Heat-related changes in cognitive performance

Information Collection Request for Office of Management and Budget (OMB) Review and Approval

Part B

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B. Collections of Information Employing Statistical Methods

1. Respondent Universe and Sampling Method

We are recruiting from 3 populations of workers: miners, construction workers, and structural/wildland firefighters. According to analyses using the National Health Interview Survey 2007-2017, current mine workers are 43.9 years of age on average and are predominantly male (91.6%) and non-Hispanic White (87.4%), while current construction workers are 41.5 years of age on average and are predominantly male (90.9%) and non-Hispanic White (65.4%). Preliminary findings from a NIOSH Western States Division cohort study on wildland firefighters found that firefighters were 29 years of age on average and predominantly male (93%); ninety-two percent of the study participants identified as White and 11% indicated they were Hispanic.

Population to be recruited

Field Study

Project staff will recruit 59 underground and surface miners of any health status, race/ethnicity, or sex. All participants will be at least 18 years of age. The majority of miners will work in areas identified as being at increased risk for heat stress. Some participants, however, may work in areas without evidence of heat stress (e.g., in a cab or supervisory position). Because this component is observational and participants will be doing their normal work tasks during their normal shifts, no restrictions regarding age or health status are needed. Participants in the field component of the study will also be eligible to participate in the environmental chamber component.

Environmental Chamber

Project staff will recruit local underground and surface miners, construction workers, and structural and wildland firefighters who are aged 18–54 years. This age group is likely to be able to meet the inclusion criteria (i.e., American College of Cardiology/American Heart Association cardiovascular risk score <10%) but includes middle-aged participants that are older than participants in many previous environmental chamber studies. Including an older age group is important because the average age of miners is higher than many other industries, and miners are an aging workforce (NIOSH, 2012; NCHS, 2007–2017). To improve generalizability, including middle-aged workers is important. A total of 30 workers will be recruited, allowing for 15% drop-out. The reason for including non-miners is to increase the sample size, because most nearby mines are approximately 1 ½ hours from Spokane, making it logistically challenging to include a sufficient number of miners. Construction workers and firefighters are exposed to heat stress and therefore would not only increase the sample size but would receive benefit from the study by gaining a better understanding of their physiologic and cognitive responses to heat exposure. Furthermore, NIOSH has specific research programs focused on these occupations.

Recruitment Plan

Field Study

Project staff will identify both surface and underground mines that have vocalized having issues with heat stress and also hold an interest in voluntarily collaborating with NIOSH on the study. Investigators will attend state mining association meetings, reach out to contacts in trade, labor, and state mining organizations, and use current mining contacts to identify mines that might be interested in working

with NIOSH on this study. Investigators will contact mine management to discuss the study and enlist their support. NIOSH team members will work with the health and safety officer of mines expressing interest in the study to identify the best ways to recruit miners. Posters and postcards will be provided to these mines.

NIOSH staff will discuss the project during group meetings (such as regularly scheduled safety meetings) to explain the purpose of the study and recruit participants. Investigators will attend these meetings to ensure that all possible miners who might be interested in participating will be able to hear the presentation and have the opportunity to ask questions. Additionally, investigators will set up smaller individual (including phone calls) or group meetings specifically to answer study questions, as requested by miners or mines. Health and safety officers at these mines will assist with identifying work positions/roles that have a higher degree of exposure to heat stress, and, of the workers that engage in such positions/roles, who might have an interest and/or willingness to participate in the study. A recruitment script (Appendix J) is included to assist NIOSH staff in discussing the study with potential participants.

Environmental Chamber

To recruit miners, investigators will contact mine management of local mines and the local mine rescue team to explain the purpose of the study and enlist their support in identifying potential participants. We will use emails and phone calls to reach out initially. NIOSH investigators will attend miner trainings and meetings at each of the mine sites to explain the purpose of the study and identify potential participants. We will supply recruitment posters to place in mine sites and will hand out postcards describing the study to interested miners. We will also contact local unions to enlist their support, attending meetings to identify interested participants. Posters and postcards will also be delivered to union offices. The posters and postcards will have contact information, and if contacted, we will set up smaller individual (including phone calls) or group meetings specifically to answer study questions and perform recruitment. A recruitment script will be followed to assist NIOSH staff in discussing the study with potential participants. At the end of the recruitment script is a list of health conditions and symptoms that are exclusion criteria. This list will be printed out and given to potential participants for review during recruitment.

