



A health study for oil spill clean-up workers and volunteers

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Overview

The Gulf Long-term Follow-up Study (GuLF Study, www.gulfstudy.nih.gov/en.index.html) was initiated in response to the April 2010 explosion of the *Deepwater Horizon* (DWH) drilling rig and resulting oil spill in the Gulf of Mexico, the largest marine oil spill in U.S. history. Individuals who participated in oil spill response and clean-up (OSRC) activities are a potentially high-risk group with exposure to multiple toxicants and stressors. The GuLF Study targeted these OSRC workers because they were more likely than community members to have had direct physical contact with crude oil chemicals, combustion products, dispersants, and a range of associated physical and psychosocial stressors, with exposure levels depending on their job/tasks, location, and dates of work. It is the largest study ever conducted on the potential health effects associated with an oil spill, with nearly 33,000 participants and is focused on both physical and mental health effects related to the oil spill. The GuLF Study collected ten years of questionnaire and clinical follow-up information between 2011-2021 and the cohort is now being passively followed via National Death Index and cancer registry linkage. Data and results from this study can be used by individuals, communities, and government agencies to better understand the consequences of oil spills and plan for future disasters.

Outcomes of interest were identified from existent literature on health effects of oil spills, studies of petroleum-exposed workers, National Institute for Occupational Safety and Health (NIOSH) surveillance reports during the spill, and media and community reports of symptoms among oil spill workers and residents of nearby communities. Of the 38 major reported oil spills prior to the DWH disaster, only seven were studied for human health effects. Most studies were cross-sectional and investigated acute symptoms. In many studies, exposure status was based on residential address in relation to the oil spill location or on performance of a small number of clean-up tasks. Studies with prospective data were generally small and had short follow-up. Early data from these studies suggested that respiratory and genotoxic effects were important to capture, as well as mental health outcomes commonly associated with disasters. Several studies reported respiratory symptoms among exposed persons, including cough and shortness of breath, but reports on changes in lung function have been limited and inconsistent. Other commonly reported acute symptoms include itchy eyes, nausea and vomiting, dizziness, headaches, and dermatological problems. Occupational and toxicological studies suggest other potential health consequences of exposure to oil spill-related chemicals, including neurological, hepatic, renal, endocrine, hematological, and other systemic effects.

Participants were recruited by telephone from lists of individuals who worked on the OSRC or received safety training but were not hired. Enrollment interviews were conducted with 32,608 participants between March 2011 and May 2013 to collect information related to OSRC activities, and demographic, socioeconomic, occupation, lifestyle, and health information, including

symptoms experienced during the time of the oil spill and at the time of the interview. Exposure measurements collected via personal badge detectors and areal monitoring taken during the oil spill and available industrial hygiene data were used with questionnaire responses to characterize chemical exposures of participants. A subset (N=11,193) of workers and non-workers residing in Gulf states completed a home visit in which biological and environmental samples were collected along with anthropometric and physiologic measurements, including measures of pulmonary function. Additional health, lifestyle, and occupational and environmental exposure information also was collected.

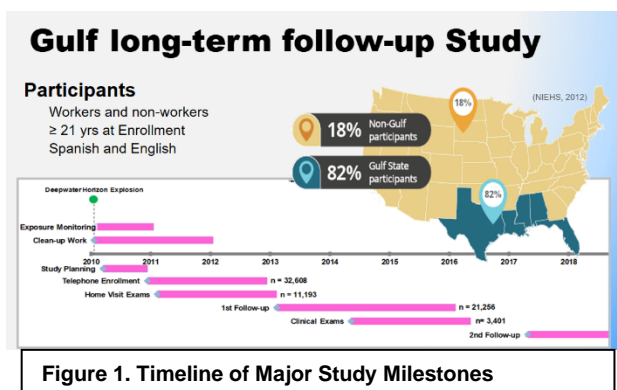


Figure 1. Timeline of Major Study Milestones

Study participants have been followed via telephone interviews every two to three years. The first follow-up interview was completed by 23,690 participants between May 2013 and May 2016. A subset of 3,401 participants completed a more comprehensive clinical exam if they met the eligibility criteria (completed a home visit; lived within ~60 miles of one of 2 study clinics, and completed the first follow-up interview). The clinic visit included additional measures of lung function, standardized measures of neurological function, questionnaires, and biological sample collection.

A second follow-up interview began late November 2017 and ended May 2021. The second follow-up questionnaire was based largely on the first with the addition of questions on reproductive health and sleep habits. While the second follow-up made attempts to reach all who enrolled, those who completed previous study activities such as the first follow-up or the clinic exam were prioritized in follow-up efforts. All participants, regardless of active participation in follow-up interviews or exam, have been linked to mortality records through 2022. Participants residing in the Gulf states (Alabama, Florida, Louisiana, Mississippi, and Texas) have been linked to state cancer registries and linkage for all participants to registries participating in the nearly nation-wide Virtual Pooled Registry Cancer Linkage System (VPR-CLS) is underway.

Eligibility and Recruitment

Recruitment was based on training and worksite records provided by BP, contractors, NIOSH, and other governmental agencies. After merging and cleaning these lists, 62,803 apparently unique individuals with presumably accurate contact information were identified and considered potentially eligible (**Figure 2**). Those eligible for the study were ≥ 21 years of age and had either worked on the OSRC in any capacity for at least one day or had completed safety training but were not hired.

