Jon Deaton, Diana Gong, Anna Jaffe
BIOE 141B
1/11/17

Milestone 1

1.0: Project Overview

Need statement: People uneducated about and at risk for non-exertional heat stroke in hot regions of India need a method to prevent the likelihood of experiencing heat stroke to decrease mortality.

To address our need statement, we are creating and testing a heat stroke risk prediction wearable device. The overall concept is a system of sensors that take environmental and the user's physiological parameters and connect to a mobile phone to estimate heat stroke risk. A complete project includes sub-projects of development of algorithms for risk assessment, wearable hardware, mobile-software, and experimental testing procedures; however, we have chosen to focus only on the first and last components (depicted in Figure 1) during BIOE 141A/B.

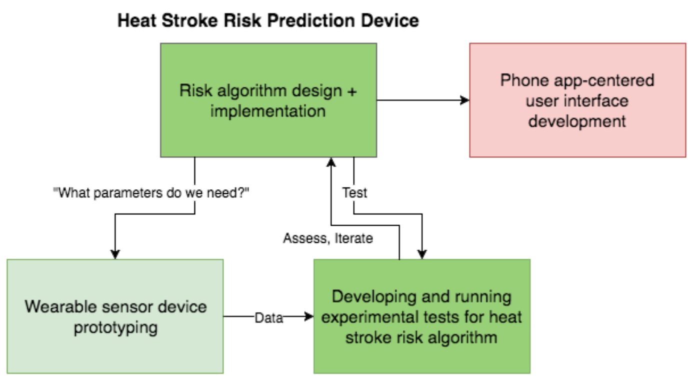

Figure 1: Complete concept subcomponent relationships and intended focus. Red indicates an area that we will not be addressing during BIOE 141A/B. Shades of green indicate areas that we will be addressing with our milestones, with dark green representing more focus and light green representing less focus.

We intend to implement a prototype that senses relevant parameters and need not necessarily be wearable, minimally intrusive, or connect wirelessly to a phone, as we aim to prove concept viability rather than produce a ready-to-use device. Our concept (Figure 2) involves sensors connected to a microprocessor that relays information to a computer, which predicts heat stroke risk using machine learning algorithms. By the end of BIOE 141B, we aim to have developed hardware and software that allow us to accurately sense and predict heat stroke, as well as a series of experimental tests verifying that our device functions as expected.

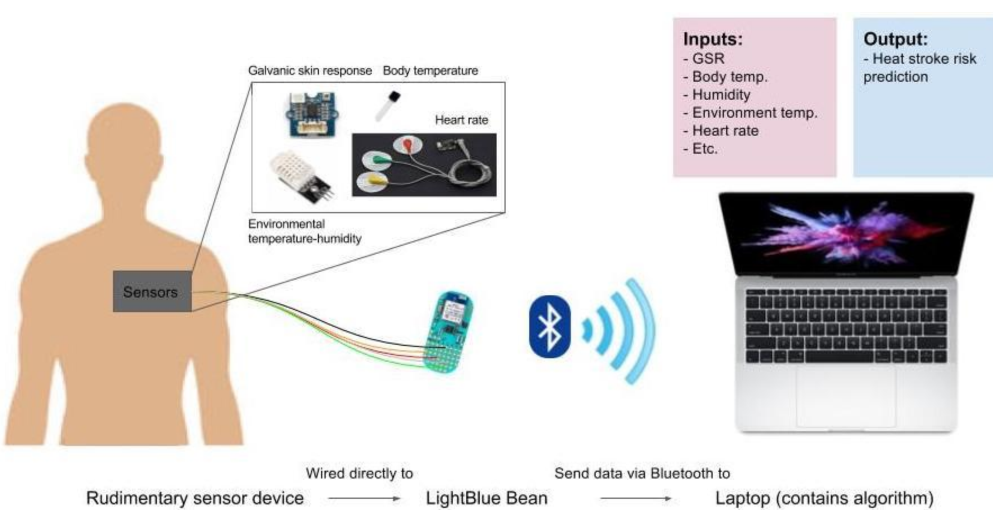

Figure 2: Graphic depicting our concept of a heat stroke risk prediction wearable device prototype.

