STFACTOR	Y	Factor, Stephanie Hope	AB, MPH, MD	PD/PI	2.0	0.0	0.0			NA
PAOLO.BOFFETTA	Y	BOFFETTA, PAOLO	MPH, MD	PD/PI	1.0	0.0	0.0			NA
	N	Desai, Vimi	MD MPH	Research Coordinator	12.0	0.0	0.0			NA

Glossary of acronyms:

S/K - Senior/Key

DOB - Date of Birth

Cal - Person Months (Calendar)

Aca - Person Months (Academic)

Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation

SS - Supplement Support

RE - Reentry Supplement

DI - Diversity Supplement

OT - Other

NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT**E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?**

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

NOTHING TO REPORT

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

Summary of U01OH011307

Project: Hepatitis C virus infection in WTC responders
 PI: Stephanie H. Factor, MD MPH
 Paolo Boffetta, MD MPH
 Organization: Icahn School of Medicine at Mount Sinai

Chronic hepatitis C virus infection places infected persons at risk for liver cirrhosis, hepatocellular carcinoma, and non-Hodgkin lymphoma. According to CDC, persons born during 1945 through 1965 are at high risk for chronic hepatitis C virus infection and are likely to be unaware of their infection. There are identified risk factors for hepatitis C virus infection (including HIV infection, history of injection drug use, selected medical conditions (receipt of clotting factors concentrates produced before 1987, on chronic hemodialysis, and persistently abnormal alanine aminotransferase levels), recipients of transfusions or organ transplants (including persons who received blood from an HCV-infected donor, persons who received a transfusion of blood or blood components before July 1992, and persons who received an organ transplant before July 1992) and person with recognized exposures (including health care, emergency medical and public safety workers after needle sticks, sharps, or mucosal exposures to blood from hepatitis C virus-infected people, and children born to hepatitis C virus-infected women). However, many people with hepatitis C virus infection do not have any of these risk factors.

Prior to 2011, treatments for hepatitis C virus infection were difficult to take (required injection) and had many side effects. Therefore, many people were not cured of their infection. In 2011, a new class of treatments became available that were easy to take (oral pills) and had few side effects. Therefore, many people are now likely to be cured of their infection. To cure people of hepatitis C virus infection, people need to be tested for hepatitis C virus infection and those with hepatitis C virus infection need to be linked to appropriate medical care.

The World Trade Center General Responder Cohort followed at the Icahn School of Medicine at Mount Sinai consists of persons who worked or volunteered during the World Trade Center Rescue and Recovery between September 2001 and June 2002. The majority were born during 1945-1965, the birth years associated with a high prevalence of infection.

In this study, we tested almost 4000 members of the World Trade Center General Responder Cohort for past and current hepatitis C virus infection.

These were some of our main findings:

- The proportion of persons who had ever had hepatitis C virus infection in this cohort is similar to the proportion of persons who had ever had hepatitis C virus infection in general population of the United States, about 3%
- Most persons who had ever had hepatitis C virus infection in this cohort (89%) did not have one of the identified hepatitis C virus infection risk factors
- People who were exposed to sewage during their work at the World Trade Center had a higher risk of hepatitis C virus infection than people who were not exposed to sewage during their work at the World Trade Center
- People who wore gloves when they were in contact with sewage during their work at the World Trade Center site had a lower risk of hepatitis C virus infection than people who did not wear gloves when they were in contact with sewage during their work at the World Trade Center site
- Most of the people who had ever had hepatitis C virus infection had either cleared their infection naturally or had been treated; we found 13 persons who had current hepatitis C virus infection
- After learning about their current hepatitis C virus infection from us, most of the persons who were found to have current hepatitis C virus infection were then seen by a liver disease specialist (11 out of 13, 85%). Of the 11 who were seen by an infectious disease specialist, most were treated and cured (9, 82%), 1 is currently on treatment (9%), and 1 was seen in a state outside of New York which does not provide treatment for hepatitis C virus infection in most cases