A comprehensive outreach plan promoted participation across the region. Before launch, the NIEHS hosted public meetings and webinars to solicit input from key stakeholders. An intensive media campaign included advertisements in newspapers, television, radio, billboards, social media, and electronic bulletin board outlets, endorsements from the Surgeon General and regional and national celebrities. The Study PI was interviewed on television and radio and in print media to promote enrollment. Targeted groups included potential study participants, families of workers, community leaders, and others who

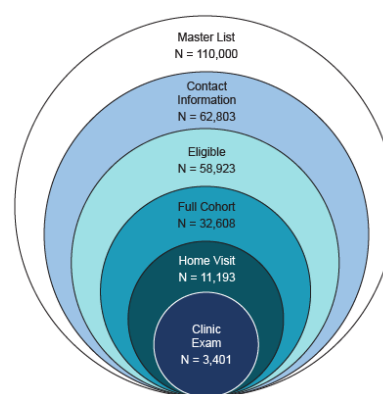


Figure 1: GuLF Study Participation Schematic

could legitimize the study and encourage enrollment. To reach potential Vietnamese-speaking participants, we enlisted the assistance of trusted community partners from groups serving local Vietnamese residents. Oil and gas industry professionals were underrepresented on the master recruitment list, largely because they were already trained and were not required to complete the new safety training for OSRC work. To find such workers, we placed recruiters at the heliport serving oil and gas professionals in Houma, Louisiana to distribute study recruitment materials and obtain contact information.

Enrollment took place between March 2011 and May 2013. Potential participants were mailed an invitation, brochure, privacy statement, and information about opting out before telephone interviewers attempted contact. Materials and interviews were available in English, Spanish, and Vietnamese. During calling, we found that 1,182 were duplicates, 308 were deceased, 1,135 were ineligible, and 1,255 had communication difficulties or were unavailable during the time window, leaving **58,923 presumably eligible participants**. Of these, 22,572 opted out or broke off telephone contact before eligibility was confirmed. Of the remaining 36,351 individuals (62% of presumed eligible participants), **32,608 completed the enrollment telephone interview** (90% of those confirmed eligible; 55% of presumed eligible participants). Of these, 999 participants completed an abbreviated interview in Vietnamese.

At the conclusion of the enrollment interview, English- and Spanish-speaking participants from eastern Texas, Louisiana, Mississippi, Alabama, and Florida were invited to participate in a home visit, which included an additional interview, collection of biological and environmental samples, and anthropometric and physiologic measurements. Because visit scheduling required a separate phone call from a home examiner, some who initially agreed were lost. Tracing efforts, including door-to-door canvassing, helped to locate participants and schedule visits. A total of **25,304 English- or Spanish-speaking Gulf state residents were eligible for the home visit**. Of those, 17,883 (70%) agreed to participate. However, 4,528 were lost to contact (25%) and 2,137 changed their minds (often on advice of lawyers or family members; 12%) before the home visit was scheduled. Of the 11,218 who had a home visit (44% of those eligible and 63% of those who initially agreed), 25 had their home visits terminated early for health or safety reasons, leaving **11,193 with complete home visit exams**. These visits were conducted between May 2011 and May 2013. Response rates for all study visits are shown in **Table 1**.

Table 1. Participation Rates for All Study Events

Study Event	Eligible	<u>Contacted</u>			<u>Completed</u>	
		N	%	N	Response Rate	Participation Rate
Enrollment	58,923	36,351	62%	32,608	90%	55%
Home Visit	25,304	13,355	53%	11,193	84%	44%
Follow-Up1	31,365	23,828	76%	21,443	90%	68%
Mental Health Modules						
Baseline	4,370	4,187	96%	2,859	68%	65%
6-Month	2,859	1,875	66%	1,822	97%	64%
12-Month	2,859	1,908	68%	1,741	91%	61%
24-Month	2,859	1,747	61%	1,506	86%	53%

Clinical Exam	5,506	4,647	84%	3,401	73%	62%
Follow-Up2	30,730	16,160	53%	14,170	88%	46%
FUP1 Responders	21,242	14,357	68%	12,874	90%	61%

Response rate = completed/contacted

Participation rate – completed/eligible

Enrollment Questionnaire

Participants completed a computer-assisted telephone enrollment interview in English, Spanish, or Vietnamese. In addition to information related to OSRC activities, participants provided demographic, socioeconomic, occupation, lifestyle, and health information, including symptoms experienced during the time of the oil spill and at the time of the interview. Where possible, the questionnaire used validated or previously used questions from major epidemiologic studies and national surveys to facilitate comparisons. Full interviews were conducted in English and Spanish. Those who spoke only Vietnamese (N=999) completed an abbreviated questionnaire. The Vietnamese questionnaire focused on clean-up experiences and current symptoms. It was abbreviated to overcome issues related to trust in researchers and tailored to account for cultural differences in reporting of physical and mental health outcomes. Questionnaires can be found at <https://gulfstudy.nih.gov/en/index.html>.

Home Visits

Cohort members residing in the Gulf states were invited to participate in baseline home visits. The home visit included an additional questionnaire, collection of biological and environmental samples, and clinical measurements. Home exams were conducted by certified medical assistants recruited from the Gulf states; examiners were trained and supervised by regional managers overseen by staff from Social & Scientific Systems, Inc. (SSS), a DLH Corporation Company (now DLH, LLC), which provides research support services for the study through a contract with NIEHS. Completion of study components is shown in **Table 2**.