To recruit construction workers, NIOSH investigators will identify local construction companies and unions and meet with company and union management to enlist support. Emails will also be used. After interested companies and unions have been identified, we will work with management to identify the best ways to contact workers. We will provide posters and postcards for worksites and will attend meetings with construction workers for recruitment. We will use the same recruitment script as that used for miners.

To recruit firefighters, we will contact local firehouses and set up meetings at the firehouses to discuss the study with firefighters, providing posters and postcards for worksites. For wildland firefighters, we will work with U.S. Forest Service (USFS) management, who will contact local USFS offices to introduce us. We will meet with firefighters at individual offices for recruitment, providing posters and postcards.

Given the amount of time required to participate (i.e., half day on visit 1 and the majority of the day on visits 2 and 3), the demands placed on participants (i.e., performing work in a hot environmental chamber), the distance that participants must travel, and the fact that participants will complete study activities while they are off duty, all participants will be compensated for participation $35/hour and

$0.545 per mile. Compensation is necessary to obtain the needed participation for this study. Compensation time will commence upon arrival to the NIOSH facility and end when participants leave the facility (i.e., participants will be reimbursed for mileage but not travel time). For participants who do not complete the study's full three days, reimbursement will be prorated for the amount of time spent in the study. Reimbursement will be made by check at the completion of the study.

All potential participants will be required to undergo a pre-participation health screening to determine eligibility. Health screening will take place after informed consent is obtained. A recruitment script (Appendix K) is included to assist NIOSH staff in discussing the study with potential participants.

Sampling Method

Convenience sampling methods will be used for both the field and environmental chamber studies. Convenience sampling will occur based on the mines, miners, firefighters, and construction workers available to participate at the point in time when the field and environmental chamber studies are conducted. For the field study, purposive sampling will be used to target miners who work in the known hot areas of a mine or who perform tasks known to increase exposure to heat. There are no restrictions, however, as to who can participate in the field study.

2. Procedures for the Collection of Information

There are two components to this data collection, a field study and an environmental chamber study. In the following section, we describe the research procedure for each component, explain sample size calculations, and provide an analysis plan.

Field Study Procedure

The field study component of the project is designed to investigate the relationship between the physiologic and environmental measurements of heat strain and cognitive performance in U.S. surface and underground miners. The study will comprise 59 miners performing their normal work activities on two different shifts. Heart rate and core body temperature will be continuously monitored. These physiological measurements will be measured and recorded using a wearable real-time monitoring device. A smart phone application has been designed by NIOSH to work in conjunction with the device to alert participants to take a brief 6-minute assessment when core body temperature reaches a designated threshold. The application was designed by a development team within the Pittsburgh Mining Research Division's Health Communication, Surveillance, and Research Support Branch to improve the efficiency of data collection without requiring the presence of NIOSH investigators or mine health and safety officers to collect the data directly. Environmental measurements will be taken using commercially available environmental data loggers. Using this technology, NIOSH investigators will not need to travel to operational/active areas of the mine sites. For this study, only equipment set-up and decommissioning will be needed at the beginning and end of each shift. Once their core body temperatures reach the designated threshold, participants will be prompted to answer a few brief questions and take a cognitive test. A 5-minute Psychomotor Vigilance Test (PVT) will be administered by the smart phone application to assess vigilance, which is the ability to maintain attention over time. The PVT involves the presentation of a stimulus (e.g., a bullseye shown on the screen) at random intervals of 2–10 seconds. Participants are instructed to respond to the stimulus by tapping the smart

phone screen as quickly as possible. Participants will be instructed to take the assessment as soon as they can safely do so after hearing the alert.

Visit 1

On the first day of the study, NIOSH staff will orient participants to the study, obtain consent (Appendix L), obtain baseline health information, and measure height, weight, and body fat percentage. The staging area for study participants will occur in a private area on the mine site that will be used by participants to prepare for the testing pre-shift and to remove monitors and other testing devices post-shift. Each identified participant will self-administer a tablet-based questionnaire (Appendix C) using ITSO/ISSO Level 2-approved FedRAMP-certified software titled Epi Info Secure Web Survey system (EISWS). If they prefer, paper-based questionnaires will also be available. Electronic data are stored on the Epi Info Secure Web Survey server. The questionnaire includes information on demographics, comorbidities, medication use, history of heat illness, physical fitness, and mental health; responses to these questions will provide information on risk factors for heat strain and confounders of decreased work performance. The questions on medications and comorbidities such as heart disease, diabetes, neurologic disease, and skin disease will be used to assess risk factors for heat illness or cognitive decline. The questions also include information on kidney disease, which can result from excessive heat exposure, and respiratory disease, which can affect heart rate and thus the interpretation of data. NIOSH staff will be available to assist miners with completing the questionnaire, if necessary. Height and weight will be measured by using a stadiometer and digital scale. Body fat percentage will be measured by using bioelectrical impedance analysis (BEI). The stadiometer, digital scale, and BEI will be calibrated according to manufacturers' specifications. During the initial orientation, the cognitive test (PVT) will be explained and participants will be trained on how to perform the task. Additionally, study participants will be introduced to all equipment used for data collection and given instructional training on how to operate the smart phone device for the purposes of the study.