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1.1: Milestone Overview

<u>Milestone 1:</u> Obtain patient, clinical trial, or study data and existing models on heat stroke risk assessment and prediction.

Milestone 1 is a key step for our project because the information collected will form the basis of our heat stroke prediction algorithm. We will create a matrix containing patient data on environmental and physiological conditions relevant to heat stroke, as well as patient outcomes. Our milestone thus involves finding heat stroke cases in the literature, extracting data from these studies, and compiling comparable parameters. Additionally, we will research existing models and equations relevant to heat stroke prediction to have a starting basis for our prediction algorithm that we will develop in future milestones. We are measuring milestone success by quantity of patient data, since a high volume of data will help minimize overfitting in our prediction algorithm. We aim for 50 sets of patient data and at least three model-based heat stroke prediction algorithms.

1.2: Milestone Methods

Our approach consisted of searching for patient data from documented heat stroke cases because we will use regression analysis with existing data to predict heat stroke in future situations. We examined 15 research articles (**Appendix A**) recommended by our clinical mentor, Dr. Lipman, to obtain patient heat stroke data. We looked for environmental and physiological information potentially correlating with heat stroke development. Our goal was to compile data into a single spreadsheet, with patients as rows and patient features and outcomes as columns.

We also searched for models estimating heat stroke. Our approach was two-fold: while searching through medical literature for individualized heat stroke cases, we considered general trends in patient and aggregate data to postulate what risk factors and signature characteristics were indicative of heat stroke. Additionally, we looked for literature attempting to predict heat stroke, perceived temperature, or core body temperature.

1.3: Milestone Results

We obtained 109 patient heat stroke data sets from medical literature (**Appendix B**). We also have an arbitrarily large number of data points from people with normal environmental and physiological conditions through writing a program (**Appendix C**) that generates normal patient data points. Each patient has up to 76 possible features (columns) that describe environmental conditions, physiological conditions, and heat stroke outcome (Figure 3). Given that these patient data points have missing fields, we also created code (**Appendix C**) that fills in missing values based on physiologically normal defaults, meaningless defaults, (e.g., “None” for a “Location” field), or defaults set as some other function of data from the same or a different column. This enables us to use our dataset for regression analysis, cross-validation, and prediction testing in subsequent modules.

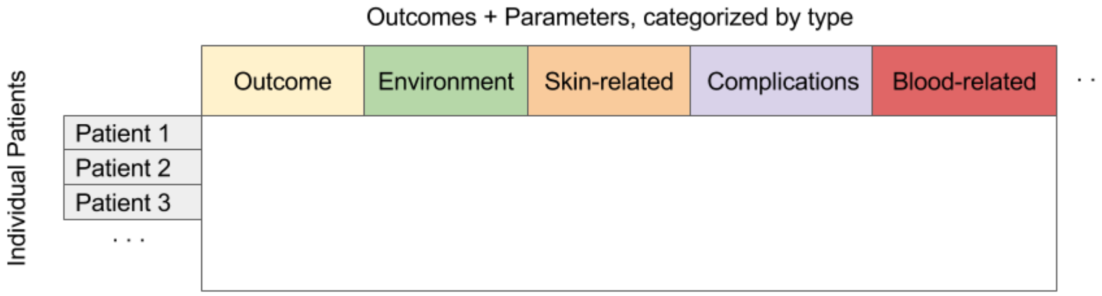

Figure 3: Representative graphic of spreadsheet of individual patient heat stroke data. Each patient is represented by a row, and each column is a patient outcome or parameter possibly relevant to heat stroke. For ease of reading, related parameters have been grouped. The actual spreadsheet is filled with numbers obtained from medical literature.

In addition, although we found/recorded aggregate patient data (e.g., “75% of patients who had heat stroke in this study were overweight”), these data are not in our individual data spreadsheet, as they cannot be easily used in regression analysis (Musicant et al., 2007), and we intend to use them in model-based predictions (Figure 4).

