

Physiological, Immunological and Contaminant Monitoring of Firefighters and Instructors

Fire Service Research and Training Trust (FSRTT) Report

Authors

Alan Richardson PhD ^{1,2*} A.J.Richardson@brighton.ac.uk

Catherine Gage MSc ¹

Ben Lee PhD ⁴

Rebecca Bradley, MSc ²

Nadia Terrazzini PhD ²

Peter Watt PhD ¹

Emily Rachel Watkins PhD ³

¹ Environmental Extremes Group, University of Brighton, UK

² Centre for Stress, Aging and Disease, University of Brighton, UK.

³ Department of Life Sciences, University of Roehampton, UK

⁴ Occupational Performance Research Group, University of Chichester, UK



University of Brighton



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Lay Summary

This study sort to evaluate the physiological responses, psychological consequences and contamination levels of Firefighters and Fire Instructors, in response to their exposure volumes and types. To do this we measured blood and urine from a large sample of Firefighters, Fire Instructors and small control group over a 6 month period. Fire personnel also provided urines samples after every exposure to look at contamination levels. In a small subset, we attempted to measure heart rate and core temperature during live fire operations.

The main findings demonstrated that:

- There is a severe inflammatory response in some Fire Instructors, which is likely to be the result of severe over exposure to extreme heat and activity. This further supports the restriction of fire exposure volume for these individuals.
- The physiological analysis equipment available at present is not sufficient for widespread use within Fire Services. Physiological monitoring set ups are possible in fixed scenario training activities with time to don equipment.
- Firefighters and Instructors are exposed to carcinogenic substances. High frequency exposure may lead to elevated levels of contamination. Methods to reduce exposure should be considered, with guidance needed regarding decontamination techniques.





Background Information

The acute health consequences of firefighting have been much interrogated over recent decades, with strong evidence to indicate an association between firefighting and cardiovascular events (Fahy *et al.*, 2015), post-traumatic stress disorder (Haslam & Mallon, 2003) and musculoskeletal injuries (Orr *et al.*, 2019). However, the long-term implications of the occupational role and the physiological impact of live operational exposures is less well documented. In recent years, Breathing Apparatus Instructors (BAI) have been highlighted as a unique population amongst the firefighting profession, with BAI completing a significantly greater monthly exposure number (~13) compared to firefighters (FF) (~1) (Watkins *et al.*, 2018). The increase in exposure numbers has been suggested to relate to elevated markers of systemic inflammation and a specific group of symptoms of ill health, although currently evidence only offers a snapshot of information (Watkins *et al.*, 2018; Watkins *et al.*, 2019a; Watkins *et al.*, 2020). The exposure of FF to contaminants has also come under recent scrutiny, with research, mainly from the USA, suggesting that FF are metabolizing PAH chemicals as a result of fire exposures. However, there is currently limited information available on the contamination from live fires in the UK or on contaminant levels past a 24 hour period. Ensuring the health of FF is optimized is vital to creating an efficient and effective Fire and Rescue Service. FF who are fit and healthy are less likely to take time off sick (Kyröläinen *et al.*, 2008) and are more likely to work safely and efficiently (Siddall *et al.*, 2016). In addition, it is important to consider the quality of life individuals will have following retirement, which can be drastically reduced after a cardiovascular event or with cancer (Lewis *et al.*, 2014; Allart-Vorelli *et al.*, 2015; Pitman *et al.*, 2018). This report will therefore have three areas of particular focus: physiological monitoring, systemic inflammation and well-being, and contamination.

Physiological Strain of Firefighting Tasks

Firefighting tasks often result in individuals working at 80-100% of their maximal aerobic capacity (Barr *et al.*, 2010). Personal protective equipment (PPE) worn by FF can add approximately 10-15kg in weight, with a breathing apparatus (BA) adding a further 10-12kg (Cheung *et al.*, 2010). The additional weight of the PPE and BA reduces maximal oxygen capacity ($\dot{V}O_2$) and cardiopulmonary abilities (Dreger *et al.*, 2006). Carrying an 11 kg BA has been reported to result in a $\dot{V}O_2$ of $28.1 \pm 3.3 \text{ mL.kg}^{-1}.\text{min}^{-1}$ compared to $21.6 \pm 2.5 \text{ mL.kg}^{-1}.\text{min}^{-1}$ without a BA at the end of exhaustive exercise (Bakri *et al.*, 2012). A theoretical model predicted that metabolic rate would





increase by 1% per kg of additional weight (Givoni & Goldman, 1971). However, based on the linear regression line formed from an assessment of a variety of PPE types, it has been more recently suggested that for each kg of additional weight metabolic rate increases by 2.7% (Dorman & Havenith, 2009). Despite this, weight alone is not the only cause of increased metabolic rate, with differences in material, number of layers and BA harness design also having an impact (Dorman & Havenith, 2009; Bakri *et al.*, 2012). This is evidenced by Taylor *et al.*, (2012) who noted that whilst the heaviest item worn by FF is their BA, during walking both the BA (11.30 kg) and protective clothing (without boots and helmet) (4.72 kg) contributed 9% to the metabolic rate increase. Increases in the metabolic rate whilst walking in PPE have been noted to be up to 14.5% (Dorman & Havenith, 2009).

Added layers to the human skin also creates a number of microenvironments in which metabolic heat must pass before exchanging into the ambient environment (Cheung *et al.*, 2010). Consequently, when ambient temperature is elevated due to fire exposure, the encapsulating PPE reduces the capacity for evaporative heat loss. In a fire situation the evaporative heat loss required to maintain a thermal steady state cannot be achieved, as a consequence of the PPE, BA, physical activity and environmental conditions (Montain *et al.*, 1994; Cheung *et al.*, 2000). This is referred to as an uncompensable heat stress situation and results in the body continually storing heat, causing a rise in core temperature (T_c) (Cheung *et al.*, 2000). Increases in T_c and HR in FF following live fire exposures range from 1.4 - 3.2°C in T_c and maximum HR of 134 - 194 b.min⁻¹ (Smith *et al.*, 1996; Smith & Petruzzello, 1998; Walker *et al.*, 2015). In comparison, BAI exhibit increases in T_c of 0.27 - 1.0°C with a maximum HR of 134 - 162 b.min⁻¹ (Eglin *et al.*, 2004; Eglin & Tipton, 2005; Watt *et al.*, 2016; Watkins *et al.*, 2019b). Data indicates that BAI experience a reduced level of physiological strain in comparison to FF, likely due to the differences in roles undertaken during training exercises or acclimation status. Although the data presented for FF is not operational data, it gives an insight into the strain they may experience.

The lack of operational data from FF is a consequence of logistical difficulties, given the emergency nature of the role, and technology available. There are numerous types of physiological monitoring systems currently available on the market, which can measure an array of variables including HR, T_c , skin temperature and breathing frequency. However, these devices are typically designed for athletes or the military. Firefighting presents a unique set of requirements for monitoring technology: it must be easy to put on quickly, it must be intrinsically sound in hot environments, it must communicate data to safe distances outside of complex environments made





of a variety of materials, it must be simple to access and understand the data, and finally it must be accurate and reliable. At the time of writing, the authors are unaware of any established device which meets all of these requirements. Review of the functionality of devices marketed to the Fire and Rescue Service as suitable for physiological monitoring is important, and this report will make use of one such device to capture training and operational data, with the aim to provide an assessment of its usability.

Systemic Inflammation

High levels of physiological strain and fire exposures have also been documented to increase markers of inflammation (Smith *et al.*, 2005; Wright-Beatty *et al.*, 2014). Interleukin-6 (IL-6) is an inflammatory cytokine, meaning that it is a small protein that is important for cell signalling and is involved in the inflammatory response. IL-6 signals white blood cells to migrate to areas of injury or tissue damage and therefore can cause inflammation to occur. Firefighting search and rescue tasks have been reported to cause increases in IL-6 (Walker *et al.*, 2015), with training exposures conducted by BAI noted to elicit increases in IL-6 of 1.13 pg.mL^{-1} and 2.5 pg.mL^{-1} (Watt *et al.*, 2016; Watkins *et al.*, 2019b). Whilst inflammation following exercise is a normal appropriate response, BAI have been reported to exhibit elevated markers of inflammation at rest (Watkins *et al.*, 2019a; Watkins *et al.*, 2020).

Elevated biomarkers in BAI at rest include IL-6, interleukin-1 β (IL-1 β) and C-Reactive Protein (CRP). A small sample of BAI ($n = 11$) displayed IL-6 levels of $2.18 \pm 2.39 \text{ pg.mL}^{-1}$ and IL-1 β values of $20.52 \pm 18.19 \text{ pg.mL}^{-1}$, which were significantly greater than a control groups values (IL-6: $0.28 \pm 0.37 \text{ pg.mL}^{-1}$ and IL-1 β $1.37 \pm 2.06 \text{ pg.mL}^{-1}$)(Watkins *et al.*, 2019a). A larger snapshot of BAI ($n=53$) inflammatory levels also documented increased IL-6 ($2.98 \pm 3.56 \text{ pg.mL}^{-1}$), IL-1 β ($11.56 \pm 19.48 \text{ pg.mL}^{-1}$) and CRP ($1.98 \pm 1.74 \text{ mg.L}^{-1}$) at rest compared to FF (Watkins *et al.*, 2020). IL-6, IL-1 β and CRP are all involved in the inflammatory response, with resting elevated levels indicating systemic inflammation in BAI. Increased levels of these three biomarkers are also related to an increased risk of atherosclerosis and cardiac events. Resting levels of IL-6 greater than 2.28 pg.mL^{-1} increases the relative risk of a cardiac event by 2.3 times compared to levels below 1.04 pg.mL^{-1} (P. M. Ridker *et al.*, 2000), whilst the American Heart Association and Centers for Disease Control and Prevention classify $< 1 \text{ mg.L}^{-1}$ of CRP as low risk, $1 - 3 \text{ mg.L}^{-1}$ as average risk and $> 3 \text{ mg.L}^{-1}$ as high risk for cardiovascular disease (Ridker, 2003). Typical healthy values for IL-1 β are $0.14 - 1.00 \text{ pg.mL}^{-1}$ and whilst the cytokine has not





yet been established as a predictor of cardiovascular events with set classifications of risk, gene polymorphisms causing increased IL1- β are associated with risk of coronary artery disease and cardiovascular events (Tsimikas *et al.*, 2014), and IL1- β is being targeted for atheroprotective interventions (Ridker, 2016).

Repeated experiences of high physiological strain which result in an inflammatory response, with limited recovery time between episodes, has been proposed to lead to gradual increases in systemic inflammation (Smith, 2000; Smith, 2003). It is suggested that whilst regular exercise can reduce inflammation, having minimal recover time does not enable inflammatory levels to return to normal (or be reduced) prior to a subsequent stimulus occurring (Smith, 2000; Smith, 2003). Cytokines such as IL-1 β and IL-6 are able to communicate with the central nervous system via directly crossing the blood brain barrier or activation of afferent neurons (Banks, 2005). Elevated levels of these cytokines can stimulate “recuperation” or “sickness” behaviours, which are a group of responses including weight loss, depression, fatigue and sleep disturbances (Dantzer *et al.*, 2008). Elevated IL-1 β and IL-6 in BAI have previously been reported to be associated with an increased likelihood of experiencing symptoms of ill health (IL-6 Odds Ratio = 5.63, IL-1 β Odds Ratio = 3.67) (Watkins *et al.*, 2020). These symptoms included fatigue, sleep disturbances, heavy sweating, headaches and colds. IL-6 and IL-1 β levels were also related to the number of wears that had been completed in the previous month, with 19% and 25%, respectively, of variance in these markers explained by wear numbers (Watkins *et al.*, 2020). Whilst this evidence begins to indicate a relationship between the symptoms of ill health described by BAI, systemic inflammation and fire exposure number, the singular snapshot nature of the data from one blood sample limits the conclusions that can be drawn. Further assessment of the inflammatory status of Fire and Rescue Service personnel is required in relation to exposures and well-being over a greater duration of time. Moreover, previous detailing of ill health symptoms were limited, with additional information required on the frequency of symptoms and expansion on the meaning of fatigue to individuals. Consequently, specific fatigue and mood related questionnaires are required to more thoroughly capture the well-being of personnel.

A previous assessment of BAI resting inflammatory status has also reported increased immunoglobulin-G (IgG), with BAI having values of $16.88 \pm 836 \text{ g.L}^{-1}$ compared to FF with values of $9.17 \pm 4.85 \text{ g.L}^{-1}$ (Watkins *et al.*, 2020). Immunoglobulins are antibodies which are produced by B-cell white blood cells in response to antigens as part of the humoral immune response (Vidarsson *et al.*, 2014). An up-regulation of humoral immunity is commonly associated with a





suppression of cellular immunity, increasing the risk of viral or bacterial infections (Buyukyazi *et al.*, 2004; Zhao *et al.*, 2012; Kakanis *et al.*, 2014). However, further information into the balance between cellular and humoral immunity is required before this postulation can be supported. IgG, whilst the most abundant antibody in the body, is not the only immunoglobulin and therefore detail of other antibodies, such as IgM, IgA and IgE, are required. Furthermore, the balance between the two sides of the immune system is also carefully controlled by the regulation of specific cytokines, with interferon gamma (IFN γ) being crucial in the development of T-helper 1 cells that are instrumental in cellular immunity, and IL-4 and IL-10 being closely involved in the development of T-helper 2 cells that are involved in humoral immunity (Glimcher & Murphy, 2000; Kidd, 2003; Smith, 2003). A larger array of cytokines and immunoglobulins than have previously been measured therefore need to be investigated to further understand the balance between humoral and cellular immunity in FSI.

Perceptual and Psychological Responses to Firefighting

In addition to understanding the physiological strain experienced during firefighting tasks, it is also important to investigate and monitor how FF and BAI *feel* in response to acute exposures and their workloads. To our knowledge this is an area that has not been thoroughly investigated. If measured appropriately, subjective measurements could be a potential indicator of fatigue severity levels and psychological mood, which may in turn influence ill health status and overall well-being.

Various inventories such as the Multidimensional Fatigue Inventory (MFI-20), (Smets *et al.*, 1995) have been developed to quantify subjective levels of fatigue severity. These are typically used in research involving patients with conditions that are related to fatigue, such as chronic fatigue syndrome (CFS) (Lin *et al.*, 2009), Parkinson's disease (Elbers *et al.*, 2012), Fibromyalgia (Williams & Arnold, 2011), and cancer (Smets *et al.*, 1996). Amongst these specific conditions, fatigue has been frequently associated with higher levels of inflammation (Bower & Lamkin, 2013; Strawbridge *et al.*, 2019). In previous work by our group (Watt *et al.*, 2016), the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) (Stein *et al.*, 2004) was used to measure BAI's perceptions of fatigue, before and after a singular wear that were conducted either side of a 4-week breathing apparatus training course (consisting of 15 wears). Prior to this, all participants carried out a 7-wk no-heat exposure period which allowed for a more accurate reflection of 'baseline' measures to be recorded. For a wear conducted that followed the 4-week training (Wear 2),





changes in general fatigue (a sub-scale measured by the MFSI-SF), significantly correlated with changes in rectal core temperature (T_{re}) for Wear 2 (after 4-wk training course).

Assessment of psychological moods, which can be measured using the abbreviated Profile of Mood States questionnaire (POMS) (Grove & Prapavessis, 1992), could give us a more holistic viewpoint of the effects of differing workloads on the overall psychological well-being of FF and BAI. As well as the presence of typical illness symptoms and ‘sickness behaviours’, depressed moods have also been associated with elevated cytokine levels (Felger & Lotrich, 2013). Investigating various psychological moods in firefighting roles, especially on a long-term basis has received little attention, and is usually limited to the effects of traumatic events causing Post-Traumatic Stress Disorder (PTSD) (Haslam & Mallon, 2003) and sleep deprivation and physical work due to consecutively working on wildfire suppression (Wolkow *et al.*, 2016).

