Assessment of Prolonged Occupational Exposure to Heat Stress

by

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DEDICATION

To my husband and son for their unselfishness, immense love and unconditional support. I have passed through difficult times, especially during this past year, you both have been my drive and my reason to stand up and keep going ahead. To my parents for their immense love and for instilling self-confidence. And to my advisors Aurora Sanchez-Anguiano and Thomas E. Bernard for believing in me, for their unselfishness, for all their care, for their priceless time, for their unwavering support, and for opening my eyes and stretching my mind to the awesome world of research.

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ABSTRACT

Heat stress is a recognized occupational hazard present in many work environments. Its effects increase with increasing environmental heat loads. There is good evidence that exertional heat illness is associated with ambient thermal conditions in outdoor environments. Further, there is reason to believe that risk of acute injury may also increase with the ambient environment. For these reasons, the assessment of heat stress, which can be done through the characterization of the wet bulb globe temperature (WBGT), is designed to limit exposures to those that could be sustained for an 8-h day. The ACGIH Threshold Limit Value (TLV) for heat stress was based on limited data from Lind in the 1960s. Because there are practical limitations of using thermal indices, measurement of physiological parameters, such as body temperature and heart rate are used with environmental indices or as their alternative.

The illness and injury records from the Deepwater Horizon cleanup effort provided an opportunity to examine the effects of ambient thermal conditions on exertional heat illness and acute injury, and also the cumulative effect of the previous day's environmental conditions. The ability of the current WBGT-based occupational exposure limits to discriminate unsustainable heat exposures, and the proposal of alternative occupational limits was performed on data from two progressive heat stress protocol trials performed at USF. The USF studies also provided the opportunity to explore physiological strain indicators (rectal temperature, heart rate, skin temperature and the Physiological Strain Index) to determine the threshold between unsustainable and sustainable heat exposures. Analysis were performed using Poisson models, conditional logistic regressions, logistic regressions, and receiver operator curves (ROC curves).

It was found that the odds to present an acute event, either exertional heat illness or acute injuries increased significantly with rising environmental conditions above 20 °C (RR 1.40 and RR 1.06, respectively). There was evidence of the cumulative effect from the prior day's temperature and increased risk of exertional heat illness (RRs from 1.0–10.4). Regarding the accuracy of the current TLV, the results of the present investigation showed that this occupational exposure limit is extremely sensitive to predict cases associated with unsustainable heat exposures, its area under the curve (AUC) was 0.85; however its specificity was very low (specificity=0.05), with a huge percentage of false positives (95%). The suggested alternative models improved the specificity of the occupational exposure limits (specificities from 0.36 to 0.50), maintaining large AUCs (between 0.84 and 0.89). Nevertheless, any decision in trading sensitivity for specificity must be taken with extreme caution because of the steeped increment risk of heat related illness associated with small increments in environmental heat found also in the present study. Physiologic heat strain indices were found as accurate predictors for unsustainable heat stress exposures (AUCs from 0.74 to 0.89), especially when measurements of heart rate and skin temperature are combined (AUC=0.89 with a specificity of 0.56 at a sensitivity=0.95). Their implementation in industrial settings seems to be practical to prevent unsustainable heat stress conditions.

CHAPTER ONE:

INTRODUCTION

Heat Stress

Heat stress is the result of the combined effects of environment, metabolic rate, and protective clothing [Havenith 1999]. It can result in a spectrum of disorders known as heat-related illness, which can include mild health conditions such as heat rashes and heat cramps; or more complicated events such as heat exhaustion and heat stroke [CDC 2008]. Heat exposure is a recognized occupational hazard that is present in many work environments [NIOSH 2013, OSHA 2015]. It induces physiological strain [Kjellström, et al. 2009], decreases work capacity [Kjellström, et al. 2009, Sahu, et al. 2013], jeopardizes worker's health [Arbury, et al. 2014, Spector, et al. 2014], and increase the risk to work related injury [Fogleman, et al. 2005, Ramsey, et al. 1983]. Environmental contributions to heat stress should include at least temperature and humidity. For this reason, the National Weather Service Heat Index and the wet bulb globe temperature (WBGT) are frequently used indices.

Heat Stress Assessment

In general, heat stress is the sum of heat generated in the body, plus the net heat exchange between the body and the surroundings, minus the heat lost to the environment by sweat evaporation [Bernard 2012, Havenith 1999, Joubert and Bates 2008, Malchaire 2006, NIOSH 2013]. Heat generated in the body depends on the metabolic rate, which in turn

depends on the work demands. The dry (or sensible) heat exchange between the body and the environment is due to convection. The direction of dry heat exchange depends on the temperature gradient between the skin and the surrounding air (convection). In addition to the gradient, the rate of this exchange depends on air motion and clothing. The other form of dry heat exchange is radiant heat. Radiation is the net heat flow between the person and the solid surroundings where the direction is dictated by the temperature gradient. The rate of heat transfer depends of the gradient and clothing. The major source of heat loss is via sweat evaporation, called insensible heat loss. The rate of evaporative cooling depends on the water vapor pressure gradient between the skin and the ambient environment, air movement, and clothing.

Clothing modifies the rate of heat exchange between the skin and the environment. Insulation affects dry heat exchange via convection and radiation. The rate of heat loss by evaporative cooling depends on the evaporative resistance of the clothing. Clothing characteristics that affect insulation and evaporative resistance are fabric type, clothing construction, air movement and body movement [Bernard 2012, Caravello, et al. 2008, Havenith 1999].

Body's thermal balance is usually described by an equation that represents the exchange of temperature between the body and the environment:

$$S = (M - W) + R + C + (C_{resp} - E_{resp}) - E$$

Where S = heat storage rate (gain [+] or loss [-])

M = metabolic rate (internal heat generation)

W = external work rate (energy delivered to environment)

R = radiant heat exchange rate (gain [+] or loss [-] to environment)

C = convective heat exchange rate (gain [+] or loss [-] to environment)

C_{resp} = rate of convective heat exchange by respiration (gain [+] or loss [-] to environment)

E_{resp} = rate of evaporative heat loss by respiration

E= rate of evaporative heat loss

When thermal balance is achieved, heat storage rate (S) equals 0.

Historically the risks associated with heat exposure have been well recognized in different types of industrial settings such as agriculture, mining, aluminum production, military, and sports among others [Hollowell 2010]. Annually millions of workers in the U.S. are exposed to heat stress [NIOSH 2013]. In order to determine the level of heat stress under which those workers are exposed, and if such levels of heat would be acceptable, different methods of assessment of hot working environments have been employed to achieve this aim [Parsons 2014].

Current occupational heat stress exposure standards were designed to limit the physiological response to safe levels [NIOSH 2013, Parsons 2014]. These standards where developed based in hot environment assessment. Parsons [2014] describes three indices commonly used: empirical, direct and rational. Empirical indices are based in physiological reactions to hot conditions; data are produced from laboratory studies, or in hot working environments and analyzed in order to provide the basis for predicting likely effects on workers exposed to similar environments to those used to generate the data. Direct indices use a standardized measurement instrument, which is responsive to radiant heat, air temperature and velocity, and humidity. The Wet Bulb Globe Temperature index (WBGT) is an example of this type of index, and is used as a direct indicator of heat stress. Lastly the rational indices are based on the biophysics of heat exchange between the human body and the environment. They

consider internal heat load from work demands, dry heat exchange, and evaporative cooling rates to estimate the rate of heat storage which predicts heat strain [Parsons 2014].

Wet Bulb Globe Temperature and Occupational Exposure Limits

WBGT is a direct index which was created in the early 1950's during a campaign to control heat illness in military training camps in the U.S [Yaglou and Minard 1957]. It was calculated using the readings of three types of thermometers, a natural wet bulb (T_{nwb}), a globe thermometer (T_g), and sometimes a dry-bulb thermometer (T_{db}); in practice WBGT is a weighted average of T_{nwb} and T_g, supplemented with T_{db} when radiant heat is present [Budd 2008].

WBGT takes into account the combined environmental effects of air temperature (T_a), radiant heat load (in T_g), air movement (in T_{nwb}), and humidity; in the absence of radiant heat load the T_g reflects the effects of air velocity and air temperature [NIOSH 2013]. The simplicity of the WBGT made this index suitable for monitoring industrial heat stress; that is the reason why in 1972 NIOSH recommended its use [Dukes-Dobos and Henschel 1973, NIOSH 2013]. In 1974 the American Conference of Governmental Industrial Hygienists (ACGIH®) chose the WBGT as the index for expressing environmental heat load in the Threshold Limit Values (TLVs®) for Heat Stress and Strain [ACGIH 2015].

Heat Strain Assessment

Heat strain results from the body's exposure to heat stress [ACGIH 2015, NIOSH 2013]. In order to sustain a core temperature equilibrium the body triggers compensatory mechanisms; that is, increments in body temperature, heart rate (HR) and sweating [ACGIH 2015, NIOSH 1972, WHO 1969]. When this physiological response is not effective to maintain a sustainable core temperature, heat is stored in the body leading to an increment of core temperature, the level of physiologic strain increases along with increasing heat stress [NIOSH 2013, Parsons 1999].

Heat stress assessment frequently requires thermal indices to develop and implement specific control measures. Nevertheless, there are some important limitations to take into account, these thermal indices have been validated in a narrow range of thermal environments and frequently workers are exposed to heat stress above the recommended occupational exposure limits [Logan and Bernard 1999]. Also, the efficacy of these environmental indices' estimates is affected by the use of work clothing and other types of personal protective equipment, therefore there is no effective method to accurately determine such exposure. For the aforementioned reasons measurement of physiological parameters, such as body temperature and HR are jointly used with environmental indices or as their alternative [Graveling, et al. 2009].

Since 1986, NIOSH recommends monitoring body temperature and recovery HR as indices to determine levels of heat strain in workers exposed to environmental conditions in excess to the recommended exposure limit (REL) [NIOSH 2013]. The ACGIH® has proposed monitoring physiological strain since 1997 and adopted it since 2000 [ACGIH 2015].

Heat Exposure Outcomes

Prolonged heat exposure can disrupt body's thermal equilibrium, resulting in heat related illness (HRI). Heat exhaustion and heat stroke are triggered by environmental exposure resulting in elevation of core temperature. Both conditions can occur in young and healthy individuals exposed to hot and humid environments and increased workloads [Spector, et al. 2014]. Heat exhaustion include heavy sweating, pallor, persistent muscular crams, urge to defecate, weakness, fainting, dizziness, headache, hyperventilation, nausea, anorexia, diarrhea, decreased urine output, a core temperature ranged from 36 °C to 40 °C, and the consequent dehydration. Such symptoms hinder the ability of continue exercise, due to sodium loss, and energy depletion [Binkley, et al. 2002].

Heat stroke has been classified in recent years in two types, classic heatstroke and exertional heatstroke (EHS) [NIOSH 2013]. The latter is frequent in occupational environments and is characterized by a rapid onset, being more common in active young adults [Glazer 2005]. Exertional Heat stroke implies core temperature above 40 °C, and is associated with failure of organ system due to hyperthermia [Binkley, et al. 2002].

When physical exertion is involved heat stress increases, and high outdoor temperatures are not required to trigger HRI [Binkley, et al. 2002]. Exertional heat illnesses (EHI) can occur with WBGT values below the limits established by the military training guidelines as allowed to perform continued exercise. There is evidence that many of these EHI were related with exposure to hot environmental conditions the day before becoming a case, underpinning the cumulative effect of the day before WBGT on the prediction of EHI [Wallace, et al. 2005].

While EHI is not always a life-threatening condition, if EHS is not timely recognized and treated can lead to fatality. It is characterized by an elevated core temperature, often more than 40 °C and failure of organ systems. It includes cardiovascular symptoms such as tachycardia, and hypotension and central nervous system disruptions with signs such as altered mental status, seizures and coma [Binkley, et al. 2002].

Low level dehydration may become a key issue if it becomes progressive or cumulative in that it develops over a period of days when the amount of water and electrolytes replaced is insufficient to restore the body to a state of proper hydration prior to beginning the next day's work. Such progressive or cumulative dehydration can impair or overwhelm the body's thermoregulatory system [Binkley, et al. 2002, Jackson and Rosenberg 2010]. Individuals involved in strenuous physical activities in hot environments can lose up to 3 liters of water and 3.5 grams of sodium each hour as they sweat [Sharp 2006]. There is evidence that found with just 2% dehydration there is a significant impairment in mental performance, short-term memory and visual-motor tracking skills [Gopinathan, et al. 1988]. Early signs of heat stress can include

thirst, fatigue and decrements in vigilance, visual tracking, response time, short-term memory, and auditory discrimination [Chen, et al. 2003, Epstein, et al. 1980, Grandjean and Grandjean 2007, Hancock and Vasmatzidis 2003].

The association between heat exposure and cognitive and psychomotor disruptions is not a new concept. Weston (1922) and Wyatt (1926) found strong evidence that factory output and accidents were affected by thermal conditions [Parsons 2014]. Vernon and Warner [1932] performed a series of studies in industries of glass, steel, tinplate and munitions manufacturing as well as coal mining, they found that with raising temperatures work rate declined and accident rates increased.

Ramsey, et al. [1983] study using the unsafe behavior index (UBI), found a U-shaped curve representative of the prevalence of unsafe behaviors in relation to the wet bulb temperature (WBGT). They also found that minimum UBI values occurred within the range of 17 °C to 23 °C-WBGT within the comfort range for light workload. As ambient temperatures rose above or dropped below this preferred temperature zone the UBI increased. They reported that higher metabolic workload levels corresponded to increases in the UBI. In this later review of 160 studies of perceptual motor performance and the hot work environment, Ramsey [1995] found that tasks requiring perceptual motor skills beyond mere mental or basic tasks showed statistically significant decrements in the range of 30 - 33 °C-WBGT.

Similar to Ramsey's inverted U shaped UBI is Hancock's maximal adaptability model. Using this model Hancock and Vasmatzidis [2003] described how under normal conditions individuals can perform at their optimal level within their comfort zone; however as environmental stressors increase, an individual's attentional resources will be tapped and progressively diminished in relation to their primary work task. They reported that continued stress within this psychological zone leads to a physiological shift out of homeostasis and toward a potential acute heat-stress injury. These cognitive depletions begin with only minor

elevations in deep body temperature. Hancock and Vasmatzidis [2003] also found that as the cognitive demands of a given task increase there is less of a shift in deep body temperature needed to impair performance. Hancock's psychological model is further supported by findings of The National Institute for Occupational Safety and Health [CDC 1986].

Thermal discomfort can negative affect cognitive and psychomotor functions, there is evidence supporting that as thermal conditions increase, the number of reports of perception of distraction also increase [Berg, et al. 2015]. Acute injuries at the workplace, such as those produced by contact with equipment, slips, and falls have been correlated with daily maximum temperatures [Adam-Poupart, et al. 2015, Morabito, et al. 2006, Xiang, et al. 2014]. The frequency of accidents, in general appears to be higher in hot environments than in more moderate environmental conditions. One reason is that working in a hot environment lowers the mental alertness and physical performance of an individual. Increased body temperature and physical discomfort promote irritability, anger, and other emotional states which sometimes cause workers to overlook safety procedures or to divert attention from hazardous tasks [CDC 1986].

