Prediction of Core Body Temperature from Multiple Variables
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ABSTRACT

This paper aims to improve the prediction of rectal temperature (T_{re}) from insulated skin temperature (T_{is}) and micro-climate temperature (T_{mc}) previously reported (Richmond et al. 2013) using additional physiological and/or environmental variables, under several clothing and climatic conditions. Twelve male (25.8 ± 5.1 yr; 73.6 ± 11.5 kg; 178 ± 6 cm) and nine female (24.2 ± 5.1 yr; 62.4 ± 11.5 kg; 169 ± 3 cm) volunteers completed six trials, each consisting of two 40 minute periods of treadmill walking separated by a 20 minute rest, wearing permeable or impermeable clothing, under neutral (25 °C, 50 %), moderate (35 °C, 35 %) and hot (40 °C, 25 %) conditions, with and without solar radiation (600 $W \cdot m^{-2}$). Participants were measured for heart rate (HR) (Polar, Finland), skin temperature (T_s) at 11-sites, T_{is} (Grant, Cambridge, UK) and breathing rate (*f*) (Hidalgo, Cambridge, UK). T_{mc} and relative humidity were measured within the clothing. T_{re} was monitored as the 'gold standard' measure of T_c for industrial or military applications using a 10 cm flexible probe (Grant, Cambridge, UK).

A stepwise multiple regression analysis was run to determine which of 30 variables (T_{is}, T_s at 11 sites, HR, *f*, T_{mc}, temperature and humidity inside the clothing front and back, body mass, age, body fat, sex, clothing, $\dot{V}O_2$, Thermal comfort, sensation and perception, and sweat rate) were the strongest on which to base the model. Using a bootstrap methodology to develop the equation, the best model in terms of practicality and validity included T_{is}, T_{mc}, HR and 'work' (0 = rest; 1 = exercise), predicting T_{re} with an SEE of 0.27 °C and adjusted R^2 of 0.86. The sensitivity and specificity for predicting individuals who reached 39 °C was 97 % and 85 %, respectively.

Insulated skin temperature was the most important individual parameter for the prediction of T_{re}. This paper provides novel information about the viability of predicting T_c under a wide range of conditions, using predictors which can practically be measured in a field environment.

INTRODUCTION

High core body temperature (T_c) is the single most reliable predictor of exhaustion during exercise in the heat (Montain et al. 1994) and the ability to monitor thermal responses could help reduce the risk of heat exhaustion for individuals working or exercising in these hyperthermic conditions (Malchaire et al 2001). However, the invasive monitoring of T_c is not practical in most cases, and to avoid the necessity to perform individual monitoring, many heat strain indices have been developed to predict human responses under certain conditions. These indices can be broken down into two main types; ‘empirical indices’ derived using samples of human subjects who’s responses to a range of thermal environments are used to form an equation or nomogram; and ‘rational indices’ that utilise several measurements (e.g. environmental and clothing) and uses heat transfer calculations to predict human responses to thermal environments, usually by means of a computer programme.

Of the two indices types, rational indices are the most comprehensive as they are designed to integrate all environmental and behavioural variables, but as there is no practical way to measure all of these directly, they are often assumed or regarded as constants (Epstein and Moran 2006). Additionally, these indices do not account for any variation in the responses between individuals, which would either place more people at risk, or necessitate a conservative limit for withdrawal from exercise (Havenith, 1997, 2001; Havenith and Fiala 2015). Physiological monitoring of individuals in thermally challenging environments to assess their heat strain could help mitigate these limitations. Moran et al (1998b) attempted to do this with the physiological strain index (PSI), to produce a simple model, valid across any conditions. The PSI is based on heart rate (HR) and rectal temperature (T_{re}), and describes the combined cardiovascular and thermal strain on a scale of 0-10. Although there are several studies which support the validity of the PSI in its ability to distinguish between different levels of hydration and exercise intensity (Moran et al. 1998a), between genders (Moran et al. 1999) and different levels of physiological strain for firefighters in personal protective equipment (PPE) (Petruzzello et al. 2009), the inclusion of an invasive measure of T_c does not provide an acceptable heat strain index for use in the occupational setting. As an alternative, other surrogate, non-invasive measurements that estimate T_c can be used that are suitable for field deployment such as tympanic, aural, forehead or axilla temperature. These however tend to show less reliable associations with T_{re} and oesophageal temperature (Ganio et al. 2009), and a viable alternative remains to be identified. A recent study showed that a prediction equation including insulated skin temperature (T_{is}) and micro climate temperature (T_{mc}) can predict T_{re} with a standard error of the estimate (SEE) of 0.2 °C in emergency service (ES) personnel wearing chemical biological, radiological and nuclear (CBRN) protective clothing (Richmond et al. 2013). However, these findings were only valid under the specific conditions used in these exposures and the study did not include other variables which may further improve the prediction of T_{re}.