Monitoring subjective feelings of fatigue and psychological mood over a 6-month period in BAI and FF would provide a more comprehensive overview of how the workloads may be affecting their overall well-being. It may also offer opportunity to demonstrate if it is lowered moods that are encouraging increased inflammatory responses as opposed to the effects of heat related illnesses or higher workloads.

Contaminants and Cancer Risk

Prevalence of cancer has been much discussed amongst the firefighting community over recent years, with numerous research studies highlighting the possible association between the occupation and disease (LeMasters *et al.*, 2006). A review of 32 studies published between 1959 and 2003 reported increased risk of multiple myeloma, non-Hodgkin lymphoma, prostate cancer and testicular cancer, with a further eight cancers were suggested to have a “possible” association with firefighting (LeMasters *et al.*, 2006). If focus is given to specific locations, Florida has reported significant cancer incidence comparison to the general population with the standardised incidence ratio (SIR) increased in males for bladder (SIR = 1.29), testicular (1.60), and thyroid cancers (1.77). Female firefighters also exhibited increased incidence rates of overall cancer (1.63), cervical (5.24), and thyroid cancer (3.97) and Hodgkin disease (6.25) (Ma *et al.*, 2006). Similar findings were reported from a 45 year follow up of firefighters from Nordic countries, with a moderate excess risk for all cancer sites combined, (SIR = 1.06), with an excesses in the age category of 30–49 years in prostate cancer (2.59) and skin melanoma (1.62), and for those 70 years





and higher for non-melanoma skin cancer (1.40), multiple myeloma (1.69), adenocarcinoma of the lung (1.90), and mesothelioma (2.59). However, in opposition to previous studies the authors noted the incidence of testicular cancer declined (0.51) (Pukkala *et al.*, 2014).

The majority of research into this area has been conducted with American FF, from a UK perspective an assessment of serving FF between 1984 and 2005 from a Scottish Fire and Rescue Service revealed overall incidence and mortality rates from cancer were considerably less than the age- matched reference groups. However, incidence rates for kidney and melanoma, were significantly higher by 200% and 121%, respectively (Ide, 2014). The reduced incidence of all cause cancer noted in some studies is likely a consequence of the “healthy worker effect” whereby firefighters are typically healthier than the general population due to the nature of the occupational and recruitment/in role fitness requirements. There is disparity between studies over the association between some specific cancers and firefighting, which is possibly a result of varying methods of data assessment and sample populations. However, the overall consensus of research suggests that there may be an increased incidence of non-Hodgkin’s lymphoma, prostate, testicular cancer and malignant melanoma amongst FF (Petersen *et al.*, 2018). In 2007, the International Agency for Research on Cancer (IARC) conducted a meta-analysis reviewing 42 existing studies in the field classifying firefighting as being possibly carcinogenic (group 2B) (IARC, 2010). A recent review by IARC reclassified occupational exposure as a firefighter as being carcinogenic to humans (Group 1), with sufficient evidence for mesothelioma and cancer of the bladder (Demers *et al.*, 2022).

The association between firefighting and cancer may be a result of multiple factors, for instance shift work and emotional stress are confounding factors in numerous cancers (IARC, 2010; Jin Shin *et al.*, 2016). Fire smoke is also considered a key contributory factor, with smoke known to include components such as benzene, polycyclic aromatic hydrocarbons (PAH), polychlorinated biphenyls, asbestos, arsenic and formaldehyde, which are all known human carcinogens (Petersen *et al.*, 2018). The full spectrum of toxins present, given the vast array of materials possibly being burnt during operational fire exposures, alongside the chemicals from extinguishing agents, can often be unpredictable (Petersen *et al.*, 2018). Exposure of firefighters to PAHs has also been noted as a consequence of fuel and biomass combustion, and vehicle traffic emissions (Oliveira *et al.*, 2017). It is likely that a combination of PAH exposure, from a variety of sources, and lifestyle factors that occur as a result of the occupational role are responsible for the documented association with cancer.





PAH chemicals have been identified in FF and FSI urine following training/simulated fire exposures and wildland fires (Oliveira *et al.*, 2016; Wingfors *et al.*, 2018; Fent *et al.*, 2019; Adetona *et al.*, 2017), with a small number of studies conducted following acute on-shift fires (Keir *et al.*, 2017; Cherry *et al.*, 2019). Recent research conducted in America by Fent *et al.*, (2019) record 30-fold increases in urinary 1-hydroxypyrene levels in FSI following training exercises burning orientated strand board (OSB). OSB also resulted in greater contamination than burning pallet and straw, although both conditions caused contaminant levels above that of simulated smoke training (Fent *et al.*, 2019). Tactical approach and job assignment may also vary contaminant exposure levels, with interior attack and search methods results in 20 – 50% increase in contamination in comparison to a transitional attack (Fent *et al.*, 2020). Whilst in some cases PAH levels recorded are not above work exposure limits, the frequency of exposures experienced may make contamination detrimental to the health.

Despite the protection from PAHs conferred by BA, evidence suggests that dermal absorption of these chemicals is likely the key method of contamination, with greatest levels reported around the neck area, where protection given by the hoods is reduced in comparison to other PPE covered areas (Fent *et al.*, 2014; Wingfors *et al.*, 2018). In addition, the inhalation of off-gasing contaminants may also occur whilst doffing gear or as a consequence of incorrect PPE storage (Kirk & Logan, 2015b; Fent *et al.*, 2014). Evidence collected in the UK by Stec *et al.*, (2018) identified PAHs on FF skin, PPE, fire appliances and in various locations in fire stations.

Research studies investigating PAH levels of FF have so far been limited to training, simulation or wildland fires (Fent *et al.*, 2017; Oliveira *et al.*, 2016; Fent *et al.*, 2019) due to the logistical complexities of occupational fire data collection. In addition, whilst evidence suggests PAH levels return to baseline 24 – 48hrs post fire exposure (Fent *et al.*, 2020), long term monitoring of Fire and Rescue Service personnel has not been conducted. Whilst the majority of research into this topic has not been conducted in the UK, the range of countries with findings of this nature highlight that this issue is not isolated to one location or continent and in fact should be of concern for all Fire and Rescue personnel globally. Consequently, this study aims to identify differences in contamination from a variety of occupational live fires and assess contaminant levels of FF and BAI over a 6-month period.





Study Aims

This study aims to investigate the immunological, physiological and psychological responses to FF and BAI fire exposure frequency over a 6 month period. The study also aims to identify the contamination experienced by Fire and Rescue Service personnel from different fire scenarios.

Study Goals and Objectives

1. To record physiological data from firefighters and fire instructors during fire exposures to assess acute physiological strain and thermal loading for the consideration of working practices.
2. To measure contaminants, inflammation and psychological factors from 100 firefighters and 40 fire instructors over a 6-month period to assess the effects of exposure on associated health risks.
3. To create recommendations for physiological monitoring, contaminant exposure risk and fire exposure workloads and working practices of firefighters and instructors across the UK.





Methods

Participants

One hundred and thirty-six UK Fire and Rescue Service personnel were recruited from the following services: East Sussex, Essex, Hampshire, Kent, Staffordshire, West Midlands and the Fire Service College. Of the 136 participants, 44 were BAI (43 males and 1 female) and 92 were operational FF (79 males and 13 females). See Table 1 for the number of participants recruited from each service. Fourteen control participants (10 males and 4 females) were also recruited from the University of Brighton. These individuals were staff members at the University. The University of Brighton's ethics committee approved the study. Informed written consent was acquired from all participants prior to initial data collection.

TABLE 1: Number of participants initially recruited from each Fire Service. BAI = Breathing Apparatus Instructor, FF = Firefighters

Fire Service	BAI (n=44)	FF (n=92)
East Sussex	12	23
Essex	7	0
Fire Service College	8	0
Hampshire	9	0
Kent	0	16
Staffordshire	0	16
West Midlands	8	37

Table 2 shows the demographic characteristics of all participants that were recruited at the beginning of the study. Some participants were unable to attend future data collections. Therefore, the number of participants whom were present and participated in data collection at 3 and 6 months are presented in Table 3.

For analysis, BAI were split into two groups based on average number of exposures per month. A High Exposure BAI (High Expo BAI) group was established based on those who had an average of ≥ 20 exposures per month, whilst a Low Expo BAI consisted of those who had an average of ≤ 15 per month. This monthly exposure cut off point was selected based on the median (15) and mean (18) monthly exposure number reported by BAI. No BAI completed 16 – 19 exposures per





month, and therefore High Expo BAI represents those with 20 – 33 exposures and Low Expo BAI represents those with 5 – 15 exposures per month.

TABLE 2: Demographics of participants initially recruited (mean \pm SD) BAI = Breathing Apparatus Instructor, FF = Firefighters, CON = Control; BMI = Body Mass Index; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure

	FF (n=91)	BAI (n=44)	High Expo BAI (n=44)	Low Expo BAI (n=44)	CON (n=14)
Age (yrs)	39 \pm 8	46 \pm 7	43 \pm 10	50 \pm 11	37 \pm 10
Height (m)	1.78 \pm 0.1	1.78 \pm 0.08	1.80 \pm 0.08	1.78 \pm 0.09	1.77 \pm 0.06
Weight (kg)	85.5 \pm 14.0	87.4 \pm 11.6	86.6 \pm 7.6	91.8 \pm 15.1	72.3 \pm 9.0
BMI (kg/m ²)	26.9 \pm 3.4	27.3 \pm 4.2	27.2 \pm 2.0	28.31 \pm 15.1	23.0 \pm 2.1
SBP (mmHg)	132 \pm 13	133 \pm 15	132 \pm 18	137 \pm 23	124 \pm 12
DBP (mmHg)	84 \pm 9	86 \pm 11	87 \pm 10	85 \pm 18	74 \pm 9
Service time (yrs)	15 \pm 10	19 \pm 8	15 \pm 6	20 \pm 9	n/a
Time in current role (yrs)	11 \pm 16	2 \pm 3	2 \pm 4	3 \pm 3	n/a
Number of current smokers	6	2	0	2	0

TABLE 3: Number of participants involved in data collection at 3 and 6 months

	FF (n=91)	BAI (n=44)	High Expo BAI (n=21)	Low Expo BAI (n=23)	CON (n=14)
3 months	62	33	17	16	14
6 months	56	34	16	18	14

Experimental Design

Experimenters visited training centres and fire stations to collect data on 3 occasions, at 0, 3 and 6-month time points. Control samples were collected at the Welkin Laboratories of the University of Brighton. At the first visit (0 months) background information and purpose of the study was verbally presented, individuals were then given time to ask questions and the option to volunteer.

For those who chose to volunteer, informed written consent, anthropometric data and blood pressure were attained at 0 months. At all three time points participants completed a working history form (see Appendix A), a health questionnaire (see Appendix B), an abbreviated Profile of Mood States questionnaire (POMS) (Grove & Prapavessis, 1992) (see Appendix C) and the Multidimensional Fatigue Inventory (MFI) (Smets *et al.*, 1995) (see Appendix D). In addition, a





resting venous blood sample and a urine sample were collected. Control participants were not required to complete the working history form but were requested to avoid ambient temperatures $>25^{\circ}\text{C}$ for the 6 month duration of the study.

Between experimenter visits, BAI and FF groups were asked to complete an online exposure log following all fire exposures (see Appendix E). BAI were also asked to log training fires. Participants were requested to provide a urine sample after fire exposures and to store the samples in freezers provided until experimenter visits, whereby the samples were taken away for analysis. BAI were asked to only provide a sample for their last exposure of each month.

A sample of participants were asked to wear Equivital physiological monitoring systems to gather data from fire exposures. Equivital systems were given to 27 participants (15 BAI). Data was stored on the logger until experimenter visits, whereby the data was downloaded for analysis.

Experimental Procedures

Health questionnaire

The health questionnaire required participants to self-report the occurrence of symptoms of ill health within the past month, and participants completed this at 0, 3 and 6 months (see Appendix B). The following symptom: broken sleep, heavy sweating, extreme fatigue, headaches, mood swings, cold, persistent coughing, heart palpitations, back pain, lower limb muscle/joint & upper limb muscle/joint pain, were included as they were specifically reported in previous work by Watkins et al., (2018); a survey of working practices of 130 UK BAI. The frequency of each symptom was identified using the following options, ‘none’, ‘once’, ‘2-3 times’, ‘once a week’, ‘2-3 times a week’, and ‘continuously’.

Abbreviated Profile of Mood States

The POMS was originally developed by McNair *et al.*, (1971) and is available in various forms to indicate dimensions of mood disturbances. Participants completed the abbreviated version of POMS (Grove & Prapavessis, 1992) (see Appendix D) at 0, 3 and 6 months. The abbreviated POMS is a 40-item questionnaire that has 7 sub-scales; Tension (6 items, 0-24), Anger (6 items, 0-24), Fatigue (5 items, 0-20), Depression (6 items, 0-24), Esteem-related Affect (6 items, 0-24), Vigour (5 items, 0-20) and Confusion (5 items, 0-20). A lower score indicates a less severe





sensation of that mood, excluding Vigour, in which a higher score is desired. Each item relates to one of the 7 sub-scales. Total mood disturbance (TMD) was calculated using the following calculation:

$$[TEN+DEP+ANG+FAT+CON] - [VIG+ESTEEM] + 100$$

A constant of 100 was added to the calculation to avoid any negative TMD scores. An elevated score may indicate general mood disturbance.

Multidimensional Fatigue Inventory

The MFI (Smets *et al.*, 1995) is a validated subjective self-report likert scale questionnaire which aims to measure and assess various aspects of fatigue (see Appendix C). The scale is self-administered, takes approximately five minutes to complete, and has been validated in chronic fatigue patients and also both training and barrack soldiers by the authors who developed the inventory (Smets *et al.*, 1995).

The questionnaire consists of 20-items. These can be rated on a scale of 1 – 5; ‘1’ signifying ‘yes, that is true’ and ‘5’ signifying ‘no, that is not true’, all of which fall into one of the five different dimensions of fatigue; (i) General Fatigue, (ii) Physical Fatigue, (iii) Mental Fatigue, (iv) Reduced Activity and (v) Reduced Motivation. Therefore, the total number reached for each sub-scale could be a maximum of 20.

Exposure logs

The exposure log was designed as a readily accessible and user-friendly online form (Jisc, Bristol, UK) (<https://brighton.onlinesurveys.ac.uk/exposure-log>) that allowed participants to conveniently log each heat exposure for a total of 6 months. Exposure number was calculated using the exposure logs. The log required individuals to identify their role at the beginning of the shift, the length of operational activity during the shift, time in BA, role during the incident, type of fire exposure, material involved in the fire and form of decontamination technique (if any) (Appendix E).



Post-Exposure Visual Analogue Scales (VAS)

Post-exposure, participants were also required to complete five visual analogue scales (VAS) rating their perceptual feelings on a scale of 0-10. The question “*How did you feel by the end of the incident?*” was answered on five different subscales:

- (i) My temperature was neutral (0) vs. I had never been so hot (10)
- (ii) I felt fresh (0) vs. I was completely fatigued (10),
- (iii) I was not thirsty (0) vs. the thirstiest I had ever been (10),
- (iv) I had no pain (0) vs. worst pain ever (10), and
- (v) I was thinking clearly (0) vs. I felt completely confused and disorientated (10).

The sum of each score was divided by the total number of exposures completed, providing an average score for each participant, for each sub-scale.

Physiological measures

Physiological data was recorded via the Equivital system, which includes a vest containing sensors and a data logger (Figure 1). The system measured heart rate, skin temperature and estimated core temperature. For further information on the estimated core temperature equation please contact Equivital. Participants were allocated a vest based on their chest measurements and were instructed to wear them next to the skin during fire exposures.



Figure 1: Equivital vest and data logger used by participants.