Significance of the Research

Heat stress is an important occupational hazard, associated with outcomes such as EHI and AI even under environmental conditions reported as "acceptable" to perform continuous physical exertion. For this reason, the assessment of heat stress is so important. This evaluation is usually accomplished by characterizing the environment through WBGT and the work demands with an estimate of the metabolic rate. The hazard decision follows from a comparison of the combination of WBGT and metabolic rate to an occupational exposure limit. The limit is a protective judgment about whether the exposure is sustainable for long periods of time or not. In addition, there are physiological responses to heat stress (called heat strain) that might provide opportunities to make a similar decision about whether the exposure is

sustainable or not. Table 1 gives an overview of the investigation process performed in the studies that are part of this dissertation work.
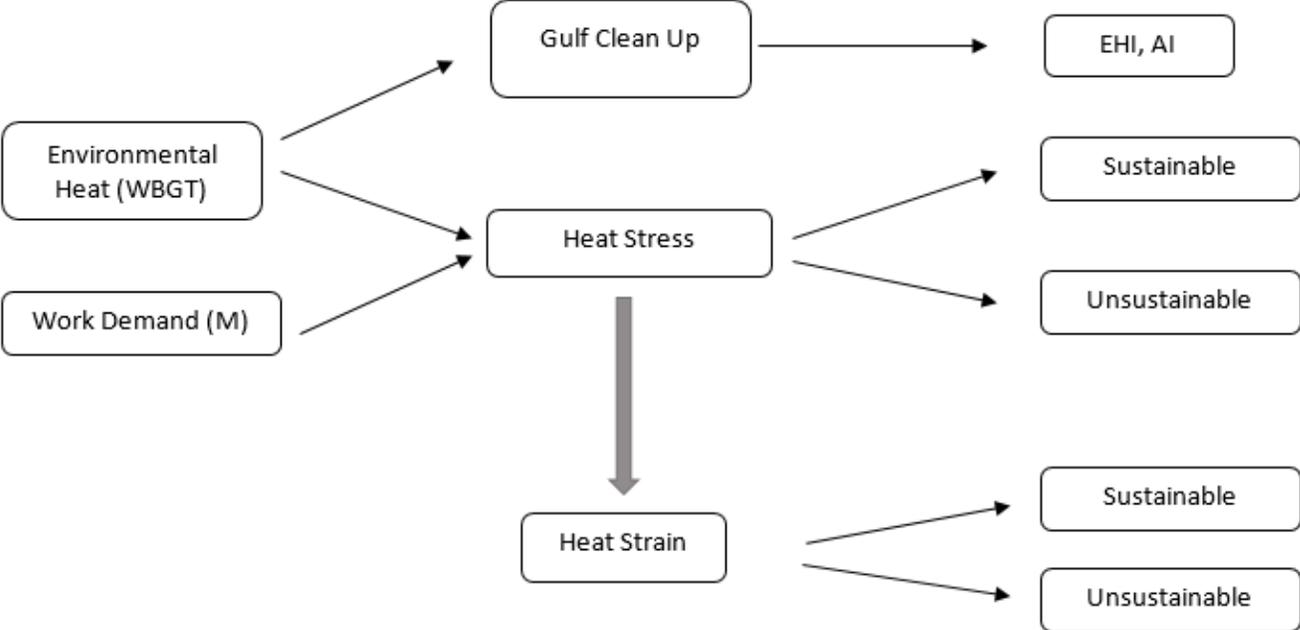
Figure 1.1. Dissertation Overview

This study provides industry, occupational health practitioners, and policy makers with evidence that can be used toward the development of new standards to improve the risk perception of prolonged heat exposure, and to reduce heat stress hazard in the workplace.

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CHAPTER TWO:

EXERTIONAL HEAT ILLNESS AND ACUTE INJURY

RELATED TO AMBIENT WET BULB GLOBE TEMPERATURE

The present is a research paper with multiple authors

Author Contributions Statement:

–   Study conception and design: Ximena P. Garzón-Villalba; Thomas E. Bernard.

–   Data management: Ximena P. Garzón-Villalba; Thomas E. Bernard; Hanna Moore.

–   Analysis and interpretation of data: Ximena P. Garzón-Villalba; Alfred Mbah; Thomas E. Bernard; Yougui Wu; Skai W. Schwartz.

–   Drafting of manuscript: Ximena P. Garzón-Villalba; Thomas E. Bernard; Michael Hiles.

–   Final approval of the version to be published: Ximena P. Garzón-Villalba; Thomas E. Bernard; Yougui Wu; Alfred Mbah; Skai W. Schwartz; Hanna Moore; Michael Hiles.

–   Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Ximena P. Garzón-Villalba; Thomas E. Bernard; Yougui Wu; Alfred Mbah; Skai W. Schwartz; Hanna Moore; Michael Hiles.

Exertional Heat Illness and Acute Injury Related to Ambient Wet Bulb Globe Temperature

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Running Head: EHI and Acute Injury Related to Ambient WBGT

KEYWORDS: Heat stress, WBGT, Wet bulb globe temperature, Occupational exposure limit, Threshold Limit Values, Sustainable, Unsustainable, ROC.

Abstract

Heat-related disorders are associated with ambient thermal conditions and there is some evidence that accidents may also be. The illness and injury records from the Deepwater Horizon cleanup effort provided an opportunity to examine the effects of ambient thermal conditions on exertional heat illness and acute injury. This study was designed to examine if increases in heat exposure result in (1) a higher risk of exertional heat illness (EHI) and (2) increased risk of acute injuries (AI). It is also hypothesized that there is a cumulative effect from the previous day's heat stress level on the risk of EHI and acute injuries.

There were 3,326 records of occupationally-related exertional heat illness and acute injury recorded by BP, and reported to a first aid station during cleanup efforts from May, 2010 through March, 2011. Day was the unit of observation, daily count of EHI and AI divided by the total number of workers on a given day was the dependent variable in the analysis. The independent variables were maximum estimated wet bulb globe temperature (WBGTmax) and severity (first aid and medical treatment). To assess the cumulative effect of the previous day, its maximum estimated wet bulb globe and an interaction term with the previous day WBGTmax were included into the model. Poisson regression models were used to explore the associations.

EHI and AI were higher in workers exposed above a WBGTmax of 20 °C (RR 1.40 and RR 1.06 / °C above 20 °C, respectively). Exposures above 28 °C-WBGTmax on the day of the EHI and/or the day before were associated with higher risk of EHI due to an interaction between previous day's environmental conditions and the current day (RRs from 1.0–10.4).

Ambient thermal conditions is a risk for those workers who perform their job in outdoor conditions, the association of an acute event increases significantly with rising temperature. There is evidence of the cumulative effect from the prior's day's temperature that becomes more evident with increasing temperatures. Further work is needed to elucidate such association.

Introduction

Heat stress is the result of the combined effects of environment, metabolic rate, and protective clothing [Havenith 1999]. It can result in a spectrum of disorders known as heat-related illness, which can include mild health conditions such as heat rashes and heat cramps; or more complicated events such as heat exhaustion and heat stroke [CDC 2008]. In the workplace, heat exposure is a known hazard, it threatens worker's health and well-being because it can induce heat illness [CDC 1986], decrease their work capacity [Kjellström, et al. 2009, Sahu, et al. 2013] and increase their risk to work related injury [Fogleman, et al. 2005, Ramsey, et al. 1983]. Environmental contributions to heat stress should include at least temperature and humidity. For this reason, the National Weather Service Heat Index and the wet bulb globe temperature (WBGT) are frequently used indices.

In the United States from 2008 through 2014, 650 deaths related to environmental heat stress were recorded by the Occupational Safety and Health Administration [OSHA 2015]. In 2011, there were 2520 lost-time cases associated with exposure to environmental heat [Bureau of Labor Statistics 2012]. Between 2012 and 2013, a total of 20 cases were cited for federal enforcement. Among them were 13 fatalities, and 7 non-fatal occupational injuries; and 15 of the 20 were among outdoor workers. These heat illness cases and deaths occurred on workdays with a National Weather Service Heat Index between 29 °C and 41 °C [CDC 2014].

Heat exhaustion and heat stroke are triggered by heat stress and both disorders can occur in exposed individuals who are young and healthy [NIOSH 2016]. Exertional heatstroke (EHS) is more common in active young adults [Glazer 2005]. Heat illnesses do not require extremely elevated outdoor temperatures especially when physical exertion is involved [Binkley, et al. 2002]. Wallace, et al. [2005] found evidence supporting that many exertional heat illnesses (EHI) occur with WBGT values well below 26.7 to 29.4 °C, levels that have been established by the military training guidelines as allowed to perform continued exercise. It is important to

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highlight that most of those EHI cases were exposed to WBGT levels above 26.7 °C the day before becoming a case [Wallace, et al. 2005].

Ramsey, et al. [1983] used an unsafe behavior index, and found a U-shaped curve representative of the prevalence of unsafe behaviors in relation to WBGT. They also found that minimum unsafe behavior index values occurred within the range of 17 to 23 °C-WBGT within the comfort range for light workload. As ambient temperatures rose above or dropped below this preferred temperature zone the frequency of unsafe behaviors increased. They reported that higher metabolic rates corresponded to increases in unsafe behaviors. Similar to Ramsey's inverted U-shaped for frequencies of unsafe behaviors is Hancock's maximal adaptability model. Hancock and Vasmatzidis [2003] described how under normal conditions individuals can perform at their optimal level within their comfort zone; however, as environmental stressors increase, an individual's attentional resources would be tapped and progressively diminished in relation to their primary work task. To explain why accidents may happen, heat could be considered as a stressor that may disrupt workers' ability to maintain a psychological homeostasis to prevent life-threatening attitudes or actions; and exposure to high levels of heat could increase the risk for acute injuries [Hancock and Vasmatzidis 2003]. In summary, the frequency of accidents appears to be higher in hot environments than in more moderate environmental conditions. One reason is that working in a hot environment lowers the mental alertness and physical performance of an individual. Increased body temperature and physical discomfort promote irritability, anger, and other emotional states which sometimes cause workers to overlook safety procedures or to divert attention from hazardous tasks.

Current Study

In response to the BP Deepwater Horizon oil platform explosion in the Gulf of Mexico in the spring of 2010, about 170,000 people worked in some capacity to clean up the Gulf spill [D'Andrea and Reddy 2013, Sandler, et al. 2013]. Heat stress was clearly a concern, and there

were 978 heat stress incidents reported as of September 2 [Michaels and Howard 2012]. OSHA

and NIOSH also reported that between April 23 and July 27 there were 2130 injuries and

illnesses, of these 281 were OSHA-recordable cases [Michaels and Howard 2012]. While not

specifically mentioned, heat stress may have contributed to an increase in acute injuries. There

was also reason to suspect an effect from the previous day's exposure, the BP illness and injury

database provided an opportunity to examine this effect.

This study was designed to examine three questions among the Deepwater Horizon

clean-up workers: (1) if increases in heat exposure result in a higher risk of exertional heat

illness (EHI); (2) if increases in heat exposure result in increased risk of acute injuries; and (3) if

there was a cumulative effect from the previous day's heat stress level on the risk of EHI and

acute injuries.

Methods

BP recorded all reports to first aid stations for the Deepwater Horizon cleanup efforts.

This database provided an opportunity to examine the hypotheses using a cross-sectional

study. The illness and injury incidents covered the period from May 2010 through March 2011.

Most of these records belonged to the Mobile and Houma Incident Command Posts (ICPs). The

Mobile ICP included base locations in Alabama, Mississippi, and Florida; and Houma included

Louisiana and Texas. The database included BP employees, BP contracted workers,

federal/state/local responders, and volunteers. There have been some local (parish) workers

involved in response efforts who did not fall under the supervision of the Unified Command, and

thus were not included in the database.

Acute Event Identification

The database was comprised of the information recorded by BP on an incident form that

was filled out for any event leading to injury or illness. This method of employer-generated data

collection was standard occupational safety and health practice. It should be noted that because the data used for this study were collected by BP, USF could not independently verify the accuracy and completeness of the data.

The first step in selecting incidents was to identify those records for which BP staff identified the visit as work-related (For database column called: "Was this determined to be an occupational injury or illness?" with an answer of Yes).

Duplicate entries were identified by first sorting records by date and time of event. Then duplicates were identified by later visit dates for the same incident date, and confirmed by similar description of incident.

The next step was to remove records with an illness code not related to heat. The BP database was sorted by OIICS code (Bureau of Labor Statistics Occupational Injury and Illness Classification System, v1.01). Incidents with a primary or secondary code that suggested a heat-related disorder (e.g., 0721- 0724) were retained. Those that were an illness (e.g. 10* - 13*) were deleted. An acute injury was likely to be retained if it was due to an individual's action (usually 01* - 06*, 08*, 09*) or deleted from the database if it was not likely due to the action of an individual (i.e., unsafe condition) (usually 14*, 15*, 19*). Examples of excluded acute injuries or illnesses were insect bites, infectious diseases, allergic reactions, etc. Sun burns, heat rash, skin chafing, and other acute skin injuries related to sun or heat exposure were also excluded from the analysis because they were not exertional. If there was not enough information to classify an injury or illness, it was excluded.

Each of the remaining acute incidence records was then categorized for incident type as acute injury (AI), or as exertional heat illness (EHI), which included acute health events related to heat such as heat stroke, heat syncope and heat exhaustion.

Severity level was assigned based on the OSHA classification of treatment. Low Severity (LS) were those incidents classified as first aid. High severity (HS) were those events where there was medical treatment, lost time, or restricted duty; that is, OSHA recordable. The original database containing 20,033 de-identified cases of recorded injury or illness, was reduced to 3326 records of occupationally-related injury and illness once the inclusion criteria were applied (Figure 1). For the purpose of this analysis, the number of exertional heat illness (EHI) and acute injuries (AI) on a given day divided by the number of workers on that day were used as dependent variables.
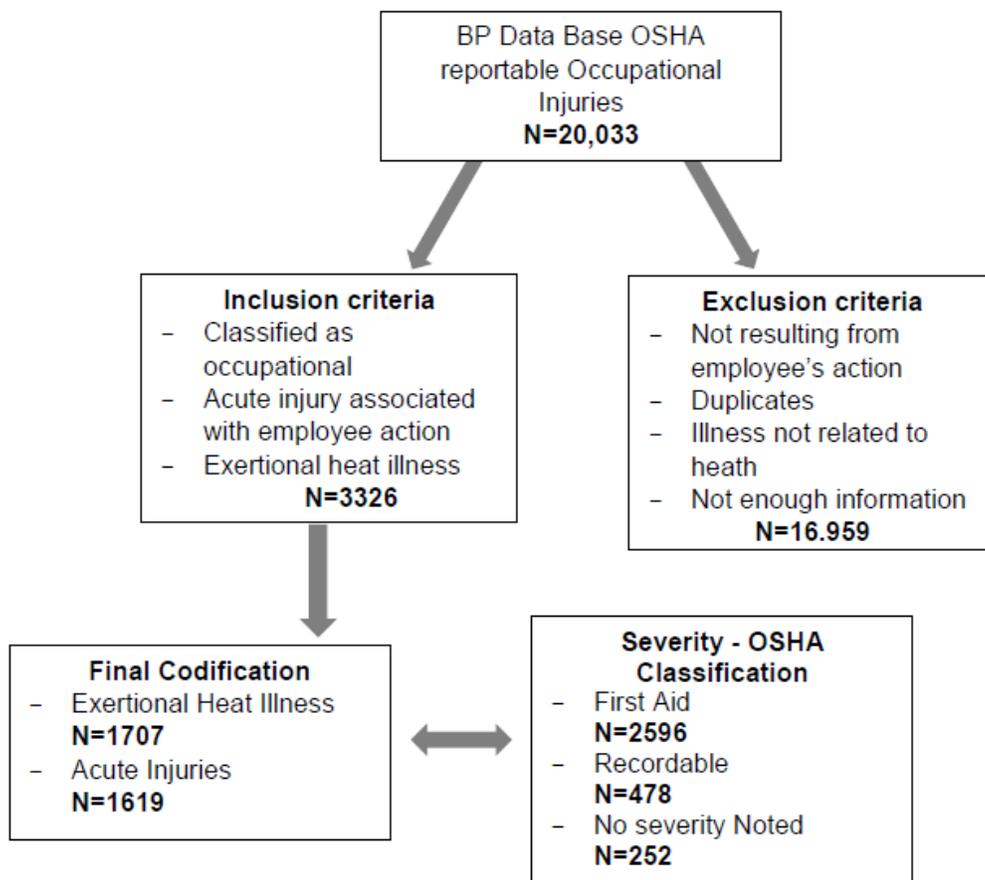
Figure 2.1. Inclusion and Exclusion Criteria Flow Diagram

Number of Workers and Environmental Conditions

Day was the unit of observation. One task was to estimate the number of workers for a given day. BP provided the total number of workers in periods of one week for May through September and monthly for October through March. Work days included 12 hours from May through December 2010, and 10 hours from January through March 2011. In spite of the difference in shift length, the total number of workers on a given day was used as denominator.

To assess the heat stress level for a given day, records from Weather Source, a company that specializes in historical weather data, were downloaded for May 2010 through April 2011. Daily weather data for New Orleans, which was assigned to Houma ICP, and for Mobile assigned to the Mobile ICP, were used to characterize each ICP region's WBGT.

The data used for this study included the maximum dry bulb temperature (T_{db}) and average dew point temperature (T_{dp}). These were used to estimate the WBGT index [Bernard and Barrow 2013]. Specifically, the water vapor pressure (P_v [kPa]) was computed from the average dew point (˚C) as $P_v = 0.1 \times 10^{(18.956-4030.18/(Tdp+235))}$. The psychometric wet bulb (T_{pwb} [˚C]) was estimated from T_{db} and P_v, by using $T_{pwb} = 0.376+5.79 P_v + (0.388-0.0465P_v) T_{db}$. The natural wet bulb temperature (T_{nwb}) was taken as 1 ˚C above the T_{pwb}. Globe temperature data were not available but adding 8 °C to the dry bulb temperature is a reasonable estimation for exposure to the sun [Bernard and Barrow 2013]. Then WBGTmax = $0.7 T_{nwb} + 0.3 (T_{db} + 8)$.

The WBGTmax for each ICP on a given day was noted and averaged for the representative WBGTmax in all analyses. That is, the overall purpose was to determine the association between WBGTmax as a measure of heat stress level (exposure variable) and the occurrences of exertional heat illness and acute injuries for all clean up areas.