Visits 2 and 3

Each participating miner will be tested during his or her shift at their work area during two shifts. Testing will be performed on days designated by mine management and miners so as to minimally disrupt mining operations; therefore, shifts in which testing will occur may or may not be consecutive for each participant.

Prior to starting his or her shift, each miner will provide a urine sample that will be tested for specific gravity, an indicator of hydration, and promptly discarded. All urine samples obtained during the study will be discarded and will not be used for anything other than urine specific gravity. Results will be recorded on a tracking form. NIOSH investigators will equip each participant with a Samsung Galaxy 8+ smart phone and bio-harness containing a data recorder for measuring heart rate and core body temperature. The smart phone will be carried using a strap on the arm or will be placed in a pocket. To minimize variability in test results from the use of different phones, each Samsung Galaxy phone will be specifically assigned to a participant to ensure that participants use the same phone during both study shifts. The investigator will input the participant's unique ID and mine site number into the smart phone application before it is given to each participant, and thus personally identifiable information will not be collected. The participants will ingest a temperature capsule as soon as they arrive to work. To ensure that participants are able to safely ingest the capsule, they will answer questions regarding swallowing difficulties in the health questionnaire administered at the beginning of the study (Appendix C). The

principal investigator is a medical officer and will review the answers to this questionnaire to exclude subjects from ingesting the temperature capsules if they report problems with swallowing or GI motility.

After donning the personal monitoring equipment, participants will be given instruments that measure environmental conditions such as air temperature and relative humidity. These instruments will be attached to their person (i.e., strapped to their hard hat or hooked to their zipper). A NIOSH team member will monitor start and stop times of the instruments.

Participants will then proceed to their work stations and begin their normal work tasks. The ingested temperature capsule and chest strap will measure core body temperature and heart rate at approximately 15 second intervals throughout the entire shift. All cognitive and questionnaire data during the underground shift will be collected by the smart phone application. The smart phone application (Appendix D) will be set to collect data twice during participants' shifts. The smart phone will be securely fastened to the person of each participant (i.e., via chest strap, arm band, or in a closed pocket) and will alert the participant to complete data collection using a combination of sounds and vibration. The participants will be provided with noise reducing ear plugs (which include ANSI-certified Noise Reduction Rating of 27 dB for miners who need double hearing protection) that will transmit the alert from the phone to the participant's ears. Additionally, the phone will vibrate to provide an additional alert mechanism. The smart phone application has been developed to communicate with the temperature capsule readings collected by the data recorder. The first alert will be set to sound directly after the miner begins work so that the assessment will be taken at normal core body temperature, and the second alert will occur when their temperature reaches 38 °C (100.4 °F). After each alert, participants will be instructed to stop work as soon as possible and begin the assessment by tapping on the 'Begin Day' button in the smart phone application (Appendix D). The application will lead them through a series of questions regarding fatigue, recent work tasks, and perceived exertion of each task (Appendix D). To minimize time requirements, the work task-related question will provide a dropdown list adapted from each participant's usual work tasks. Investigators will have the flexibility to modify each participant's task list based on tasks that he or she normally completes during the shift. These tasks will be added to the application by the investigators after asking the participant about their usual work tasks.

After the questions have been completed, the application will administer the cognitive test (5-minute PVT). After the cognitive test has been completed, participants will return to their work tasks. Once a temperature threshold has been reached once, the application will not signal the participant to repeat the assessment if that temperature threshold is reached later in the shift. The total expected time for each of the two assessments is approximately six minutes (i.e., one minute for the questions, five minutes for the cognitive test).