Anthropometric and Clinical Measurements – Home Visit

Height, weight, hip and waist circumference, resting blood pressure, and heart rate were measured and recorded following standard protocols. Pulmonary function testing (PFT) was performed according to American Thoracic Society and European Respiratory Society standards using a portable ultrasonic spirometer (Easy on-PC; ndd Medical Technologies). The spirometer had automated quality control software that provided real-time quality feedback to examiners and an overall quality score for each testing session. The central field manager aggregated weekly scores and provided direct feedback on PFT quality to field managers and staff. Dr. Robert Jensen, a spirometry expert, independently reviewed and scored all tests to ensure that quality scores assigned by the software were accurate and adjusted scores as needed. Dr. Jensen also provided training and ongoing support to field staff in conjunction with the central and regional field managers. After medical exclusions, pulmonary function testing was completed by 10,040 (94%) participants. Blood pressure, heart rate, height, weight, hip and waist circumference and urinary glucose levels were measured on nearly all participants.

Biological and Environmental Sample Collection – Home Visit

Biologic specimens collected during the home visit included toenail, blood, hair and urine samples. A total of 52.5 mL of venous blood was collected. A small subgroup provided additional blood for quality assurance. Saliva for DNA analysis was obtained if blood could not be collected. If the participant had not collected a first morning urine void, a clean catch spot urine sample was

collected during the visit. A hair sample was collected if the participant's hair was at least 1 cm long. Toenail clippings were collected from each toe. If toenails were too short, participants were given a self-collection kit to collect and return samples by mail. Study staff recorded GPS coordinates at the doorstep and collected alcohol dust wipe samples from the participant's house. For a small subset of participants in selected counties/parishes in Alabama and Louisiana, a vacuum dust sample was also collected.

Over 99% of participants provided at least one biological sample. Urine was obtained from 11,061 (99%) participants, one or more blood specimens from 10,389 (93%), toenail clippings from 9,993 (89%), a hair sample from 4,428 (40%), and house dust from 10,615 (95%).

Table 2. Home Exam Component Completion Rates (N=11,193)		
Component	Completed	Percent
Biologic samples		
Urine	11,061	99
Blood (1 or more tubes)	10,389	93
Saliva (if no blood)	566	5
<i>DNA (blood/saliva)</i>	<i>10,996</i>	<i>98</i>
Toenail clippings	9,993	89
Hair samples	4,428	40
House dust	10,615	95
Blood pressure	11,138	99
Anthropometrics	11,004	98
Pulmonary function tests	10,040	94

Biological samples were processed, labeled, and packaged for shipping in the home, and were shipped by priority overnight service to the central processing and clinical laboratories. The samples were processed at the central laboratory on the day of receipt, following standardized protocols. The central processing laboratory aliquoted samples, cryopreserved lymphocytes (32% sample) or whole blood (59% of cohort), and prepared samples for delivery to the nearby NIEHS biorepository at Experimental Pathology Laboratories (Durham, NC) where they are stored in environmentally controlled conditions (hair and nail samples) or in -20°C, -80°C or liquid nitrogen (blood and urine samples) for future analyses. **Tables 3 and 4** provide additional information about the biological sample collection, processing, shipping, and storing. A commercial clinical laboratory provided complete blood count and urinalysis results for selected participants.

Table 3. Collection and Processing of Home Visit Specimens

Blood collection tube	Order of draw	Processing in home	Disposition	Shipment temperature	Storage temperature ^a
Red top tube (2x10 mL)	1, 2	Clot and centrifuge	Serum	4°C	LN2
			Clot	4°C	-80°C
Lavender top EDTA tubes					
10 mL	3	Centrifuge	Plasma	4°C	LN2
			Packed cells	4°C	LN2
			HVS: Stored	Ambient	LN2
2 mL	6	None	BSS: CBC analysis	Ambient	N/A
6 mL	7	Centrifuge	Plasma	4°C	LN2

Blood collection tube	Order of draw	Processing in home	Disposition	Shipment temperature	Storage temperature ^a
Yellow top ACD-B tube (6 mL)	4	None	Packed cells HVS: 10% DMSO added, step frozen	4°C Ambient	LN2 LN2
Royal blue top EDTA tube (6 mL)	5	None	Stored	4°C	-20°C
PAXgene RNA tube (2.5 mL)	8	None	Stored	4°C	-20°C

^a LN2=vapor phase of liquid nitrogen

DNA Extraction

Blood leukocyte DNA was extracted from packed red cells, clots, or saliva for 10,996 Home Visit participants. BioServe Biotechnologies, Ltd. (Beltsville, MD) performed the extraction and aliquoting.

Report Back of Findings to Participants

At the conclusion of the home examination, participants were given reports with their body mass index, blood pressure, heart rate, and dipstick urinary glucose test results and interpretation. Participants later received a mailed report of findings shared during the visit, along with pulmonary function testing and complete blood count results (done in a selected sample). The reports included graphics to aid in interpretation of results and recommendations for seeking medical advice based on findings, as appropriate. Abnormal results were sent to participants' physicians, if requested. Field staff were trained to identify urgent physical or mental health issues (e.g., hypertensive crisis or acute mental distress). If necessary, participants were referred to a nearby federally qualified health center or emergency facility. Overall, 1,000 referrals were made; most were for non-emergency medical issues (mostly for participants with health concern related to the oil spill that they wanted addressed) (89%), followed by mental health (9%), and other reasons (2%). Field staff contacted emergency services when needed, and participants were connected to suicide prevention hotlines when appropriate.