Similarly, Buller et al. (2011), proposed a model to estimate core temperature, heat production and heat loss from the body using real-time physiological measurements of heart rate, accelerometer and skin heat flux using a dynamic Baysian Network model and a Kalman filter to enable forward predictions, but results may not be reliable enough to protect individuals in high heat stress conditions. Yokota et al. (2008), presented a model for predicting core temperature based on measured heart rate and environmental conditions, observing SEE's up to 0.31°C for the various datasets, and finally in 2013, Buller et al. (2013) used a Kalman filter approach in the estimation of human body core temperature from sequential heart rate observations as a single parameter with 95% of predictions falling within ±0.63°C. Though all these methods may be acceptable for prediction of group responses, for individual's protection the discrepancies were too large. Further, the datasets used had only a limited amount of data at very high core temperatures, and thus most of these statistics are based on the lower core temperature values, where the deviation is not relevant in any case (Havenith and Fiala, 2015).

As indicated by the studies mentioned above, there are known physiological responses that occur in association with exercise and climate induced hyperthermia which could be included in the model to help explain more of the variance in T_{re} than can be attributed to T_{is} and T_{mc} only. Heart rate increases during passive heat stress as a result of the changes in skin blood flow (SkBF). As T_c increases, cutaneous vasodilation occurs to allow increased volumes of blood to flow to the skin to aid dry heat loss. Elevated skin temperature (T_s) is associated with reduced cardiac filling and stroke volume; therefore, the way to maintain cardiac output is by increasing HR. However, identifying the cardiovascular response to hyperthermia during exercise is complex because HR increases not only to assist cooling, but also to meet the additional oxygen requirement by the working muscles. The inclusion of a variable in the model which changes only in response to the increase in metabolic rate due to ‘work’ may improve the predictive power of HR. One such possibility is to investigate changes in breathing frequency (*f*) as another physiological response which may reflect an increase in T_c. Around 100 years ago it was first established by Haldane (1905) that hyperthermia increases ventilation (V_E) (Tidal volume, [V_T] * *f*) in humans. The study showed that HR increased by about 36 $b \cdot min^{-1}$ for every 1 °C rise in T_c, and that as T_c rises, the alveolar CO_2 decreases (suggesting hyperpnea has occurred). While some papers suggest that the change in V_E during passive heat stress is due to an increase in *f* (Fan et al. 2008; Petersen and Vejby-Christensen 1977), other show that the change in V_E is due to an increase in V_T (Cabanac and White 1995; Gaudio and Abramson 1968). During exercise, identifying the thermal component of the increase in V_E is complicated due to the added impact of exercise on breathing; however the relationship between V_E and thermoregulation may result in *f* explaining some of the variance in T_{re}.

The aim of this study was to investigate the potential of using a combination of simple non-invasive measures associated with T_c to improve the prediction of T_{re} over several, substantially different heat stress scenarios. Variations in the environment were introduced (work/rest cycles; clothing; environmental conditions; solar radiation) to ensure a more general applicability and validation of any prediction model developed. In order to assess the accuracy of T_{re} prediction, a pre-defined ‘acceptable’ limit should be set; however, opinion in the literature is divided on this point. While some authors have agreed that the standard deviation (SD) of a measurement site should not be greater than 0.1 °C (Moran and Mendal 2002), other are less stringent, accepting an SEE of 0.3 °C (Gant et al. 2006) and ± 0.5 °C (Gunga et al. 2009) between a ‘gold standard’ and a surrogate measure of T_c. However, accepting such large prediction errors would require work to stop at quite low predicted T_c’s to avoid placing workers at the extremes of the T_c distribution at risk. Based on evidence from the literature, and the SEE achieved using non-invasive measures in previous work (Richmond et al. 2013), this study aimed to achieve an SEE of ≤ 0.2 °C.

1.1 METHODS

Twenty one participants volunteered to take part in the trial. All participants were verbally briefed, issued with a participant information sheet and gave written informed consent. Ethics approval for the procedures was secured from the Loughborough University ethics committee. All participants completed a health screening questionnaire prior to taking part in the study.