Cutoff Point

A reference point of 20 °C-WBGT for WBGTmax data was selected to represent a very low heat stress level, and it was in the range of minimum of the Ramsey, et al. [1983] unsafe behavior index. In practice, the threshold included most of the incidents. In the current study, all the exposures under 20 °C-WBGT were assigned a value of 20 °C-WBGT. The low threshold was supported by Wallace, et al. [2005] who reported an uptick in risk at 75 °F-WBGT (24 °C-WBGT) at relatively high metabolic demands (i.e., jogging); and by Cooper Jr, et al. [2006] who also reported a noticeable increase in EHIs when WBGT exceeded 23 °C for high metabolic rates (i.e., college football practice). To further explore the effect of ambient thermal conditions, the Poisson model treated WBGTmax (referenced to 20 °C) as a continuous variable. Overall, 20 °C-WBGT was considered as an appropriate reference point because it is a thermally neutral environment.

Analyses

All analyses were performed using SAS 9.4 [SAS Institute Inc 2013]. Descriptive statistics were generated for total number of exertional heat illness (EHI) and acute injuries (AI). Daily frequencies of the outcome variables (counts of EHI and AI) were used as numerator, and total number of workers on that day (unit of observation) as the denominator in the outcome variable. A WBGTmax referenced to 20 °C-WBGT was chosen based on the approximate minimum point for unsafe behavior and the fact that represents a comfortable environment. That is, WBGTmax was transformed to a continuous variable referenced to 20 °C-WBGT by subtracting 20 from the values for the purposes of analysis. All temperatures under 20 °C-WBGT were assigned a value of 0 and became the intercept (α) in the regressions.

Proc GENMOD [SAS Institute Inc 2013] was used to fit a Poisson regression model Log $(E(Y|X)) = \alpha + \beta_1$ MAX(WBGTmax – 20, 0) to determine associations between WBGTmax and the outcomes. Two associations were explored: (1) between frequency of EHI and WBGTmax,

and (2) between frequency of AI and WBGTmax. Severity of the injury was assessed as a confounder and effect modifier.

In order to estimate a possible cumulative effect of WBGTmax on EHI risk or AI risk, a Poisson model was fitted with WBGTmax referenced to 28 °C-WBGT. That is, for the day of the event all temperatures under 28 °C-WBGT were assigned a value of 0 and became the intercept (α) in the regression. The main model was adjusted for the effect of the previous day conditions with a new variable, the WBGTmax from the previous day (priorWBGTmax). The prior WBGTmax variable included all temperatures under and above 28°C-WBGT. The decision to limit the day of event WBGTmax to at or above 28 °C was taken due to the lack of contrast at lower WBGTmax. Effect modification was assessed with an interaction term between the WBGTmax from the day of the injury and priorWBGTmax. The resulting model was Log (E(Y|X)) = α + $\beta 1$ MAX(WBGTmax-28, 0) + $\beta 2$ priorWBGTmax + $\beta 3$ MAX(WBGTmax-28, 0)*priorWBGTmax.

Results

Table I shows the distribution of the incidents. There were 1707 exertional heat illness and 1619 acute injuries. There were 2596 events with low severity (i.e., first aid), 478 with high severity (i.e., OSHA recordable), and 252 events for which the incident type was assignable but severity was not. Of the 335 days from May 2011 through March 2011, there were 97 days with no incidents reported by BP.

In the model where only WBGTmax referenced to 20 °C was included [Log (E(Y|X))= α +β_1 MAX(WBGTmax – 20, 0)], the association between each category of acute event and temperature showed that the risk to present with an EHI or an AI increased with °C-WBGTmax. Table II provides the rate ratios (RR) associated with elevated WBGTmax. For both outcomes (EHI and AI), the association was statistically significant. The unadjusted RRs from the

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association between the outcome variables and WBGTmax were statistically significant (See

Table II). The model results are illustrated in Figure 2.

Table 2.1. Number of Incidents by Type and Severity

Severity	Exertional Heath Illness	Acute Injury	All
Recordable	223	255	478
First Aid	1358	1238	2596
No Severity Noted	126	126	252
Total	1707	1619	3326

Table 2.2. Unadjusted Rate Ratios per °C-WBGTmax above 20 °C.

Effect	Rate Ratio	Lower 95% C. I.	Upper 95% C.I.
Exertional Heat Illness	1.40	1.35	1.44
Acute Injuries	1.06	1.04	1.07
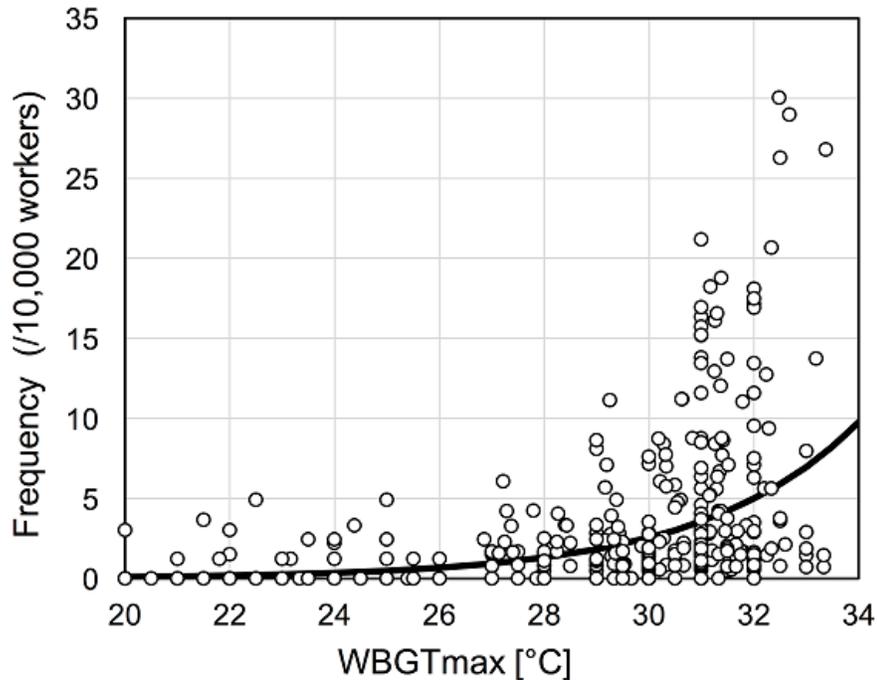
Figure 2.2. Frequency of all Events (EHI + AI) on a Given Day, with a Log-Linear Trend Line

Severity was statistically significant when added to the main model, low severity was used as comparison group. There was a 43% greater probability to be an EHI with high severity per 1°C increment in °C-WBGTmax (RR 1.43, 95% C.I. 1.38 – 1.47); and for acute injury, there was 5% higher probability to be an AI with high severity per 1°C increment in °C-WBGTmax (RR 1.05, 95% C.I. 1.04 – 1.07). Even though severity was considered as a possible effect modifier, its effect on the association between the outcome and WBGTmax was considered as negligible because the increase in RR was only 2%.

There was not enough contrast in conditions below 28 ˚C-WBGT to examine the effects of the day before. The inclusion of the previous day's temperature (priorWBGTmax) into the main Poisson model (referenced to 28˚C-WBGT) was assessed as significant only for EHI (p-value< 0.001). Its interaction term with the day of the injury's WBGTmax was found as statistically significant (p-value< 0.001).

The magnitude of the effect of the day of the injury's WGBTmax varies depending on the level of the previous day's WBGTmax. Table III provides the model-based rate ratios with the interaction term. In addition, this table has the rate ratios for the unadjusted model in the second column, where the risk ratios were referenced to 28 °C-WBGT by dividing the model's risk ratio by the predicted risk ratio at 28 °C.

Table 2.3. Rate Ratios of EHI for Combinations of Day of the Injury °C-WBGT and Previous Day °C-WBGT with Interaction Term.

		Rate Ratios of EHI (referenced to 28 °C-WBGT)			
	Unadjusted Model	Model with Previous Day Interaction			
34	7.40	7.69	8.50	9.40	10.40
32	3.80	3.89	4.15	4.41	4.70
30	1.95	1.97	2.02	2.07	2.12
28	1.00	1.00	--	--	--
	--	28	30	32	34

Day of the injury's °C-WBGT (left axis label)

Previous Day °C-WBGT

All of the models are summarized in Table IV.

Table 2.4. Summary of Significant Poisson Models with Coefficients and 95% Confidence Intervals.

Outcome	Poisson Models
	Unadjusted
EHI	α=-11.60 (-11.9 to -11.2); β_1=0.336 (0.300 to 0.365) Log(E(Y|X))=-11.6 + 0.336 MAX(WBGTmax-20, 0)
AI	α=-8.75 (-8.92 to -8.58); β_1=0.0548 (0.0377 to 0.0719) Log(E(Y|X))= -8.75 + 0.0548 MAX(WBGTmax-20, 0)
	Adjusted for Severity
EHI	α=-11.0 (-11.4 to -10.7); β_1=0.354 (0.322 to 0.387); β_2=-1.71 (-1.85 to -1.56) Log(E(Y|X))= -11.04 + 0.354 WBGTmax-20 -1.71 Severity[0=first aid, 1=recordable]
AI	α=-8.00 (-8.19 to -7.82); β_1=0.053 (0.035 to 0.071); β_2= -1.41 (-1.54 to -1.27) Log(E(Y|X))= - 8.00 + 0.053 WBGTmax-20 -1.41 Severity[0=first aid, 1=recordable]
	Effect of Prior Day
EHI	α = -8.80 (-10.34 to -7.26); β_1= 0.0711 (-0.0692 to 0.211); β_2=-0.276 (-0.448 to -0.104); β_3= 0.0096 (0.005 to 0.0141) Log(E(Y|X))= -8.80 + 0.0711 MAX(WBGTmax-28, 0) -0.276 priorWBGT + 0.0096 MAX(WBGTmax-28,0) x priorWBGT

Discussion

Exposure to hot temperatures in outdoor work has been associated with increased risk of heat related illness and accidents. The present study assessed the association between daily rates of exertional heat illness and acute injuries to increases in environmental heat exposure using the BP injury and illness database.

For this study, a maximum estimated WBGT for the region was selected as the thermal exposure index. The daily average WBGT for the study period was collinear with WBGTmax (r^2 = 0.96) with a systematic difference of about 3.7 °C-WBGT. The use of the indoor formulation for WBGT rather than direct sunlight adjustment added a systematic increase of 0.8 °C-WBGT. Thus, the WBGTmax overstated the ambient conditions for a given day, and the WBGT

threshold for the observed associations would be somewhat lower, likely between 1 and 4 °C less.

Looking at Table I it is evident that there were over 5 times as many events (either EHI or AI) categorized as first aid (low severity) than recordable (high severity). Thus, 80% of the analyzed cases were classified as low severity. The RRs from the unadjusted model, shows a statistically significant association between WBGTmax and the outcome (see Table II and Figure 2). The association between ambient heat stress conditions and EHI was not surprising [Binkley, et al. 2002, CDC 2013, Lucas, et al. 2014, Morabito, et al. 2006].

Severity was found statistically significant on the main model, corroborating what was seen on the outcome's distribution (Table I), that is the majority of the analyzed cases had low severity. It is worth emphasizing that it was statistically significant only for predicting EHI (p < 0.001). Severity was assessed as a possible effect modifier, nevertheless is effect on the association between the outcome and WBGTmax was considered as negligible due that it increased the RR in just about 2%.

An increase in EHI risk with ambient WBGT was observed by several investigators. Cooper Jr, et al. [2006], found 55 cases of EHI related with exposures to 23 to 28 °C-WBGT, and 68 cases at conditions above 28 °C-WBGT, among 139 cases reported during football practice. To compare the present results with previous research outcomes, it is important to recall that when the outcome occurs in less than 10% of the unexposed population (as in the case of the present study), ORs provide a reasonable approximation of rate ratios [Viera 2008]. Bernard [2012] found a significant association between heat stress and EHI in an unpublished analysis of 174 acute outcomes. Bernard's study classified workplace exposures in three categories, the reference group included exposures below the ACGIH® TLV® [ACGIH 2015]; the low category comprised exposures between 0 °C and 3 °C-WBGT above the TLV; and high included those greater than 3 °C-WBGT above the TLV. He reported an OR of 25 (95% C.I. 3.3

- 202) in the low group and an OR of 158 (95% C.I. 21 - >1000) in the high group. Bernard's

high ORs were likely due to the low number of observations in the reference category. For

agricultural workers, Spector, et al. [2014] reported a 25th percentile HImax (maximum Heat

Index for the day) of 94 °F, which is equivalent to about 28 °C-WBGT [Bernard and Iheanacho

2015]. The metabolic demands of agriculture workers would likely be closer to the cleanup

workers of this study.

Wallace, et al. [2005] presented in their Figure 1 a four-fold increase in the OR for EHIs

while jogging, associated with categories of WBGT going from about 23 °C-WBGT (OR 1.5) to

32 °C-WBGT (OR 6), as compared to an RR of 7 for the current study at 34°C-WBGTmax when

referenced to 28 °C-WBGT (See Table III, unadjusted model); clearly supporting a higher risk of

EHI associated with exposures to increasing ambient thermal conditions. In this study, 10% of

events occurred at ambient thermal conditions below 28 °C-WBGTmax. This finding was similar

to Spector, et al. [2014] on the study on agricultural workers in which the mean (interquartile

range) HI_{max} was100 (94 to 106) °F. Using 94 °F, which was equivalent to 28 °C-WBGT

outdoors with high radiant heat [Bernard and Iheanacho 2015] as the reference point, 25% of

cases were below 28 °C-WBGT, which indicates a substantial HRI probability below 28 °C-

WBGT.

There was a statistically significant trend for AIs to increase with WBGTmax, but it was

much more gradual than for EHIs. The unadjusted model shows a 5% of increment in risk to

experience an AI when the ambient thermal conditions increase 1 °C-WBGT (See Table II).

Those workers exposed at 28 °C-WBGTmax, had 55% greater risk to present an acute injury.

Fogleman, et al. [2005] also reported increasing acute injury risk referenced to a baseline

exposure (baseline: 0.15/1000 person-hours), such that the risk almost doubled at the highest

exposure category. Bernard [2012] reported similar findings from an unpublished analysis for

operations personnel in an aluminum smelter (i.e., tappers and anode setters) using a subset of

the Fogleman, et al. [2005] data. The resulting OR from the association between acute injuries

and low heat stress level (0°C - 3°C WBGT above TLV) was 1.4 (95% C.I. 1.1 – 2.9), and an

OR 2.4 (95% C.I. 1.4 – 4.3) resulted from the association with high stress level (>3°C WBGT

above TLV). The association between AI and increasing ambient thermal conditions is

supported by the results reported by Ramsey, et al. [1983] in the study about the effects of

workplace thermal conditions on unsafe work behavior; in which unsafe behaviors would

increase about 1.3 times going from 23 to 33 °C-WBGT.

Severity was found statistically significant only in the model fitted to predict EHI (p

<0.001), and its effect as effect modifier was negligible. This finding coincides with Spector's

study, where most of the heat related injuries (HRI) were not severe (89%), but 6% required

intensive care [Spector, et al. 2014]

Prior day's ambient thermal conditions appeared to be associated with higher risk to

present an EHI. The effect of the previous day, and the interaction term between the day of the

injury's WBGT and the previous day's WBGT was statistically significant, behaving as an effect

modifier on the association between the variables under study (See Table III). Table III must be

interpreted with caution due to the lack of determination of the nature of the interaction. The rate

ratios should not be taken as the actual measure of association between the independent

variables and the outcome in this study because other variables not assessed in the present

study could have played an explanatory role in such relationship. Perhaps due that in the

present study only 10% of events occurred at ambient thermal conditions below 28 °C-

WBGTmax, we could not find any significant carry over effect of the day before on temperatures

below 28°C WBGT.

This carry over effect was also found by Wallace, et al. [2005], who reported a significant

association between EHI and temperatures between the current and previous day. They stated

that the prediction of EHI risk increased when the previous day average WBGT was included in

their models. The findings of the present study underpinned their conclusion that the combined effect of current day and previous day WBGT was more important in predicting risk of EHI than current day WBGT alone.

One of the strengths of this study was that the assessment of prevalence of acute injuries and exertional heat injuries was based on a large population of workers, exposed to diverse temperatures and environmental conditions for almost one year. Due to its cross-sectional design, only associations can be assessed.

There were several important limitations to this study. Unified Command and BP with the advice of OSHA and NIOSH were very concerned about heat stress; and this concern may have translated into a larger number of reported heat-related disorders. Acute injuries and exertional heat injuries could have been related to other personal risk factors, which could be prevalent among a large population of unselected workers, such as alcohol consumption, chronic diseases, medications, etc. The study was susceptible to bias due to selection and/or misclassification of records. Another source of bias was the decision to use number of daily workers instead of labor hours. For instance, the shift length changed from 12 hours to 10 hours in October through March. The break periods were longer during the 12 hour shifts, which reduced this bias. Finally, because (1) metabolic demands and clothing are important considerations that were not included in the analysis, and (2) the metric was WBGTmax using the indoor formulation for WBGT causing the actual exposures to be systematically lower than the reported WBGTmax, care must be taken not to generalize to other work settings.