Table 4. Non-blood Biological and Environmental Sample Collection and Processing

Specimen	Processing in home	Disposition	Shipment temperature	Storage temperature ^a
Urine	Reagent strip urinalysis on small sample; 16 mL transferred to preservative tubes; 24 mL left unpreserved	Urinalysis of ~8 mL for selected participants; remainder stored	4°C	LN2 and -80°C
Toenail clippings (n=10)	None	Stored	Ambient	Ambient
Hair	None	Stored	Ambient	-20°C
Saliva (for DNA) ^b	None	Stored	4°C	-20°C

Specimen	Processing in home	Disposition	Shipment temperature	Storage temperature ^a
House dust wipes	None	Stored	Ambient	-20°C
Vacuum dust	None	Stored	Ambient	-20°C

^a LN2=vapor phase of liquid nitrogen

^b Among participants who refused or were unable to provide blood samples

Exposure Monitoring Sub-Study

During baseline home visits conducted between July 2012 and May 2013, we collected additional blood samples and questionnaire data on current environmental exposures from a subset of home visit participants (n=1,046); ~200 participants also wore a personal air monitor for 24 hours. This was done as part of an Exposure Monitoring (EM) sub-study designed to address ongoing concerns among Gulf state residents (fueled by advocate and media reports) about potentially higher current blood levels of oil-spill related chemicals and implications for current and future health. Since the half-lives in blood of relevant volatile organic compounds (VOCs) is short (12-24 hours), reports of high levels of chemicals such as benzene, toluene, ethylbenzene, and xylene (BTEX) in blood from Gulf area residents were likely from ongoing environmental, lifestyle, and occupational exposures rather than the DWH oil spill. We hoped to provide reassurance about persistent oil spill exposures, in part, by determining the factors that contributed to any apparently higher levels of oil-related chemicals and evaluating the relationship between oil spill work exposures and measured levels after taking known and discovered contributing factors into account (e.g., cigarette smoking). A secondary aim was to evaluate associations between current chemical levels and symptom reporting or other health outcomes.

Collaborators at the National Center for Environmental Health (NCEH) analyzed samples for selected heavy metals and VOCs and provided a comparison dataset (from The National Health and Nutrition Examination Survey, NHANES). Developed with input from community advisors, reports to participants included a description of overall results for VOCs and blood metals, simplified visually appealing graphs showing participant exposure levels in relation to national and clinically relevant levels (if available), and fact sheets with information about how to reduce potential exposures. State-level reports were shared with state and local health departments. As expected, levels of most VOCs did not differ from those reported in NHANES after adjusting for smoking, and exposure levels were unrelated to OSRC work.

Cohort Characteristics

Demographic characteristics of the full cohort and home visit participants are shown in **Table 5**. Most participants (82%) lived in Alabama, Florida, Louisiana, Mississippi, or Texas, but those affiliated with the Coast Guard and other federal agencies, as well as others came from elsewhere in the United States. The majority were ≤ 45 years old (56%), male (80%), and had an annual household income ≤ \$50,000 (54%), with nearly 40% reporting their race as nonwhite (23% black, 4% Asian, 9% other/multi-racial). Most participants worked ≥ 1 day(s) (76%). There were few noteworthy differences between workers and those who trained but were not hired (non-workers). Fewer workers than non-workers were > 45 years of age (41% vs. 50%) and fewer were women (18 vs. 25%). Home visit participants (restricted to the Gulf states) largely did not differ from the full cohort although they reported fewer years of schooling and lower incomes.

Table 5. Characteristics of Full Cohort and Home Visit Participants at Enrollment

Characteristic	Full Cohort N=32,608 %	Workers N=24,937 %	Nonworkers N=7,671 %	Home Visit N=11,193 %
Age				
< 30	19.2	20.1	16.3	17.7
30-45	37.0	38.2	33.2	35.1
> 45	43.4	41.3	50.2	47.2
Gender				
Male	80.8	82.5	75.1	78.2
Female	19.2	17.5	24.8	21.8
Race				
White	63.4	64.6	59.8	54.6
Black	22.8	22.6	23.5	34.7
Asian	4.1	3.1	7.1	0.7
Other/multi-racial	9.3	9.3	9.1	9.8
Hispanic Ethnicity	6.5	6.9	5.3	6.0
Location at Enrollment				
Alabama	18.2	18.0	18.6	26.4
Florida	21.4	20.2	25.3	28.8
Louisiana	24.1	22.5	29.4	24.5
Mississippi	13.0	13.3	12.1	17.2
Texas	5.6	6.1	4.1	3.0
Other	17.7	20.0	10.4	0.0
Marital Status				
Married/living as married	56.2	56.5	55.3	49.8
Divorced/separated/widowed	18.8	18.4	20.1	23.3
Never married	24.0	24.3	23.1	26.5
Educational Attainment				
< High school/equivalent	15.6	15.3	16.6	21.2
High school diploma/GED	28.9	28.7	29.7	33.9
Some college/2-year degree	28.8	29.3	27.1	29.9
4-year college graduate or more	23.3	24.2	20.3	14.7
Annual Household Income				
≤ \$20,000	25.8	24.7	29.5	37.2
\$20,001 - \$50,000	28.3	28.7	27.1	30.9
> \$50,000	34.3	36.3	27.9	24.8
Worked ≥ 1 Day on Clean-Up	76.5	100.0	0.0	80.1