1.1.1 Experimental protocol

The study took place in the environmental chamber at Loughborough University. Prior to the trial, all participants carried out a sub maximal and maximal intensity fitness test on a treadmill to determine maximum HR and maximum oxygen uptake ($\dot{V}O_{2\,max}$). Participants were measured for height and body mass, as well as estimated body fat (%) (Durnin and Womersley 1974). All participants completed between 2-6 trials under different environmental and clothing conditions (Table 1). Though temperatures were very different in conditions C1 to C5, vapour pressures/concentrations were kept almost identical, and moisture load was instead induced by wearing PPE with different permeability. The experimental protocol involved sitting in the chamber for ten minutes, followed by 2 x 40 minutes walking on a treadmill at a set speed and gradient (depending on the fitness and capability of the participant). The exercise intensity was ~ 40 % $\dot{V}O_{2\,max}$, which was set using the corresponding HR identified from the fitness test. This was regarded as a reasonable work rate that could be sustained over the duration of a work shift. The 40 minute periods of exercise were separated by seated rest outside the chamber. The rest was included because a heat strain monitor needs to be valid during rest as well as exercise, not only so that T_c can continue to be monitored once exercise has ceased, but because heat exhaustion can still occur at rest. The length of the rest was determined by the T_c of the individual, with participants returning to the chamber once T_c had dropped by 0.4 °C. In C6 the work period was increased to 60 minutes in order to elicit a greater hyperthermic response.

Two different PPE ensembles were worn: one permeable (PERM) and one impermeable (IMP). The PERM ensemble was a cotton coverall (Arco Ltd, Hull, UK) and the IMP ensemble was a coated nylon coverall (FRS Countryware limited, Bridgnorth, UK). The same clothing was worn underneath the coveralls by all participants which consisted of black Lycra shorts and a long-sleeved cotton t-shirt. The clothing ensembles had the same total local thermal resistance (0.166 $m^2K \cdot W^{-1}$), but the total local evaporative resistance was considerably higher for IMP (213 $m^2P_a \cdot W^{-1}$) than PERM (42.4 $m^2P_a \cdot W^{-1}$)[1]. In the two solar conditions, two 1000 watt metal halide Compact Source Iodide lamps (GE Lighting) were used to simulate solar radiation; directed to the back of the participants. The amount of direct radiation was measured with a Pyranometer (CM11, Kipp & Zonen, Netherlands) and kept at a fixed level of ~530 $W \cdot m^{-2}$.

There were five termination criteria:

- T_{re} of 39.5 °C
- T_s of 45 °C
- HR >95 % max
- Voluntary withdrawal
- Withdrawal by experimenter

Table 1- Experimental conditions, including the 'real-life' conditions replicated

Condition	**T_{amb}, RH, P_a and PPE**	**Real-life conditions**
C1	25 °C, 50 %, 11.5 $g \cdot m^3$, IMP	Indoors, cool conditions, protective clothing
C2	40 °C, 25 %, 10.2 $g \cdot m^3$, PERM	Indoors, hot factory conditions, basic level PPE
C3	40 °C, 25 %, 10.2 $g \cdot m^3$, IMP	Indoors, hot factory, protective clothing
C4	30 °C, 35 %, 10.7 $g \cdot m^3$, PERM, solar	Outdoors, hot sunny day, basic level PPE
C5	40 °C, 25 %, 10.2 $g \cdot m^3$, PERM solar	Desert environment, basic level PPE
C6	40 °C, 35 %, 17.9 $g \cdot m^3$, PERM	Indoors, hot factory, basic level PPE

[1] The thermal and evaporative resistance of the clothing was measured using thermal manikin by EMPA, Switzerland

T_{amb} = ambient temperature, RH = relative humidity, P_a = water vapour pressure, PPE = personal protective equipment, PERM = permeable and IMP = impermeable

1.1.2 Measurements

On arrival, approximately one hour prior to the start of a trial commencing, participants were issued with, and inserted a rectal probe (Edale Instruments, Cambridge, UK) to a depth of 10 cm. Rectal temperature was chosen as the 'gold standard' measure of T_c for the purposes of this study. Participants were then asked to change into their standardised t-shirt and Lycra shorts, and return to the prep room for nude weight and clothed weight to be recorded (Sartorius IS 150 I GG-H scale, Sartorius, Goettingen, DE). Skin temperature was measured (iButton DS1192L, Homechip, Milton Keynes, UK) at 11 sites (forehead, chest, upper back, upper arm, lower arm, hand, lower back, abdomen, thigh, calf and foot), and secured using a soft cloth hypoallergenic tape (3M Medipore, 3M Healthcare, UK). Insulated skin temperature was measured at the lower part of the neck between C7 and T2 (spinous process) using skin probes (Grant Instruments, Cambridge, UK) connected to a Squirrel SQ800 data logger (Grant Instruments, Cambridge, UK) which recorded data every 20 s. The probe was covered by a 5 cm x 5 cm x 1 cm block of closed-cell cross linked polyethylene foam (Rubber Astic International, Birmingham, UK), which was secured around the probe head and onto the skin surface by use of a double-sided adhesive patch (3M Health Care, UK). A further layer of 11 cm x 11 cm single-sided adhesive patch (woven spun lace tape 1776, 3M Health Care, UK) was used to cover the polyethylene block and provide additional skin adhesion. Micro-climate temperature was measured on the outer side of the insulation foam, also using a Grant thermistor. Heart rate, f and ECG were measured using the Equivital monitor (Hidalgo, Cambridge, UK). Heart rate was also measured using a polar heart rate monitor and watch (RS 800, Polar, Finland). Rectal temperature and HR were monitored 'live' throughout the trials for safety, and recorded at five minute intervals so changes in the rate of rise could be observed. At the end of each trial, participants were re-weighed, both nude and with their clothing, to enable sweat rate and evaporative heat loss to be estimated. Participants were asked for their subjective rating of thermal comfort (TC), thermal sensation (TS) and thermal preference (TP) at the start and end of each exercise bout.