The results of this investigation could be used to generate new hypotheses. For instance, the experience argues for a study design that more fully considers the exposure (environment, metabolic rate and clothing) and accounts for personal risk factors. Another study design could consider the role that low level dehydration might play in cumulative dehydration, leading to an impairment of the body's thermoregulatory system [Binkley, et al. 2002, Jackson

and Rosenberg 2010], consequently decreasing mental performance, short-term memory and visual-motor tracking skills [Gopinathan, et al. 1988], and increasing the risk for occupational accidents. Further investigation could clarify the physiopathology of this behavior.

Conclusion

This study clearly demonstrated that ambient thermal conditions are a risk factor for exertional heat illness and acute injury among outdoor workers. There was an evident progressive increase in risk as the ambient WBGTmax increased above a thermally neutral environment.

There was evidence of the cumulative effect from the prior day's thermal conditions, the association between rising temperature and the risk to present an EHI increased significantly. When the previous day was hotter than the current day, there was an increase that was greater than the current day analysis alone would suggest. If both days were above 28 °C, the risk was even higher. The increased risk for EHI might be explained by insufficient recovery from the previous day; that is, the effect is cumulative. Further work is needed to elucidate the nature of this interaction.

The most important findings from this study were (1) that the level of heat stress affects the risks for heat-related disorders and acute injuries and (2) that there is a cumulative effect from the exposure to heat stress on the prior day.

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CHAPTER THREE:

ABILITY OF WBGT EXPOSURE LIMITS TO DISCRIMINATE

BETWEEN SUSTAINABLE AND UNSUSTAINABLE HEAT STRESS

The present is a research paper with multiple authors

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- Study conception and design: Ximena P. Garzón-Villalba; Thomas E. Bernard.

- Data management: Candi D. Ashley; Thomas E. Bernard; Ximena P. Garzón-Villalba.

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- Drafting of manuscript: Ximena P. Garzón-Villalba; Thomas E. Bernard.

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Ability of WBGT Exposure Limits to Discriminate Between Sustainable and Unsustainable Heat Stress Exposures

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Running Head: Ability of WBGT to Discriminate Unsustainable Conditions

Abstract

Heat stress exposure limits based wet bulb globe temperature (WBGT) were designed to limit exposures to those that could be sustained for an 8-h day. The exposure limit was based on limited data from Lind in the 1960s. In this research the results from two progressive heat stress studies were used to determine the accuracy of the current WBGT-based occupational exposure limits (specifically the ACGIH® Threshold Limit Value - TLV®) to discriminate Unsustainable heat exposures, and to propose alternative occupational exposure limits. The progressive heat stress studies included 176 trials with 352 pairs of Sustainable and Unsustainable exposures over a range of relative humidities and metabolic rates using 29 participants. To assess the discrimination ability of the TLV, the exposure metric was the difference between the observed WBGT and the TLV adjusted for metabolic rate. Conditional logistic regression models and Receiver Operating Characteristic curves (ROC curve) were used. Four alternative OEL models were proposed, their corresponding areas under the curve (AUCs) were compared against the existing TLV's, to determine the improvement of the proposed limits. The conditional logistic regression model fitted with the current TLV, found that the odds of being unsustainable increased 2.5 times per 1 °C-WBGT of difference above the TLV (C.I. 2.12 – 2.88). Its AUC was 0.85 (C.I. 0.81 – 0.89). For the alternative models, the odds ratios were about 2.5, with AUCs between 0.84 and 0.88, which were statistically significant from the TLV. The three most important findings from this study were (1) confirming that the TLV is appropriate for heat stress screening; (2) assessing the OEL's discrimination accuracy through an ROC curve; and (3) establishing the odds ratio for unsustainable exposures. The TLV has a high sensitivity, meaning that the exposed working population is protected but its specificity is very low, which is translated as a high percentage of false positive cases. There were no important improvements with alternative OELs; and there was weak evidence to support adjustment of metabolic rate for populations with small body surface area.

Introduction

The assessment of heat stress considers the effects of environmental conditions, metabolic rate (M) and clothing. The wet bulb globe temperature (WBGT) index is used as a direct indicator of environmental contributors to heat stress [Parsons 2014].This index considers the combined environmental effects of air temperature, radiant heat load, air movement, and humidity [NIOSH 2016]. Despite its limitations [Alfano, et al. 2014, Budd 2008], WBGT is the most widely used heat stress index because it is convenient and easy to interpret [Budd 2008, NIOSH 1972, NIOSH 1986, NIOSH 2016]. In 1974 the ACGIH® adopted WBGT as the index for expressing environmental contributions in heat stress Threshold Limit Values (TLVs®) [ACGIH 2015]. Because the ACGIH TLV was the first widely used WBGT-based occupational exposure limit for heat stress, it is the stand-in for the same occupational exposure limits as the NIOSH Recommended Exposure Limit (REL) [NIOSH 2016] and the ISO 7243.

Based on ordinary work clothes, the TLV for heat stress has its origin from the upper limit of the prescriptive zone (ULPZ) proposed by Lind [1963] using three different metabolic rates. The combinations of effective temperature and metabolic rate where core temperature maintained consistent values independent of the environment was called the prescriptive zone (PZ), and the upper limit of the PZ was named the ULPZ. Lind reported that above the ULPZ, there was a trend of rising core temperatures with increasing levels of environmental heat. In three additional studies, Lind and colleagues [Lind 1963, Lind 1970, Lind, et al. 1970] confirmed that subjects as a group could not maintain thermal equilibrium above the ULPZ. In the current paper such a condition was called Unsustainable. Conversely, thermal equilibrium could be sustained for a long period at and below the ULPZ heat stress exposures, and these exposures were called Sustainable. Dukes-Dobos and Henschel [1973] used Lind's data as the primary rationale to support the TLV and NIOSH REL (NIOSH 1986).

The TLV was later examined by Kuhlemeier, et al. [1977] in assumingly acclimatized workers (working in hot industries in the summer) and another group of assumingly unacclimatized workers (from cold and neutral industries such as meat packing, janitorial service, and hospital orderlies, men working in the winter) were assumed to be unacclimatized. The investigators exposed workers randomly to environments either below or above the TLV at three levels of metabolic rate. They confirmed that as a group, exposures below the TLV yielded consistent core temperatures and heart rates (HR), and above the TLV the data showed an upwards trend with increasing WBGT. For their unacclimatized population they used a lower threshold to distinguish between Sustainable and Unsustainable.

In one study, Lind [1970] reported outcomes for individuals for four environments at one metabolic rate (350 W) as Sustainable (able to go 3 hours), and Unsustainable (reaching termination criteria before 3 hours). With respect to the TLV of 27.4 °C-WBGT, two environmental conditions were clearly above (30.7 and 33.3 ˚C-WBGT); one was well below (22.8 ˚C-WBGT); and another one was closer to, but higher than, the TLV (28.9 ˚C-WBGT). Although the subjects were seminude and unacclimatized, these two effects were considered by Dukes-Dobos and Henschel [1973] as equivalent to being acclimatized and wearing work clothes. We classified Lind's individual data as 22 Unsustainable cases, all of them above the TLV, and 73 Sustainable cases with 47 of them above the TLV and 26 below. This resulted in a sensitivity of 1.00 and a specificity of 0.35. It is worth noting that many exposures above the TLV in this study were Sustainable. Exposures for the individual data were assigned as the difference between the WBGT of the exposure minus the value for the TLV (27.4 °C-WBGT) for the metabolic rate of 350 W. Based on a logistic regression model using this difference to assess its association with the outcome of Unsustainable, we found a significant OR = 2.00 (C.I. 1.44 – 2.81) / °C-WBGT. That is, the odds to become a case increased two fold for each 1 ˚C of difference between the TLV and the observed WBGT.

Kuhlemeier, et al. [1977] provided individual data graphically (not in tables). Their experimental design purposely had exposures above and below the TLV. For classification purpose, we classified all exposures below the TLV as Sustainable. Above the TLV, the classification was Sustainable if the reported rectal temperature (T_{re}) was at or below the average T_{re} for the observations below the TLV. If the individual was above the average T_{re}, the exposure was classified as Unsustainable. There were 67 Unsustainable cases above the TLV; and 88 Sustainable conditions, 71 of them under the TLV. From the 2x2 table, sensitivity was 1.00 and specificity was 0.81. The odds ratio from the logistic regression model was OR= 2.10 (1.56 – 2.83) / °C-WBGT. That is, the odds to become a case was also about two times larger for each 1 °C of difference between the observed WBGT and the current TLV. In a similar fashion for the unacclimatized trials against the ACGIH action limit (AL) [ACGIH 2015], we examined the sensitivity, specificity and OR. There were 86 Unsustainable conditions above the AL, and none below it, yielding a specificity of 1.00. There were 62 Sustainable below the AL and 4 above it, resulting in a specificity of 0.94. The OR from the logistic regression model was 2.45 °C-WBGT (C.I. 1.63 – 3.71)

While the sensitivity and specificity described above from the Lind [1970] and Kuhlemeier, et al. [1977] studies appear strong, they were based on categories of metabolic rate and not individual values; and for the Kuhlemeier data, there was a potential for classification bias. This paper used a progressive heat stress protocol dataset that was designed to find the individual critical conditions where thermal equilibrium was no longer supported. The critical condition was approximately equivalent to an individual ULPZ. Thus individually known metabolic rates and WBGTs were available to assess the ability of the current and candidate WBGT-based occupational exposure limits to discriminate between Sustainable and Unsustainable heat exposures.

A secondary hypothesis was the effect of body surface area (BSA); grounded on a commonly accepted premise that body surface affects heat loss capacity [Havenith 2001]. Current thresholds assume a nominal BSA of 1.8 m^2; therefore, the present study explored if the reference metabolic rates should be adjusted for populations systematically smaller.

Methods

The data used for this paper were taken from two previous studies at USF [Bernard, et al. 2008, Bernard, et al. 2005]. The progressive heat stress protocol used in these studies began with a comfortable environment that was easily Sustainable. After thermal equilibrium was established, the temperature and humidity were slowly increased in 5-minute intervals. That is, once the participant reached thermal equilibrium (no changes in T_{re} and HR for at least 15 minutes), dry bulb temperature (T_{db}) was increased about 0.8 ˚C at a fixed relative humidity every 5 minutes. Rectal temperature (T_{re}), heart rate (HR), skin temperature (T_{sk}), and ambient conditions were recorded. Metabolic rate was estimated from the assessment of oxygen consumption via expired gases sampled every 30 minutes in a trial. The transition from a steady value for T_{re} to values that were steadily increasing were marked as the critical condition (see Figure 1). A compensable point was selected as 15 minutes before the critical condition; and an uncompensable point was selected as 15 minutes after the critical condition.
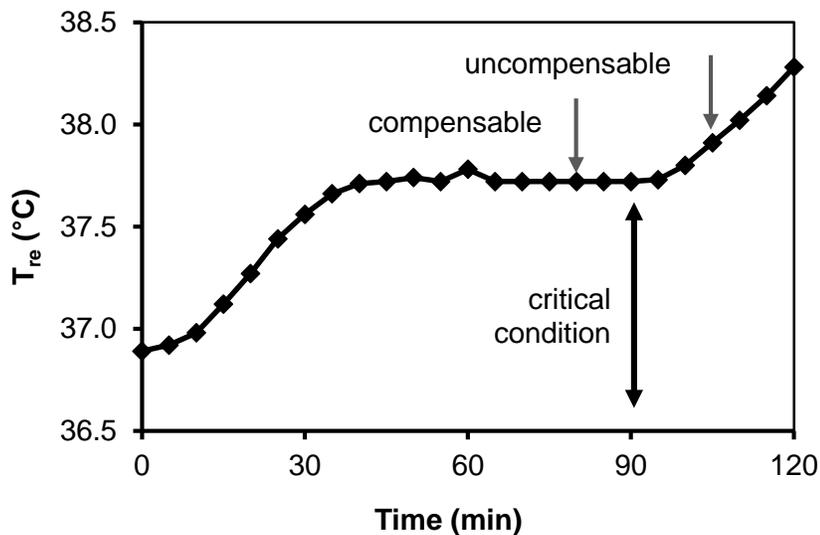
Figure 3.1. The Time Course of T_{re} for an Example Trial with Arrows to Indicate the Critical Condition, the Compensable Condition Established 15 Minutes before the Critical Condition, and Uncompensable 15 Minutes after It.

Bernard, et al. [2005] used the progressive heat stress protocol to find the effect of relative humidity on critical WBGT (WBGT$_{crit}$) for five clothing ensembles that included work clothes (4 oz./yd^2 cotton shirt and 8 oz./yd^2 cotton pants), and cotton coveralls (9 oz./yd^2). The metabolic rate was fixed at approximately 160 W m^{-2} to approximate moderate work. The subjects were exposed to three environments: warm, humid at 70% RH; hot, dry at 20% RH; and a moderate at 50% RH. In the other study, Bernard, et al. [2008] were interested in the effects of varying metabolic rates at a relative humidity of 50%. The three metabolic rates were 115, 175 and 250 W m^{-2} to approximate light, moderate, and heavy work. The characteristics of the participants who took part in these trials are summarized in Table I. All participants were acclimatized.

Table 3.1. Physical Characteristics (Mean ± Standard Deviation) of Participants

	N	Age (yr.)	Height (cm)	Weight (kg)	Body Surface Area (m^2)
Relative Humidity Study (Bernard, et al. 2005)					
Men	9	29 ± 6.8	183 ± 6	97.2 ± 18.5	2.18 ± 0.20
Women	5	31.8 ± 9.1	161 ± 7	63.5 ± 17.2	1.66 ± 0.23
Metabolic Rate Study (Bernard, et al. 2008)					
Men	11	28 ± 10	176 ± 11	81.7 ± 12.0	1.98 ± 0.47
Women	4	23 ± 5	165 ± 6	64.2 ± 18.0	1.70 ± 0.22
Pooled					
Men	20	29 ± 9	179 ± 34	88.7 ± 23.2	2.07 ± 0.41
Women	9	28 ± 8	163 ± 7	63.7 ± 16.6	1.74 ± 0.29

To explore if the metabolic rates should be adjusted for populations with lower BSA, a subset of the data was created for those with a BSA at or below 1.65 m^2. For this group, the metabolic rate was adjusted by multiplying the observed metabolic rate by a nominal BSA of 1.8 m^2 and divided by the individual's BSA. This effectively increased the metabolic rate for those participants with low BSA.

Statistical Analyses

For the case definition, an observation was called Unsustainable (case) if it was uncompensable (15 min. after the critical condition); its control (Sustainable) was the compensable exposure (15 min. prior to the critical condition). In addition, the data at the critical condition were classified as Sustainable if T_{re} was less than 38 °C or if the change in T_{re} was less than or equal to 0.1 °C over the preceding 20 min. The critical condition observation was classified as Unsustainable if T_{re} was greater than or equal to 38 °C, and T_{re} increased by more than 0.1 °C over the preceding 20 min. The method of assigning case status (Sustainable v

Unsustainable) resulted in a cross-over study design. That is, each individual served as their own control, and therefore the data obtained were dependent observations.

To assess the TLV, the exposure metric was the difference between the observed WBGT and the TLV value of WBGT adjusted for metabolic rate. That is, the TLV = 56.7 – 11.5 * $\log_{10}$ (M) [NIOSH 2016]; and the metric was ΔTLV = WBGT$_{observed}$ – TLV.

To characterize the data, descriptive statistics and bivariate distributions of the outcome by exposure were obtained using the SAS functions Proc Univariate and Proc Freq. The association between the exposure metric and the outcome was assessed with SAS Proc Logistic [SAS Institute Inc 2013]. Due to the dependency of the data, a conditional logistic regression model fitted with the binary outcome and a continuous predictor was performed.

Alternative WBGT-based limits were also addressed using conditional logistic regression models using the same binary outcome (Sustainable v Unsustainable). To suggest an alternative adjustment to the TLV only one independent variable was used, that is ΔTLV. The other alternatives used both WBGT and metabolic rate as the independent variables. First, WBGT was verified as the main predictor (p-value < 0.001), then metabolic rate was added to be assessed for confounding and effect modification. The metabolic rate variables used were metabolic rate (M) in W; $\log_{10}$ (M); metabolic rate divided by body surface area (MSA) (W m^{-2}); and $\log_{10}$ (MSA).

The ability of the TLV, and its alternatives to accurately discriminate Sustainable versus Unsustainable was assessed using a Receiver Operating Characteristic curve (ROC curve). The ROC curve graphically displays the predictive accuracy of the logistic regression model, and its area under the curve (AUC) is a measure of the overall ability to discriminate between Sustainable and Unsustainable. A SAS ODS statement along with a request to produce the ROC plotted the fitted logistic regression models [SAS Institute Inc 2013]; the logistic

regressions produced j-ordered pairs of 1-specificity, sensitivity at j probabilities. Working from the premise that a WBGT-based occupational exposure limit functions as a screening method, a cut point of 0.95 for sensitivity was chosen. The AUCs, their correspondent confidence intervals (C.I.), and the p-values from the comparison between the alternative models' AUC against the TLV's AUC, were obtained using R [R Development Core Team 2015], and following the method described by Wu and Wang [2011].