Percentages may not total 100 due to missing values

Exposure Assessment

OSRC workers performed a range of jobs/tasks, from stopping the leak to cleaning beaches to administrative support, with varied exposure profiles (**Table 6**). Many reported multiple different jobs/tasks often performed on the same day. Due to weathering of the oil, exposure levels within each activity varied based on location, time period (defined by key OSRC foci) and vessel type (if applicable). Quantitative exposure estimates for total hydrocarbons (THC) and BTEX-H (benzene, toluene, ethylbenzene, xylene, hexane) are of interest as these oil-related chemicals comprised most of the air measurements taken during the spill and are generally considered to be the more toxic components. Exposure estimates for dermal contact, dispersants, and particulate matter (PM_{2.5}) from burning were also desired because of their association with some health effects and because of concerns raised by the public.

The GuLF Study began after most of the oil spill clean-up effort had ended and it was not possible to directly monitor study participants for exposures. Instead, we relied on data from study questionnaires and personal and ambient monitoring done by BP and its contractors during the OSRC to determine what the exposures of study participants would have been, given the tasks and jobs they performed. The enrollment interview captured detailed histories of participant job activities, start/stop dates, average number of days worked/week, average number of hours worked/day, use of personal protective equipment, and dermal contact with chemical agents. These detailed participant work histories were linked to exposure estimates from Job Exposure Matrices (JEMs) to develop ordinal and quantitative exposure metrics.

Much of this effort depended on the more than 28,000 full-shift, personal air monitoring samples obtained by BP contractors to characterize worker exposure to OSRC chemicals from April 2010 to through June 2011. Collaborating industrial hygienists, chemists, and biostatisticians, overseen by Dr. Patricia Stewart (Stewart Exposure Assessments, LLC), used the air measurement data to identify factors associated with exposure levels. Statistical methods were evaluated and/or developed to deal with large amounts of missing data (due to levels of chemicals below limits of detection) and leverage more complete data on total hydrocarbons to develop estimates for exposure to correlated chemicals. Unique combinations of factors were identified that were expected to lead to similar distributions of chemical exposures. The measurement data were used to determine average chemical exposures for each job or task/vessel or vessel type/location/time period combination, which was translated into both ordinal and quantitative exposure estimates. An ordinal job-exposure matrix (JEM) was first developed for THC inhalation exposure and used in publications through 2020. Later, quantitative THC, BTEX-H, PM_{2.5}, and oil mist JEMs were developed to provide more detailed levels of inhalation exposures. A customized theoretical (since no direct dermal measurements were made) model to estimate THC and BTEX-H dermal exposures was published (Gorman Ng et al., *Annals of Work Exposures and Health* 2022). Using the JEMs, a range of exposure estimates for each chemical can be evaluated such as average daily exposure or cumulative maximum daily exposures across days worked (Table 6). The development of the ordinal metrics has been described (Stewart et al., *J Exp Science Environ Epid* 2018). A monograph describing the development of the continuous exposure estimates and the Job Exposure matrices is published in the *Annals of Work Exposures and Health*.

Table 6. Exposure Characteristics of Oil Spill Response and Clean-up Workers

Exposure measure	Full Cohort N=24,736 %	Home Visit N=8,912 %
Number of Jobs/Tasks		
1	19.4	9.9
2-5	25.4	19.2
6-10	23.6	27.2
≥11	31.5	43.7
Duration of Work		
≤ 14 Days	4.5	3.6
15-180 Days	61.6	58.2
More than 180 Days	33.9	38.2
Work Timing		
Only Before Capping	14.3	12.4
Only After Capping	14.1	12.2
Before and After Capping	71.6	75.5
Still Working at Time of Interview	2.6	2.7
Cumulative Daily Maximum THC (ppm-days)		
0.01-11.852	25.0	18.0
11.854-49.332	25.0	26.2
49.339-131.014	25.0	26.4
131.02-1243.761	25.0	29.4
Hierarchical Job Class[^]		
Response	10.1	10.9
Support of Operations	24.6	30.7
Clean-up on Water	25.5	22.0
Decontamination	11.6	14.0
Clean-up on Land	12.1	14.5
Administrative Support	16.1	7.9
Potentially Exposed to Burning/Flaring (IH classification)		
Yes	9.7	9.2
No	88.3	88.9
Unknown	2.0	1.9

[^] based on likely exposure to THC from highest (Response) to lowest (Administrative Support)

Workers Only

	Full Cohort (N=2,124)	Home Visit (N=842)
Modeled PM_{2.5} 12HR MAX		
Offshore in situ (10 ug/m)	2.5	1.7
Hotzone/Source (29 ug/m)	82.2	85.2
Hotzone (97 ug/m)	15.3	13.2

Cohort Follow-up

Two cohort-wide follow-up interviews (except for Vietnamese-only-speaking participants) have been conducted to date. Contact information has been updated annually since 2013, usually in connection with newsletter mailings. Additional follow-up activities include a longitudinal assessment of mental health, a comprehensive clinical exam conducted in conjunction with the first follow-up interview, validation of self-reported health conditions, and linkage to the National Death Index (NDI) and state cancer registries.