1.1.3 Statistical analysis

All values are presented as mean ± SD and statistical significance was accepted at the $p<0.05$ level. Multiple linear regression and univariate ANOVA were used to develop the prediction equation for T_{re}. The data from each condition for every participant taken at 10 minute intervals were entered into SPSS in order to run an exploratory linear multiple regression analysis. Thirty potentially relevant variables (T_{is}, T_s at 11 sites, HR, f, T_{mc}, temperature and humidity inside the clothing front and back, body mass, age, body fat, height, sex, clothing, $\dot{V}O_2$, T_C, TS and TP and sweat rate) were entered into the model and a stepwise regression was performed. Using the results of that analysis, variables were added one by one to the model using the 'enter' method. In cases where the relationship between T_{re} and the primary variable in the equation was better described as a curvilinear model, the covariates were centred to reduce colinearity (Bland 2000). Once the best equation was determined using this model, fixed factors were added to the model using univariate ANOVA. In determining the most significant and practical covariates to include in the model, the improvement in the SEE and adjusted (adj) r^2 were examined as variables were added and removed.

Adherence to the assumptions of multiple regression was assessed (Havenith and Fiala, 2015). Independence of data points was determined using the Durbin-Watson statistic (1950) which tests a regression model for serial correlation. A value near 2 indicates non-autocorrelation, a value near 0 indicates positive autocorrelation and a value near 4 indicates negative autocorrelation. Although there are some specific tables for determining upper and lower bounds of acceptability depending on the number of variables in the model and the number of data points, a value of between 1 and 3 is often regarded as 'acceptable' and is a useful rule of thumb for assessing the autocorrelation in a model. Data were also checked for outliers and heteroscedasticity.

Once the model structure in terms of included variables had been determined, it was validated using the same data set, with a 'leave-one-out' bootstrapping approach. Twenty one different equations (same variables, different coefficients) were developed, using 20 participants for each equation, leaving one out each time. Rectal temperature was then predicted for each participant using the equation from which they were excluded. The mean of the twenty coefficients was then taken to produce a more 'robust' equation based on an independent sample.

The validity of the model was assessed by 1) the SEE and 2) by calculating the sensitivity (number of individuals over 39 °C correctly identified) and specificity (number of individuals under 39 °C correctly identified) of the model. Determining the sensitivity and specificity of the model was chosen as an additional assessment as it shows how many individuals are correctly or incorrectly identified as ‘safe’ or ‘at risk’ and therefore provides a tangible way of describing the validity of a measure.

1.2 RESULTS

The physical characteristics of the 21 participants are shown in Table 2.

Table 2- Descriptive characteristics of the participants (mean ± SD) (range)

	Male (n=12)	**Female (n=9)**
Age (years)	25.8 ± 5.1 (19 – 36)	24.2 ± 5.7 (19 – 36)
Body mass (kg)	73.6 ± 11.5	62.4 ± 6.1
Height (cm)	177.9 ± 5.6	168.7 ± 3.4
$\dot{V}O_{2\,max}$ (ml·kg·min^{-1})	52.3 ± 11.4	52.5 ± 11.6
Body fat (%)	13.3 ± 4.6	19.3 ± 8.1