Immunological measures

Whilst in a resting state, a trained phlebotomist collected a 20ml venous blood sample from the antecubital fossa. Samples were divided into 5ml tubes containing EDTA anticoagulant. Within two hours, whole blood was centrifuged at 4°C at 4500 rpm for 10 minutes. Blood plasma was aliquoted into 1.5ml eppendorfs and stored at -86°C, for future analysis. Blood samples were collected before midday prior to fire exposure, with time of collection remaining consistent for each station across the three visits. Blood plasma was analysed for Interleukin-6 (IL-6), Interleukin 1-β (IL-1β), Interleukin-10 (IL-10), Interleukin-4 (IL-4), Interferon gamma (IFN-γ), C-reactive protein (CRP), Immunoglobulin-G (IgG), Immunoglobulin-A (IgA), Immunoglobulin-E (IgE) and Immunoglobulin-M (IgM) using a Sandwich Enzyme-Linked Immunosorbent Assay (ELISA) kit (R & D Systems, Minneapolis, US and Thermo Fisher Scientific, Massachusetts, US). Intra-assay coefficient of variation was 4.1% for IL-1β, 4.9% for IL-6 and 4.7% for IL-10, 3.4% for IL-4, 5.0% for CRP, 5.7% for IFN-γ, 3.2% for IgG, 3.9% for IgM, 4.1% for IgA and 3.0% for IgE.

Ratios between IFN γ and IL-4 and IL-10 were also assessed to give indication of T helper 1/2 balance. All biomarker data was classified as above or below healthy reference values, excluding IL-6 and CRP, which were classified by future cardiac event risk classification. Values used for classification can be seen in table 2.

TABLE 2: Biomarker classifications according to reference values. High risk classification for cardiovascular event denoted by #

Biomarker	Limit (\geq)	Reference
CRP (mg.L⁻¹)	3.00 [#]	(Ridker, 2003)
IL-6 (pg.mL⁻¹)	2.28 [#]	(Ridker <i>et al.</i> , 2000)
IL-1β (pg.mL⁻¹)	2.00	(Di Iorio <i>et al.</i> , 2003; Hennø <i>et al.</i> , 2017)
IgG (g.L⁻¹)	16.00	(Fuggle, 2017)
IgM (g.L⁻¹)	2.59	(Fuggle, 2017)
IgA (g.L⁻¹)	4.00	(Fuggle, 2017)
IgE (ng.mL⁻¹)	513.60	(Martins <i>et al.</i> , 2014)
IL-10 (pg.mL⁻¹)	16.70	(Kleiner <i>et al.</i> , 2013)
IL-4 (pg.mL⁻¹)	2.00	(Hennø <i>et al.</i> , 2017)
IFN-γ (pg.mL⁻¹)	121.00	(Hennø <i>et al.</i> , 2017)



Contaminant measures

All urine samples were frozen until analysis. Samples were analysed for urinary 1-Hydroxypyrene (1-HP). 1-HP is a PAH metabolite and is a biological indicator of exposure to PAH. It is well recognised as a reliable indicator of exposure to fire produced contaminants.

Urine samples (1 mL) were acidified with the addition of 100 μ L 1 M HCl and extracted with methyl tertiary butyl ether (MTBE 500 μ L twice) for ten minutes. Extracts were dried under a stream of nitrogen and resolubilised in 0.05 % NH_3OH (10 μ L) and transferred to glass autosampler vials with fused inserts. Samples were injected (5 μ L) and subjected to reversed phase chromatography (Ascentis® Express C18, 5 μ m HPLC Column) at a flow rate of 200 μ L/min, using a gradient of A: water (0.05% NH_3OH) and B: acetonitrile (0.05% NH_3OH), starting from 12% B to 25% B over 3 min, up to 100% B in 1 min and held at 100% B for 1 min, down to 12% B in 30 s and held at 12% for 1 min. The mass spectrometer, a Thermo-Scientific Orbitrap, was operated in the negative mode using PRM (parallel reaction monitoring) from 1.6 to 5 min. Default charge state was set to 1. MS2 was acquired with a resolution of 70,000@200 m/z , using an AGC target of $2e5$ and a maximum IT of 250 ms. Isolation window was set to 3.0 m/z with an isolation offset of 0.5 m/z and a first fixed mass of 140.0 m/z , using a normalized collision energy of 35. An inclusion list of 393.09798 m/z and 402.15450 m/z , corresponding to light and heavy 1-HP glucuronide, respectively, was used. Spray voltage was set to 3.5 kV. Sheath, auxiliary and sweep gas were held at 20, 4 and 1, respectively. Capillary temperature was set to 320 °C and auxiliary gas heater temperature was set to 350 °C.

Peak areas for the light and heavy 1-HP glucuronide were generated from the reconstructed ion chromatogram of the fragments 217.0648 and 226.1213 m/z , respectively, at a mass accuracy of 10 ppm. The Genesis peak detection method was used, with 5 smoothing points for integration (Xcalibur V 4.1.31.9).

Urinary creatinine was used to correct the values of 1-HP glucuronide to urine production rate. Creatinine was analysed using the Jaffe method, reaction of creatinine with alkaline picrate and analysis by spectrophotometry (Heinegård & Tiderström, 1973). Samples were diluted to provide values within the standard curve range of 0-80 μ g/ml. Diluted urines were corrected for their dilution to provide values of creatinine in the urine (g/l).





All participants provided at least 1 urine sample and all samples (n = 667) were analysed for 1-HP. Samples provided by smokers and those who recently had eaten barbequed meat were excluded from the statistical analysis (n=11 participants, n = 33 samples). Forty-four samples were not included due to lack of a significant internal standard signal, or a signal below a signal to noise ratio of 1000. In total 590 samples were included in statistical analysis.

Data and Statistical analysis

Data was analysed using IBM SPSS Statistics v25, with a statistical significance accepted at $p \leq 0.05$. Demographic characteristics of participants are presented as means and standard deviation (\pm SD), and non-parametric data is presented as median and interquartile range (\pm IQR). Normal distribution of the data was analysed prior to analysis; using skewness and kurtosis ($+2$ or -2) and inferentially through a Kolmogorov Smirnov test. Where the data violated the assumptions of normal distribution, non-parametric tests were used or data was log transformed.

Perceptual, Physiological and Immunological Analysis

To test the differences in POMS and MFI sub-scales and all blood markers between the three time points (0, 3 and 6 months) within groups; a Friedman Test was conducted. If/where there were any significant differences, a Wilcoxon-Signed rank test was used as a post-hoc to see where those differences emerged. Bonferroni adjustments were applied to follow up tests.

A Kruskal Wallis H test was used to test for differences in all exposure variables between High Expo BAI, Low Expo BAI and FF. A Kruskal Wallis H test was also conducted to test for differences between groups for VAS, POMS, MFI, illness symptoms and all blood markers at each of the time points. Mann-Whitney U follow up tests were conducted to detect where differences occurred, with Bonferroni correction applied to p-values.

Due to the non-parametric nature of the biomarker data, average 6 month biomarkers were log transformed. The association between log biomarkers and average monthly fire exposures were assessed using linear regression analysis (model 1). The model was then adjusted for age, BMI, systolic blood pressure and diastolic blood pressure (model 2). Regression analysis was also conducted to identify the association between fire exposures and psychological factors and fire





exposures and symptoms of ill health, the same adjusted models were followed.

Contaminant Analysis

Data which violated normality assumptions was log transformed for statistical analysis. A two way mixed methods ANOVA was conducted to identify differences between 0, 3 and 6 month time points between the four exposure groups (HBAI, LBAI, FF, CON). Independent samples t-test analysis was conducted to compare differences in 1-HP between pre vs post fire exposure samples and between two training scenarios, demonstration and attack single box scenarios vs multiple compartment training scenarios. A one way independent measures ANOVA was conducted to assess differences in 1-HP as a result of numerous independent variables (exposure type, occupational task and fuel type in training). A one way independent ANOVA was also performed to identify differences in exposure duration between exposure types. In the presence of a significant effect, Tukey post hoc tests were utilised to identify where differences occurred. Where Levene's test revealed violations of homogeneity Welch's test was conducted and subsequent Games-Howell post hoc follow up tests. A Pearson's correlation analysis was conducted to identify if a relationship was present between exposure duration and 1-HP levels. Significance was accepted at $p < 0.05$.





Results and Discussion

Fire Exposures

There was a large range in exposure number across the groups. The study purposely set out to recruit the busier fire stations and training centres. Two training centres had a particularly heavy workload with BAIs each averaging approximately 25-30 exposures per month. Participants were asked to log exposures. This was not always completed by those taking part, although there were still 1234 logged exposures from a total of 85 participants (49 FF, 19 High Expo BAI and 17 Low Expo BAI). Subsequently, participants were also asked to provide the number of exposures completed in each 3-month period, details are shown in Table 4

TABLE 4: Details stating the number of exposures that were estimated from baseline data, then subsequently logged by participants. Data presented as mean \pm SD. # = significantly different from FF, † = significantly different from High Expo BAI, § = significantly different from Low Expo BAI. BAI = breathing apparatus instructor, FF = firefighter.

	FF (n=92)	High Expo BAI (n=21)	Low Expo BAI (n=23)	BAI (n=44)
Estimated number of fire exposures in 6 months	30 \pm 15 ^{†§} (Range 0-54)	135 \pm 66 ^{#§} (Range 93 - 207)	60 \pm 30 ^{#†} (Range 6 - 75)	74 \pm 76
Total number of fire exposures logged in 6 months	3 \pm 2 ^{§†} (Range 1 – 33)	29 \pm 34 [#] Range (4 – 97)	12 \pm 14 [#] (Range 2 – 41)	22 \pm 28
Average number of fire exposures per month	5 \pm 2	26 \pm 7	10 \pm 5	15 \pm 15
Duration of exposure (min)	45 \pm 20	60 \pm 15	60 \pm 25	60 \pm 15
Exposures wearing BA (%)	43 \pm 39 ^{§†}	100 \pm 0 [#]	100 \pm 0 [#]	100 \pm 0
Average time wearing BA (min)	20 \pm 11 ^{§†}	45 \pm 12 [#]	45 \pm 15 [#]	43 \pm 15





Fire Exposure Types

A total of 1234 exposures were logged (Figure 2). 885 (71.7%) of all exposures were BA training exercises (Attack: 274/22.2%, Compartment Fire: 486/39.4%, Demo: 124/10.0% and Hazmat: 1/0.1%). The further 349 (28.3%) exposures were logged as various other fire types such as: Dwelling Fire (105/8.5%), Industrial Building Fire (75/6.1%) and Vehicle Fire (37/3.0%),

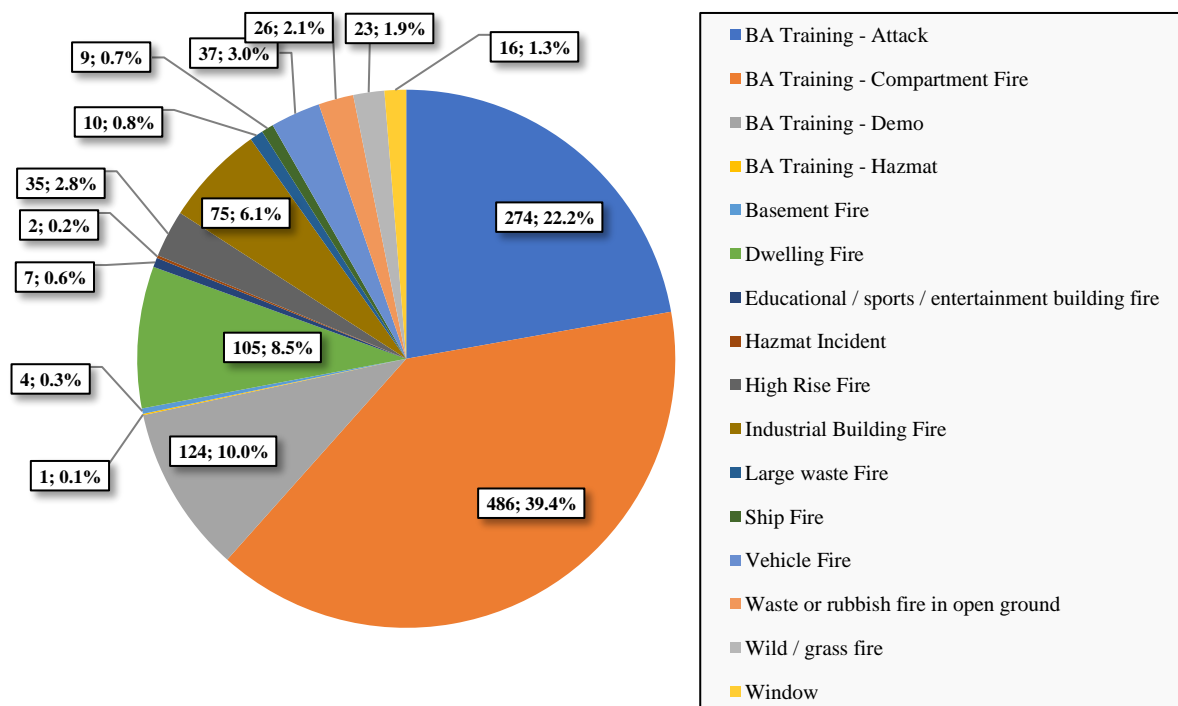


FIGURE 2: Pie chart representation of fire type logged by all participants over 6 months





Post-Exposure Visual Analogue Scale

A total of 85 participants (49 FF, 19 High Expo BAI and 17 Low Expo BAI) logged exposures over the duration of the study. A 6-month average score for each post-exposure VAS sub-scale was calculated, the median and IQR are presented. In response to “*my temperature was neutral vs. I had never felt so hot*”, both High Expo BAI (5.0 ± 1.4 , $p = 0.001$) and Low Expo BAI (5.1 ± 1.8 , $p = 0.004$) reported significantly higher scores compared to FF (2.7 ± 2.0). Similarly, High Expo BAI recorded a significantly higher perceptual response compared to FF (4.5 ± 2.7 vs. 2.7 ± 2.2 , $p = 0.012$) in response to “*I felt fresh and ready to go vs. I was completely fatigued*”, however, Low Expo BAI (4.4 ± 2.4) was no different to FF ($p = 0.075$). This pattern was repeated in response to “*I had no pain vs. worst pain ever*” with High Expo BAI reporting a significantly higher perceptual response compared to FF (2.2 ± 3.0 vs. 0.4 ± 1.0 , $p = 0.015$) with no difference between Low Expo BAI (1.2 ± 2.3) and FF ($p = 0.258$). In response to “*I was thinking clearly vs. I felt completely confused and disorientated.*”, both High Expo BAI (2.6 ± 2.2 , $p = 0.004$) and Low Expo BAI (2.8 ± 3.4 , $p = 0.012$) reported significantly higher scores compared to FF (0.8 ± 1.7). However, there was no differences in VAS thirst scores detected between groups ($p = 0.091$).

TABLE 5: BAI and FF perceptual responses to the Visual Analogue Scales (median \pm IQR), # = significantly different from FF ($p < 0.05$). BAI = breathing apparatus instructor, FF = firefighter

	FF (n=49)	BAI (n=36)	High Expo BAI (n=19)	Low Expo BAI (n=17)
Temperature	3.0 \pm 2.0	5.0 \pm 2.0	5.0 \pm 2.0 [#]	5.0 \pm 3.5 [#]
Fatigue	3.0 \pm 2.0	4.5 \pm 2.8	5.0 \pm 3.0 [#]	4.0 \pm 3.5
Thirst	4.0 \pm 3.5	5.0 \pm 2.8	5.0 \pm 3.0	5.0 \pm 3.0
Pain	0.0 \pm 1.0	2.0 \pm 3.0	2.0 \pm 4.0 [#]	1.0 \pm 3.0
Confusion	1.0 \pm 2.0	3.0 \pm 3.0	3.0 \pm 3.0 [#]	3.0 \pm 3.5 [#]

The results from the VAS suggest that BAI, regardless of exposure number, felt hotter and were more confused than FF after an acute exposure. High Expo BAI also experienced more fatigue and pain than FF. The high exposure frequency completed by High Expo BAI may mean that these individuals do not have sufficient recovery time between exposures and perceive an exposure as more strenuous. It is important to note that the type of exposure completed varied greatly in this study due to the operational nature of FF exposure logs. Data presented in Table 4 demonstrated





that BAI wore BA for longer durations of time compared to FF, which may also have contributed to the increased fatigue sensations.