At the end of the shift, the application will signal the participants to take a post-shift questionnaire (Appendix E). An alert will be scheduled at the end of shift as a reminder. To minimize schedule disruptions during the shift, each miner will be instructed to take the post-shift questionnaire directly after their shift ends. Underground miners can take the post-shift questionnaire while waiting for the hoist to return aboveground at shift's end. The post-shift questionnaire will provide information on factors relevant to heat strain that vary over time: alcohol consumption over the past 24 hours, acute illness, medication use, sleep amount and quality during the night prior to testing, and number and type of shifts worked during the current shift rotation. At the end of each shift, participants will provide

another urine sample for specific gravity measurement, and NIOSH investigators will collect the smart phone, bio-harness and data recorder, and environmental temperature monitor. Data will then be immediately extracted and transmitted from the devices to an encrypted CDC hard drive using offline USB data transfer on a password protected CDC issued computer. Recorded notes will be maintained in locked file cabinets in a secure NIOSH building.

Environmental Chamber Study Procedure

The laboratory study component of the project, performed within an environmental chamber, is designed to investigate the relationship between physiologic and environmental measurements of heat strain and cognitive performance within highly controlled environmental conditions. Testing will occur on three days for each participant. The study will comprise 30 workers aged 18–54 years performing moderate physical activity in a heated environmental chamber. Moderate physical activity is defined by ACSM as metabolic equivalents (METs) of 4.8–7.1 and 4.0–5.9 for persons 20–39 and 40–64 years of age, respectively (ACSM, 2016). Participants will perform a combination of resistance and aerobic exercises to simulate moderate exertion activities that are performed during a typical work shift. To ensure that participants can safely complete the exercise protocol, a brief physical examination (i.e., heart and lung exam, Appendix F) and health screening questionnaire (Appendix G) will be used to collect data on current health conditions and symptoms, in addition to demographics, health history, history of heat illness, physical activity history, and work characteristics. The health history form is similar to the form used for participant screening in the field component of the study, with the addition of questions to establish inclusion and exclusion criteria. The medical history form was modified from the health screening form that was used for a pilot heat stress study. Included in the questionnaire are questions based on the recommended health screening algorithm by the American College of Sports Medicine (ACSM), which has the following priorities (ACSM, 2016):

- Determine current physical activity levels
- Identify persons with symptoms consistent with underlying cardiovascular, metabolic, and kidney disease
- Identify persons with diagnosed cardiovascular disease (CVD) and metabolic disease

Because ACSM recommends that asymptomatic, healthy persons who do not regularly participate in exercise can proceed directly to light or moderate exercise, participants will exercise to the moderate range (ACSM, 2016). Participants who regularly participate in exercise can proceed directly to vigorous exercise without further evaluation (ACSM, 2016). The exercise protocol will target a moderate metabolic work intensity not to exceed a heart rate of 76% of age-adjusted maximal heart rate by greater than 10%. Maximal heart rate will be estimated using the equation 208 – (0.7 x age) (ACSM, 2016).

The exercise protocol comprises one-minute alternating cycles of resistance and aerobic exercises for a total of 20 minutes. The resistance cycle consists of weighted squats to simulate the frequent lifting performed by mine workers. Prior to the exercise cycles, participants will be tutored on proper form for the squats. They will squat to pick up 10-pound weights in each hand, stand fully erect while holding the weights, and then will replace the weights on the ground or on a raised surface (for those who cannot reach the ground using proper squat techniques during tutoring). Investigators will prompt them to complete one squat every 5 seconds, for a total of 10 squats in 50 seconds. At the end of this round, they will have 10 seconds to transition to the aerobic exercise component. During minute two (i.e.,

aerobic exercise component), they will hold 5-pound weights in each hand and step up and back down on a low step (8 inches high). They will complete the step-ups for 50 seconds at a pace of approximately one step-up and step-down per four seconds and then will have 10 seconds to transition back to the squats.

During testing in the environmental chamber, heart rate and core body temperature will be continuously monitored. When participants' core body temperatures reach the designated thresholds, participants will take two computer-based cognitive tests (PVT and N-back) that evaluate different aspects of cognitive functioning (i.e., vigilant attention, reaction time, and working memory).

Participants will be randomly assigned to one of two groups. During visits two and three, each group will perform two rounds of exercise followed by cognitive tests. The only difference between groups will be the order of testing. Group one will take the cognitive tests when their core body temperatures reach a threshold of 38 ℃ in round one and when core body temperatures reach 38.5 ℃ in round two. Group two will take the cognitive tests in the opposite order, when their core body temperatures reach a threshold of 38.5 ℃ in round one and when core body temperatures reach 38 ℃ in round two (see table).