1.2.1 Prediction of T_{re}

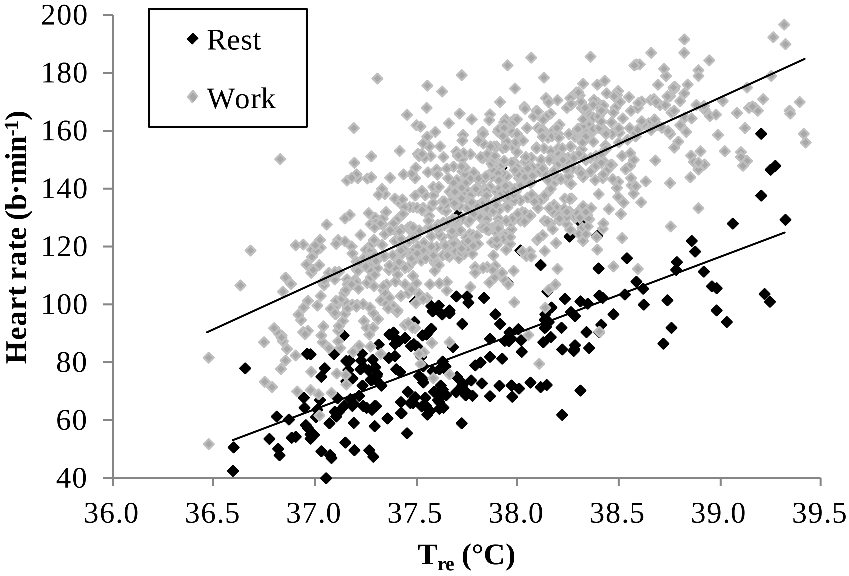

Figure 1 Rectal temperature (T_{re}) and heart rate during work and rest for all conditions

Figure 1 shows T_{re} and HR for all conditions, with data points coded by work or rest. The HR associated with a given T_{re} is lower during rest.

The exploratory stepwise regression analysis produced an equation that explained 82 % of the variance with an SEE of 0.25 °C, and included 13 variables (with most significant first; T_{mc}, T_{is}, HR, $\dot{V}O_2$, chest temperature, lower arm temperature, upper arm temperature, age, sweat rate, hand temperature, mean T_s and TC). The next step was to determine the most appropriate model using all the data. Due to the outcome of the stepwise prediction, T_{is} and T_{mc} were chosen as the first physiological measure on which to base the prediction model. The T_{re} and T_{is} at 10 minute intervals from all participants (n=1091) is shown in Figure 2. This figure shows that the relationship between T_{is} and T_{re} is better described as a curvilinear model (r^2=0.54) than a linear model (r^2=0.46), therefore a curvilinear model was applied. All input variables were centred in order to reduce the problem of multicollinearity, which can occur when a single variable is used twice in a model (x and x^2) (Bland 2000).

The first model included centred T_{is} (cT_{is}) and cT_{is}^2 and both variables were significant ($p<0.05$, $adjr^2$=0.54, SEE=0.38 °C). The addition of centred T_{mc} (cT_{mc})

improved $adjr^2$ to 0.76 and the SEE to 0.28 °C ($p<0.05$). In an attempt to improve this prediction, factors which might help distinguish between periods of work and rest were added to the model separately. Breathing rate and $\dot{V}O_2$ were significant, but only marginally reduced the error ($p<0.05$, $adjr^2=0.76$, SEE=0.27 °C). Heart rate provided the greatest increase in $adjr^2$ (0.80) and decrease in the SEE (0.25 °C)[2].

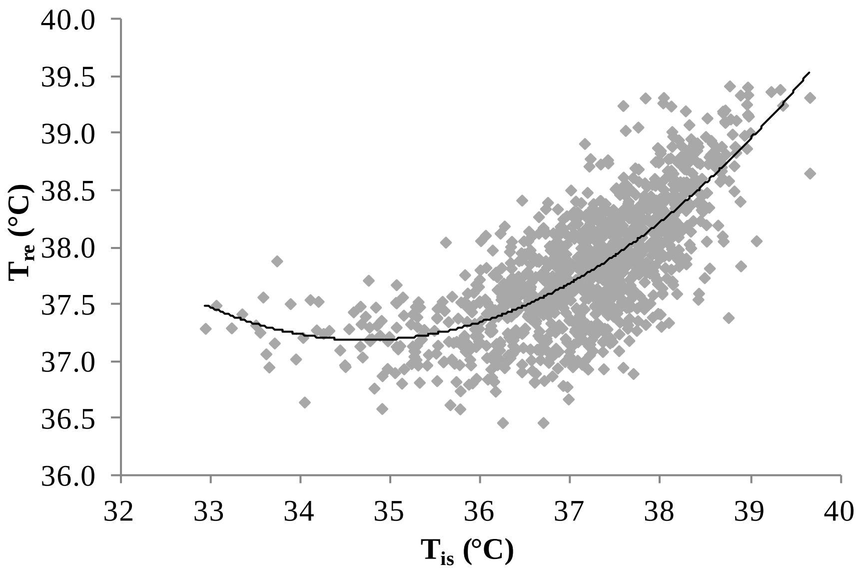

Figure 2- Measured rectal temperature (T_{re}) against measured insulated skin temperature (T_{is}) (°C) for all conditions

When 'participants' was added into the model as a fixed factor, there was an interaction effect between participant and T_{is}, which resulted in an increase in $adjr^2$ to 0.83 and a decrease in the SEE to 0.23 °C. This shows that the model provides a closer prediction of T_{re} when each participant has a different equation, but as this is impractical, this option was not followed-up. Finally, PPE, sex, work and training status (individuals were classed as 'trained' or 'untrained' based on their $\dot{V}O_{2\ max}$) were added to the model as fixed factors. Only sex and work had an interaction effect with T_{is} ($adjr^2=0.80$, SEE=0.25 °C and $adjr^2=0.81$, SEE=0.24 °C respectively, $p<0.01$).