Physiological Measurements

A total of 27 (15 BAI and 12 FF) participants were provided with, or already had access to, an Equivital vest and data logger at the experimenters' first visit to the station or training centre (Table 6). Nineteen (12 BAI and 7 FF) of those 27 participants produced valid data sets over 6 months and therefore, a total of 172 full and valid data sets were suitable for review and analysis. See Table 7 for summary of valid data sets.

TABLE 6: A summary of equivital system use for the duration of the study

	FF	BAI	Total
Number of participants with the system	12	15	27
Participants with valid data sets	7	12	19
Total number of valid data sets	19	153	172

TABLE 7: Summary of valid data taken from the equivital systems, including measures and various components of Core Temperature Estimate (CTE), Heart Rate (HR), Breathing Rate (BR) and Skin Temperature (T_{skin}).

	FF (n=7)	BAI (n=12)
Number of Days Recorded	15	157
Core Temperature Estimate (CTE) ($^{\circ}\text{C}$) <i>Mean \pm SD (Range)</i> <i>Time spent above 38.5$^{\circ}\text{C}$ (mins)</i> <i>Time spent above 39$^{\circ}\text{C}$ (mins)</i>	37.0 \pm 0.2 (36.3 - 38.5) 0 (0 - 0) 0 (0 - 0)	37.4 \pm 0.2 (36.3 - 39.1) 1.8 (0 - 37) 0 (0 - 2)
Heart Rate (HR) (bts.min$^{-1}$) <i>Mean \pm SD (Range)</i> <i>Time spent above 80%HRmax (mins)</i>	79 \pm 14 (48 - 182) 2.5 (0 - 25)	98 \pm 18 (50 - 189) 7.5 (0 - 58)
Breathing Rate (BR) (breaths.min$^{-1}$) <i>Mean \pm SD (Range)</i> <i>Time spent above 35 breaths per min (mins)</i>	18 \pm 4 (7 - 38) 0 (0 - 0)	19 \pm 5 (7 - 59) 2 (0 - 54)
Skin Temperature ($^{\circ}\text{C}$) <i>Mean \pm SD (Range)</i> <i>Time spent above 38$^{\circ}\text{C}$ (mins)</i>	34.7 \pm 1.1 0 (0 - 0)	34.4 \pm 2.1 7 (0 - 55)

Following this data are some examples of various data sets presented as case studies of different types of wear scenarios.

Instructor Example 1A:

This data is from a 51-year old male (BMI 25.4kg/m²) with 22 years' experience in the Fire Service 14 months experience as a BAI.

On this day (Figure 3), the exposure was recorded by the instructor as two high rise training fires. The data demonstrates a handful of key observations;

- (i) Following the first wear, CTE did not return back to resting (36.98°C) before the instructor continued to carry out their afternoon wear (37.09 °C)
- (ii) Compared to the morning wear, both peak HR and peak CTE were higher during the afternoon wear
- (iii) CTE continued to rise following peak HR during both wears, as indicated by the blue patterned area. In the morning wear, peak HR was 161 bts.min⁻¹ and the CTE continued to increase after the end of the wear for approximately 13 mins by 0.2°C (37.82 °C to 38.02 °C). In the afternoon wear, peak HR was 173 bts.min⁻¹ and the CTE continued to increase for approximately 8 minutes, by 0.23 °C (38.12 °C to 38.35 °C). This data demonstrates that individuals continue to heat up for approximately 10 mins after exposure finishes.
- (iv) It took 63 mins for the instructor to recover to near resting values.

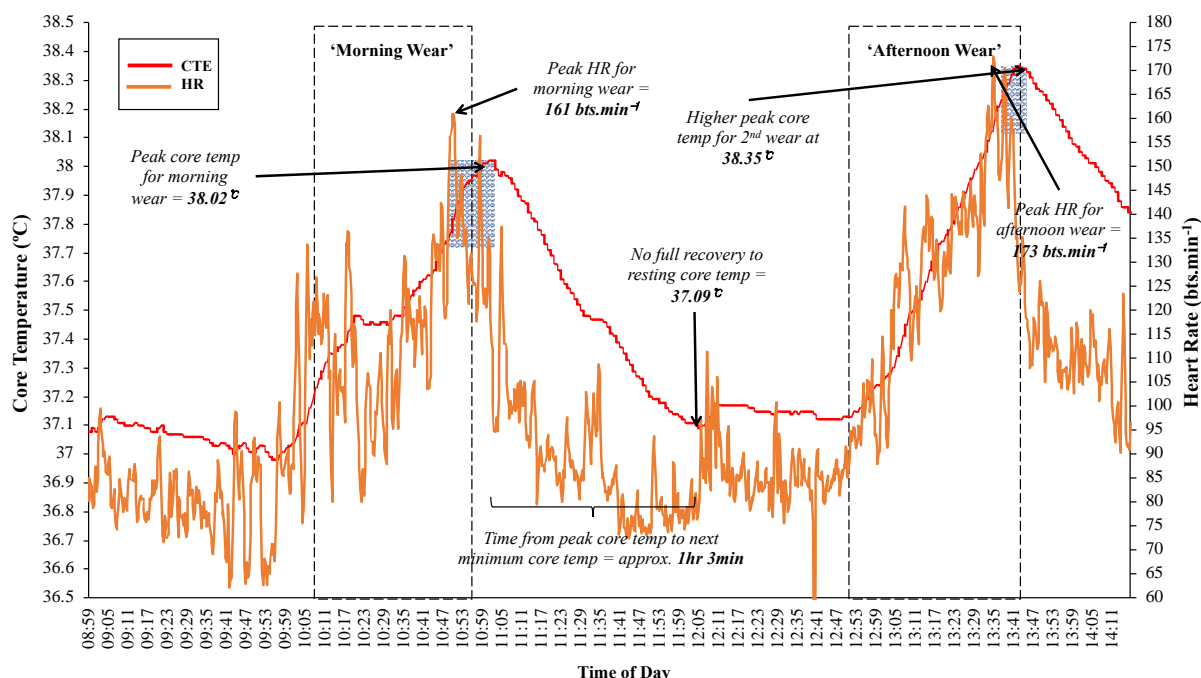


FIGURE 3: Annotated trace of Core Temperature Estimate (CTE; °C), and Heart Rate (HR; bts.min⁻¹) for an instructor recorded by an Equival system. Patterned area = further increase in CTE following activity end.

Instructor Example 1B:

Recordings from the same participant followed a similar trend on a different day during the same type of BA training exercise. On this day (Figure 4), the exposures were again recorded by the instructor as two high rise training fires. The data demonstrates similar key observations;

- (i) Following the first wear, CTE did not return back to resting (37.01°C) before the instructor continued to carry out the afternoon wear
- (ii) Compared to the morning wear peak CTE (38.41°C) was higher during the afternoon wear (38.54°C)
- (iii) CTE continued to rise following both wears, as indicated by the blue patterned area. In the morning wear, peak HR was 182 bts.min^{-1} and the CTE continued to increase for approximately a further 24 minutes by 0.35°C (38.05°C to 38.40°C). In the afternoon wear, peak HR was 175 bts.min^{-1} and CTE continued to increase for approximately a further 10 minutes, by 0.17°C (38.37°C to 38.54°C).
- (iv) It took 82 mins for the instructor to get to a minimum CTE after the morning exposure, by which point preparation for the next wear started. This was still 0.2°C above resting CTE. This demonstrates that there was not full recovery from the morning wear.

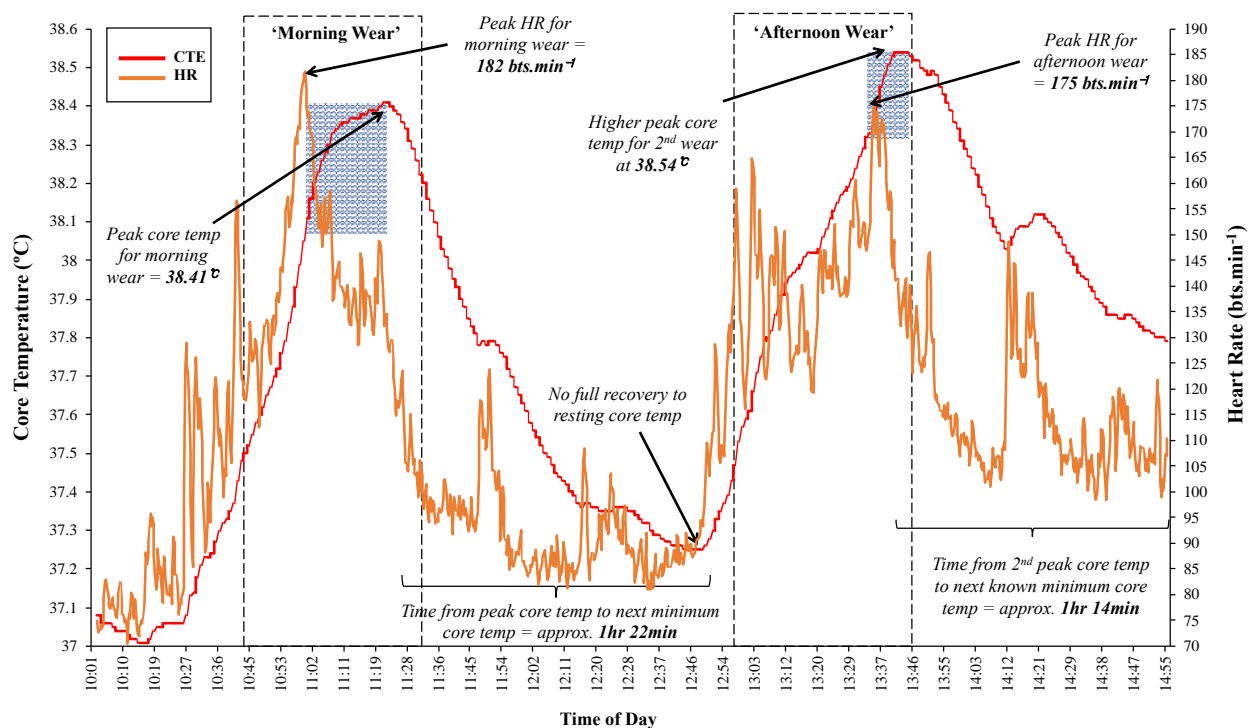


FIGURE 4: Annotated trace of Core Temperature Estimate (CTE; $^{\circ}\text{C}$), and Heart Rate (HR; bts.min^{-1}) for an instructor recorded by an Equival system. Patterned area = further increase in CTE following activity end.

Instructor Example 2:

The following data is from a 39-year-old male instructor (BMI 26.0kg/m²) with 13 years' experience in the fire service 21 months experience as a BAI. The exposure (Figure 5) was recorded by the BAI as a single exposure and identified the exercise as a BA Training - Compartment Fire.

From the data provided, the data demonstrates a handful of key observations;

- (i) CTE continued to rise after the wear for a further 9 minutes by 0.14 °C (38.87 °C to 39.01 °C), as indicated by the blue patterned area.
- (ii) The participant spent nearly 40 minutes with a CTE above 38 °C and HR above 80% HRmax, which is a very hot and heavy workload.
- (iii) The BAI had to remove all equipment (inc Equivital) immediately following exposure due temperature.

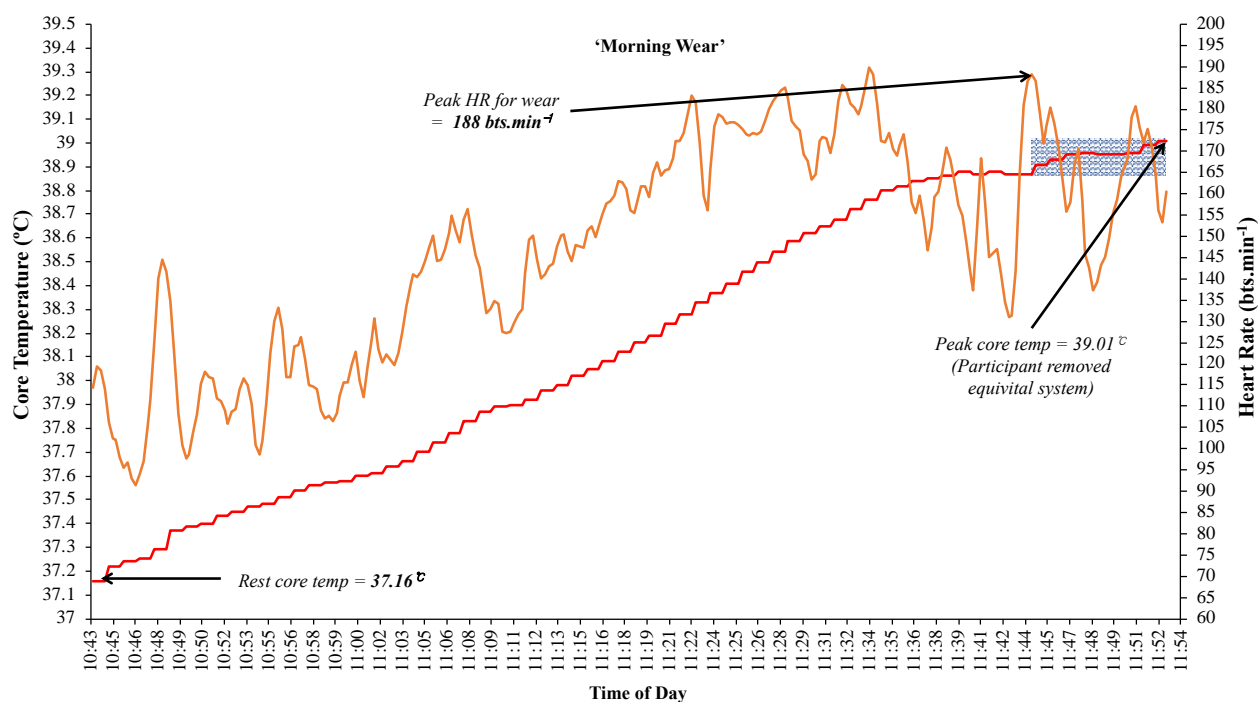


FIGURE 5: Annotated trace of Core Temperature Estimate (CTE; °C), and Heart Rate (HR; bts.min⁻¹) for an instructor as recorded by an Equivital system. Patterned area = further increase in CTE following peak HR/activity end.

Instructor Example 3:

The following data is from a 43-year-old male instructor (BMI 25.3kg/m²) with 19.4 years' experience in the fire service 22 months experience as a BAI. This exposure (Figure 6) was recorded by the instructor as a single exposure and identified the exercise as BA Training - Compartment Fire. The data provided demonstrates a handful of key observations;

- (i) CTE continued to rise after the exposure for approximately 12 minutes by 0.28°C (38.0°C to 38.28°C), as indicated by the blue patterned area,
- (ii) The instructor spent 26 minutes above 38°C.
- (iii) It took 46 mins for the instructor to get CTE back to within 0.5 °C, however the instructor did not get back a resting CTE by the end of shift.