To assess the effect of heat stress for a population that is systematically smaller than the nominal BSA of 1.8m^2, the analysis procedure that was described above was performed for 96 observations corresponding to study subjects with a BSA less than or equal to 1.65 m^2.

Development of Alternative Exposure Models

Logistic regression using Proc log [SAS Institute Inc 2013] was used to find the alternative models' estimates to compare their equivalent threshold limit lines expressed as WBGT = f(metabolic rate) at a case probability=0.05 . A three step process was followed:

1. The weights associated with WBGT and each of the four functions of metabolic rate were determined from the conditional logistic equation based on the full dataset of 3 conditions (compensable, transition, and uncompensable) in 176 progressive heat stress trials. In general, the exposure metric (Ω) was Ω = $β_1$ WBGT + $β_2$ f(M). For instance for MSA, Ω = $β_1$ WBGT + $β_2$ MSA. In other words, this step provided the optimal weighting of WBGT as the alternate function of metabolic rate.

2. A second database of just critical conditions was used to estimate a threshold value for Ω. When the data were rank ordered by increasing Ω, this approximated a dose-response curve. The logistic regression was used based on the progressive count of cases divided by 176 as the dependent variable. The result was log (p / (1-p)) = α + β Ω.

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3. The threshold value for Ω was determined for $p = 0.05$ so that log (p / (1-p)) = -2.94 = α + β Ω. From this, the threshold value for Ω was (-2.94 – α) / β.

Results

Descriptive Statistics

Table II provides the mean, standard deviation and 5% - 95% quantiles for the metabolic rate (M), rectal temperature (T_{re}) and heart rate (HR) for Sustainable and Unsustainable conditions.

Table 3.2. Summary Statistics for Metabolic Rate, Rectal Temperature (T_{re}) and Heart Rate (HR) by Case Status

Outcome	N	Metabolic Rate			Rectal Temperature			Heart Rate		
		Mean	SD	Quantiles 5%-95%	Mean	SD	Quantiles 5%-95%	Mean	SD	Quantiles 5%-95%
Sustainable	273	326.3	103.9	166 - 506	37.6	0.31	37.1– 38.1	108	17	82 - 136
Unsustainable	255				37.9	0.33	37.4 – 38.5	130	20	100 - 164

The frequency distribution of Sustainable heat exposure as a function of ∆TLV began with conditions under the TLV, but it was notable that most of Sustainable conditions were distributed above the TLV. All Unsustainable heat exposures were distributed above the TLV.

Bivariate Analysis

The 2x2 contingency table showed the same trend as the frequency distribution, 255 pair of observations were Unsustainable cases, all of them above the TLV. There were 259 sustainable conditions above the TLV, and 14 under it. Therefore, sensitivity = 1.00 and specificity = 0.05.

For the population with a BSA under $1.65m^2$, there were 49 Unsustainable cases above the TLV, there were no Unsustainable under it. There were 39 Sustainable conditions above, and 8 Sustainable under the TLV, with a sensitivity = 1.00 and a specificity = 0.17.

Multivariate Analysis and ROC Curves

For the ΔTLV, the conditional logistic regression model showed that the odds of being Unsustainable increases 2.5 times per 1 °C-WBGT of difference above the TLV (OR=2.47, C.I. 2.12 – 2.88). The ROC curve had an area under the curve (AUC) of 0.85 (C.I. 0.81 – 0.89), see Figure 2.
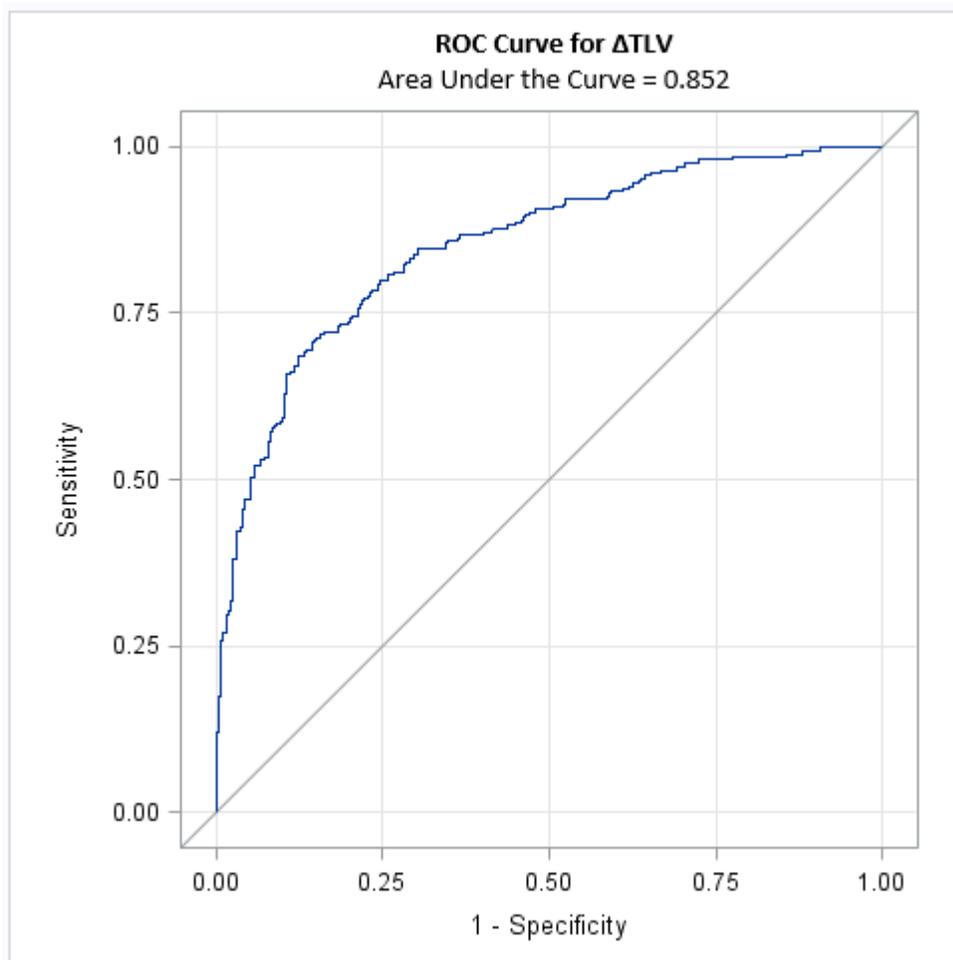
Figure 3.2. ROC and AUC for ΔTLV

There were four alternative OELs developed from the data based on the treatment of metabolic rate. The treatments were metabolic rate (M) in W; $\log_{10}$ (M); metabolic rate divided by body surface area (MSA) (W m^{-2}); and $\log_{10}$ (MSA).

The ORs and their respective confidence intervals were obtained from the conditional logistic regression model. The AUCs for the TLV, and for the alternative models with their confidence intervals, as well as the p-values from the comparison between each one of the alternative models' AUCs against the AUC for the ΔTLV were obtained using R [R Development Core Team 2015], and the method described by Wu and Wang [2011]. For all five models, the odds to become a case were about 2.5, with AUCs between 0.84 and 0.88. A ROC's sensitivity of 0.95 was chosen as optimal operating point (OOP) [Gallop 2001], due that a higher probability for the OEL's prediction of true Unsustainable was preferred over the probability to accurate determine false positives. The specificities were ranged from 0.36 to 0.50; Table III is a summary of these results.

TABLE 3.3. ORs from the Conditional Logistic Models; AUCs and P-Values from the Comparison of the Adjusted TLV to the Alternative Models; and their Specificity at an OOP Sensitivity of 0.95.

Model	OR (C.I.)	AUC (C.I.)	p-value	Specificity at sensitivity = 0.95
ΔTLV				
	2.47	0.85		0.36
	(C.I. 2.12 – 2.88)	(C.I. 0.81 – 0.89)		
AEL_M			ΔTLV v AEL_M	
	2.55	0.85	0.139	0.41
	(C.I. 2.17 – 2.99)	(C.I. 0.81 – 0.89)		
AEL_{log10M}			ΔTLV v AEL_{log10M}	
	2.53	0.84	0.004	0.40
	(C.I. 2.16 – 2.96)	(C.I. 0.79 – 0.88)		
AEL_{MSA}			ΔTLV v AEL_{MSA}	
	2.57	0.88	0.02	0.50
	(C.I. 2.19 – 3.01)	(C.I. 0.85 – 0.91)		
$AEL_{log10MSA}$			ΔTLV v $AEL_{log10MSA}$	
	2.53	0.88	0.02	0.49
	(C.I. 2.16 – 2.96)	(C.I. 0.85 – 0.91)		

For the model using an adjusted metabolic rate for smaller BSAs, the odds to become a case was 2.4 times for the exposed population. The AUC was 0.86, with a specificity of 0.53 at a cut point of sensitivity of 0.95.

Table IV summarizes the development process for an adjusted TLV and the four alternatives. The table also shows the limit lines at a $p=0.05$.

TABLE 3.4. Model Development for the Adjusted TLV and the Four Alternative Models; and the Equivalent Threshold Limit Lines Expressed as WBGT = f(metabolic rate) at a $P=0.05$.

OEL	Alternative Exposure Limit Development
ATLV	$\Omega = 0.903\ \Delta$TLV
	$\log(p/(1-p)) = -4.77 + 0.861\ \Omega$
	$\text{ATLV}_{@p=0.05}$ [WBGT] = 59.1 - 11.5 $\log_{10}$M
AEL: M	$\Omega = 0.936$ WBGT + 0.0188 M
	$\log(p/(1-p)) = -30.3 + 0.795\ \Omega$
	$\text{AEL}_{M@p=0.05}$ [WBGT] = 36.8 – 0.0201 M
AEL: $\log_{10}$M	$\Omega = 0.928$ WBGT + 13.8 $\log_{10}$M
	$\log(p/(1-p)) = -51.0 + 0.770\ \Omega$
	$\text{AEL}_{\log 10M@p=0.05}$ [WBGT] = 67.2 – 14.9 $\log_{10}$M
AEL: MSA	$\Omega = 0.943$ WBGT + 0.0346 M
	$\log(p/(1-p)) = -35.74 + 0.932$ WBGT, MSA
	$\text{AEL}_{MSA@p=0.05}$ [WBGT] = 37.3 – 0.0386 MSA
AEL: $\log_{10}$MSA	$\Omega = 0.928$ WBGT + 13.8 $\log_{10}$MSA
	$\log(p/(1-p)) = -58.0 + 0.931\ \Omega$
	$\text{AEL}_{\log 10MSA@p=0.05}$ [WBGT] = 63.7 - 14.9 $\log_{10}$MSA

Discussion

Table II shows that the mean metabolic rate found among the participants of the present study was 325 W, and the range was from 170 to 500 W [Bernard, et al. 2008]. In the Kuhlemeier, et al. [1977] study, mean metabolic rate was 394 W and again with a wide range (280 – 540 W) based on the study design. While Lind (1970) reported only one group metabolic rate at 350 W, the present and Kuhlemeier studies reflected the range of metabolic rates to promote validity in a wide range of jobs and exposures.

The mean and 95th percentile values for T_{re} among the Sustainable data were 37.1 and 38.1, respectively. These values were very close to those found in Kuhlemeier, et al. [1977], with a mean T_{re} for Sustainable exposures of 37.7 ˚C, and a T_{re} value of 38.2 ˚C at the 95% quantile. These results were lower than the range of T_{re} found in Lind [1970] with a mean T_{re} of 38.2 ˚C; and 38.6 ˚C for the 95% quantile. These T_{re} values fall between the WHO limits of 38.0 °C and 39 °C [NIOSH 2016, WHO 1969]. In the present study mean HR was 106 bpm for Sustainable exposures with a 95th percentile value of 136. The HR values found in Kuhlemeier, et al. [1977] for Sustainable exposures were also very similar than those found in this study; the mean HR was 107 bpm, with a 95th percentile value of 139 bpm.

The distribution Sustainable heat exposure began with Sustainable classifications under the TLV. Most of Sustainable conditions were distributed above the TLV, extending up to 12 ˚C; all Unsustainable heat exposures were distributed above the TLV. The ability of the TLV to discriminate between cases and controls was first assessed by calculating its sensitivity and specificity directly from its 2x2 contingency table. The sensitivity for the TLV was high with a value of 1.00, with a poor specificity of 0.05. It is important to highlight that such sensitivity and specificity were obtained directly from the observations, without taking into account the probability of becoming a case (Unsustainable) from a generalized population.

The assessment of predictive accuracy is a critical aspect of evaluating and comparing models that produce predictions, and the receiver operating characteristic (ROC) curves are commonly used for such purposes when probabilities change with a decision threshold [Gonen 2006]. These ROC curves plotted sensitivity on the vertical axis and 1-specificity on the horizontal axis for all possible cut-points in the study dataset. The AUC was the average sensitivity of the metric over the range of specificities, and was used in the current study as a summary statistic representing the overall performance of an occupational exposure limit. For reference, Shin and Coulter [2009] and Gallop [2001] pointed out that a metric with no predictive value would have an AUC of 0.5, while a metric with perfect ability to predict outcome would have an AUC of 1.

The AUC was 0.85 for the TLV. The AUCs of the four alternative limits were very close with AUCs between 0.84 and 0.88. Generally, all of the metrics had similar capabilities to discriminate between Sustainable and Unsustainable. The ideal occupational limit would to have high values of sensitivity as well as high values of specificity, nevertheless achieving such conditions is very difficult due to practical constraints.

The present study assessed the possibility of using a cut point to improve the OEL's specificity with minimal trade-off of sensitivity. Gallop [2001] called this threshold as the optimal operating point (OOP). Being conscious that any occupational exposure limit must be designed to protect the majority of the exposed population, an OOP of 0.95 for sensitivity was chosen to increase the accuracy of the occupational exposure limit, preventing loss of sensitivity.

Looking at the ROC for the TLV and reducing the sensitivity to 0.95, the specificity increased from 0.05 to 0.36. The increment in the risk associated with the higher threshold plus the uncertainty of the assessment is an important practical constraint related to increasing the cut point to improve specificity, despite the little loss of sensitivity. For instance, the odds ratio for going 2 °C-WBGT above the TLV (p=0.03) had an OR of 6.3, and at 3 °C-WBGT above the

TLV the OR became 15.6 (p=0.33) for an Unsustainable exposure. The ORs pointed to a similar increased risk of exertional heat illness found by Garzon, et al. [2016]. Before making any decision to increase the exposure threshold, it is worthwhile to take into account that Wyndham and Heyns [1973] also found a steep increase in risk for heat stroke over a small range of environmental conditions.

Four alternative OELs based on the statistically significant association between the outcome and WBGT (p-value < 0.001) were developed in the current study. The main model was fitted with WBGT and metabolic rate, which included metabolic rate (M) in W; $\log_{10}$ (M); metabolic rate divided by body surface area (MSA) (W m^{-2}); and $\log_{10}$ (MSA). The odds to become a case was around 2.5 / °C-WBGT for all the models, all with significant and tight confidence intervals.

The OOP chosen for the alternative occupational exposure limits followed the same criteria used for the TLV; that is, the cut-point was set at a sensitivity of 0.95, which was maximized over the specificity. The resultant AUCs for the four alternative OELs had areas between 0.85 and 0.88, with specificities ranged from 0.36 to 0.50. All of the proposed models kept a high sensitivity, decreasing the proportion of false positives above the occupational exposure limit from 8 to approximately 18%.

The accuracy of each one of the four alternative OELs to detect Unsustainable exposures above the threshold, was assessed contrasting their AUCs with the current TLV. Shin and Coulter [2009] stated that such comparison can be executed with a method that exploits the mathematical equivalence of the AUC to the Mann-Whitney U-statistics [DeLong, et al. 1988]. Thus, the ROCs of any two OELs can be compared by evaluating the difference of the AUCs which is asymptomatically normal. It seemed that MSA (reflecting metabolic rate normalized to body surface area) was a better predictor, because those alternative models had larger and statistically significant differences with the TLV's AUC. In addition the sensitivities

were 0.99 and a specificities of around 0.17. Nevertheless, the apparent improvements were statistically significant, but still low (see Table III).

Compared to the TLV, the AUCs for the two BSA alternatives were significantly different, with a slight improvement from 0.85 to 0.88. These AUC's accuracies, however, were not practically different. The slight improvement in the AUCs was seen in somewhat better specificities at the same sensitivity. Again, the improvement was unremarkable going from 0.10 to 0.17.

Despite the widely accepted premise that a high body surface area is beneficial in the heat [Havenith 2001], the present investigation could not find an association between BSA and increased odds to become Unsustainable in the population under study with BSA less than or equal to $1.65m^2$. The distribution in the 2x2 contingency table, the OR, and the AUC were very close to these results from the analysis performed in the whole study population. By the same token, the specificity of the model considering a small BSA at a sensitivity of 0.95, was similar to those resultant from the whole study population.