Using all the data, and taking into consideration practicality (limiting the number of predictors and considering the ease of obtaining them) and accuracy of the prediction, the following equation provides the optimal prediction of T_{re}:

[2] Using a linear model, T_{is}, T_{mc} and HR produce an r^2 of 0.70 and SEE of 0.30, supporting the use of a quadratic equation in this case.

T_{re} = 37.06 + (0.520 * [T_{is}-37.1]) – (0.061 * [T_{mc}-35.5]) + (0.089 * [T_{is}^2-1378]) + (0.007 * HR) - (0.294 * work) (*eq1*)

rest = 0; work = 1
adjr^2=0.82, SEE=0.24 °C

In an attempt to improve the SEE, the next stage of the analysis involved developing prediction equations for a sub-set of data (accurate prediction of low core temperatures was deemed irrelevant, and the focus was put on the higher values: T_{is} ≥36.5 °C, n=886). For this subset of data there was little difference in the relationship between T_{re} and T_{is} (≥ 36.5 °C) when described as a linear (r^2=0.43, SEE=0.40 °C) or quadratic (r^2=0.44, SEE=0.39 °C) equation, so a linear equation was developed.

In order to remove the impact of any possible dependency between development and validation of the equation, twenty one regression equations were developed, leaving one participant out from each analysis and using that person to validate the equation (bootstrap method). Rectal temperature was then predicted for each participant using the equation they were left out of in the development process. Figure 3 shows the regression line for predicted against measured T_{re}. The equations were developed using only T_{is} data points above 36.5 °C, so with the exclusion of these data points the adjr^2 = 0.86 ($p<0.05$) and SEE = 0.27 °C. The following equation was developed by averaging the coefficients from the 21 equations:

T_{re} = 15.35 + (0.648 * T_{is}) – (0.064 * T_{mc}) + (0.008 * HR) – (0.381 * work) *(eq 2)*
rest = 0; work = 1

Figure 3 also shows the sensitivity and specificity of predicted T_{re} with a theoretical upper threshold of 39 °C. The vertical dashed line takes into account the 0.27 °C error. To protect 97.5 % of individuals from exceeding a T_{re} of 39 °C, they need to stop at a predicted T_{re} of 38.46 °C (39 – (2 * SEE)). The sensitivity is increased to 97 % (27 out of 28 data points correctly identified as >39 °C), but the specificity is reduced to 85 %. In protecting most individuals from possible heat illness, many individuals would be stopped at an actual T_c of below the designated T_{re} limit (bottom right quadrant of the graph). The solid horizontal line indicates the current safe recommendation by the World Health Organisation of 38 °C (WHO 1996).

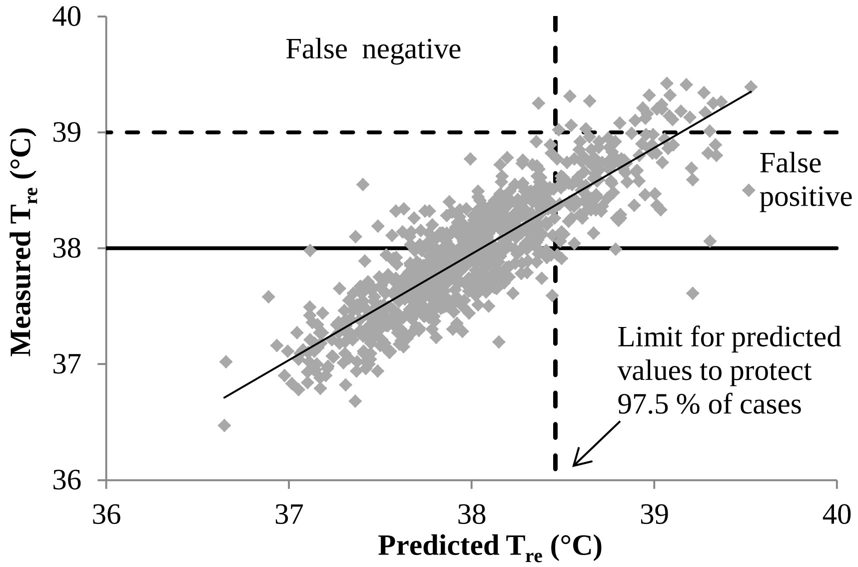

Figure 3 – Measured vs predicted rectal temperature (Tre) (°C). The vertical dashed line show participants would need to be stopped at a Tre of 38.46 °C to prevent 97.5 % of the population exceeding 39 °C. The horizontal line shows the recommended safe limit for a group of workers, as set by th World Health Organisation.