First Follow-up Interview

The first follow-up telephone interview was conducted between May 2013 and May 2016, targeting the entire cohort, except for the 999 participants who spoke only Vietnamese. A total of **21,443 participants completed the first follow-up** (90% of those contacted; 68% of those eligible). Of these, 2,115 completed an abbreviated interview offered to those who refused the longer interview. Efforts to maximize participation included various mailings, extensive calling, use of commercial tracing services to update contact information, refusal conversion strategies, gift card drawings, door-to-door canvassing with in-person interviewing, and offering the survey through additional modes (i.e., mail, web, or telephone).

Mental Health Trajectories

With support from the Substance Abuse and Mental Health Services Administration (SAMHSA), a subset of participants completed longitudinal telephone assessments of mental health status and service use. The first assessment was conducted in conjunction with the first follow-up interview in 2013, with additional assessments conducted approximately 6, 12, and 24 months thereafter. The mental health sample was limited to those who participated in both the home visit and first follow-up survey and included participants with signs of potential mental health distress at the time of the home visit and a sample of those without any apparent distress. Of 4,370 a priori selected participants, 2,859 (65%) completed the first supplemental mental health interview. A total of **1,059 participants completed all four mental health interviews by August 2016**.

Clinical Exam

A subgroup of 5,510 participants who completed the home visit and the first follow-up telephone interview and lived within ~ 60 miles of clinics in Mobile, Alabama, or New Orleans, Louisiana, were invited to complete a comprehensive clinical exam. Clinical collaborators from the University of South Alabama (USA) in Mobile and Louisiana State University (LSU) in New Orleans carried out the standardized study exams. While many of the same measures from the Home Visit were repeated, participants underwent more comprehensive lung function testing, completed a battery of computer-assisted behavioral and physiological tests to assess neurological function and provided additional biological samples (**Table 7**). Neurobehavioral testing protocols were developed and overseen by Drs. Frederick Gerr and Diane Rohlman from the University of Iowa. A subset of participants from the Alabama site were asked to provide repeat saliva samples (collected at home after training in the clinic) for evaluation of changes in stress-hormone response over the course of two days. Participants also completed a comprehensive clinical mental health assessment, including a self-administered module to assess substance abuse. The exams began in August 2014 and concluded in June 2016. **Overall, 3,401 of eligible participants (62%) completed the exam.**

Second Follow-up Interview

The second cohort-wide follow-up interview began in late November 2017 and ended June 2021. Based on response rates from a pilot study of 1000 participants and recommendations from the

study's Scientific Advisory Board, efforts (and resources) to obtain a completed follow-up interview were primarily targeted to those who completed the first follow-up interview. Those who had not but had either provided biological specimens at the home visit or had higher OSRC exposures were also targeted for more aggressive follow-up (i.e. could be most informative in future analyses). Efforts to reach the remainder were less extensive, involving mailings and email or text outreach alone. Overall, 46% of the non-responders to the first follow-up interview completed the second follow-up, with the majority being from the group specifically targeted. Participation among responders to the first follow-up was higher, as expected (61%). The second follow-up interview covered most topics addressed in the first follow-up and added questions on reproductive health and sleep habits. Participants had the option to complete the second follow-up questionnaire online or by telephone. To further increase participation, we offered an abbreviated version of the questionnaire starting in late 2019. Demographic characteristics of the study population at each of the main study events were similar (not shown).

Validation of Self-reported Health Conditions

We attempted to validate self-report of selected health conditions through requests for medical records. First efforts focused on cancer, myocardial infarction and stroke. Of the 1,197 cases of interest, we have thus far collected medical record releases for 40%, with provider records obtained for 87% of these. Many of the cases of interest (72%) had reported incident disease at the time of enrollment or follow-up 1, and some had died, become too sick to continue participating, or were lost to follow-up. Consent for medical records was better for participants who were prospectively asked to provide releases (54% vs. 34%).

Mortality Surveillance

We have been following participants through linkage with the National Death Index (NDI) since a first linkage in 2016 (which provided data through 2014). We currently have data on deaths through December 2022. Linkage to the NDI identified N= 2,218 (7.2%) GuLF Study participants who had died during 12 years of follow-up. We plan to continue these requests on bi-yearly basis.

Cancer Linkage

Late in 2017 we began communicating with cancer registries for the purpose of identifying cancer diagnoses among cohort members. We directly contacted registries in the 5 Gulf States in which 80% of our cohort participants reside. We also have submitted requests to additional states via the Virtual Pooled Registry-Cancer Linkage System (VPR-CLS) which is intended to streamline the process for cancer linkage studies. We currently have data from a total of 11 states and have been in contact with another 18 states to conduct linkages via the VPR. The VPR states we have contacted will account for 95.6% of the cohort. We are not pursuing linkage in 25 states due to low numbers of participants in these states or because the state doesn't participate in the VPR or imposes restrictions on data sharing. We plan to use the data for validation of self-reports (to the extent there are overlapping timeframes for questionnaire and registry data) and as an independent ongoing source of cancer incidence data, especially for those lost to follow-up.