The five models increased the OEL threshold about 2 ˚C. As it was stated before, this models sacrificed a bit of sensitivity, with some improvement in specificity, but increasing the risk for Unsustainable. Figure 3 shows the comparison among the lines from the current TLV, the adjusted TLV and the other four alternative models.
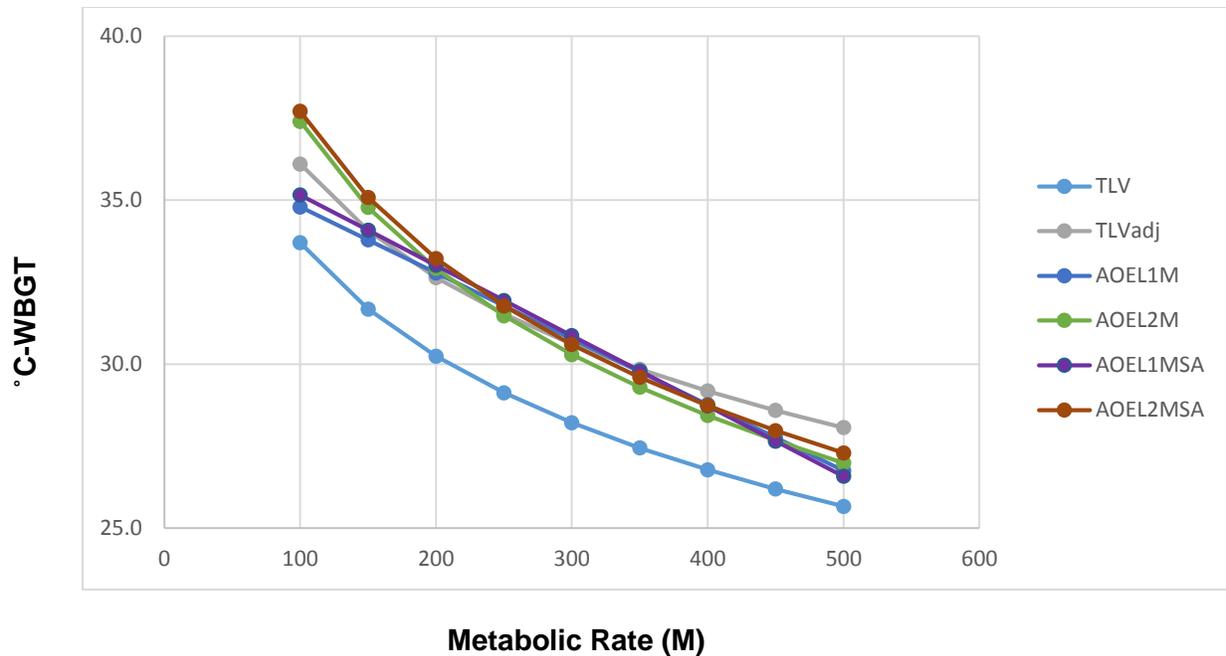
Figure 3.3. Comparison of the TLV to the Five Proposed Models Adjusted for *P*=0.05.

One possible limitation of the present study was that the participants were relatively young with a mean age of about 30 years. Lind, et al. [1970] reported on the average physiological responses of two age groups to exposure below and near the ULPZ and above the ULPZ, finding stable physiological responses and no differences due to age at and below the ULPZ. Age was not a factor in establishing a Sustainable exposure.

Another limitation is that the data obtained in both USF studies were collected on laboratory trials, under controlled conditions with acclimatized participants which were not similar than those present in real work settings, and therefore generalization could be affected.

Although the cross-over design of the present study removes the between-subject variation, the participants' responses to the exposures were likely to be correlated, which complicated the analysis and interpretation of the data. Particularity affecting the accuracy of

our case probability (p=0.05), due that the SAS ROC request uses a logistic regression model instead of a conditional regression.

The observations' dependency did not allow us to directly set a probability of an Unsustainable exposure. The model building process allowed us to estimate the probability for the TLV by using the Adjusted TLV model and find the probability when the intercept value was 56.7, as it is for the TLV. The predicted case probability for the current TLV was 0.01.

Conclusion

The three most important findings from this study were (1) confirming that the TLV is appropriate for heat stress screening; (2) The accuracy to discriminate was assessed through a ROC curve; and (3) establishing the odds ratio for unsustainable exposures, which was relatively large. An increase in WBGT of a couple of degrees above the TLV resulted in ORs on the order of 10. Of course, the current TLV has a high sensitivity, meaning that the exposed working population is protected. Because its specificity is very low, it has a high percentage of false positive cases.

The original TLV was based on few subjects and limited qualitative approach. This study provided data-driven exposure limits. The proposed alternative OELs had also very high sensitivity, and slightly improved specificities compared with the current TLV. The alternative models that were adjusted for body mass index seems to be more accurate to predict Unsustainable heat stress due to their large AUC, its specificity is higher than the TLV and the other alternative models suggested in this paper. Based on the logistic regression results, the current TLV has a case probability of 0.01.

Any decision in decreasing sensitivity in favor of improving the specificity of the OEL must be taken with extreme caution, because of the high probability to become Unsustainable even with little increments of environmental temperatures.

Acknowledgments

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CHAPTER FOUR:

ABILITY OF PHYSIOLOGICAL HEAT STRAIN INDICES TO DISCRIMINATE

BETWEEN SUSTAINABLE AND UNSUSTAINABLE HEAT STRESS

The present is a research paper with multiple authors

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- Study conception and design: Ximena P. Garzón-Villalba; Thomas E. Bernard.

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- Analysis and interpretation of data: Yougui Wu; Ximena P. Garzón-Villalba; Thomas E. Bernard.

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Ability of Physiological Heat Strain Indices to Discriminate Between Sustainable and Unsustainable Heat Stress Exposures

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Running Head: Ability of PHSI to Discriminate Unsustainable Conditions

Abstract

Heat strain results from the body's exposure to heat stress. Heat strain indicators have been used for decades as tools for monitoring physiological responses to work in hot environments. Common indicators of heat strain are body core temperature (assessed as rectal temperature T_{re}), heart rate (HR), skin temperature (T_{SK}), and a composite index called Physiological Strain Index (PSI). Data collected from progressive heat stress trials at USF gave the opportunity to develop an alternative method using physiological heat strain indicators to heat stress exposure assessment to determine the threshold between cases and non-cases, and to assess the accuracy of discrimination of Sustainable and Unsustainable heat exposure. To assess the discrimination ability of the physiological heat strain indices (PHSI), several conditional logistic regression models, and a stepwise logistic regression were performed to find the best combinations of predictors to set a practical equation to predict Unsustainable cases. The accuracy of the models were assessed using receiver operating characteristic curves. Resultant areas under the curve were compared among them to determine which of the models had more accuracy along with its correspondent sensitivity, and its specificity at an optimal operating point for sensitivity at 0.95. Metabolic rate was found as not statistically significant associated with Unsustainable conditions; it was assessed as confounder and effect modifier. To be able to compare the proposed PHSIs models among them, a probability of 0.05 was chosen as cut point. The dependency of the data and consequently the conditional logistic regression used in the analysis, did not allow to obtain the estimated values for the intercept. A logistic regression model performed in a reduced data set with only critical conditions was performed to overcome such limitation. The combination of T_{SK}, HR, and T_{re} was suggested by the stepwise logistic regression as the best model to predict Unsustainable conditions (AUC=0.89). Due its practicability the combination of HR and T_{SK} (AUC= 0.88) could be used to prevent heat stress outcomes in industrial settings.

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Introduction

      Heat stress is the sum of heat generated in the body, plus the net heat exchange between the body and the surroundings, minus the heat lost to the environment by sweat evaporation [Bernard 2012, Havenith 1999, Joubert and Bates 2008, Malchaire 2006, NIOSH 2013]. Heat stress assessment frequently requires thermal indices that account for at least the environment and work demands and some include clothing effects. Heat strain results from the body's exposure to heat stress [ACGIH 2015, NIOSH 2013]; and heat strain indicators have been used for decades as tools for monitoring physiological responses to work in hot environments [Brouha 1960, Fuller and Smith 1981, NIOSH 1972, NIOSH 1986, NIOSH 2013, OSHA 2015]. Common indicators of heat strain are body core temperature, heart rate (HR), and skin temperature (T_{SK}), and a composite index developed by Moran, et al. [1998] called Physiological Strain Index.

      Rectal temperature (T_{re}) is considered an accurate measure of core temperature, it is used commonly in scientific research for heat exhaustion [Dukes-Dobos 1976, Dukes-Dobos and Henschel 1973, Kuhlemeier, et al. 1977, Lind 1970, Moran and Mendal 2002]. A WHO scientific group on health factors involved in working under conditions of heat stress [WHO 1969], stated that deep body temperature rises during work to a level that is not affected by the environment and is only controlled by the rate of work. Nevertheless, under increasing thermal stress, body temperature does not remain dependent only on the rate of work, but it is forced to rise to become sustainable in a higher equilibrium than in cooler environments. This statement corroborated Lind's conclusion that under the upper limit of the prescriptive zone (UPLZ) body's core temperature was dependent primarily on work demands, and that core temperature increases steadily on exposure to climate above the ULPZ [Lind 1963]. Under this approach the WHO's scientific group set 38 ˚C as a limit on deep body temperature for prolonged daily exposures to heavy work [NIOSH 2016]. The investigations on which this limit was established

used as measurement T_{re} [Lind 1963, Lind 1963]. NIOSH states that a core temperature of 39 ˚C is indicative of terminate the exposure during closely monitored conditions [NIOSH 1986]. Current NIOSH recommended exposure limits (RELs) recommends sustainable heat stress conditions under which it is believed that most of all workers may be repeatedly exposed without negative health effects (unacceptable strain), that is keeping core temperature +1 ˚C of normal (37 ˚C) in unacclimatized individuals; acclimatized workers may be able to achieve a sustainable heat strain and to work safely with a core body temperature up to 38.5 ˚C for extended periods of time. Another measure that could be considered as accurate as T_{re} is intestinal temperature, which can be measured with ingestible sensors. This method gives investigators the advantage of monitoring core temperatures on industrial sites during actual work performance [CDC 2011, Minard, et al. 1971, Ruddock, et al. 2014, Yamasue, et al. 2012].

One of the first procedures developed to determine the association between heat stress and heat strain was introduced by Brouha [1960]. He concluded that HR during work and recovery varies according to work load and ambient condition; he found a linear relation between HR increments and ambient temperature [Brouha 1960]. In 1963 [Maxfield and Brouha] reported that during environmental stress, the recovery of the HR was prolonged with the increase in work load and increase of environmental temperature. WHO [1969] recognized HR as an index of heat strain. In their document "Health Factors involved in Working Under Conditions of Heat Stress", they described three possible measures of HR that could be used as an index of thermoregulatory strain: increased HR during or at the end of work; increments of HR along a working period or day; and the time of HR recovery to resting levels after work. This document highlight that sometimes HR at the end of the work shift is less significant than peak rates achieved throughout the work day, because such peak rates could imply peak periods of work or peak of heat exposures. To prevent excessive or cumulative effects, they recommended a HR of 100 beats/minute (b/min) for men exposed to steady light work [WHO 1969]. Minard, et

al. [1971] demonstrated that HR could be used as a physiological index to evaluate heat strain due to its association with metabolic heat load (M). Assessing recovery HR of workers exposed to heat stress was proposed by NIOSH [1986] as a safe and relatively simple method to ensure that heat strain does not exceed pre-established values. NIOSH considered indicators of excessive heat strain a recovery HR of ≥ 90 b/min taken during the third minute of seated rest after a work cycle; and/or a recovery hear rate taken during the first minute of seated rest, minus the third minute recovery HR of ≤ 10 b/min [NIOSH 1986]. Bernard and Kenney [1994] stated that while it is true that HR is a physiological indicator of heat strain, it is important to take into account that momentary peaks of high HR are not physiologically significant, and that sustained high HR are significantly representative of physiological strain. In consequence, they recommended limits based on a range of moving-time averages; for shorter averaging windows, the threshold HR was higher than for the longer averaging windows. Recently ACGIH® recommended discontinuing a heat stress exposure (unsustainable heat stress) if the worker presents a sustained HR ≥180 b/min minus the individual's age in year (e.g. 180 – age) [ACGIH 2006].

The social acceptance and costs for ingestible sensors hinder the possibility of real-time monitoring of core temperature. To cope with this limitation, there has been some attempts to develop indirect measurement of core temperature using T_{SK} [Buller, et al. 2008, Fuller and Smith 1981, Gunga, et al. 2008, Kim and Lee 2015]. T_{SK} can be measured with wired thermistors and thermocouples, and more recently with the use of iButtons. They are accurate and can be used in industrial settings for long periods of time [Smith, et al. 2009, Van Marken Lichtenbelt, et al. 2006]. There are few publications that assess T_{SK} as a single predictor of core temperature, one of them performed by Niedermann, et al. [2014] in which T_{SK} along with skin heat fluxes and HR were used to monitoring core body temperature for early detection of heat strain. Kim and Lee [2015] found that the relationships between T_{re} and T_{SK} were not linear, in

their study forehead temperature was the most stable and valid site to predict T_{re} in a fluctuating ambient temperature. NIOSH [2013] noted that even though T_{SK} is usually about 2 to 4 °C lower than core temperature, and recommends T_{SK} be at least 1 °C below T_{re} [Pandolf and Goldman 1977].

Due to the complexity of the interaction between the factors associated with heat strain, there is no accepted universal physiological strain index. To address this issue, Moran, et al. [1998] proposed the physiological strain index (PSI), which was developed as a simple method based on only two physiological parameters. It uses HR and T_{re} to represent both the cardiovascular and thermoregulatory systems and assuming that both contribute equally to the strain by assigning the same weight function to each one.

$$PSI = 5 (T_{ret} - T_{re0}) * (39.5 - T_{re0})^{-1} + 5 (HR_t - HR_0) * (180 - HR_0)^{-1}$$

PSI evaluates heat strain on a common scale of 0 to 10, where 0 represents no strain and 10 represents strenuous (near maximal) physiological conditions. It can be applied at any time including rest or recovery periods; PSI can rate and compare the heat strain resultant from any combination of climate and clothing [Moran, et al. 1998]. The index has been evaluated in experimental and observational studies [Buller, et al. 2008, Cuddy, et al. 2013, Meade, et al. 2015]. A modified PSI was designed by Gunga, et al. [2008] using T_{SK} instead of T_{re} to determine heat strain through the implementation of a heat flux sensor to monitor real-time core temperatures. Despite its limitations their new device allows continuous heat strain monitoring using a non-invasive method, with an accuracy that differ less than 1 PSI score form the calculations done recording T_{re}.

Workers exposed to combinations of environmental and metabolic heat stress would experience different levels of physiological strain, depending on their body's responses to thermal stress to maintain thermal balance. Such changes in the response of a particular heat

strain indicator (T_{RE}, HR, and T_{SK}) could be very useful to prevent unsustainable heat strain when environmental conditions are difficult to measure; or to assess physiological responses to thermal stress increased by a third factor, besides environment and metabolic rate (M), such as clothing.

Changes in the body's response to heat stress can be used to set a threshold between sustainable and unsustainable heat strain. The objective of the current study is to determine if physiological heat strain indicators T_{RE}, HR, and T_{SK} or their combinations could accurately discriminate Sustainable from Unsustainable heat exposure. It is also of interest in this study to assess the accuracy of PSI to discriminate Unsustainable outcomes.

The association of physiological strain indices and M is difficult to assess, many investigators agree that core temperature is mainly determined by M below certain environmental temperatures [Kuhlemeier and Wood 1979, Lind 1963, Lind 1963, Lind, et al. 1970]. On the other hand, T_{SK} is largely independent of M, and mainly associated with environmental temperatures [Nielsen 1966, Wyndham, et al. 1965]. A secondary objective of the present study is to assess if M increases the accuracy of the PHSI models to predict Unsustainable outcomes.

Methods

For the current study, data collected from progressive heat stress trials at USF gave the opportunity to develop an alternative method to heat stress exposure assessment using physiological heat strain indices (PHSI), to determine the threshold between sustainable and unsustainable heat strain, and to assess the accuracy of discrimination of Sustainable and Unsustainable heat exposure.

The USF progressive heat stress studies [Bernard, et al. 2008, Bernard, et al. 2005] began with an environment that allowed the participants to achieve thermal equilibrium; once it

was established, the environmental conditions (temperature and humidity were slowly increased). T_{re}, HR, T_{sk}, and ambient conditions were recorded every 5 minutes; M was calculated from oxygen consumption via expired gases sampled every 30 minutes in a trial. The transition from a steady value for T_{re} to values that were steadily increasing were marked by the critical condition (see Figure 1). These cross over studies, where their volunteers served as their own control, were designed to test five clothing ensembles that included work clothes (4 oz./yd^2 cotton shirt and 8 oz./yd^2 cotton pants), and cotton coveralls (9 oz./yd^2).