1.3 DISCUSSION

This study aimed to determine whether or not T_{re} changes during exercise can be modelled using non-invasive physiological, physical and/or environmental measures. To avoid the criticisms on earlier studies, rather than focussing of a single condition, the experimental trials included as many conditions and measurements as was feasible, with an exercise protocol developed to elicit physiological responses indicating high strain levels. This project covered 4 different, low humidity external climates, and by using impermeable garments too also produced skin microclimates with very high humidity, whereby a very wide range of skin microclimate conditions were achieved.

Insulated skin temperature was the most important individual parameter for the prediction of T_{re}, followed by T_{mc}. During heat stress, blood flow to the skin increases to dissipate the heat generated in the muscle (Bernard and Kenney 1994). Through conduction, convection, radiation and mostly evaporation, the blood loses heat through the skin before it is returned to the working muscle. The purpose of the insulation material at the surface of the skin is to impede this heat loss, therefore causing the temperature of the skin to become close or equal to T_c. The origin of the concept for using T_{is} to predict T_{re} comes from the convergence of T_s and T_c in conditions of uncompensable heat stress. As the temperature gradient between the core and environment reduces, the capacity for heat dissipation from core to skin is removed. Therefore, T_s will converge with T_c and the temperature of the skin will eventually reflect changes in T_c (Pandolf and Goldman 1978). Covering the skin thermistor with an insulation material should mimic this condition and provide an estimate of T_c.

In addition to T_{is} and T_{mc}, several other potentially relevant physiological measures were added to the equation to see whether they could improve the prediction. When added to the equation in combination with 'work', HR explained a significant amount of the variance in T_{re}; thus improving the predictive capacity of the equation. During passive heat stress, SkBF increases in response to rises in T_c and T_s. This elevation in SkBF occurs through an increase in cutaneous vascular conductance and cardiac output (Crandall et al. 1999). Rowell et al. (1969) showed an increase in HR of 82 $b \cdot min^{-1}$ following 30 min of passive heating from a T_{re} of 37.12 °C to 38.23 °C. Similarly, Crandall et al. (1999) reported an increase in HR of 23 b·min^{-1} when T_{es} increased from 36.5 °C to 37.2 °C during passive heating, showing a cardiovascular response to hyperthermia. During exercise, this relationship becomes more complex. The onset of exercise is accompanied by an initial increase in cutaneous vasoconstriction as blood is directed away from the skin and towards the working muscles (Hunold et al. 1992). Therefore, any increase in HR at the onset of exercise is due to the increased requirement of blood to the working muscles. As exercise continues and metabolic heat production causes internal temperature to rise, a threshold is reached at which thermoregulatory reflexes are evoked (Johnson and Park 1982). Above this threshold, cutaneous vasodilation occurs to allow an increase in SkBF which enables dry heat loss from the skin. This redistribution of fluids from the blood plasma to the skin tissue, as well as the increased demand for SkBF, causes a decrease in stroke volume, which results in an increase in HR to maintain cardiac output. This is known as cardiovascular drift and although it is influenced by an increase in body temperature, it is also affected by the increased oxygen cost of exercise. It was hypothesised that by identifying the proportion of the rise in HR during exercise which is due *only* to the thermoregulatory response, HR may provide an even stronger prediction of T_{re}. Figure 1 shows a comparison of the regression lines for HR against T_{re} during 'work' and 'rest'. This shows two things; firstly the increase in HR that occurs with increasing T_{re} during rest; and secondly, the increase in HR between rest and work (for a given T_{re}) that occurs due to exercise. By including 'work' in the equation, the different intercepts of the two regression lines are accounted for; going some way to distinguishing between the cardiovascular response due to 'work' and due to the thermoregulatory response.

Breathing rate was included as a measurement due to the relationship that exists between V_E and changes in T_c (Fujii et al. 2012; Haldane 1905). However, there were issues in this experiment with the measurement of *f*. Firstly, analysis of the data was difficult due to the many factors that affect *f* including talking, drinking or sporadic deep intakes of breath. Secondly, measurement of *f* using the Equivital monitor was deemed unreliable: the monitor detects *f* in two ways; one using impedance of the chest strap; and, one using the ECG signal. The values reported by these two methods were different, and it was not possible to determine which was more reliable. Despite these problems with the measurement of *f*, it was found to be significant in the model, albeit not powerful enough to warrant inclusion in the model. However, the effect of changes in T_c on V_E is well established, and this is a measure worthy of further investigation if the problems associated with its measurement can be overcome.