	Visit 2		Visit 3	
	Round 1	Round 2	Round 1	Round 2
Group 1	Cognitive tests when CBT reaches 38 °C	Cognitive tests when CBT reaches 38.5 °C	Cognitive tests when CBT reaches 38 °C	Cognitive tests when CBT reaches 38.5 °C
Group 2	Cognitive tests when CBT reaches 38.5 °C	Cognitive tests when CBT reaches 38 °C	Cognitive tests when CBT reaches 38.5 °C	Cognitive tests when CBT reaches 38 °C

These temperature thresholds were chosen because national and international organizations recommend that temperatures not exceed 38 ℃, in general, but it is unclear if there is a specific temperature threshold above this threshold where cognitive dysfunction begins to occur. The WHO has noted that core temperatures of 39 ℃ under controlled conditions may be acceptable.

Visit 1

Informed consent (Appendix M) will be obtained during the first visit. After the consent form has been reviewed, discussed, and signed, medical screening will be performed.

Medical screening

Participants will complete the health screening form (Appendix G) on a tablet (i.e., Epi Info Secure Web Survey software) or if they prefer, on paper. The medical officer will review all health screening forms, identify any responses that need further clarification, and discuss these clarifications with the potential participant. If participants answer in the affirmative to any exclusionary condition, the medical officer will explain to them that these conditions increase the risk for cardiovascular, heat, or musculoskeletal complications from the study and that we cannot allow them to participate for their safety. The medical officer will also request that they follow-up with their health provider to ensure that the conditions are properly evaluated and treated. The health screening will be performed one-on-one with participants.

Once the medical officer/health professional has reviewed all health screening forms and excluded potential participants who do not meet health requirements for the study, he or she will perform a

physical examination that will include blood pressure at rest, heart rate, and heart/lung auscultation (Appendix F). Team members will also measure height and weight (clothed but with shoes off) and body fat percentage. The physical examination will be performed separately to ensure privacy. Blood pressure will be measured after participants have been sitting quietly for five minutes, using either an automated blood pressure device or manual device with appropriate arm cuff sizes.

Most participants will be directly excluded or included by the medical officer based on the health questionnaire and physical examination, but some participants will require further screening for certain populations. For persons aged ≥40 years, point-of-care fingerstick cholesterol testing will be performed, and results will be entered into an ACC/AHA CVD risk stratification tool (ACC/AHA 2013), along with information from the health screening and physical examination. Only persons with a 10-year risk score of <10% will be able to participate. For persons with diabetes and pre-existing kidney disease, point-of-care testing for blood sugar, hemoglobin A1c, or kidney function and electrolytes, respectively, will be performed. Health screening results for all participants will be recorded on a form for NIOSH use only, but participants will also receive their results.

On occasion, the medical officer may request further information from potential participants' healthcare providers before determining if they can be included in the chamber study. These participants will forego the control exercise cycle on day 1 and will be rescheduled for the control cycle after health consultation has been completed. They will sign a release of information form (Appendix N) and provide the name and contact information of their health provider. After the release of information form has been received by the health provider, the medical officer will call the health provider to explain what the participant will be doing during the study and to request pertinent medical information.

Cognitive testing

After medical screening and risk stratification has taken place, eligible persons will undergo a brief tutorial for the two cognitive tests that will be used during the study. Each cognitive test will be explained and demonstrated to the participants, and each participant will practice each test at least once to ensure that they understand the test procedures before undergoing baseline testing. The tests will assess different aspects of cognitive performance, including vigilant attention and working memory. The 10-minute PVT (Lim and Dinges, 2008) will be administered by tablet to assess vigilant attention, which is the ability to maintain attention over time. The PVT involves the presentation of a stimulus (e.g., a bullseye shown on the screen) at random intervals of 2–10 seconds. Participants are instructed to respond to the stimulus by tapping the smart phone screen as quickly as possible. Reaction times for each stimulus will be automatically recorded by the computer for downloading to secure NIOSH servers at a later time. The N-Back cognitive test (Jaeggi et al., 2010) will also be administered by computer to assess working memory, reaction time, and vigilant attention. A sequence of letters is presented one at a time, and participants are instructed to press a button whenever a letter is shown that is the same as what was presented two letters ago.

Environmental chamber test – control

After cognitive testing is completed, participants who are not excluded and who do not need further health consultation will proceed directly to the environmental chamber for one cycle of testing at room temperature (i.e., control cycle). Participants will ingest a core body temperature pill directly after the health questionnaire in order to provide sufficient time (i.e., 2 hours) for the pill to exit the stomach. The

control cycle will comprise an exercise protocol in the environmental chamber at room temperature (70 °F, 40% relative humidity) directly followed by the cognitive tests.