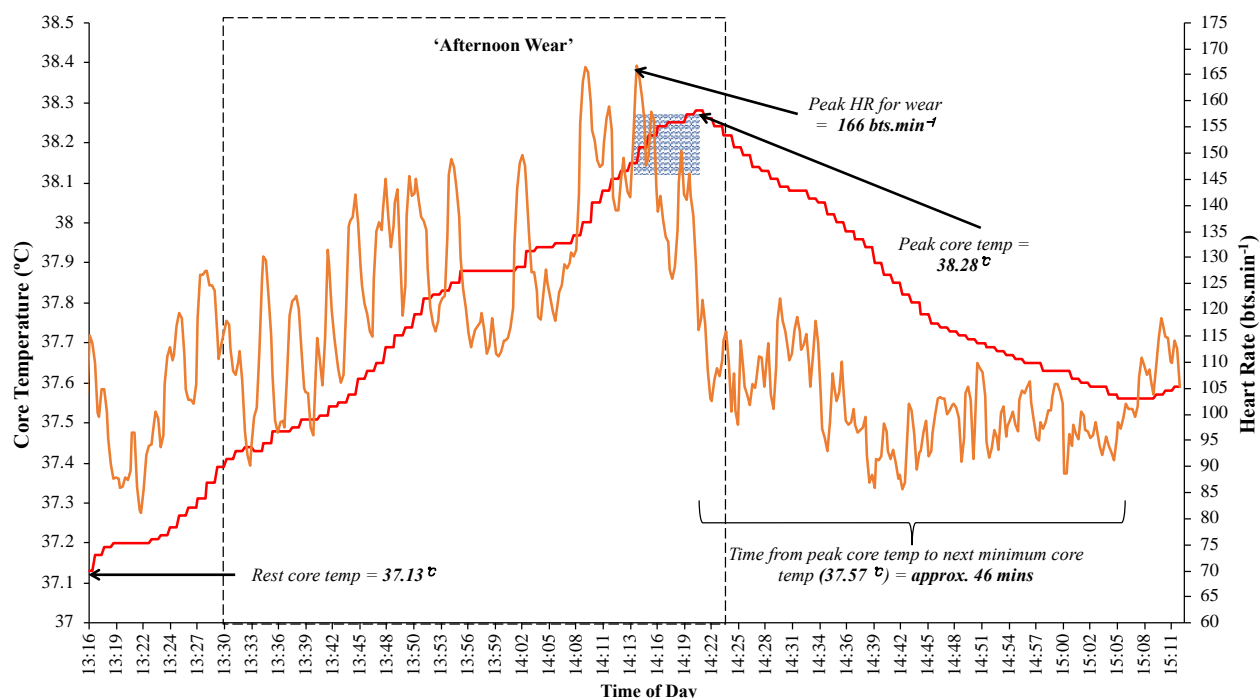


FIGURE 6: Annotated trace of Core Temperature Estimate (CTE; °C), and Heart Rate (HR; bts.min⁻¹) for an instructor as recorded by an Equival system. Patterned area = further increase in CTE following peak HR/activity end.

Firefighter Example 1:

The following data is from a 41-year-old female firefighter (BMI 22.3kg/m²) with 20 years' experience in the Fire Service. This was a training fire exposure (Figure 7). The data provided demonstrates a handful of key observations;

- i) Core temperature remained elevated after the exposure for approximately 10 minutes before slowly declining.
- ii) Heart rate returned to baseline in around 20 minutes, whereas core temperature remained 0.9°C above resting core temperature when the vest was removed 30 mins after completing the wear.
- iii) Adequate time needs to be given for effective recovery during training sessions.

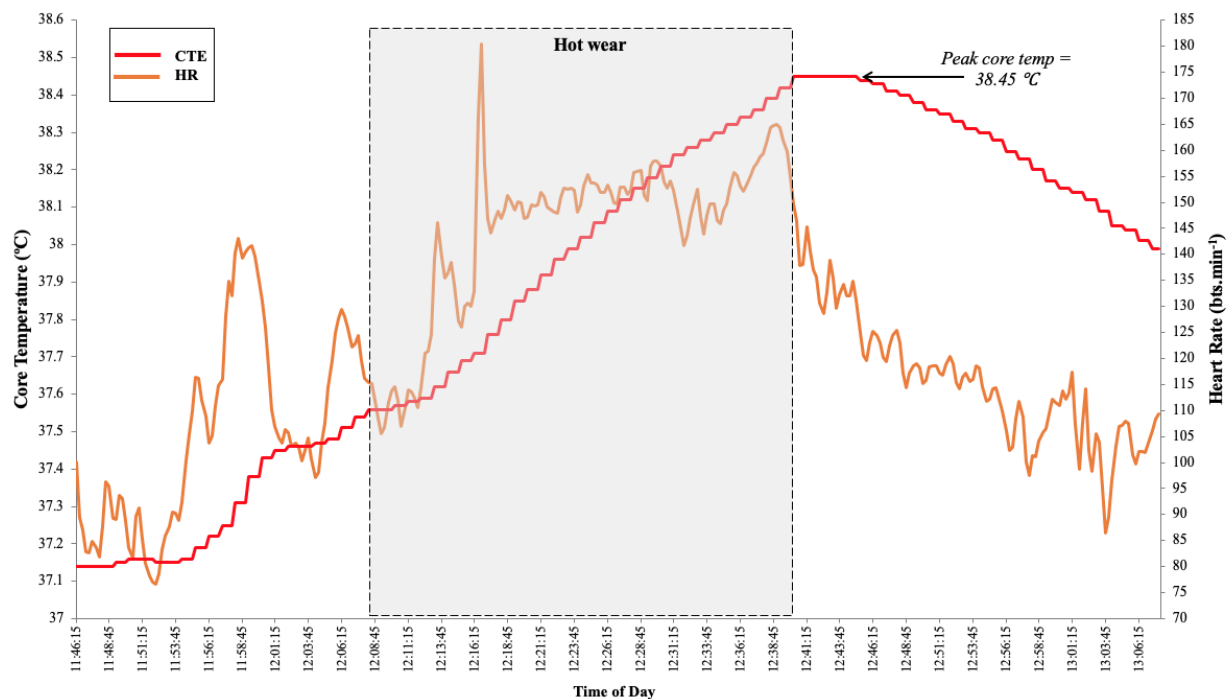


FIGURE 7: Annotated trace of Core Temperature Estimate (CTE; °C), and Heart Rate (HR; bts.min⁻¹) for a firefighter, recorded by an Equivital system.

Firefighter Example 2:

The following data is from a 49-year-old male firefighter (BMI 25.5kg/m²) with 23 years' experience in the Fire Service. This was a vehicle fire exposure (Figure 8). The data provided demonstrates a handful of key observations;

- i) Firefighters tend to experience multiple tasks, but do not experience necessarily high core temperatures when dealing with short duration work while outdoors.
- ii) The spikes in heart rate over the afternoon demonstrate the short, repeated tasks being carried out.
- iii) Even though the firefighter is outdoors, working in PPE has cumulative effect, meaning the body progressively stores heat over these repeated short tasks.
- iv) In this scenario a period of 21 mins recovery allowed core temperature to return to near rest values before completing another task.

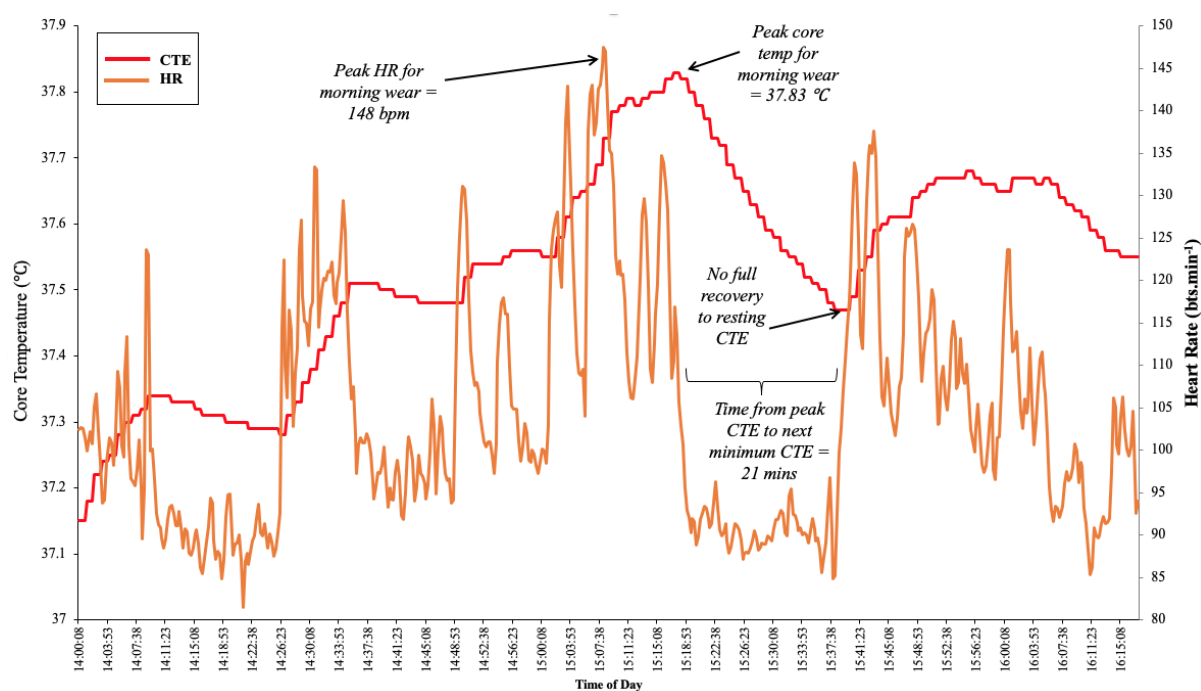


FIGURE 8: Annotated trace of Core Temperature Estimate (CTE; °C), and Heart Rate (HR; bts.min⁻¹) for a firefighter recorded by an Equival system.

New Recruits Example 1A:

The following data is from a group of six new recruits on their second day of BA training. This was a compartment fire behaviour training session with various short tasks over a 90 minute period. The data provided demonstrates a significant increase in core temperature in all individuals. While four of the six participants end the session with a core temperature in excess of 39°C. Two individuals reached 40°C. This puts them at a high risk for heat illnesses.

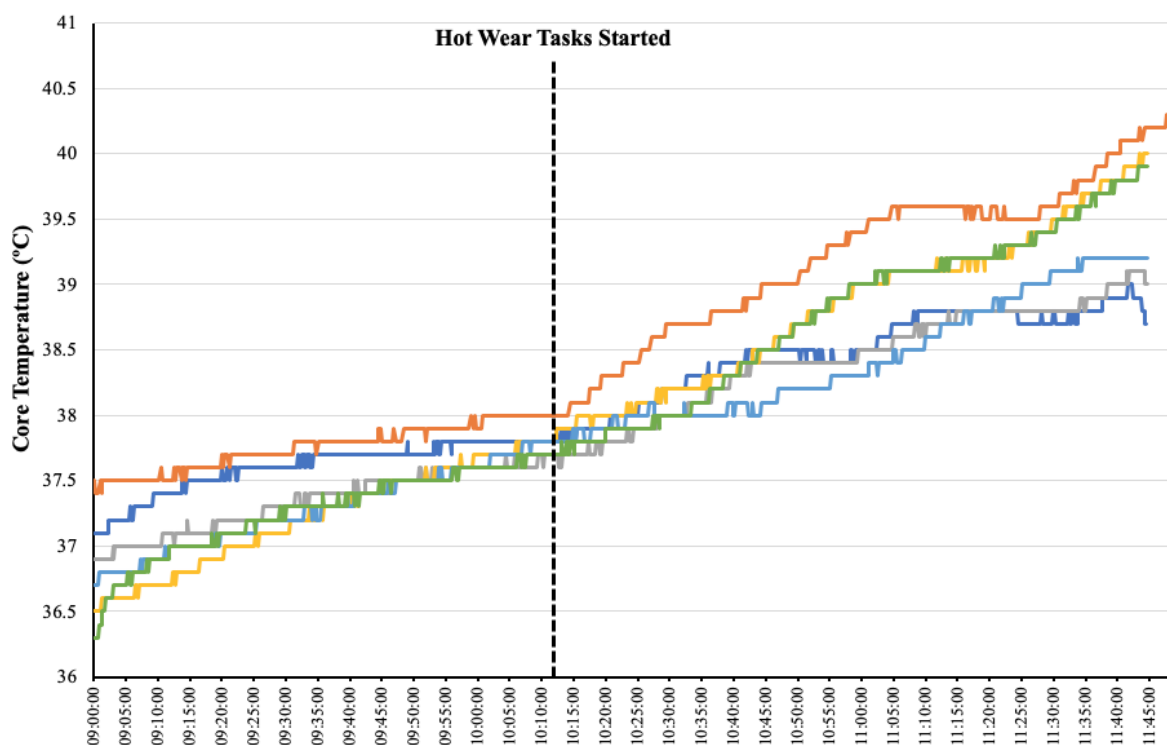


FIGURE 9: Core Temperature (°C) for a group of trainee firefighters during a morning wear. Dotted line indicates the starting of hot wear activities.

New Recruits Example 1B:

Similarly, this is another set of data from day 6 of the BA basic training for five of the new recruits during an afternoon wear. Core temperature systems were donned with PPE at 13:40. Recruits reached similar core temperatures to that seen throughout the 2-week basic training and that shown in the previous example (Figure 10). This again demonstrates the potential for heat illness in this particular group. This data also demonstrates that recruits were starting to heat up well before starting the wear by donning PPE.

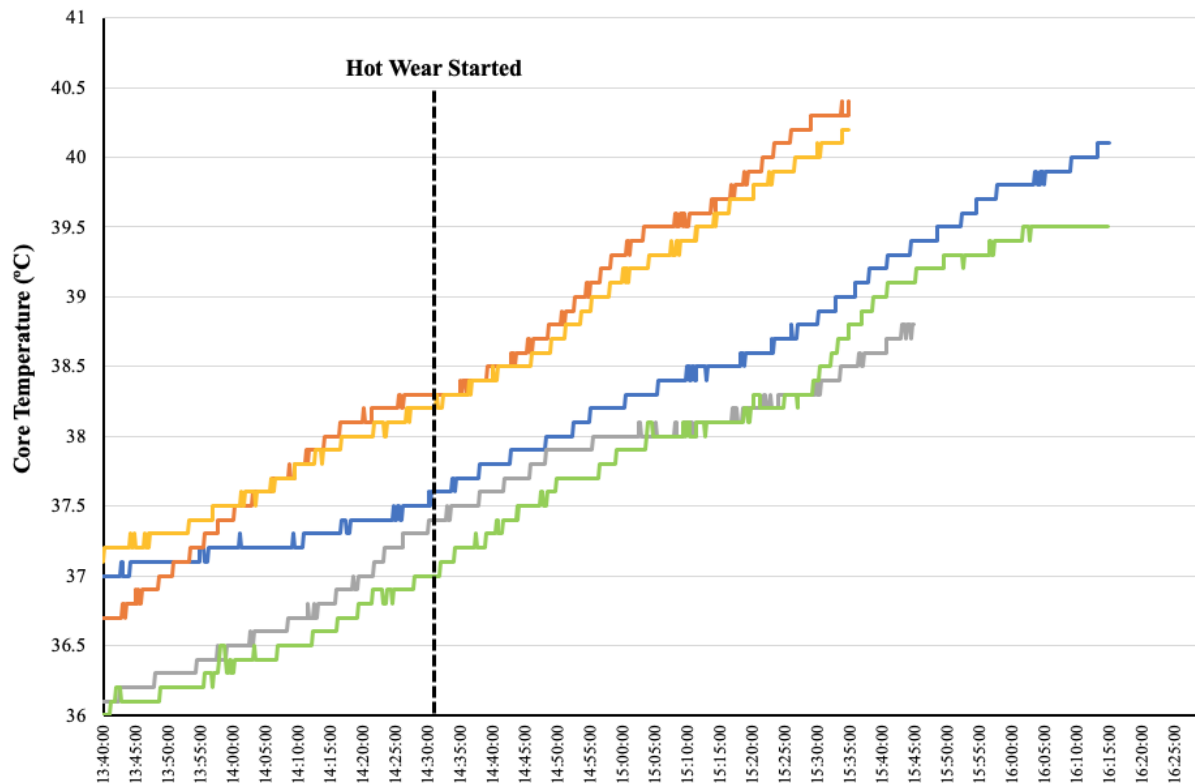


FIGURE 10: Core Temperature (°C) for a group of trainee firefighters during an afternoon wear.

Training Fire with Ice Slurry Example:

The following data is from a training fire and show the BA trainee ingesting ice slurry during a briefing period (15 mins duration) prior to donning PPE and then undertaking a hot wear. The decline in gastrointestinal core temperature of $\sim 0.25^{\circ}\text{C}$ is quite fast. Temperature then returns back to resting levels while donning PPE and activities on the fire-ground, although it is important to note that in the previous figures core temperature exceeded resting levels during this phase. This initial reduction in temperature may help reduce the final temperatures seen during BA training activity. The BA trainee in this instance only increased to 38.37°C over the wear.