The prediction of T_{re} from T_{is}, T_{mc}, HR and 'work' using the bootstrap method of validating the equation has a lower SEE (0.27 °C) and explained more of the variance in T_{re} (86 %) than previous work that has used similar non-invasive measures to monitor heat strain. Xu et al. (2013) reported that T_s and heat flux measured at the sternum explained ~75 % of the variance in observed T_c in hot environments for participants wearing army combat uniform and body armour. Niedermann et al. (2013) developed a model for participants exercising in hot (30 °C) and ambient (10 °C) conditions, and included three T_s, two skin heat fluxes and HR. The root mean square deviation ranged from 0.28 °C to 0.33 °C in the various conditions, and the variables in the model explained a maximum of 73 % of the variance in observed T_{re}. Taylor and Amos (1998) compared 4 T_{is} sites with T_{es}, while cycling at different intensities under five thermal loads. Oesophageal temperature was regressed against T_{is} and the best prediction under all conditions was using T_{is} on the spine ($r^2 = 0.86$). Although no values for error were given, the report states that temperatures were offset by as much as 2 °C during the temperate conditions, whereas they converged in the heat, particularly when T_{es} approached 39 °C. Bernard and Kenney (1994) reported lower errors in the prediction of T_{re} from non-invasive measures. Three thin copper disks each containing a thermocouple were placed on the skin with a thermal insulator between each disk. Under hot conditions in impermeable (T_{amb} 55 °C) and cotton (T_{amb} 45 °C) coveralls there was a high correlation of disk temperature with T_{re} (0.93) and an SEE of 0.2 °C.

Despite the positive findings from the current study in relation to much of the published literature, the model developed, using many more predictors, did not predict T_{re} with a lower SEE than the previous work by our group (Richmond et al. 2013) in which T_{is} and T_{mc} only were used to model T_{re} with an SEE of 0.2 °C and an $adjr^2$ of 0.85 in ES personnel wearing CBRN protective clothing. One reason is the inclusion of several different climate and clothing conditions to develop a more universal equation. When the $adjr^2$ and SEE were calculated for each individual condition, the equations for three of the six conditions gave an SEE of 0.21 °C; closer to the value deemed as 'acceptable' prior to the start of the study. However, when all the data were combined in order to develop a universal model, the additional variation added by the other conditions increased the error. Another possible reason is the different clothing that was used in this trial compared with previously. The PPE worn by ES personnel in our earlier study was fully encapsulated which reduces the exchange of heat between the surface of the skin and the environment. The impermeable clothing worn in the current study did not cover the head and neck of the participant, leaving the sensor patch and surrounding skin exposed to the environment. While the insulating material over the skin thermistor should minimise evaporative heat loss from the skin, it is possible that cooling of surrounding tissue caused a reduction in T_{is} when exposed to open air conditions.

Although the SEE of 0.27 °C fell outside the pre-defined acceptable error of 0.20 °C, the impact of the error of the model developed on drop-out rate is still worthy of consideration. The sensitivity and specificity plot showed that to prevent 97.5 % of the population from exceeding 39 °C, they would need to be stopped at a predicted T_{re} of 38.4 °C. This would result in 50 % of the population being withdrawn from work at a true T_{re} of 38.65 °C; considerably lower than many people can tolerate in compensable conditions. This would have a negative impact on work productivity and efficiency. Despite the SEE being lower than hoped, it is clear from Figure 3 that using *eq 2* to predict T_{re} would improve considerably on the WHO standards (withdrawal at 38°C), with fewer individuals being stopped before reaching potentially critical temperatures, and therefore improving work productivity.

1.3.1 Conclusion

For the current study, which included six environmental conditions, two clothing ensembles, and a wide variety of physiological and environmental measurements, it was not possible to predict T_{re} within the SEE of 0.2 °C. However, the inclusion of ‘work’ and HR into the equation provided a better estimation of T_{re} than T_{is} and T_{mc} alone; with ‘work’ helping to distinguish between the different regression lines observed for HR at work and at rest. It was hoped that *f* might improve the prediction due to the relationship between V_E and increasing T_c, but this was not possible due to problems with the measurement of *f*. Nevertheless, the relationship between *f* and hyperthermia may be worth further investigation under other conditions (e.g. when the individuals are not drinking or talking), and using different monitoring equipment. The findings from this work could be used to implement a practical, valid prediction of body temperature under certain conditions in the workplace (i.e. for selected conditions), thereby improving health, safety and productivity. As these findings are specific only to the conditions trialled here, future work might also include repeating this study under additional conditions, and using fully-encapsulated PPE to establish whether the addition of ‘work’ and HR improved further the errors reported previously (Richmond et al. 2013). However, given that in this study prediction models were investigated with the largest possible number of predictors, but in the end not achieving the required predictive power to work over the whole range of conditions tested here (which was extensive compared to other studies but not exhaustive), the idea that it is possible to create a universally usable non-invasive heat stress monitor may be unachievable.

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