Participants will alternate between squats with 10-pound weights in each hand and step-ups onto an 8-inch step with 5-pound weights in each hand. Each individual cycle (i.e., 50 seconds of one exercise followed by a 10-second transition to the other exercise) will alternate for 20 minutes total, and each of the exercise cycles (squats with weights, step ups with weights) will therefore be completed 10 times each (Table A).

Table A: 20-minute exercise round

Minute	Monitoring activity	Activity	METs
1		Squats with 10-lb weights	5.0
2	Ask about symptoms	Step-ups with 5-lb weights	5.0
3		Squats with 10-lb weights	5.0
4	Ask about symptoms	Step-ups with 5-lb weights	5.0
5	Ask about thermal sensation and exertion level	Squats with 10-lb weights	5.0
6	Ask about symptoms	Step-ups with 5-lb weights	5.0
7		Squats with 10-lb weights	5.0
8	Ask about symptoms	Step-ups with 5-lb weights	5.0
9		Squats with 10-lb weights	5.0
10	Ask about symptoms; ask about thermal sensation and exertion level	Step-ups with 5-lb weights	5.0
11		Squats with 10-lb weights	5.0
12	Ask about symptoms	Step-ups with 5-lb weights	5.0
13		Squats with 10-lb weights	5.0
14	Ask about symptoms	Step-ups with 5-lb weights	5.0
15	Ask about thermal sensation and exertion level	Squats with 10-lb weights	5.0
16	Ask about symptoms	Step-ups with 5-lb weights	5.0
17		Squats with 10-lb weights	5.0
18	Ask about symptoms	Step-ups with 5-lb weights	5.0
19		Squats with 10-lb weights	5.0
20	Ask about symptoms; ask about thermal sensation and exertion level	Step-ups with 5-lb weights	5.0

Core body temperature and heart rate will be monitored at all times during the test, and every two minutes participants will be asked whether they have any symptoms of heat strain, cardiovascular or respiratory strain (i.e., chest pain, shortness of breath, muscle pain or cramps, lightheadedness). Thermal sensation using a thermal sensation scale (Appendix N) (Young et al., 1987) and exertion level using ratings of perceived exertion (Appendix O) will be assessed every 5 minutes and will be recorded by NIOSH investigators.

At the end of the exercise protocol, participants will be seated and will undergo the cognitive tests. The Karolinska Sleepiness Scale (KSS; Åkerstedt and Gillberg, 1990), Positive and Negative Affect Schedule (PANAS; Watson et al., 1988), and fatigue rating will be taken prior to cognitive testing to measure the influence of sleepiness, affect, and fatigue on cognitive performance (Appendix H). The PVT will be administered first, with a duration of 10 minutes, followed by N-back, with a duration of approximately 45 seconds.

The following table (Table B) summarizes the environmental chamber visit 1 study process, with a total estimated time of 3–4 hours.

Table B: Environmental chamber visit 1 overview

Consent form reviewed, questions answered, and form signed.
Participant completes initial health screening form.
Medical officer/health professional reviews health screening form, clarifies responses, and excludes participants based on responses.
Participant ingests temperature pill to measure core body temperature and heart rate.
Medical officer performs physical examination: blood pressure, heart rate, heart/lung auscultation.
Height, weight, and body fat percentage measured
Persons aged ≥40 years only: medical officer or other team member measures cholesterol using point-of-care Cholestech LDX machine. CVD risk stratification using ACC/AHA calculator is performed for all participants ≥ 40 years; subjects with score ≥10% are excluded. Medical officer explains results to participants. Participants receive results of their cholesterol testing.
Persons with diabetes have fingerstick blood sugar and fingerstick Hemoglobin A1C measured. Persons with chronic kidney disease have fingerstick electrolytes and kidney function measured. Participants receive results.
Participants receive the results of their physical examination (blood pressure, height/weight, BMI), regardless of whether they are excluded or not.
For persons who meet inclusion criteria, cognitive tests are explained and practiced. Baseline testing for PVT and N-back are performed once each.
Persons for whom medical officer/health professional needs further information from healthcare provider: release of information form signed, and person is rescheduled to return for baseline cognitive testing and control exercise cycle (to be performed after medical officer has contacted participants' health provider).
Control exercise cycle in environmental chamber is performed.
Control cognitive testing is performed (KSS, PANAS, fatigue, PVT, N-back).
Schedule visit 2 with at least 2 week gap between visit 1 and visit 2

Visits 2 and 3

At least two weeks following visit 1, participants will return to the laboratory for visit 2. An additional two weeks after visit 2, participants will again return to the laboratory for visit 3. Visits 2 and 3 will follow the same procedures. The exercise protocol and cognitive tests will be the same as that of the control cycle except that testing will now take place in hot conditions (100 °F, 80% relative humidity). Two rounds of exercise testing and cognitive tests will occur each day. Cognitive tests will take place when core body temperatures reach specific thresholds.