Bernard, et al. [2005] exposed the study participants to a M fixed approximately 160 W m^{-2} to approximate moderate work, and to three environments: warm, humid at 70% RH; hot, dry at 20% RH; and a midrange (50% RH). In the other study, Bernard, et al. [2008] exposed the subjects to three M 115, 175, and 250 W m^{-2}, to approximate light, moderate, and heavy work. It is worth to highlight that all the participants were acclimatized, and every one of them contributed with two outcomes (case and control), therefore due to the study design the obtained observations were dependent.

The outcome was defined as Unsustainable 15 minutes after the critical condition in which the study subject was not able to maintain thermal equilibrium when exposed to a progressive heat stress. A matching control (Sustainable) was the compensable exposure, 15 minutes prior to the critical condition (See Figure 1). The data at the critical condition were also classified as Sustainable if Tre was < 38 °C, and if the change in T_{re} was ≤ 0.1 °C over the preceding 20 minutes [Garzon, et al. 2016]
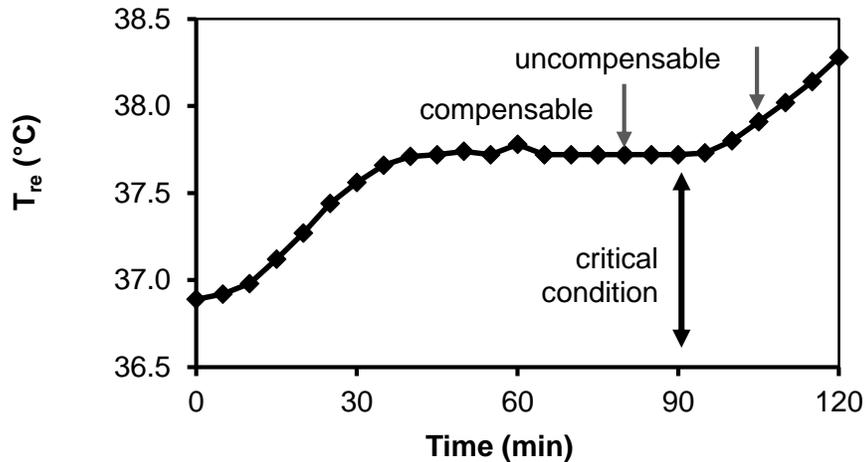
Figure 4.1. The Time Course of T_{re} for an Example Trial with Arrows to Indicate the Critical Condition, the Compensable Condition Established 15 Minutes before the Critical Condition, and Uncompensable 15 Minutes after It.

Statistical Analysis

Once the characteristics of the variables were assessed using Proc Univariate SAS 9.4 [SAS Institute Inc 2013], an alternative method to determine physiological limits between Sustainable and Unsustainable heat stress was explored. Proc Log [SAS Institute Inc 2013] was used to fit conditional logistic regression models with PHSI as predictors, and Unsustainable and Sustainable conditions as the dichotomous outcome. Several models were built, beginning with unadjusted models, which later were fitted with the other PHSI predictors, added one by one until the best combination of predictors was achieved, leaded to increase the predictability of the model.

Main Models

Unadjusted conditional regression models were fitted with a single continuous predictor (T_{re}, HR, $T_{SK,}$ M, or PSI) to assess its association with the outcome; the statistical significance was accepted at the p-value=0.05.

The accuracy of each unadjusted model to discriminate Unsustainable versus Sustainable was assessed using a Receiver Operating Characteristic curve (ROC curve). The ROC curve graphically displays the predictive accuracy of the logistic regression model, and its area under the curve (AUC) is a measure of the overall ability to discriminate between Sustainable and Unsustainable. A SAS ODS statement along with a request to produce the ROC plotted the fitted logistic regression models [SAS Institute Inc 2013]; the logistic regressions produced j-ordered pairs of 1-specificity, sensitivity at j probabilities. Working from the premise that an indicator function as screening method, a cut point of 0.95 for the ROC sensitivity was taken.

Due to its wide recognition as an appropriate measurement of heat strain, T_{re} was used as the comparison predictor. Its ROC curve was contrasted with the other models' curves to determine if the accuracy of the different physiological models differ one from the other. The AUCs, their correspondent confidence intervals (C.I.), and the p-values from the contrast between T_{re} AUC and the other PHSI's AUCs, were obtained using R [R Development Core Team 2015], and following the method described by Wu and Wang [2011].

Multivariate Models

Stepwise logistic regression [SAS Institute Inc 2013], helped to determine which second predictor (T_{re}, HR, T_{SK}) was added into the model, the statistical significance was kept at $p=0.05$. ROCs were generated for the adjusted models, keeping a cut point of 0.95 for sensitivity. The order of the predictors was changed, that is the second predictor was assessed as main predictor, to determine which order improved the model. A covariate was maintained into the model only if it increased the association between the main predictor and the outcome in more than 10%, or if it increased its ability to predict Unsustainable conditions (increasing its AUC).

Depending on the AUC, the conditional regressions' results, and the stepwise regression, a third predictor was added to the models to evaluate if it increased the accuracy of the model's prediction or not.

Metabolic Rate as Effect Modifier

M was added to the unadjusted and to the adjusted models, to assess its effect and to evaluate if its addition into the models increased their predictability.

Once the best model was determined, only the most significant predictors were included to set a practical equation to predict Unsustainable cases.

Predictor Model Building

The conditional logistic regression [SAS Institute Inc 2013] used to analyze dependent observations did not allow to get the intercept (α) values required to build models at any fixed probability. To overcome such limitation, and to be able to use a cut point of p=0.05 for comparison purposes, a three step process was followed:

1. The weights associated with each independent variable were determined from the conditional logistic equation based on the full dataset of 3 conditions (compensable, transition, and uncompensable) in 176 progressive heat stress trials. In general, the physiological metric (Ψ) was $\Psi = \beta_1 x_1 + \beta_2 x_2$. For instance for Tre and HR, $\Psi = \beta_1 T_{re} + \beta_2 HR$. In other words, this step provided the optimal weighting of the physiological values.

2. A second database of just critical conditions was used to estimate a threshold value for Ψ. When the data were rank ordered by increasing Ψ, this approximated a dose-response curve. The logistic regression was used based on the progressive count of cases divided by 176 as the dependent variable. The result was $\log (p / (1-p)) = \alpha + \beta \Psi$.

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3. The threshold value for Ψ was determined for p=0.05 so that log (p / (1-p)) = -2.94 = α + β Ψ. From this, the threshold value for Ψ was (-2.94 – α) / β.

Results

Descriptive Statistics

The progressive heat stress studies included 176 trials, with 352 pairs of Sustainable and Unsustainable exposures over a range of relative humidities and metabolic rates using 29 participants. The characteristics of the study's volunteers are summarized in Table I.

Table 4.1. Baseline Characteristics (Mean ± Standard Deviation) of Participants

	N	Age (yr.)	Height (cm)	Weight (kg)	Body Surface Area (m^2)
Relative Humidity Study (Bernard, et al. 2005)					
Men	9	29 ± 6.8	183 ± 6	97.2 ± 18.5	2.18 ± 0.20
Women	5	31.8 ± 9.1	161 ± 7	63.5 ± 17.2	1.66 ± 0.23
Metabolic Rate Study (Bernard, et al. 2008)					
Men	11	28 ± 10	176 ± 11	81.7 ± 12.0	1.98 ± 0.47
Women	4	23 ± 5	165 ± 6	64.2 ± 18.0	1.70 ± 0.22
Pooled					
Men	20	29 ± 9	179 ± 34	88.7 ± 23.2	2.07 ± 0.41
Women	9	28 ± 8	163 ± 7	63.7 ± 16.6	1.74 ± 0.29

Table II provides descriptive statistics of the predictors, which are mean, standard deviation, and 5% - 95% quantiles for T_{re}, HR, T_{SK}, and M.

Table 4.2. Summary Statistics for Metabolic Rate, Rectal Temperature and Heart Rate by Case Status

N	Rectal Temperature in ˚C			Heart Rate in bpm			Skin Temperature in ˚C			Metabolic Rate in W			PSI scale from 1 to 10		
	Mean	SD	Quantiles	Mean	SD	Quantiles	Mean	SD	Quantiles	Mean	SD	Quantiles	Mean	SD	Quantiles
			5%-95%			5%-95%			5%-95%			5%-95%			5%-95%
273 Sustainable	37.6	0.31	37.1– 38.1	108	17	82 - 136	35.6	0.9	34.0 - 36.9	326.3	103.9	165 - 506	2.81	1.22	0.65 – 4.86
255 Unsustainable	37.9	0.33	37.4 – 38.5	130	20	100 - 164	36.8	0.77	35.5 - 38.1	331.3	104.2	170 - 506	4.44	1.39	2.37 – 6.71

Main Models

Three conditional logistic regression models were fitted with every single PHSI as main predictor. The association between the outcome and T_{re}, HR, T_{SK}, and PSI was found statistically significant (p-value 0.001), unlike M which was not significantly associated with the outcome (p-value 0.13).

The accuracy of the main models to predict Unsustainable was assessed plotting ROC curves. A ROC's sensitivity of 0.95 was chosen as optimal operating point (OOP) [Gallop 2001], due that a higher probability for the OEL's prediction of true Unsustainable was preferred over the probability to accurate determine false positives. Table III presents the results from the conditional logistic models, ORs and p-values from the main associations, as well as their AUCs with their respective specificities.

Table 4.3. Results from the PHSI Models, Their Correspondent AUCs and their Specificities at a Sensitivity of 0.95.

Parameter	OR	p-value	AUC	Specificity
Main models				
TRE	103.00	0.001	0.74	0.15
HR	1.15	0.001	0.80	0.36
TSK	9.90	0.001	0.85	0.41
PSI	5.47	0.001	0.81	0.36
Multivariate models				
TRE+TSK	128.56		0.88	0.47
HR+TSK	1.14		0.89	0.56
TSK+TRE	10.35		0.88	0.47
TSK+HR+TRE	9.65		0.89	0.53
Models adjusted for M				
HR+TSK+MW	1.15		0.90	0.62
TSK+HR+TRE+MW	8.39		0.90	0.59
PSI + MW	9.35		0.81	0.34

Multivariate Models

Six conditional regression models were fitted with the PHSI predictors (the three main predictors plus each one of the others), to assess which was the best combination to improve the predictability of each main model. We selected the pair that increased the association between the main predictor and the outcome in more than 10%, or if the increment on the AUC was at least 5%.

Stepwise regression was used to determine which other PHSI could be introduced into the model, and which predictors' combination would be the best to increase the model's prediction ability. The combination of T_{sk}, HR, and T_{re} was found by the stepwise logistic regression as the best model to predict Unsustainable cases (OR=9.65, C.I. 5.73-16.26), with an AUC of 89%, Table III shows the results from the best combination for each one of the physiological indices.

Models Adjusted for Metabolic Rate

M was found as not statistically associated with Unsustainable, it was assessed for confounding and effect modification in the unadjusted and adjusted models. M was found as a confounder for the models with T_{re} and/or T_{SK} as predictors (increasing respectively the ORs 159% and 46%), the effect modification was not statistically significant for the model with T_{re} as main predictor. For the model with T_{SK} as main predictor, the effect modification had a marginal significance (p-value=0.0572).

There was a slightly increment in the OR when M was added to the model with HR as only predictor (from 1.15 to 1.19), the AUC remained the same. In the model that had PSI as predictor, M was found statistically significant (p-value< 0.001), it increased the OR in around 71%, its interaction term was found as not significant (p-value=0.223), and was deemed as a confounder for the main association.

The model with T_{re} and T_{SK} as predictors, the fitting of M into the model decreased its OR 39%, and its AUC remained the same. M was found as a confounder for this model. The OR from the model with HR and T_{SK} as predictors as well as its AUC increased 1% once M was fitted. M was not statistically significant in the model with T_{SK} and T_{re} (in that order). And was found as not statistically significant in the model that used the combination of T_{SK}, HR and T_{re} as predictors.

Predictor Model Building

Table IV reports the resulting physiological limits for the PHSI models at a $p=0.05$. The first row on each index have the Psi (Ψ) from the multiplication of betas from the conditional logistic regressions times the correspondent values of each index, on the whole data set. The second row have the estimates yielded by the logistic regression model were the outcome was the frequency of critical conditions at each ranked value of the index Ψ, divided by the total of critical conditions. On the bottom of the same row are the threshold limit lines at $p=0.05$, along with the equivalent values on ˚C and bpm.

Table 4.4. Estimates from the Conditional Regression Models and Logistic Regression Models, PSI Calculation and PHSIs Indices at P=0.05

PHSI Model	Conditional Regression
T_{re}	$\Psi = 4.64 * T_{re}$
	Logistic Regression
	$\log(p/(1-p)) = -204.7 + 1.17\,\Psi$ Threshold at p 0.05 = 172 equivalent to 37 ˚C
HR	**Conditional Regression**
	$\Psi = 0.1404 * HR$
	Logistic Regression
	$\log(p/(1-p)) = -11.17 + 0.68\,\Psi$ Threshold at p 0.05 = 12.1 equivalent to 100 bpm
T_{SK}	**Conditional Regression**
	$\Psi = 2.29 * T_{SK}$
	Logistic Regression
	$\log(p/(1-p)) = -95.8 + 1.15\,\Psi$ Threshold at p 0.05 = 80.74 equivalent to 36 ˚C
$T_{re} + T_{SK}$	**Conditional Regression**
	$\Psi = 4.86 * T_{re} + 2.37 * T_{SK}$
	Logistic Regression
	$\log(p/(1-p)) = -199 + 0.744\,\Psi$ Threshold at p 0.05= 263.8 equivalent to T_{re} 37 ˚C + T_{SK} 36 ˚C
$HR + T_{SK}$	**Conditional Regression**
	$\Psi = 0.135 * HR + 2.18 * T_{SK}$
	Logistic Regression
	$\log(p/(1-p))= -55.6 + 0.587\,\Psi$ Threshold at p 0.05= 89.7 equivalent to HR 100 bpm + T_{SK} 36 ˚C
$T_{SK} + T_{re}$	**Conditional Regression**
	$\Psi = 2.33 * T_{SK} + 4.85 * T_{re}$
	Logistic Regression
	$\log(p/(1-p)) = -199.4 + 0.75\,\Psi$ Threshold at p 0.05= 263.4 equivalent to T_{SK} 36 ˚C + T_{re} 37 ˚C
$T_{SK} + HR + T_{re}$	**Conditional Regression**
	$\Psi = 2.27\,T_{SK} + 0.114 * HR + 2.11 * T_{re}$
	Logistic Regression
	$\log(p/(1-p)) = -97.9 + 0.56\,\Psi$ Threshold at p 0.05= 169.77 equivalent to T_{SK} 36 ˚C + HR 100 + T_{re} 37 ˚C

AUC Contrast

The model fitted with T_{re} as predictor was chosen as comparison model, its accuracy to predict Unsustainable cases was contrasted with the other PHSI models. Table V shows the

AUCs, their correspondent C.I., and the values from the contrast between the PHSI models'

AUC against the T_{re}'s AUC. These results were obtained using R [R Development Core Team

2015], and following the method described by Wu and Wang [2011]. Figure 2 shows the

contrast between T_{re} model's ROC and the model fitted with HR and T_{SK} as predictors. There is

an evident 13% of difference between the AUCs.