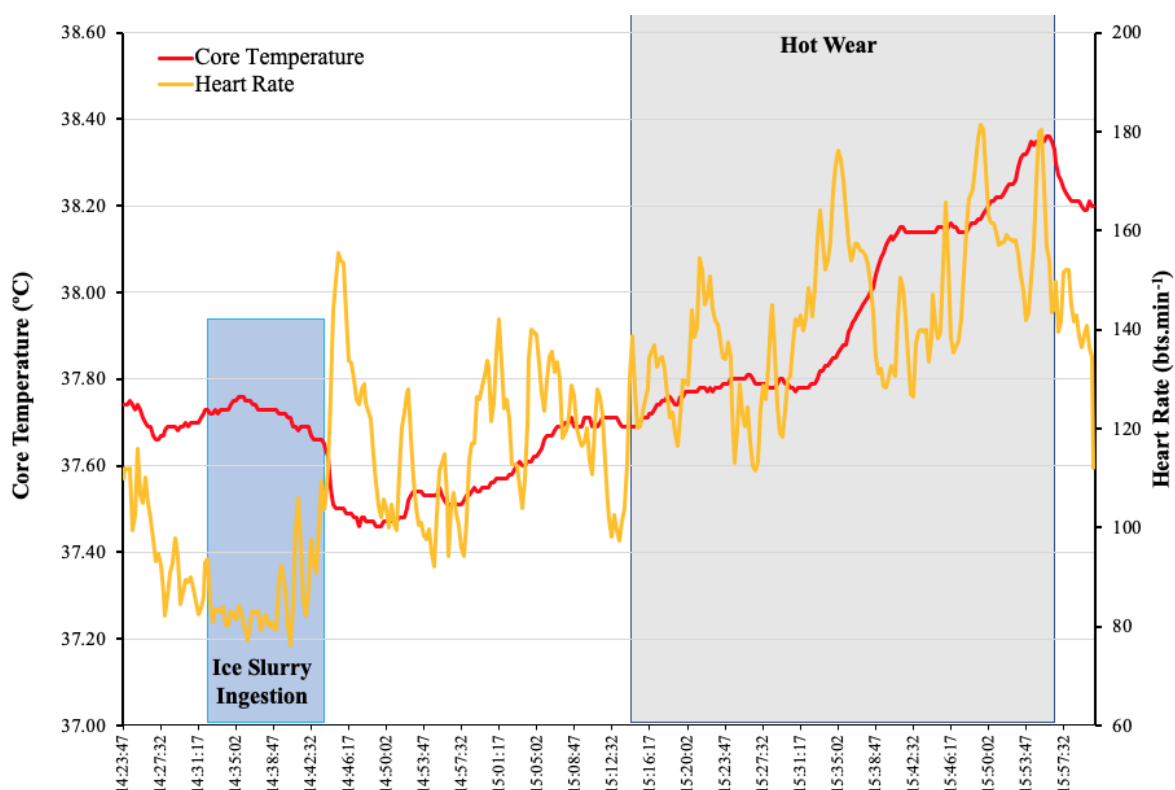


FIGURE 11: Annotated trace of Core Temperature ($^{\circ}\text{C}$), and Heart Rate (HR; $\text{bts}\cdot\text{min}^{-1}$) for a firefighter recorded by a telemetry pill system.



Physiological Measurement Considerations

The measurement of core temperature during firefighting tasks is particularly challenging due to logistics, safety, accuracy and implementation of the findings. Subsequently we along with many others have spent a great deal of time and effort attempting to test and consider the best practices to physiological assessment of firefighting.

Core Temperature Options and Accuracy

The gold standard measurement of core temperature is measured using rectal core temperature, which is simply not feasible or fair to consider. The other direct measurement option would be the gastrointestinal telemetry pill, however these are not possible in an emergency environment as they have to be consumed 6 hours prior to use, they also cost ~£50 per pill making training based activities impossibly expensive. The Equivital system uses an algorithm based on heart rate and skin temperature to calculate core temperature. This is in the process of becoming optimised for accuracy in the Fire Service, with firefighting tasks being modelled against the core telemetry pill. Whilst the temperature presented by the algorithm appears reasonable and realistic, the exact accuracy of the algorithm has not yet been defined when worn during firefighting tasks. The data obtained within this study uses the algorithm method. Finally, in-ear devices offer a feasible option, taking a temperature from the aural canal. BodyTrak and Cosinuss use this method. However, we found the versions available at the time not to be safe or robust enough to be feasible for use by Fire Service personnel outside of training fires.

Logistics

Wearing a device can be challenging especially while wearing PPE in a fire scenario. During training activities this can be feasible as there is time to don the PPE and device appropriately in order for it to be set correctly. Firefighters could wear devices throughout shifts but over this study we have found that firefighters generally do not wish to wear anything extra, certainly anything that could be uncomfortable. Equivital vests or Cosinuss and Bodytrak ears pieces are possible to wear all day but can be uncomfortable. Meanwhile, the feasibility of donning these during an emergency call is challenging, especially the Equivital vest. During this study, most firefighters chose to wear the vest throughout the shift in case of an emergency call. This subsequently led to significant volumes of firefighter data being of resting periods. Conversely, BAIs when knowing they were going to have an exposure wore the Equivital vest and obtained data. Even so, a lot of





data was lost by participants putting in the logging device incorrectly. Approximately 80% of the sessions with vests worn did not provide useable data.

Safety

Many devices that are to be taken into a fire need to be intrinsically safe, yet all these devices require a battery to run. Many devices even require a mobile phone to receive and download data. The consequence of this is that many of the best devices available are not possible to use within the Fire Service.

Implementation

Once a device can be used a clear method of implementing its use must be considered. Measuring numbers alone offers little meaning. The data shown in this study demonstrates very heavy workloads of BAIs, with physiological strain further elevated in new recruits unacclimatised to firefighting tasks, PPE and anxious of the training activities. Given the values shown here, it would be expected that recruits during training will often experience core temperatures in excess of 39-40°C. For this population monitoring of temperatures should be considered, especially in regard to an upper temperature limit. Likewise, monitoring of BAIs longer term will help them understand how long it takes for them to recover or how severe the exposure was. It would also help with effective rotation of staff during exposures or between wears and shifts.

For firefighting, the firefighter, incident commander or central control team need to know if an individual is approaching a core temperature threshold. A simple alert (vibration, alarm etc) needs to be used to inform welfare and act as a means of rotating personnel effectively. However, an effective device is still not available yet. It must be quick to don or be wearable all shift, be comfortable, intrinsically safe and easy to obtain data from quickly, with little need for set up by the firefighter. At present all available options fall short of being appropriate for effective use.



Perceptual Scales at 0, 3 and 6 months

Multidimensional Fatigue Inventory

Results from the responses to the MFI at 0, 3 and 6 months are presented in Appendix F. Responses did not significantly differ between 0, 3 and 6 months within each group ($p > 0.05$); suggesting that all participants experienced the same level of fatigue at each dimension over the 6-month duration.

Additionally, no differences in any sub-scales between groups were reported at any time point ($p > 0.05$) or for the 6-month average ($p > 0.05$) (Table 8).

TABLE 8: 6-month average results from the Multidimensional Fatigue Inventory for FF, BAI (High & Low Exposure) and CON (median \pm IQR). FF = firefighter, BAI = breathing apparatus instructor, CON = control.

	FF (n=56)	BAI (n=34)	High Expo BAI (n=16)	Low Expo BAI (n=18)	CON (n=14)
General Fatigue	9 \pm 4	11 \pm 4	11 \pm 3	10 \pm 5	8 \pm 3
Physical Fatigue	7 \pm 3	8 \pm 4	8 \pm 3	8 \pm 4	7 \pm 3
Mental Fatigue	9 \pm 5	9 \pm 5	7 \pm 4	9 \pm 4	9 \pm 6
Reduced Activity	6 \pm 4	7 \pm 3	7 \pm 2	6 \pm 5	5 \pm 3
Reduced Motivation	7 \pm 3	9 \pm 4	9 \pm 3	9 \pm 3	7 \pm 4

MFI provides a valid assessment of fatigue in this study, as correlation analysis reveals that each subscale average positively corresponds with 6 month average POMS measurements of fatigue ($r = 0.298 - 0.730$, $p < 0.001$) and reports of extreme fatigue symptoms ($r = 0.247 - 0.501$, $p = 0.002 - < 0.001$). Only one subscale (reduced activity) was not correlated with extreme fatigue symptom reports ($r = 0.150$, $p = 0.068$).

The results noted for BAI are similar to that noted by Watt *et al.*, (2016) whereby fatigue levels reported on a variation of the MFI was not altered in BAI across a 4 week training instruction course. Scores on the MFI subscale recorded by FF (6 – 9) and BAI (7 – 11) are similar, if slightly elevated, in relation to those reported by a well population from America (7 – 8), and lower than that of a chronically ill population (9 – 13) (Lin *et al.*, 2009). Values were also lower than that reported by cancer patients both pre (9 – 12) and post (10 – 13) radiotherapy (Purcell *et al.*, 2010).



A change of 1 – 2 points on a subscale, with the exact value dependent on scale, have been identified as the minimal clinically important difference to note changes in MFI, although this was determined specifically within patients undergoing radiotherapy and therefore is not necessarily applicable to an alternate population (Purcell *et al.*, 2010). Whilst not statistically significant, average 6 month values of general fatigue and reduced motivation are 2 or more points greater in High Expo BAI compared to FF and CON. VAS fatigue reports taken post fire exposure suggest elevated fatigue amongst BAI in comparison to FF. Being fatigued at work may be associated with impaired performance and compromised safety (Williamson & Friswell, 2013). However, it remains unclear if this post exposure fatigue conveys to chronic fatigue.

Abbreviated Profile of Mood States Questionnaire

Low Expo BAI demonstrated some variability in mood subscales between 0 and 6 months, with variations in Tension ($p = 0.005$), Fatigue ($p = 0.032$) and Depression ($p = 0.032$) (Appendix G). Otherwise, the data suggests that there were no inconsistencies in these perceptual feelings as measured by POMS over the 6 months.

There were also no differences between groups for every sub-scale at each time point (Appendix G) or for the 6-month average (Table 9).

TABLE 9: 6 month- average from all POMS sub-scales for FF, BAI (High and Low Expo). Data presented as median \pm IQR. (TMD = Total Mood Disturbance)

	FF (n=56)	BAI (n=34)	High Expo BAI (n=16)	Low Expo BAI (n=18)	CON (n=14)
Tension	2 \pm 3	2 \pm 4	2 \pm 4	2 \pm 4	2 \pm 2
Anger	1 \pm 4	1 \pm 3	1 \pm 2	1 \pm 3	1 \pm 3
Fatigue	4 \pm 5	5 \pm 5	5 \pm 7	5 \pm 5	4 \pm 4
Depression	1 \pm 3	1 \pm 4	1 \pm 4	2 \pm 3	2 \pm 3
Esteem	18 \pm 4	18 \pm 4	19 \pm 2	17 \pm 4	15 \pm 5
Vigour	10 \pm 5	10 \pm 5	11 \pm 4	10 \pm 5	11 \pm 3
Confusion	2 \pm 3	2 \pm 5	2 \pm 4	2 \pm 5	1 \pm 3
TMD	84 \pm 19	85 \pm 25	85 \pm 26	85 \pm 21	87 \pm 16

The use of POMS amongst high stress occupations is limited and there exists a large variation between different POMS questionnaires, consequently normative data for Fire and Rescue Service Personnel is not available (Perroni *et al.*, 2009). When comparing data to other studies using the





abbreviated POMS, TMD values recorded in this study are greater than that reported by rested military personnel (75.8 ± 3.4), but not dissimilar to values recorded mid military training (85.0 ± 2.9) (Fry *et al.*, 1994). Values are also in the region of those reported by endurance athletes (94 ± 10) (Robson-Ansley *et al.*, 2009). It can therefore be suggested that POMS scores reported by Fire and Rescue Service personnel are similar to that reported in other similar populations.

It is interesting to consider that both FF and BAI had similar POMS scores to the CON group, despite the very different occupations. POMS is not specific to firefighting tasks and is therefore sensitive to everyday life stresses. It could be postulated that the similarity between CON and FF may be a consequence of CON also experiencing mood disturbances from either their work or lifestyle.

Low psychological moods such as depression and fatigue have previously been associated with elevated markers of inflammation (Brydon *et al.*, 2009; Howren *et al.*, 2009). However, literature is conflicting as to the causal direction in linkage between inflammation and depression (Das, 2016; Huang *et al.*, 2019; Howren *et al.*, 2009). The lack of differences detected in these groups of participants indicates that any biomarker elevations are likely not caused by altered mood states.



Illness Symptoms

Participants were given a health questionnaire to complete consisting of a list of 11 symptoms that relate to ill health; requiring them to self-report any occurrence of these symptoms within the past month. The frequency of each symptom was identified using the following options, ‘none’, ‘once’, ‘2-3 times’, ‘once a week’, ‘2-3 times a week’, and ‘continuously’.

The total number of symptoms (TotSymp) reported at least once at each time point (0, 3 & 6 months) were calculated for each participant and presented in Table 10, the maximum score possible being 11. No differences were found between time points for each group ($p > 0.05$), suggesting that TotSymp reported were consistent over the 6 months.

No difference in TotSymp between groups was found at 6 months however, at 0 and 3 months, High Expo BAI reported significantly more symptoms of ill health in the previous month, compared to CON (5 ± 3 vs. 2 ± 2 ; $p = 0.04$, 6 ± 5 vs. 3 ± 4 ; $p = 0.046$) respectively. Analysis of the average score across from the 6-month was revealed a differences between High Expo BAI and CON (6 ± 3 vs. 3 ± 2 ; $p = 0.006$).

TABLE 10: Number of symptoms reported (out of 11) in the previous month by FF, HighExpo BAI, LowExpo BAI and CON. At 0, 3 and 6 months. Also showing the 6-month average. Data is presented as median \pm IQR (range). * = significantly different to CON ($p < 0.05$).

	Group	Total number of Symptoms
0 months	FF (n=92)	4 ± 4 (0 - 9)
	High Expo BAI (n=21)	$5 \pm 3^*$ (0 - 10)
	Low Expo BAI (n=23)	4 ± 4 (0 - 10)
	CON (n=14)	2 ± 2 (0 - 8)
3 months	FF (n=62)	3 ± 4 (0 - 10)
	High Expo BAI (n=17)	$6 \pm 5^*$ (1 - 10)
	Low Expo BAI (n=16)	4 ± 2 (2 - 8)
	CON (n=14)	3 ± 4 (0 - 8)
6 months	FF (n=56)	4 ± 4 (2 - 7)
	High Expo BAI (n=16)	7 ± 5 (1 - 10)
	Low Expo BAI (n=16)	4 ± 4 (2 - 7)
	CON (n=14)	3 ± 4 (0 - 10)
6 – month average	FF (n = 92)	4 ± 3 (1 - 7)
	High Expo BAI (n = 21)	$6 \pm 3^*$ (1 - 9)
	Low Expo BAI (n = 23)	3 ± 3 (0 - 8)
	CON (n = 14)	3 ± 2 (1 - 9)

Out of the 11 illness symptoms, ‘broken sleep’ reoccurred the most frequently (Table 11). Although it is difficult to argue, it may be a concern that some symptoms (such as broken sleep and heavy sweating) were reported by the participants as a reflection of their normal duties, as opposed to a symptom of ill health when not on duty. For example, FF often experience periods of disturbed sleep which may be a consequence of their shift patterns and reduced psychological well-being (Åkerstedt & Kecklund, 2017; Smith *et al.*, 2019). Both FF and BAI may experience heavy sweating as a physiological response to exercising in the heat. Table 9 presents the occurrence of each symptom which they reported to have experienced in the previous month.