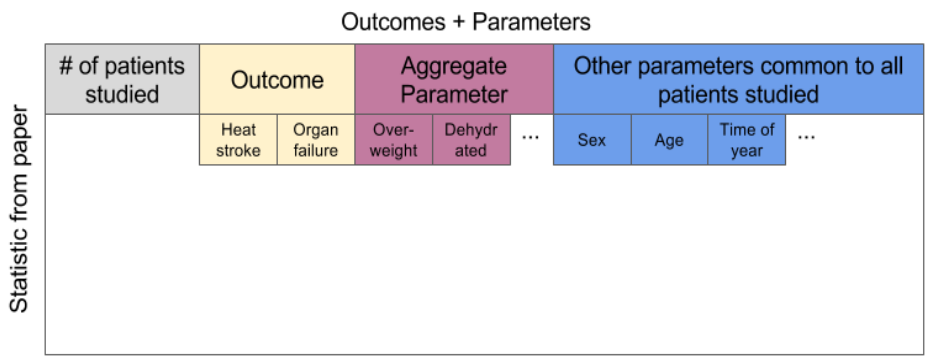

Figure 4: Representative graphic of aggregate data spreadsheet of individual data. Each aggregate data statistic is represented by a row, and the columns are the number of patients studied, patient outcomes, aggregate parameters, and other parameter common to patients involved in the statistic. The actual spreadsheet is filled with numbers obtained from medical literature.

To supplement the aforementioned data collected from medical literature, we also accumulated four model-based predictions (described in Appendix D) that we intend to use and test to predict heat stroke risk:

1. Hypothalamic regulation failure
2. Heat Index (HI)
3. Wet Bulb Globe Temperature (WBGT)
4. Estimation of Core Temperature (CT) from Heart Rate (HR)

1.4: Milestone Interpretation/Discussion

- We accumulated 109 patient data points and 4 model-based predictions.
    - We have >50 positive (heat stroke) data points. We were unable to obtain negative data in literature, so we wrote a program that generates these data.
    - We met our success metric of at least 3 model-based predictors, as we have 4 that we intend to use and test.
- We originally set the due date for Milestone 1 as 12/10/16, but we extended our final milestone report deadline to the end of week 1 of winter quarter (1/15/17; see Appendix E for Gantt chart). This extension was warranted because data collection is a critical part of our project, and it can occur concurrently with initial algorithm development. By meeting the success criteria that we set, we have completed this milestone.

1.5: Supporting Material/Appendices

Appendix A: List of articles from Dr. Lipman:

1. Austin MG, Berry JW. Observations on one hundred cases of heatstroke. J Am Med Assoc. 1956;161(16):1525-1529.
2. Backer HD, Shopes E, Collins SL, Barkan H. Exertional heat illness and hyponatremia in hikers. Am J Emerg Med. 1999;17(6):532-539.
3. Beller GA, Boyd AE, 3rd. Heat stroke: a report of 13 consecutive cases without mortality despite severe hyperpyrexia and neurologic dysfunction. Military medicine. 1975;140(7):464-467.
4. Bouchama A. Features and outcomes of classic heat stroke. Ann Intern Med. 1999;130(7):613; author reply 614-615.
5. Epstein Y, Moran DS, Shapiro Y, Sohar E, Shemer J. Exertional heat stroke: a case series. Med Sci Sports Exerc. 1999;31(2):224-228.
6. Ferris EB, Blankenhorn MA, Robinson HW, Cullen GE. HEAT STROKE: CLINICAL AND CHEMICAL OBSERVATIONS ON 44 CASES. The Journal of clinical investigation. 1938;17(3):249-262.
7. Khogali M, Weiner JS. Heat stroke: report on 18 cases. Lancet. 1980;2(8189):276-278.
8. Khogali M, al Khawashi M. Heat Stroke during the Makkah Pilgrimage. Saudi Med J. 1981;2:85-93.
9. Robine JM, Cheung SL, Le Roy S, et al. Death toll exceeded 70,000 in Europe during the summer of 2003. Comptes rendus biologies. 2008;331(2):171-178.
10. Shapiro Y, Seidman DS. Field and clinical observations of exertional heat stroke patients. Med Sci Sports Exerc. 1990;22(1):6-14.
11. Sithinamsuwan P, Piyavechviratana K, Kitthaweesin T, et al. Exertional heat-stroke: early recognition and outcome with aggressive combined cooling--a 12-year experience. Military medicine. 2009;174(5):496-502.
12. Varghese GM, John G, Thomas K, Abraham OC, Mathai D. Predictors of multi-organ dysfunction in heatstroke. Emergency medicine journal : EMJ. 2005;22(3):185-187.
13. Weiner JS, Khogali M. A physiological body-cooling unit for treatment of heat stroke. Lancet. 1980;1(8167):507-509.
14. Yaqub BA, Al-Harthi SS, Al-Orainey IO, Laajam MA, Obeid MT. Heat stroke at the Mekkah pilgrimage: clinical characteristics and course of 30 patients. Q J Med. 1986;59(229):523-530.
15. Zeller L, Novack V, Barski L, Jotkowitz A, Almog Y. Exertional heatstroke: clinical characteristics, diagnostic and therapeutic considerations. European journal of internal medicine. 2011;22(3):296-299.