Table 4.5. AUCs and their Correspondent C.I., and P-Values from the Comparison of the T_{re} Model to Other PHSI Models

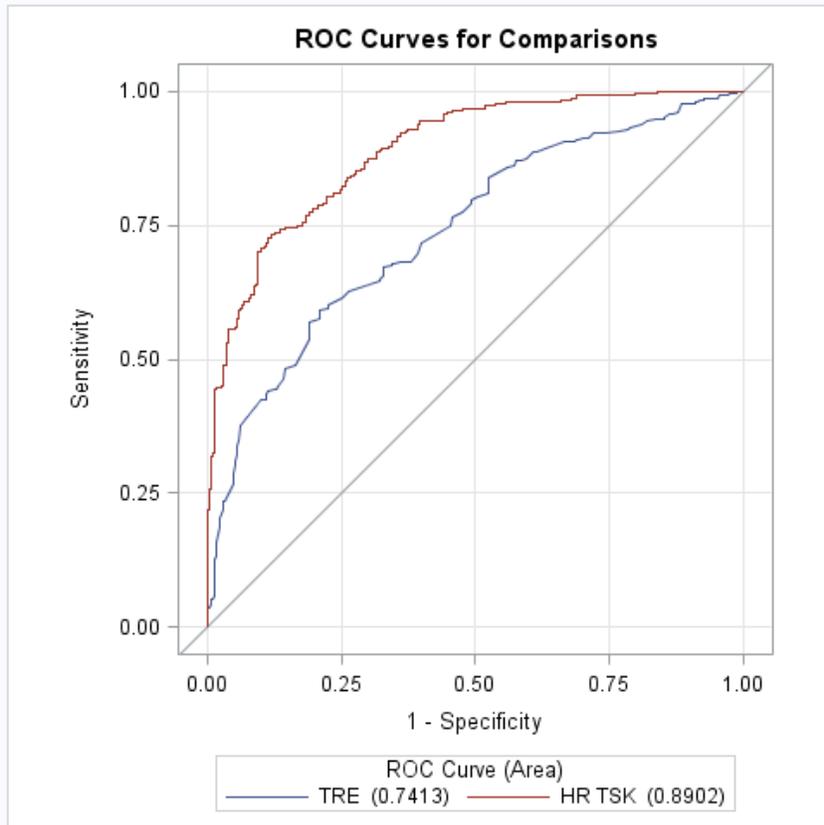| Model	AUC (C.I.)	p-value
T_{re}		
	0.74 0.70 - 0.78	
HR		T_{re} v HR
	0.80 0.77 - 0.84	0.003
T_{SK}		TSK
	0.85 0.82 - 0.89	0.001
T_{re} + T_{SK}		T_{re} v T_{re} +T_{SK}
	0.88 0.85 - 0.91	0.001
HR + T_{SK}		T_{re} v HR + T_{SK}
	0.89 0.86 - 0.92	0.001
T_{SK} + T_{re}		T_{re} v T_{SK} + T_{re}
	0.88 0.85 - 0.91	0.001
T_{SK} + HR + T_{re}		T_{re} v T_{SK} + HR + T_{re}
	0.89 0.87 - 0.92	0.001
PSI		T_{re} v PSI
	0.81 0.77 - 0.85	0.001

Figure 4.2. Contrast between T_{re}'s AUC and HR T_{SK}'s AUC

Discussion

Heat strain is the consequence of the exposure of human body to heat stress [ACGIH 2015, CDC 2013]. Many compensatory mechanisms such as increments in core temperature, HR, and sweating are triggered to maintain the body's thermal equilibrium [ACGIH 2015, NIOSH 1972, WHO 1969]. When this physiological response is not effective to keep a sustainable core temperature, heat is stored in the body leading to an increment of core temperature; the level of physiologic strain increases along with increasing heat stress exposure [NIOSH 2013, Parsons 1999].

Heat stress assessment frequently requires thermal indices to develop and implement control measures. Nevertheless, there are some important limitations to take into account when

using thermal indices, such as that they were validated in a narrow range of thermal environments, and frequently workers are exposed to heat stress above the recommended occupational exposure limits [Logan and Bernard 1999]. Also, the efficacy of environmental heat indices' estimates would be affected by the use of work clothing and other types of personal protective equipment, therefore there is no effective method to accurately determine such exposure.

For the aforementioned reasons, and being conscious that heat strain indicators have been used for more than 50 years as tools for monitoring physiological responses to work in hot environments [Brouha 1960, Fuller and Smith 1981, NIOSH 1972, NIOSH 1986, NIOSH 2013, OSHA 2015], the present study's purpose was to assess if physiological strain indices or their combinations accurately discriminate whether heat exposure is sustainable for long periods of time or not.

The USF progressive heat studies provided a data set with physiological strain values (T_{re}, HR, and T_{SK}) resultant from the exposure to a wide range of combinations of M and environmental temperatures, which allowed us to explore occupational exposure limits based on physiological strain indices.

It is worth remembering that our study considered Unsustainable (case) if it was uncompensable (15 min. after the critical condition); its control (Sustainable) was the compensable exposure (15 min. prior to the critical condition). In addition, the data at the critical condition were classified as Sustainable if T_{re} was less than 38 °C or if the change in T_{re} was less than or equal to 0.1 °C over the preceding 20 min. The critical condition observation was classified as Unsustainable if T_{re} was greater than or equal to 38 °C, and T_{re} increased by more than 0.1 °C over the preceding 20 min.

Main Models

Rectal Temperature

T_{re} is well known for its precision to determine heat exhaustion. Our population under study presented a mean T_{re} of 37.6 ˚C, and 38.1 ˚C at the 95% quantile for sustainable conditions, and a mean T_{re} of 37.9 ˚C, with 38.5 ˚C at the 95% for unsustainable conditions. These mean values are below the value recommended by the WHO's scientific group, which in 1969 set 38˚C as an advisable limit value of deep body temperature for prolonged daily exposures to heavy work [NIOSH 2016]. The values corresponded to the 95% percentile are under the limits established by the NIOSH RELs (38 ˚C for unacclimatized individuals, and 38.5 ˚C for acclimatized) as a safety core body temperature to work for extended periods of time. Contrary to what could had been expected, the present study found an AUC of 0.74 for T_{re}, with a very low specificity of 0.15 at the OOP of 95% for sensitivity.

Heart Rate

Brouha [1960] found that HR varies during work and recovery according to M and environmental conditions, he concluded that there is a linear association between HR and ambient temperature. This finding was underpinned by Maxfield and Brouha [1963] who concluded that recovery HR was prolonged with increasing M and increments on environmental temperature. The present study had the opportunity to assess HR under different combinations of M and environmental conditions (ambient temperature and humidity). A mean HR of 108 beats per minute (bpm), with a highest value (95% quantile) of 136 bpm was found for Sustainable conditions; and a mean of 130 bpm with 164 bpm as highest value for Unsustainable. ACGIH® recommends discontinuing a heat stress exposure if the worker presents a sustained HR ≥ 180 bpm minus the individual's age in years [ACGIH 2006]. The accuracy to predict Unsustainable conditions using HR resulted in an AUC of 0.80, with a specificity of 0.36 at an OOP for sensitivity of 95%.

Skin Temperature

This physiological strain index has been widely accepted due to its accuracy and its easy use for long periods of time on industrial settings [Smith, et al. 2009, Van Marken Lichtenbelt, et al. 2006]. There are few publications that assess T_{SK} as a single predictor of core temperature, Niedermann, et al. [2014] concluded that multiple physical and physiological parameters at different body sites should be measured for a reliable prediction of body temperature. The present study collected data from skin thermistors located in four body sites (arm, chest, thigh, and calf). The mean T_{SK} for Sustainable was 35.6 ˚C, with a high value of 36.9 ˚C (95% quantile); and for Unsustainable a mean value of 36.8 ˚C with 38.1 ˚C at the 95% quantile. T_{SK} is usually about 2 to 4 ˚C lower than core temperature [NIOSH 2013], therefore it is recommendable to maintain T_{SK} at least 1 ˚C below T_{re} for prolonged exposures to heat stress [Pandolf and Goldman 1977]. Our study found an AUC of 0.85 for T_{SK} as single predictor of Unsustainable conditions, with a specificity of 0.41 at an OOP of 0.95 for sensitivity.

Physiological Strain Index

PSI was developed by Moran, et al. [1998] as a physiological strain index based on T_{re} and HR, assuming that both variables contribute equally to the strain, the same weight was assigned to each. It evaluates heat strain on a nominal scale from 0 to 10, where 0 represents no strain, and 10 represents near maximal physiological conditions. Our study found a PSI mean of around 3, and a value close to 5 at the 95% quantile for Sustainable conditions, and a mean of about 4, with a 95% quantile of 7 for Unsustainable. The accuracy to predict Unsustainable for PSI resulted in an AUC of 0.81, with a specificity of 0.36 at the OOP of 0.95 for sensitivity.

Multivariate Models

Rectal Temperature Plus Skin Temperature

The OR between T_{re} and the outcome was increased by approximately 25 % once T_{sk} was added to that model, in the same token, its AUC increased 14%, and its specificity increased from 0.15 to 0.41 at a sensitivity of 0.95.

Heart Rate Plus Skin Temperature

The model fitted with HR as main predictor and T_{SK} as covariate had the largest AUC (0.89), and the highest specificity compared with the other models. While is true that the OR from the main association between HR and the outcome remained almost the same, once T_{sk} was added to such model the accuracy to predict Unsustainable conditions was reflected in an AUC that increased 9%, with a specificity that improved 20%, from 0.36 to 0.56. Due to its practicability and easy implementation, this model could be used in industrial settings to predict unsustainable heat exposures at low cost.

Skin Temperature Plus Rectal Temperature

Once T_{re} was added as a covariate, the OR between T_{SK} and the outcome increased around 5%, its AUC increased 3% compared with the unadjusted model. The specificity increased 6% at an OOP of 0.95 specificity.

Skin Temperature Plus Heart Rate Plus Rectal Temperature

The addition of HR to the model fitted with T_{SK} and T_{re} increased the AUC only 1 %; its specificity increased considerably, from 0.47 to 0.53. As it is reflected with these results, the accuracy to predict Unsustainable for the model with T_{SK} as single predictor, did not improve much with the adjustment for T_{re}, and it did not improve with the addition of HR. This model was found by the stepwise regression [SAS Institute Inc 2013] as the best combinations of indices to predict Unsustainable cases. Nevertheless, the accuracy to predict cases kept practically

identical contrasted to the model with only T_{SK} and T_{re} as predictors, although the specificity of the model did increase, being a proposed OEL, the prediction of true Unsustainable (sensitivity) is preferred over the probability to accurate determine false negatives (specificity). Therefore it is difficult to state that the model with the three variables would be preferred over that with HR and T_{SK} as predictors.

It is important to highlight that we are discussing only the main models and the best multivariate models; that is, only those models adjusted for a second variable or a third statistically significant, and that increased the main model AUC at least 5%.

Adjusting for Metabolic Rate

M is considered as a measure of internal heat generation, and it is closely related with body core temperature. The achievement of thermal equilibrium depends on the amount of heat exchange as a function of M and the heat gained from the environment. The procedures for assessing M are designed for short duration activities. For long period exposures there are tables of energy expenditure, pitifully they are not accurate, and have been reported errors as high as 30% [NIOSH 2016].

ACGIH [2015] recommends an exposure limit of 30 ˚C-WBGT for a light workload (117-233 W), 26 ˚C-WBGT for a moderate workload (234-407 W), and 25 ˚C-WBGT for a heavy workload (407 -581 W). The present study had the opportunity to assess physiological heat strain indices in a variety of combinations of light, moderate, and heavy M and environmental conditions. The mean M for Sustainable conditions was 326.3 W, and 506 W at the 95% quantile. The mean M for Unsustainable was 331.3 W, keeping the same 506 W at the 95% quantile, see Table III.

The present study found M as not statistically associated with Unsustainable. Due to the widely accepted association between environmental conditions and M [ACGIH 2015, ISO 1989,

Ramsey 1995, Ramsey, et al. 1983], it was assessed for confounding and effect modification. M behaved as a confounder in all the models where T_{re} was present, and as a confounder and as a marginal effect modifier (p-value=0.0572) at a significance on 0.05 for the models with T_{SK} as predictor. The confounding effect is related with the close association of M with body core temperature, therefore the assessment of the effect of M to predict Unsustainable conditions is uncertain, and even more complicated by the fact that it is very difficult to accurately measure M in groups of individuals, due that it depends of how each body reacts to different workloads.

AUC Contrast

T_{re} was chosen as comparison model because T_{re} has been used as predictor of unsustainable heat exposure for decades [Brouha 1960, Fuller and Smith 1981, NIOSH 1972, NIOSH 2013, OSHA 2015]. The resultant AUC for the model with T_{re} as main predictor was 0.74, and it was the lower area under the curve among the seven models assessed, followed by HR with an AUC of 0.80. PSI had a slightly better AUC, nevertheless the best main single predictor was found T_{SK}, see Table IV.

Among the models with two predictors, HR plus T_{SK} had the best AUC 0.89, which was 15% larger than T_{re}'s AUC. This model also has the best specificity (0.56), meaning that if it is use as a predictor of Unsustainable, this model will detect 95% of true unsustainable conditions, and 56% of true sustainables, therefore percentage of false positives will be lower compared with the other models.

The model recommended by the stepwise regression [SAS Institute Inc 2013], as the best combination of variables (T_{SK}, HR and T_{re}) to detect Unsustainable conditions yielded the same AUC than the model with HR and T_{SK}, therefore it was 15% larger than the comparison AUC, but the specificity of this model was 3% lower than the model HR +T_{SK}. For practical reasons this model is not easy to apply, due to the limitations associated with T_{re} measurements

(discomfort, prejudice, difficult to measure in industrial settings). Therefore, despite it was statistically chosen as the best model, comparing its advantages and disadvantages against the model adjusted for HR+T_{SK}, the second seems to be more effective to predict Unsustainable conditions in real work settings.

A possible limitation of this study is that the data obtained in both USF studies were collected on laboratory trials, under controlled conditions with acclimatized participants which were not similar than those present in real work settings, and therefore generalization could be affected. Nonetheless, this probable lack of generalization could have been attenuated by the fact that the study volunteers were exposed to a large combination of M and environmental conditions (ambient heat and humidity).

Another limitation was the dependent observations from the cross-sectional design of the USF Progressive Heat Studies. Such dependence hindered the possibility to find the estimates for the proposed PHSI at a probability of 0.05. Which drove us to manipulate the data in order to assess the predictability of the model in a data set using just the critical conditions (before becoming cases), and to create a new metric with the combination of the estimates for the intersection and betas from the conditional logistic models, which was used as a predictor in consequent logistic regressions were the outcome was the proportion of critical conditions related with such metric.

Conclusion

The present study found that physiologic heat strain indices (T_{re}, HR, and T_{SK}) can accurately predict Unsustainable heat stress exposures. There was a progressive improvement in the ability to predict Unsustainable conditions from T_{re} to HR, to T_{SK} with AUCs from 0.74, 0.80, and 0.85, respectively. Adding a second predictor had only a marginal improvement (3 to 4%). PSI had an accuracy barely better than T_{re} and HR alone; its ability to predict

Unsustainable conditions was between 4 to 8% less than the other multivariate physiological indices. HR plus T_{SK} was found as a very accurate and practical model that can be used in industrial settings, it would have an easy and economical implementation, well accepted by the workers.

Acknowledgments

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CHAPTER FIVE:

CONCLUSIONS

The second chapter of this dissertation (BP Study) demonstrated that heat stress is a hazard for workers exposed for extended periods of time to ambient conditions above thermally neutral environment. We found evidence that the risk to present exertional heat illness and acute injuries steeply increased with rising temperatures (ORs of 1.4 and 1.06 respectively). The odds to present an exertional heat illness was described by an interaction between the day of heat exposure and the day before when WBGTmax was above 28 °C (ORs from 1 to 10.4).

Because the WBGT based TLV is used worldwide, we wanted to assess its accuracy to discriminate unsustainable heat stress exposures. The third chapter of this dissertation (WBGT Validation Study) used conditional logistic regressions and the receiver operator characteristic (ROC) curve to assess the TLV. ΔTLV was used as the exposure metric, which was the difference between the observed WBGT and the TLV value adjusted for metabolic rate. Unsustainable heat stress was the outcome in a logistic regression that yielded a risk of 2.5 per 1°C-WBGT of difference between the current TLV and the observed WBGT. TLV was found as extremely sensitive to predict unsustainable conditions (sensitivity = 1.00). While it is true that the percentage of false positives due to an extremely low specificity (0.05) could be considered as a limitation, it is important to highlight that an occupational exposure limit is designed to protect the majority of the exposed workers, a higher prediction of true cases is preferred over the probability to accurately determine false positives. Such decision does not convey major

implications, but the other way around could be associated with an increment in morbidity and mortality associated with heat exposure. Alternative metabolic rate based models were also developed and assessed using the same approach used to evaluate the current TLV. Those alternative models sacrificed a little percent of sensitivity in favor of an improvement in their specificity, trying to maintain a high predictability of unsustainable conditions (sensitivities from 0.84 to 0.88). Any decision to apply these alternative models have to take into account the risk to become a case associated with heat stress increases exponentially with raising environmental conditions. Taking into account that more than fifty years ago the investigators that set the current TLV did not have the technology that is present today, we can conclude that they succeeded in they aim.

Sometimes it is not practical to use environmental indices to evaluate heat stress. Assessing heat strain was examined on chapter four as an alternative approach; physiologic heat strain indices were found as accurate models to predict Unsustainable heat exposures (AUCs from 0.74 to 0.85. The addition of a second predictor did not significantly improve the predictability of the models (AUCs from 0.88 to 0.89). The prediction ability of PSI was lower than T_{SK}, and even lower that all the adjusted PHSI models assessed. The accuracy to predict Unsustainable conditions of the adjusted PHSI models were very similar to those found for the environmental models reported in chapter three (AUCs 0.85 $\pm$ 4). It is noteworthy that the specificity of the PHSI adjusted models at a sensitivity of 0.95 are somehow better than the environmental models, specificities of 0.47 to 0.53 for the PHSI, compared with specificities of 0.36 to 0.49 at the same sensitivity cut point. The combination of heart rate and skin temperature had a high sensitivity, and better specificity than the other PHSI. Its implementation in industrial setting seems to be more practical, well accepted and economical than other physiological strain indices commonly used, and could be a good option to replace or as a complement of environmental indices.