TABLE 11: The occurrence of each symptom at 0, 3 and 6 months

		BROKEN SLEEP	HEAVY SWEATING	EXTREME FATIGUE	HEADACHES	MOOD SWINGS	COLD	PERSISTENT COUGHING	HEART PALPITATIONS	BACK PAIN	LOWER LIMB/JOINT PAIN	UPPER LIMB/JOINT PAIN
0	FF	77	36	43	38	34	24	16	9	45	40	23
	HighExpo BAI	17	12	12	14	6	8	7	4	12	7	6
	LowExpo BAI	17	9	11	12	11	7	3	2	8	10	9
	CON	8	1	2	5	5	4	0	0	2	5	2
	Overall	119	58	68	69	56	43	26	15	67	62	40
3	FF	54	30	36	24	21	10	8	7	27	23	11
	HighExpo BAI	16	12	12	13	8	4	2	5	12	7	8
	LowExpo BAI	15	5	10	7	8	4	2	0	3	8	4
	CON	10	2	3	7	6	2	0	0	8	3	2
	Overall	95	49	61	51	43	20	12	12	50	41	25
6	FF	48	29	25	20	23	21	10	5	25	21	17
	HighExpo BAI	14	15	11	9	9	7	3	3	9	11	11
	LowExpo BAI	13	8	10	6	9	4	1	0	4	10	4
	CON	11	3	3	6	5	2	0	2	7	5	3
	Overall	86	55	49	41	46	34	14	10	45	47	35



The results discussed so far do not demonstrate the frequency at which these symptoms were reported. For further analysis, the responses to the illness symptoms questionnaire were scored accordingly;

- ‘None’ = 0
- ‘Once’ = 1
- ‘2 – 3 times’ = 2
- ‘Once a week’ = 3
- ‘2 – 3 times a week’ = 4
- ‘Continuously’ = 5

Sum of symptoms scores are displayed in Table 12. There were no changes in sum of symptom scores over time for each of the groups ($p < 0.05$). Comparison between groups revealed differences in sum of symptom scores at all time points and for the 6 month average ($p < 0.05$). At 0 months both High Expo BAI and FF reported an increased sum of symptoms compared to CON ($p = 0.005$ and $p = 0.009$, respectively). At 3 months High Expo BAI exhibited greater sum symptom scores than both CON ($p = 0.006$) and FF ($p = 0.048$). High Expo BAI was also greater than CON at 6 months ($p = 0.004$). Collective 6 month averages revealed that High Expo BAI and FF reported greater sum symptom scores than CON ($p = 0.001$ and $p = 0.013$, respectively).

TABLE 12: Sum of symptoms scores at 0, 3 and 6 months. 6- month average also presented (data presented as median \pm IQR) * denotes a significant difference from CON, # denotes a significant difference from FF.

	0 months	3 months	6 months	6-month average
FF	9 \pm 9*	8 \pm 9	9 \pm 9	8 \pm 8*
HighExpo BAI	11 \pm 14*	15 \pm 16*#	16 \pm 15*	14 \pm 14*
LowExpo BAI	9 \pm 12	8 \pm 7	9 \pm 8	8 \pm 9
CON	4 \pm 6	5 \pm 8	5 \pm 8	5 \pm 5

Please refer to Appendix H for a more in-depth presentation of results for illness symptom reports.

Illness symptom data demonstrates that symptoms experienced are consistent over a 6 month period and it can therefore be suggested that these issues are chronic in nature. High Expo BAI report an increased number of symptoms in comparison to CON, whilst no differences were detected between CON and Low Expo BAI or FF. This is similar to the increased cluster of symptoms reported previously by BAI (Watkins *et al.*, 2018; Watkins *et al.*, 2019a; Watkins *et*





al., 2020). The data collected in this study also provides further detail than previous research by enabling an understanding of symptom frequency to be gained. High BAI displayed consistently increased frequency of symptom expression compared to CON, and on occasion also increased expression in comparison to FF. FF symptom frequency varied in comparison to other groups, which may reflect the altering sample size as a result of non-attendance. Joint/back pain and disturbed sleep were the most commonly reported symptoms by FF, this support previous reports of increased prevalence of these issues in the occupation (Lusa *et al.*, 2015; Negm *et al.*, 2017; Kim *et al.*, 2013).





Blood Measures

Due to call outs, staffing changes and drop outs, blood samples were not collected from all 150 participants at each 3 time points. Data analysis was therefore conducted on complete data sets ($n = 55$) and a comparison between groups also made on average data from those providing a sample at any time points.

Across Time Points

Each of the groups displayed some variations in biomarkers over time (see Table 13). For the CON group there were variations in five of the variables, CRP, IL-6, IL-4, IL-10 and IgM, with levels being lowest at the 6 month time point ($p < 0.05$). For FF, six of the variables displayed changes across the months, with IL-6, IL-10, IL-4, IgG, IgE and IgM being greatest at 0 months ($p < 0.05$). For LBAI IL-10 and IL-6 were greatest at 0 months, IgG, IgM, IgE were greatest at 3 months, and IgA greatest at 6 months ($p < 0.05$). In contrast, HBAI demonstrated little variation, with only CRP and IgE varying between time points, with greatest levels detected at 3 and 6 months, respectively.

Overall fluctuations between months, whilst statistically significant, did not cause the median values to change between being above or below healthy reference values in the majority of cases. IL-1 β , IL-6 and IL-10 for both LBAI and FF medians demonstrated fluctuations, with the three variables being above reference values at 0 months only within the FF group, whilst LBAI median was only below upper values at 6 months for IL-6 and IL-10. See Table 6 for number of participants above reference ranges within each group and time point.





TABLE 13: Biomarker data for participants with complete data sets. CON n = 12 , FF n = 18 , LBAI n = 11 , HBAI n = 14 . Data presented as Median IQR. * = different from 0 months, # different from 3 months, † different from CON, ‡ different from FF, \$ different from LBAI.

	0 Months				3 Months				6 Months			
	CON	FF	LBAI	HBAI	CON	FF	LBAI	HBAI	CON	FF	LBAI	HBAI
CRP (mg.L⁻¹)	0.46 ± 0.12 (0/0%)	0.39 ± 0.16 (1/6%)	0.51 ± 0.31‡ (1/9%)	0.59 ± 0.57‡ (1/7%)	0.60 ± 0.38* (0/0%)	0.46 ± 0.71 (0/0%)	0.52 ± 1.68 (2/18%)	1.13 ± 2.56 (4/29%)	0.14 ± 0.23* (0/0%)	0.29 ± 0.51 (0/0%)	0.24 ± 1.25 (2/18%)	0.92 ± 5.48*† (5/36%)
IL-6 (pg.mL⁻¹)	0.99 ± 0.89 (1/8%)	2.52 ± 2.56 (9/50%)	9.24 ± 12.51†(9/82%)	12.27 ± 92.18† (10/71%)	2.16 ± 1.61 (3/25%)	0.86± 1.05 (0/0%)	2.93 ± 11.57‡ (6/55%)	3.93 ± 53.57‡ (8/57%)	0.61 ± 0.71# (0/0%)	1.36 ± 0.81 (2/11%)	1.46 ± 1.87* (2/18%)	4.93 ± 40.67† (8/57%)
IL-1β (pg.mL⁻¹)	1.00 ± 2.35 (3/25%)	3.18 ± 6.64 (9/82%)	7.99 ± 41.39† (9/82%)	3.74 ± 35.17†(10/71%)	1.43 ± 5.00 (5/42%)	1.07 ± 1.25 (3/17%)	11.32 ± 37.51†‡ (10/91%)	9.86 ± 109.92†‡ (10/71%)	1.28 ± 0.97 (3/25%)	1.26 ± 1.30 (3/17%)	3.59 ± 7.53# (5/45%)	8.81 ± 139.08†‡ (11/79%)
IgG (g.L⁻¹)	7.04 ± 2.32 (0/0%)	10.68 ± 4.30† (0/0%)	9.33 ± 1.40 (0/0%)	9.63 ± 2.74 (0/0%)	7.89 ± 11.15 (3/25%)	7.29 ± 2.08* (0/0%)	14.33 ± 5.25‡ (3/27%)	11.98 ± 6.10 (0/0%)	7.49 ± 1.59 (0/0%)	7.33 ± 1.67* (0/0%)	7.28 ± 1.45** (0/0%)	8.13 ± 4.97* (0/0%)
IgM (g.L⁻¹)	1.79 ± 1.36 (2/17%)	0.98± 0.29 (3/17%)	1.08 ± 0.48 (1/9%)	0.98 ± 0.29† (0/0%)	1.86 ± 2.20 (4/33%)	1.15 ± 0.99* (0/0%)	1.13 ± 0.34 (1/9%)	0.96 ± 0.22† (0/0%)	1.59 ± 1.51*# (1/8%)	1.17 ± 0.65* (0/0%)	0.99 ± 0.27 (1/9%)	0.97 ± 0.17† (0/0%)
IgA (g.L⁻¹)	1.09 ± 1.05 (0/0%)	1.21 ± 1.53 (1/6%)	0.99 ± 0.14 (0/0%)	1.40 ± 1.10 (1/7%)	1.24 ± 0.97 (0/0%)	1.23 ± 0.87* (0/0%)	0.96 ± 1.01 (1/9%)	1.17 ± 0.87 (0/0%)	1.02 ± 0.68 (0/0%)	1.13 ± 0.69 (0/0%)	1.21 ± 0.88* (0/0%)	1.25 ± 0.69 (0/0%)
IgE (ng.mL⁻¹)	40.54 ± 39.79 (0/0%)	40.90 ± 44.19 (0/0%)	97.02 ± 68.42 (0/0%)	75.68 ± 173.29 (0/0%)	41.57 ± 28.09 (0/0%)	52.35 ± 36.24*(1/6%)	132.43 ± 139.18† (0/0%)	114.56 ± 152.30† (0/0%)	44.58 ± 32.7 (0/0%) ⁹	54.69 ± 28.54 (1/6%)	101.96 ± 116.08† (0/0%)	74.60 ± 203.14† (0/0%)





IL-10 (pg.mL⁻¹)	9.98 ± 12.08 (2/17%)	53.43 ± 94.86 (13/72%)	64.62 ± 280.06 [†] (11/100%)	251.06 ± 714.05 ^{†‡} (14/100%)	14.87 ± 22.64 (4/33%)	4.45 ± 6.81 (2/11%)	85.02 ± 81.96 [‡] (9/82%)	121.89 ± 604.81 [‡] (1 1/79%)	4.15 ± 8.29 [#] (1/8%)	1.34 ± 11.73 (2/11%)	5.58 ± 22.63 ^{*#} (3/27%)	119.68 ± 614.94 [‡] (10/71%)
IL-4 (pg.mL⁻¹)	1.45± 1.47 (1/8%)	1.39 ± 1.08 (0/0%)	1.04 ± 1.25 (1/9%)	4.25 ± 9.72 ^{\$} (6/43%)	1.13 ± 1.57 (1/8%)	0.80 ± 1.97 (1/6%)	1.05 ± 1.87 (1/9%)	4.28 ± 18.43 (7/50%)	1.33 ± 1.67 [*] (1/8%)	0.76 ± 1.41 [*] (2/11%)	1.12 ± 2.10 (1/9%)	6.90 ± 19.73 [‡] (8/57%)
IFN-γ (pg.mL⁻¹)	78.98 ± 4.48 (0/0%)	75.44 ± 4.51 (0/0%)	73.23 ± 4.25 (0/0%)	79.22 ± 106.79 (4/29%)	80.09 ± 6.13 (0/0%)	75.62 ± 5.44 (0/0%)	73.68 ± 4.62 [†] (0/0%)	77.21 ± 43.72 (3/21%)	78.43 ± 3.22 (0/0%)	76.18 ± 10.80 (0/0%)	75.45 ± 4.44 (3/21%)	81.21 ± 48.29 (0/0%)
IFN-γ /IL-4	53.575 ± 39.22	53.77 ± 39.97	75.59 ± 58.57	33.69 ± 37.75 ^{\$}	53.73 ± 57.94	107.23 ± 362.38 [*]	72.08 ± 248.88	30.88 ± 206.71	62.15 ± 78.57	101.60 ± 180.69 [*]	68.67 ± 80.01	17.69 ± 56.58 [‡]
IFN-γ /IL-10	8.28 ± 14.64	1.39 ± 14.01	1.33 ± 1.20 [†]	0.32 ± 0.71 ^{†‡}	4.07 ± 10.89	17.06 ± 63.53 [*]	0.88 ± 0.59 [‡]	0.51 ± 1.62 [‡]	20.19 ± 63.39 ^{*#}	57.68 ± 69.66 [*]	19.88 ± 71.56 ^{*#}	0.62 ± 13.33 [‡]





Complete Data Sets - Difference between Groups

Excluding CRP, IL-4, IgA, IgG and IFN- γ , analysis of complete data sets revealed differences between groups for biomarkers at all time points ($p < 0.05$). No differences in IgA were noted at any point ($p = 0.781$, $p = 0.995$, $p = 0.876$) whilst IgG and IFN- γ exhibited differences only at months 0 ($p = 0.003$, $p = 0.050$) and 3 ($p < 0.001$, $p = 0.011$). Groups did not differ in IL-4 at 3 months ($p = 0.203$) or CRP at 3 months ($p = 0.061$) (see Table 13).

HBAI was greater than either FF or CON at all three time points for IL-6, IL-1 β and IL-10 ($p < 0.05$). HBAI also exhibited IgM and IFN- γ /IL-10 ratio values lower than CON for all time points ($p < 0.05$). In addition, IL-4 was elevated in HBAI above FF levels at 6 months ($p = 0.004$), with corresponding IFN- γ /IL-4 ratios being reduced in HBAI ($p = 0.006$). LBAI also exhibited values greater than FF or CON for CRP, IL-6, IL-1 β , IgG, IgE, IL-10, although these differences did not persist across the 6 month observation period. There was only one occurrence of FF biomarker values being greater than CON, which were noted at 0 months in IgG ($p = 0.002$).

6 Month Average between Groups

Excluding IgA ($p = 0.846$), IL-4 ($p = 0.423$) and IFN- γ ($p = 0.054$) the 6 month average of all variables displayed a significant difference between groups ($p < 0.05$), see Table 14 CRP and IgG displayed an effect of group ($p = 0.019$ and $p = 0.023$, respectively), however follow up tests did not reveal significant differences, with only a trend indicating greater CRP for HBAI in comparison to FF ($p = 0.063$) and greater IgG in LBAI than FF ($p = 0.083$).

HBAI exhibited greater levels of IL-6, IL-1 β , IgE, IL-10, and reduced levels of IgM, in comparison to CON and/or FF ($p < 0.05$), see Table 14. LBAI also exhibited biomarker values greater than CON for IL-6, IgE, IL-10 ($p < 0.05$). There were no differences noted between FF and CON for any biomarkers ($p > 0.05$). The percentage of participants with IL-10 above the upper reference limit is also notably greater in HBAI (48%) compared to all groups (FF: 7%, CON: 0%, BAI LOW: 13%).

There was no difference between groups for IFN- γ /IL-4 ($p = 0.545$). Alternatively, IFN- γ /IL-10 data indicated group differences ($p < 0.001$), with the ratio being lower in both HBAI and LBAI compared to both CON ($p < 0.001$ and $p = 0.001$, respectively) and FF ($p < 0.001$ and $p = 0.017$, respectively). There was no difference between FF and CON ($p = 0.368$).





TABLE 14: Average six month biomarker data, CON n = 12, FF n = 81, LBAI n = 23, HBAI n = 21. Data presented as Median IQR. † different from CON, ‡ different from FF, \$ different from LBAI.