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Appendix B: Matrix containing compiled literature data. There is a tab for individualized data which will be used for regression analysis, a tab for aggregate data that can be used in model-based predictions, a tab for data content which delineates the parameters that each paper contains, and a tab for our personal notes.

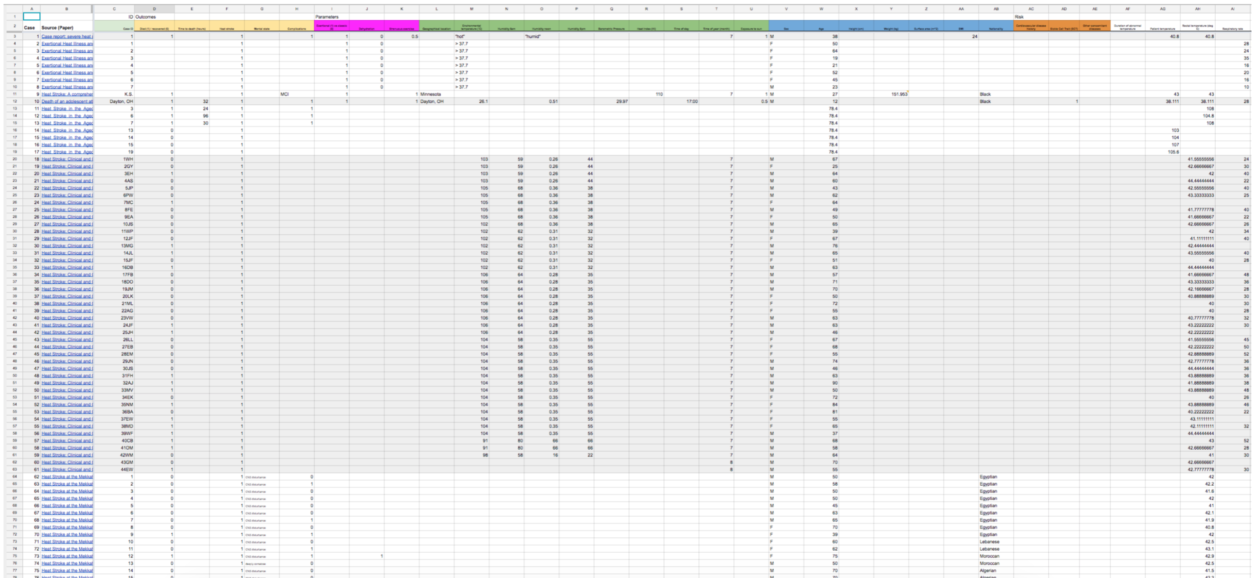
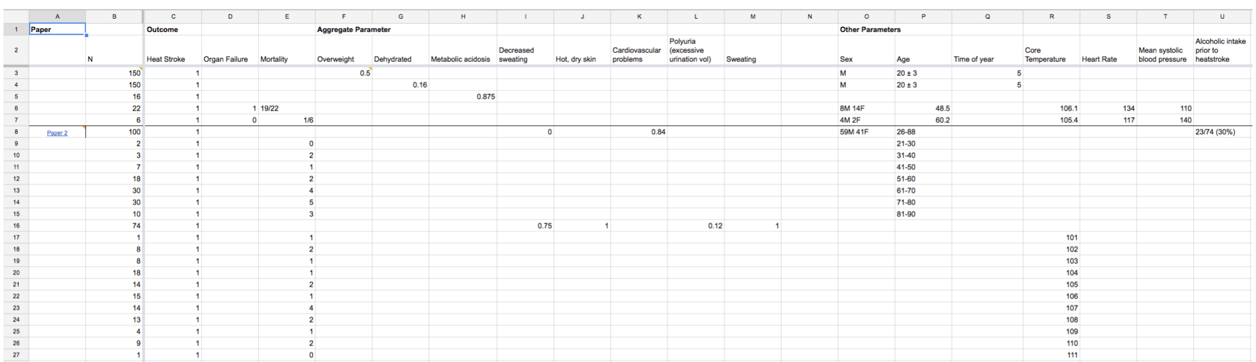