Biomarker Studies

Kidney and Liver Injury Biomarkers: In 2018, a small pilot study (N=72) of biomarkers of very early kidney and liver injury showed that all but two markers of interest could be detected, with most measures above the limits of detection (LOD) in all pilot subjects, with an appreciable range in the measurements for each marker. Although few differences were seen between those with high and low exposure to THC, the study was small, and comparisons may have been confounded by factors such

as obesity or other baseline health characteristics that were not accounted for in the design. We completed a larger study (N=924) in May 2019 and are currently analyzing results. A second small study of biomarkers for chemically induced liver injury was completed in collaboration with Matt Cave from the University of Louisville School of Medicine (*Werder et al., 2020*).

Table 7. Clinical Exam Components and Completion (N=3,401)

Exam Component	% complete
Biological Specimens	
Hair	61.3
Toenail	85.1
Urine	99.3
Saliva ¹	99.3
Blood	98.5
Hemoglobin A1c and Lipid Panel	99.6
Peripheral Nerve Tests	
Visual Acuity	99.5
Visual Contrast Sensitivity	99.4
Single leg Stance	97.4
Long Distance Corridor Walk (400m)	93.0
Trail Making Test	99.8
Handgrip Strength	99.2
Vibrotactile Threshold	97.5
Postural Stability	98.8
Neurobehavioral Tests	
Finger Tapping	99.8
Symbol-Digit	95.3
Simple Reaction Time	95.3
Digit Span	95.1
Match-to-Sample	95.0
Continuous Performance	98.9
Progressive Ratio	98.8
Lung Function	
Exhaled Nitric Oxide	98.5
Pulmonary Function Test	98.4

Epigenome-wide DNA Methylation and Genetics: In 2019, we measured DNA methylation at 863,904 CpGs using a high-density microarray (Illumina Infinium MethylationEPIC Beadchip; Illumina, Inc) to evaluate OSRC exposures in relation to epigenetic effects (n=1547). We selected individuals from a biomarker sampling pool intended to maximize overlap of participants with multiple biological measurements and prioritize participants with samples at two time points (home and clinic visits). Participants were selected for the pool if they were 1) male (too few

participants were female for stand-alone analyses), 2) 21 to 65 years old, 3) participated in oil spill cleanup efforts, 4) had a urine or serum sample collected at the home visit meeting quality control standards (N=6,323). We selected a weighted sample of non-Hispanic Black and White participants with varying levels of oil-related exposures (to ensure sufficient sample sizes across exposure levels) who also contributed biological samples at a subsequent clinic visit (N=1,206) and augmented the sample with an additional 200 never-smokers and 141 opioid users for a total of 1,547 participants. Participants were genotyped using the Global Screening Array (Illumina, Inc) to support studies of gene by environment interactions and to control for possible ancestry-related confounding in other genomic work. As part of this project, we collaborated with researchers at RTI to identify DNA methylation signatures related to marijuana use (Fang et al., *Molec Psy* 2024) and plan to study epigenetic changes associated with reduced pulmonary function.

Proteomics: In mid- 2025 we received assay results on peripheral blood-based proteomic profiles comprising 11,000 proteins measured via the SomaLogic SomaScan Assay at the CHI Lab at NIAID. N=1,215 participants were selected from the pool 1,392 males previously selected for genome- and epigenome-wide studies and evaluation of biomarkers of liver, kidney, and metabolic function to maximize biomarker overlap. Participants were also selected to have a range of environmental and sociodemographic characteristics. Planned analyses include assessment of proteomic signatures related to natural hazards, extreme heat, and neighborhood deprivation. We will also explore OSRC work related exposures in relation to protein patterns in peripheral blood.

Hemoglobin A1C and related biomarkers: In early 2021, we sent 3,228 packed cell samples and 3,216 plasma samples to The University of Minnesota to obtain measurements of hemoglobin A1C and related biomarkers (insulin, glucose, C-reactive protein, creatinine, and lipids) for studies of diabetes and other metabolic outcomes.

Study Funding and Oversight

GuLF Study enrollment and early follow-up was funded by the NIH Common Fund, the NIEHS Office of the Director, and the NIEHS Intramural Research Program (now the sole funder). An Interagency Agreement with SAMHSA supported enhanced mental health data collection. While in development, the study received review and oversight from the NIH OD, the Institute of Medicine, and multiple Federal agencies. DLH, LLC provides support for study management, operations, data collection and analysis activities through a contract with NIEHS. Through 2019, scientific oversight was provided by a Scientific Advisory Board. Advisory board members included internationally recognized scientists and representatives from the affected community. A Community Advisory Group with representation from local community groups and OSRC workers and an Exposure Assessment Working Group also met regularly.

Data Sharing and Collaboration

Collaborative research using GuLF Study data and samples is encouraged. Procedures for requesting data or proposing new research can be found on the study website – <https://gulfstudy.nih.gov/en/index.html>.