Sample Size Determination

Our power calculation to determine the number of subjects needed in the current study is based on data from our pilot testing (unpublished). The data from 8 subjects include a control session and two hot chamber sessions, with each of the three sessions followed by a PVT. For the environmental chamber study, we base our expected effect size on the increase in PVT lapses from control to the second hot chamber session in the pilot test, which produced a medium effect size (Cohen's d) of 0.703. For analyses in the current environmental chamber study, we will make pairwise comparisons between the control and hot chamber conditions. As such, we must base our Type I error threshold on a correction for multiple (i.e., 3) comparisons, and therefore set α=0.017. Avoiding Type II error is important in this study as well, and therefore we set our statistical power requirement to 90%. We chose 90% for the chamber and 80% for the field study based on resources. To achieve 90% statistical power at a one-sided

Type I error threshold of 0.017, we will need a sample size of at least *n*=26 subjects, which we will round up to a total of *n*=30 subjects to account for approximately 15% attrition.

For the field study, we based our power calculation on the effect size from our pilot testing data with the increase in PVT lapses from control to the first hot chamber session (as there will only be one hot core body temperature measure per day in the field). This yielded a small effect size (Cohen's d) of 0.353. For the current field study, we set our Type I error threshold α=0.050. We maintain our statistical power requirement of 80% to avoid Type II error. It follows that, to achieve 80% statistical power at a one-sided Type I error threshold of 0.050, we will need a sample size of at least *n*=51 subjects, which we will round up to *n*=59 subjects to account for approximately 15% attrition (nQuery Advisor 4.0).

Holding all other variables constant (and excluding the attrition estimate), Table C shows the benefit of additional study participants for minimizing the chances of a type II error.

Table C. Sample size estimates for improving the likelihood of Type II error

	Sample Size Needed	
Type II error (β)	Environmental Chamber	Field
80%	21	51
85%	23	60
90%	26	71
95%	32	89

Analysis Plan

There are a number of measures and variables included in this data collection. The following table (Table D) provides a summary.

Table D. Variables and outcomes

Cognitive test	Outcome measure	Independent variable	Covariates
KSS	Subjective sleepiness score	Maximum core body temperature (CBT) (>38 vs >38.5 °C) ΔCBT (CBT start of exercise to CBT start of PVT) Rate of rise of CBT (ΔCBT per minute from start of exercise to start of PVT)	Age Sex Race/ethnicity BMI Chronic disease (diabetes, heart disease, kidney disease, other) Medication use (blood pressure, antihistamines, decongestants) History of heat illness Fitness level Acclimatization status
PANAS	Positive affect score		
	Negative affect score		
	Individual item ratings		
PVT	Mean reaction time (RT)		
	Number of		

	lapses (RT >500 ms)		PANAS, sleepiness scores Number of days between chamber tests Thermal sensation scale Urine specific gravity Wet bulb globe temperature or air temperature and humidity
N-back	Correct response (Y/N)		
	Mean RT		

We will perform a descriptive analysis of the mean reaction times (PVT/N-back); lapses of attention (PVT RTs >500 ms); number of correct N-back responses; maximum, rate of rise, and overall change in core body temperature; and each of the covariates listed in table L. We will fit a log-logistic time to event frailty model, which accounts for repeated measures, to evaluate the effect on mean reaction time of three separate independent variables: 1) maximum core body temperature, 2) overall change in core body temperature from start of exercise or shift to maximum temperature, and 3) rate of rise of core body temperature. We will repeat these models using number of lapses as the outcome measure. We will fit a generalized linear mixed model to evaluate the binary right/wrong outcome of each N-back response as a function of each of the three independent variables used in the previous model. We will also perform time series analyses to evaluate the time to reach certain temperatures. Potential confounding factors that will be evaluated in the models are included in the above table and include physiologic measures, personal factors, and environmental factors. Inclusion of some of the demographic variables will depend on the diversity of the sample population.