Figure B.1: Representative screenshot of individualized data tab (not all data shown). Alternating white/gray shading shown in rows helps with blocking off/visualizing each literature source. Columns are roughly grouped by similar or related characteristics (e.g., orange columns are all skin parameters).



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	Paper		Outcome			Aggregate Parameter									Other Parameters						
2		N	Heat Stroke	Organ Failure	Mortality	Overweight	Dehydrated	Metabolic acidosis	Decreased sweating	Hot, dry skin	Cardiovascular problems	Polyuria (excessive urination vol)	Sweating		Sex	Age	Time of year	Core Temperature	Heart Rate	Mean systolic blood pressure	Alcoholic intake prior to heatstroke
3		150	1			0.5									M	20 ± 3	5				
4		150	1				0.16								M	20 ± 3	5				
5		16	1					0.875													
6		22	1	1	19/22										8M 14F	48.5		106.1	134	110	
7		6	1	0	1/6										4M 2F	60.2		105.4	117	140	
8	Paper 2	100	1						0		0.84				59M 41F	26-88					23/74 (30%)
9		2	1		0											21-30					
10		3	1		2											31-40					
11		7	1		1											41-50					
12		18	1		2											51-60					
13		30	1		4											61-70					
14		30	1		5											71-80					
15		10	1		3											81-90					
16		74	1						0.75	1		0.12	1								
17		1	1		1													101			
18		8	1		2													102			
19		8	1		1													103			
20		18	1		1													104			
21		14	1		2													105			
22		15	1		1													106			
23		14	1		4													107			
24		13	1		2													108			
25		4	1		1													109			
26		9	1		2													110			
27		1	1		0													111			
28		27	1		9															<100 mmHg	

Figure B.2: Representative screenshot of aggregate data tab. Data are split by paper, and then primary measured parameters, and other associated parameters.

Appendix C [GitHub]: Python code that fills in missing parameters in heat stroke case studies with physiologically normal values. This code can also generate an arbitrary number of "negative" data points with features drawn from probability distributions meant to represent normal physiological ranges.

Appendix D: Descriptions of our current model-based predictions:

1. Hypothalamic regulation failure

Heat stroke is accompanied by neurologic degeneration that can impair hypothalamic function, which often manifests as a cessation of sweating and a loss of skin flushness (Bouchama 2002). Dr. Lipman mentioned this is a key feature of heat stroke, and trends in patient data also support this (Austin 1956, Ferris 1938, Yaqub 1986). By monitoring skin sweating (using a galvanic skin response monitor), skin paleness (using an optical transmitter and receiver), and core temperature, we may be able to predict when a person is experiencing hypothalamic dysregulation. In future milestones, we will determine thresholds for perspiration cessation, paleness, temperature elevation, and time.

2. Heat Index

Heat index (HI) is an estimate of “perceived temperature” and may be a reasonable estimate of how much heat stress a person is experiencing. To calculate HI, an equation that takes relative humidity and temperature into account may be used. We will make use of pre-implemented calculators of these parameters (https://pypi.python.org/pypi/meteocalc/1.0.0).