GuLF Study Collaborators

NIH Collaborators

Linda Birnbaum	Office of the Director, retired
Aaron Blair	National Cancer Institute, retired
Chandra Jackson	Epidemiology Branch, NIEHS
Lenore Launer	Laboratory of Epidemiology and Public Health, NIA
Stephanie London	Epidemiology Branch, NIEHS
Aubrey Miller	Office of the Director, NIEHS
Jack Taylor	Epidemiology Branch, NIEHS
Shanshan Zhao	Biostatistics and Computational Biology Branch, NIEHS

Outside Collaborators

Susan Arnold	University of Minnesota
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Patricia Stewart	Stewart Exposure Assessments, LLC
Anna Strasma	Duke University, Duke Department of Medicine
David Welsh	Louisiana State University Health Sciences Center
Casey Zuzak	FEMA

NIEHS Fellows

Dazhe Chen	Postdoctoral Fellow, Epidemiology Branch
Hanna Jardel	Pre- and Postdoctoral Fellow, Epidemiology Branch
Kaitlyn Lawrence	Pre and Postdoctoral Fellow, Epidemiology Branch, now Senior Epidemiologist DLH, LLC
Opal Patel	Predocotrual Fellow, Epidemiology Branch
Emily Werder	Postdoctoral Fellow, Epidemiology Branch, now Assistant Professor, Department of Radiology, University of North Carolina Medical School

Other Students and Trainees

Kieran Aguirre	Summer Intern and Master Student, Emory University, Rollins School of Public Health
Cailey Cranny	Summer Intern, Tulane University School of Public Health and Tropical Medicine

Geihae Choi	Doctoral Student, University of North Carolina, now Assistant Professor, Johns Hopkins University
Kristen Cowan	Doctoral Student, University of North Carolina
Xinlei Deng	Postdoctoral Fellow, now Principal Biostatistician, Novartis Pharmaceutical
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Caroline Groth	Doctoral Student, University of Minnesota, now Assistant Professor, West Virginia University
Michael Hu	NIEHS Medical Fellow, University of Miami, now Intern, University of Chicago, IL
Tran Huynh	University of Minnesota (Doctoral Student), now Assistant Professor, Drexel University
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Faye Koenigsmark	Postdoctoral Fellow, University of North Carolina
Joyce Lin	Doctoral Student, Johns Hopkins University, now Post-doctoral fellow, Harvard University
Craig McGowan	Summer Intern, University of North Carolina (Masters Student), now Data Scientist, ZeniMax Media, Washington, DC
Rachel Nethery	Summer Intern, Univ. of North Carolina (Doctoral Student), now Assistant Professor of Biostatistics, Harvard University
Sam Neally	Summer Intern, University of North Carolina
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Rebecca Noga	Doctoral Student, University of North Carolina
Opal Patel	Doctoral Student, University of North Carolina
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Arbor Quist	Doctoral Student, University of North Carolina, now Assistant Professor, Ohio State University
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Kyle Roell	Doctoral Student, University of North Carolina
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Jake Thistle	Doctoral Student, University of North Carolina
Jing Xu	Visiting Student, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, now Assistant Professor, Peking Union Medical College, China
Xian Zhang	Summer Intern, Univ. of California, Irvine (Doctoral Student), now Research Associate, Univ. of North Carolina Division of Gastroenterology and Hepatology

Completed Doctoral Dissertations

- Dazhe Chen, University of North Carolina at Chapel Hill (2020-2023). Exposure to Crude Oil Chemicals and Burning-Related PM_{2.5} among Deepwater Horizon Oil Spill Workers and Incident Coronary Heart Disease.
- Kaitlyn Gam, Tulane University (2015-2018). Pulmonary function in oil spill clean-up workers: Impact of exposure to oil spill chemicals and community level point source VOC exposures.
- Caroline Groth, University of Minnesota (2013-2017). Bayesian Models for Analysis of Airborne Chemical Exposure During the *Deepwater Horizon* Oil Spill Response and Cleanup
- Tran Huynh, University of Minnesota (2009-2014). An assessment of occupational inhalation exposures to volatile oil components on four rig vessels for the GuLF Study.
- Hanna Jardel, University of North Carolina at Chapel Hill (2018-2024). Occupational exposure to volatile organic compounds and glycemic dysregulation among oil-spill cleanup workers.

- Rachel Nethery, University of North Carolina at Chapel Hill (2013-2018). Special Topics in Latent Variable Models with Spatially and Temporally Correlated Latent Variables.
- Opal Patel, University of North Carolina at Chapel Hill (2019-2024). Association of volatile hydrocarbons with hypertension and other CVD-related biomarkers among Gulf Long-term Follow-up Study participants.
- Tyler Prussiz, Louisiana State University (2021-2024). The Impact of Air and Oil Spill Pollution on Health in the Gulf South.
- Harrison Quick, University of Minnesota (2010-2013). Exploration of the use of Bayesian modeling of gradients for censored spatiotemporal data from the *Deepwater Horizon* oil spill.
- Jean Strelitz, University of North Carolina at Chapel Hill (2014-2018). BTEX, PAH and PM2.5 exposure during oil spill clean-up work and incident cardiovascular disease in the GuLF Study.
- Emily Werder, University of North Carolina at Chapel Hill (2014-2018). Ambient and personal styrene exposure and adverse neurobehavioral outcomes in the GuLF Study.

Doctoral Dissertations in Progress:

- Rashida Callender, Johns Hopkins Bloomberg School of Public Health (2025-date). Evaluation of community and individual resilience and their associations with mental health outcomes after disasters in the Gulf Long-term Follow-up (GuLF) Study.

GuLF Study Publications (Oct 2021 to Oct 2025)

2025

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Jardel HV, Keil AP, Martin CL, Richardson DB, Stenzel MR, Stewart PA, **Sandler DP***, Engel LS* (co-senior authors). Prospective study of oil spill cleanup-related exposure to volatile organic compounds and glycemic dysregulation. In press, *Environmental Health* 2025.

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