To assess patterns of heat strain among U.S. surface and underground miners, only physiologic data from the field will be used. We will use the same methodology described in Yeoman et al. (2019) to categorize core body temperatures into four zones: <37.5, 37.5 to <38, 38 to <38.5, and ≥38.5 °C. Core body temperatures during each participant's entire shift will be grouped into zones based on consecutive temperatures within the same temperature zone. We will calculate mean, maximum, and range of number of times participants move from one CBT zone to another, the number of times participants cross the 38 °C threshold, and the mean, maximum, and range of minutes spent in each zone per shift. We will also calculate maximum CBT by self-reported work task.

3. Methods to Maximize Response Rates and Deal with Nonresponse

For the field, it is anticipated that the majority (at least 80%) of individuals who are recruited to participate, will complete the study. We make this assumption because data collection for the field study will take place at the mine where the miner is employed during his or her shift. In addition, the field data collection research protocol was specifically designed to take a minimal amount of time to complete during the workers' shift. Miner feedback collected during recent pilot testing was used to guide development of the field protocol (see a description of the pilot test in Section 4 below).

For the environmental chamber, it is also anticipated that the majority (at least 80%) of individuals who complete the health questionnaire and physical examination will be meet the requirements, based on the risk stratification assessment. It is expected that at least 90% of those participants who qualify and then choose to take part in the study will successfully complete testing within the environmental chamber. Because of the nature of the environmental chamber study, it is necessary to conduct the research at the NIOSH/SMRD Spokane Research Laboratory (SRL) facility. All data will be collected one-

on-one with participants. Efforts will be made to coordinate with participants ahead of time to minimize time spent on site in the environmental chamber. This means that efforts will be made to not have participants wait to complete any parts of the study while on site. Given the amount of time required to participate (i.e., half day on visit 1 and the majority of the day on visits 2 and 3), the demands placed on participants (i.e., performing work in a hot environmental chamber), the distance that participants must travel, and the fact that participants will complete study activities while they are off duty, all participants will be compensated for participation $35/hour and $0.545 per mile. Compensation is necessary to obtain the needed participation for this study. Compensated time will commence upon arrival to the NIOSH facility and end when participants leave the facility (i.e., participants will be reimbursed for mileage but not travel time). For participants who do not complete the study's full three days, reimbursement will be prorated for the amount of time spent in the study. Compensation will be made by check at the completion of the study. Our previous experience with data collection efforts in the environmental chamber with mine workers suggest that the expected response rate of at least 90% is an achievable response rate. An example of a recent NIOSH/SMRD research project that achieved a 90% response rate is 18-SMRD-02 Validating heat strain responses among miners, which saw between 90 and 95% of the mine workers recruited complete the study.

The project team developed a plan to maximize response rates and manage nonresponse. Participants are free to withdraw from participation in the study at any time upon request. If a participant withdraws from the field or environmental chamber study, they will be replaced by another person from the pool of recruits if time permits. The reason for participant discontinuation or withdrawal from the study will be recorded by NIOSH investigators. An investigator may discontinue a participant from the study for the following reasons:

- Lost-to-follow up; unable to contact subject
- Any event or medical condition or situation that occurs (e.g., heat exhaustion, chest pain requiring medical evaluation) such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

For the field study, a participant will be considered lost to follow-up if he or she fails to return for a previously scheduled shift, and study staff are unable to either contact the participant after 5 attempts or are unable to reschedule their shift prior to completing data collection for the rest of the participants at that mine.

For the environmental chamber study, a participant will be considered lost to follow-up if he or she fails to return for a previously scheduled study visit, and study staff are unable to contact the participant after at least 5 attempts.

The following actions must be taken if a participant fails to return to the laboratory for a required study visit:

- NIOSH investigators will attempt to contact the participant, reschedule the missed visit, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.

- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant with 5 telephone calls and/or 5 emails. These contact attempts will be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

4. Tests of Procedures or Methods to be Undertaken

All data collection materials used in these studies have been developed based on similar research in other areas. The individual questionnaires and questions have been pilot tested by eight mine workers to ensure questions, as posed, elicit the intended responses. Pilot testing was also conducted to ensure feasibility of data collection methodology and procedures. No additional pilot testing will be necessary.

5. Individuals Consulted or Statistical Aspects and Individuals Collecting and/or Analyzing Data

The persons who were consulted and those who will collect and/or analyze the data are listed below.

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