NWS Heat Index — Temperature (˚F)

Relative Humidity (%)	80	82	84	86	88	90	92	94	96	98	100	102	104	106	108	110
40	80	81	83	85	88	91	94	97	101	105	109	114	119	124	130	136
45	80	82	84	87	89	93	96	100	104	109	114	119	124	130	137	
50	81	83	85	88	91	95	99	103	108	113	118	124	131	137		
55	81	84	86	89	93	97	101	106	112	117	124	130	137			
60	82	84	88	91	95	100	105	110	116	123	129	137				
65	82	85	89	93	98	103	108	114	121	128	136					
70	83	86	90	95	100	105	112	119	126	134						
75	84	88	92	97	103	109	116	124	132							
80	84	89	94	100	106	113	121	129								
85	85	90	96	102	110	117	126	135								
90	86	91	98	105	113	122	131									
95	86	93	100	108	117	127										
100	87	95	103	112	121	132										

Likelihood of Heat Disorders with Prolonged Exposure or Strenuous Activity

Caution Extreme Caution Danger Extreme Danger

Figure D1: This chart shows the output values and their associated risk (color) for relative humidity and temperature ranges. Source: "NWS Heat Index." *National Weather Service: National Oceanic and Atmospheric Administration*. 12 Nov. 2016. Web. 12 Jan. 2017. <http://www.nws.noaa.gov/om/heat/heat_index.shtml>

Heat Index	Risk Level
80˚F – 90˚C	Low Risk
90˚C – 105˚C	Moderate Risk
105˚C – 130˚C	High Risk
≥ 130˚C	Extreme Risk

Table D1: Interpretation of Heat Index: We will use this table to calculate risk from the heat index value. Source: "NWS Pueblo, CO." US Department of Commerce, NOAA, National Weather Service. NOAA's National Weather Service, 31 Aug. 2010. Web. 12 Jan. 2017. <http://web.archive.org/web/20110629041320/http://www.crh.noaa.gov/pub/heat.php>

3. Wet Bulb Globe Temperature (WBGT)

Wet Bulb Globe Temperature (WBGT) uses temperature, humidity, wind speed, and radiation to calculate an apparent temperature in direct sunlight, whereas HI is used in shady areas and does not take radiation into account.

The system involves three thermometers: a natural wet bulb (NWB), a globe (GT), and a dry bulb (DB). By comparing with DB, GT measures radiation, air temperature, and wind speed. Meanwhile, NWB senses humidity. Calculating WBGT involves a weighting of the three bulbs:

When not in sun, WBGT = 0.7NWB + 0.3GT
When in sun, WBGT = 0.7NWB + 0.2GT + 0.1DB

Sources:
Budd GM. “Wet-bulb globe temperature (WBGT)--its history and its limitations.” J Sci Med Sport. 2008 Jan;11(1):20-32. Epub 2007 Aug 31.
"WetBulb Globe Temperature." *Weather.gov*. NOAA's National Weather Service, n.d. Web. 15 Jan. 2017.

4. Estimation of Core Temperature (CT) from Heart Rate (HR)

Buller et al. (2013) provide a model and method for estimating CT from HR. This calculation takes the form:

$$CT_t = a_1 \bullet CT_{t-1} + a_0 + N(0, \gamma)$$

$$HT_t = b_2 \bullet CT_t^2 + b_1 \bullet CT_1 + b_0 + N(0,\ \sigma)$$

“Where CT = core temperature, subscript *t* = time point, *a*1 = time update model coefficient, *a*0 = time update model intercept, *f* = noise drawn from a Gaussian distribution (*N*) with mean 0 and SD *γ*.

Where *b*2 = observation model quadratic coefficient, *b*1 = observation model coefficient, *b*0 = observation model intercept, *g* = noise drawn from a Gaussian distribution with mean 0 and SD σ.”

Essentially, constants *a, b,* σ, and γ are given by results from experimental tests in the paper. We can use their model and these equations to generate a more accurate estimate of core body temperature than we might with skin temperature alone. Given that core body temperature is one of the most important factors in heat stroke risk, the more proxies that we can use to estimate it, the more accurate our risk assessment will be.

Source: Buller MJ et al. “Estimation of human core temperature from sequential heart rate observations.” Physiol Meas. 2013 Jul;34(7):781-98. doi: 10.1088/0967-3334/34/7/781. Epub 2013 Jun 19.

Appendix E: Gantt chart, made using TeamGantt and updated with current timeline for finishing Milestone 1.