	6 Month Average Months			
	CON	FF	LBAI	HBAI
CRP (mg.L⁻¹)	0.43 ± 0.20	0.47 ± 0.66	0.53±0.94	0.73 ± 1.69
IL-6 (pg.mL⁻¹)	1.22 ± 0.69	1.85 ± 2.08	3.86 ± 4.97 [†]	3.60 ± 26.18 ^{†‡}
IL-1β (pg.mL⁻¹)	1.68 ± 1.56	2.87 ± 3.87	4.86 ± 9.93	8.92 ± 32.78 ^{†‡}
IgG (g.L⁻¹)	7.38 ± 4.09	8.43 ± 3.57	10.00 ± 3.00	10.03 ± 4.31
IgM (g.L⁻¹)	1.82 ± 1.70	1.18 ± 0.65	1.04 ± 0.33	0.99 ± 0.26 [†]
IgA (g.L⁻¹)	1.27 ± 0.87	1.09± 0.82	1.06 ± 1.16	1.17 ± 0.85
IgE (ng.mL⁻¹)	39.99 ± 19.31	58.17 ± 64.46	89.29 ± 102.86 [†]	94.18 ± 153.20 [†]
IL-10 (pg.mL⁻¹)	8.88 ± 12.92	24.90 ± 48.21	54.80 ± 46.10 [†]	125.85 ± 452.93 ^{†‡}
IL-4 (pg.mL⁻¹)	1.21 ± 1.57	1.28 ± 1.27	1.26 ± 1.22	1.28 ± 1.82
IFN-γ (pg.mL⁻¹)	78.02 ± 2.92	76.50 ± 7.82	74.22 ± 4.48	75.09 ± 16.27
IFNY/IL-4	63.98 ± 56.95	61.92 ± 47.88	66.07 ± 62.12	44.97 ± 73.39
IFNY/IL-10	9.70 ± 14.12	3.39 ± 11.10	1.30 ± 1.42 ^{†‡}	0.60 ± 0.87 ^{†‡}

Biomarker Association with Exposure Number

Average monthly fire exposure number was significantly associated with levels of IL6 ($p < 0.001$), IL1b ($p < 0.001$), IL10 ($p < 0.001$) and IgM ($p = 0.002$). Trends also suggested an association with CRP ($p = 0.052$). After adjustment for age, BMI, systolic blood pressure and diastolic blood pressure associations remained between monthly exposure number and IL6, IL1-b, IL10 and IgM. Adjusted models suggest monthly fire exposure number accounts for 15.4% of the variance in IL6 values, 11.8 % of the variance of IL1b and 25.2% of IL10. See Table 15 for full regression analysis results.

TABLE 15: Regression analysis statistical results demonstrating the association between average monthly fire exposures over a 6 month period and average 6 month biomarker values (model 1)





and the adjusted model (model 2). Adjustments made for BMI, age, systolic and diastolic blood pressure. * denotes a significant model ($p < 0.05$). # denotes average monthly fire exposure as a significant predictor to the model ($p < 0.05$)

AVERAGE NUMBER OF MONTHLY FIRE EXPOSURES

	MODEL 1					MODEL 2 (adjusted)				
	R ²	Model P value	β	β 95% CI	Predictor P value	R ²	Model P value	B	β 95% CI	Predictor P value
CRP	0.033	0.052	0.007	0.00, 0.015	0.052	0.183*	<0.001	0.006	-0.002, 0.013	0.128
IL-6	0.127*#	<0.001	0.020	0.010, 0.030	<0.001	0.154*#	0.002	0.020	0.010, 0.029	<0.001
IL-1β	0.106*#	<0.001	0.027	0.012, 0.041	<0.001	0.118*#	0.016	0.028	0.013, 0.042	<0.001
IgG	0.017	0.159	0.002	-0.001, 0.005	0.159	0.199	0.482	0.002	-0.001, 0.005	0.186
IgM	0.078*#	0.002	-0.005	-0.09, -0.002	0.002	0.093#	0.054	-0.005	-0.009, -0.002	0.004
IgA	0.042	0.656	0.001	-0.004, 0.005	0.656	0.183	0.581	0.001	-0.004, 0.005	0.834
IgE	0.011	0.265	0.004	-0.003, 0.011	0.265	0.076	0.116	0.004	-0.003, 0.011	0.247
IL-10	0.249*#	<0.001	0.042	0.028, 0.055	<0.001	0.252*#	<0.001	0.042	0.28, 0.055	<0.001
IL-4	0.023	0.112	0.008	-0.002, 0.018	0.112	0.065	0.209	0.009	-0.001, 0.019	0.090
IFN-γ	0.003	0.534	0.001	-0.001, 0.002	0.534	0.047	0.0382	0.001	-0.01, 0.003	0.852

Biomarker Association with Psychological Factors

Regression analysis was also conducted to identify associations between 6 month average psychological factors (the five fatigue scales and TMD) and biomarker levels (Model 1). Significant associations were present only for CRP ($R^2 = 0.119$, $p = 0.029$), with Reduced Motivation identified as a predictor variable ($\beta = 0.060$, 95% CI: 0.019, 0.102, $p = 0.005$). This association was still present when adjusted for age, BMI, systolic blood pressure and diastolic blood pressure (Model 2) ($R^2 = 0.223$, $p = 0.002$: $\beta = 0.046$, 95% CI: 0.005, 0.087, $p = 0.027$). Trends suggest IL1b may also be associated with psychological factors ($R^2 = 0.105$, $p = 0.054$), with General Fatigue a significant predictor ($\beta = 0.115$, 95% CI: 0.037, 0.193, $p = 0.004$). Although this trend was not apparent in the adjusted model ($p = 0.194$).





Exposure Number Association with Symptoms

Exposure number was associated with the 6 month average total symptom score ($R^2 = 0.033$; $\beta = 0.145$, 95% CI: 0.005, 0.285, $p = 0.042$), with confounding factors of age, BMI, systolic and diastolic blood pressures not altering the predictor variables contribution.

Discussion of Biomarker Data

Systemic Inflammation

Whilst biomarker levels varied across the 6 month period for BAI LOW, FF and CON, consistent levels were demonstrated by BAI HIGH. IL6 ($3.60 \pm 7.23 \text{ pg.mL}^{-1}$), IL1b ($8.93 \pm 17.85 \text{ pg.mL}^{-1}$) and IL10 ($125.85 \pm 356.00 \text{ pg.mL}^{-1}$) were notably increased in BAI HIGH in comparison to CON and FF. BAI LOW was also increased in comparison to CON in both IL6 and IL10, but only in comparison to FF for IL10. Previous research by Watkins et al., (2020) reported similar findings from a singular snapshot of inflammatory status ($n = 110$), with IL6 ($1.66 \pm 2.26 \text{ pg.mL}^{-1}$) and IL1b ($2.50 \pm 9.99 \text{ pg.mL}^{-1}$) being elevated in BAI in comparison to FF, in addition to increases in CRP ($1.62 \pm 2.40 \text{ pg.mL}^{-1}$). Research studies with smaller sampler sizes further corroborate these findings, with increased levels of IL6 reported as $17.0 \pm 5.7 \text{ pg.mL}^{-1}$ (Watt et al., 2016) and $2.18 \pm 2.39 \text{ pg.mL}^{-1}$ (Watkins et al., 2019), and elevated IL1b of $20.52 \pm 18.19 \text{ pg.mL}^{-1}$ (Watkins et al., (2019) in comparison to FF and CON groups. The variation in absolute levels between studies may be a consequence of the differing Fire and Rescue Services recruited and therefore the variation in working practices. BAI in this study completed on average 15 ± 15 fires a month with BAI HIGH completing 26 ± 5 and FF competing 5 ± 2 . In comparison, Watkins et al (2020) reported BAI completed 5 ± 8 exposures and FF 1 ± 1 , and BAI participating in the study conducted by Watt et al., (2016) all completed 15 exposures. Arguably, the use of a 6 month study design, instead of a singular collection time point as used by Watkins et al., (2020), indicates that this study provides a more valid reflection of the chronic inflammatory status of Fire and Rescue Service personnel, whilst offering an assessment of personnel from a range of geographical locations across the UK, unlike the work of Watt et al., (2016). Overall, increases in levels of biomarkers suggest that BAI chronically experience systemic inflammation.

Furthermore, this study identifies that the systemic inflammation may be related to the frequency of fire exposures experienced. Regression analysis suggests that 11 - 25% of the variation in IL6, IL1b and IL10 is a consequence of monthly exposure number. This is similar to the 19 - 25%





variance in IL6 and IL1b explained by exposure number reported by Watkins et al., (2020). Data collected in this study was controlled for additional contributory factors, such as systolic and diastolic blood pressure, and further analysis conducted to assess the prediction capacity of psychological variables. Psychological factors contributed only to CRP in the case of Reduced Motivation. Consequently, this study builds on the work of Watkins et al., 2020, by giving further consideration to other possible factors that were theorised to be associated with inflammation. In Fire and Rescue Service personnel, the leading cause of chronic systemic inflammation is fire exposure number.

Systemic inflammation may be associated with “sickness behaviours” and symptoms of ill health commonly exhibited with overtraining, such as: fatigue, sleep disturbances, headaches and flu like illnesses (Booth *et al.*, 2006; Gomez-Merino *et al.*, 2003; Konsman *et al.*, 2002). The likelihood of reporting these symptoms of ill health has also previously been documented to be associated with elevated IL6, IL1b and CRP in Fire and Rescue Service personnel (Watkins et al., 2020). The findings of this study also indicate increased reports of symptoms of ill health amongst BAI, with exposure number being associated with the average total number of symptoms reported. This is the first study to indicate that these symptoms are consistent over time in BAI. Cytokines may stimulate these responses due to their ability to travel into the brain and effect central nervous system function (Dantzer, O’Connor, Freund, Johnson, & Kelley, 2008; Johnson, 2002). It is of interest to note that there were no significant differences in TMD reported in the POMS questionnaire between groups. TMD is an indicator of depressed mood and has been associated with increased cytokine levels (Dantzer *et al.*, 2008; Wright *et al.*, 2005; Irwin *et al.*, 2019). However, the direction of this causal relationship remains unclear and an elevated cytokine level does not predetermine depression (Cho *et al.*, 2019). Walker et al (2016) proposes that increased cytokine levels may increase the risk of Fire and Rescue Service personnel experiencing depression in the future. Limiting exposure numbers therefore may minimise the level of systemic inflammation and the expression of ill health symptoms in BAI.

Systemic inflammation may also increase the risk of future cardiovascular events, due to the association of inflammation with atherosclerosis. Atherosclerosis is the formation of plaques in blood vessels that result in luminal narrowing or precipitating thrombi that obstruct blood flow (Bentzon *et al.*, 2014). Thrombus blood flow obstruction can cause myocardial infarction. IL6 and IL1b are associated with increased cell adhesion molecules, platelet reactivity and procoagulant activity, which can contribute to atherosclerosis development (Lindmark,





Diderholm, Wallentin, & Siegbahn, 2001; Schuett, Luchtefeld, Grothusen, Grote, & Schieffer, 2009). BAI in this study have a median IL-6 in the upper quartile of the general population, being greater than 2.28 pg.mL^{-1} , at this level the relative risk of a cardiac event is 2.3 times those in the first quartile below 1.04 pg.mL^{-1} (P. M. Ridker *et al.*, 2000). It is not possible to offer a similar assessment of IL1b values exhibited by BAI, as predictive values for the occurrence of cardiovascular events have not yet been established for this cytokine, possibly as a consequence of the variability in its measurement in plasma (Ridker *et al.*, 2011). Alternatively, CRP has been known to have strong associations with cardiovascular disease with clear classifications of risk. Whilst only trends indicated differences between group medians in this study, it may be of importance to consider the percentage of participants exhibiting CRP levels in the high risk category ($> 3 \text{ mg.L}^{-1}$) (Ridker, 2003): 0% CON, 4% FF, 14% BAI HIGH. The cumulative assessment of these three biomarkers indicates that BAI may be at an increased risk of a cardiovascular event as a consequence of systemic inflammation.

The profile of IL10 must also be considered in relation to inflammatory status and cardiovascular events. IL10 is an anti-inflammatory cytokine which has been reported to be protective against to progression of atherosclerosis through its actions to regulate proinflammatory cytokine production (Goldwater *et al.*, 2019). Animal studies have indicated that IL10 can prevent plaque development and improve plaque stability (Caligiuri *et al.*, 2003), although this is yet to be documented in humans. However, the findings of studies investigating the association between cardiovascular events and IL10 have been inconsistent. Analysis of IL10 gene polymorphisms in relation to cardiac event predictors identified that the high producer polymorphism results in decreased arterial elasticity in men ages 24 – 39 yrs (Heiskanen *et al.*, 2010). Preliminary studies also report that the risk of adverse cardiovascular events are increased with higher IL10 concentrations in elderly men (Welsh *et al.*, 2011) and postmenopausal women (Lakoski *et al.*, 2008). It is postulated that this may be because IL10 is produced in response to cytokines such as IL6, and therefore may acts as a marker of an overall proinflammatory status (Goldwater *et al.*, 2019). Alternatively, a recent longitudinal prospective study of 930 individuals aged 45 – 85 yrs noted that although IL10 displays a weak positive correlation with IL6 ($r = 0.086$, $p < 0.01$), there was no association between IL10 and cardiovascular events (Goldwater *et al.*, 2019). It is therefore unclear if IL10 can be used as a predictor of cardiovascular events. The importance of this biomarkers elevation in this study may therefore lay in the role it plays in the balance between T helper 1 and T helper 2 cells.





T helper 1/ T helper 2 Balance

The T helper 1/ T helper 2 balance can be investigated through the review of cytokine profiles. T helper cells are a type of lymphocyte which differentiation into type 1 or type 2 cells. T helper 1 cells are associated with increases in IFN- γ and are involved in the cellular immune response, whereas T helper 2 cells are primarily associated with IL4 and IL10 and are involved with the humoral immune response. The cellular and humoral response operate in opposition, consequently an elevation in one response will result in a reduction in the other. Cellular immunity acts through cytotoxic lymphocytes to remove antigens that are found within infected host cells. Alternatively, humoral immunity acts through the process of antibody production, with the antibodies present in plasma binding to antigens and working to eliminate the infection. The ratio of IFN- γ with IL4 (IFN- γ /IL4) and IL10 (IFN γ /IL10) provides an indicator of this T helper balance. A greater ratio value indicates a swing towards T helper 1 response, whereas a reduction in values suggests an increase in T helper 2 response.

Furthermore, this study assessed humoral immunity via the measurement of IgE, IgA, IgM and IgG antibodies. BAI HIGH exhibited increased IgE and reduced IgM in comparison to the CON group. Previous research has identified elevated IgG in BAI ($16.49 \pm 8.65 \text{ g.L}^{-1}$) (Watkins *et al.*, 2020), however this was not reported in this study ($10.03 \pm 4.15 \text{ g.L}^{-1}$).

IgE is considered as the allergic response antibody, playing a dominant role in the pathology of allergies. An increased IL4 release from T Helper 2 cells can induce secretion of IgE from B cells (Amarasekera, 2011). Although, this IgE in response does not occur in all individuals, with some people having a genetic predisposition to develop IgE in response to otherwise harmless allergens (Navinés-Ferrer *et al.*, 2016). Exposure to PAHs via diesel exhaust fumes have been reported to increase the prevalence of IgE in blood (Mastrangelo *et al.*, 2003). Although values reported in this study are substantially lower than those reported in dock yard workers ($191.1 - 363.6 \text{ ng.mL}^{-1}$) (Mastrangelo *et al.*, 2003) and coke-oven workers ($429.12 \text{ ng.mL}^{-1}$) (Wu *et al.*, 2003). Dock yard workers may present a greater IgE expression than FF and BAI as a consequence of increased respiratory intake of PAHs, as FF and BAI commonly wear BA to protect from smoke inhalation. However, dermal absorption of PAHs has also been noted to increase IgE and therefore may be the cause of the moderate increase noted in the firefighting occupation (Mastrangelo *et al.*, 2003). Whilst only High Expo BAI exhibited increased IgE in comparison to the CON group, there was no association with exposure numbers. It can be postulated that it is not necessarily the exposure





number that is relevant here, but the cumulative exposure to PAHs which may vary in accordance to BA usage, decontamination practices, dirty equipment/PPE storage and fuels burnt.

IgM is the first class of antibody produced during an infection and therefore acts as an early defence mechanism against mucosal and systemic pathogens. The antibody has been reported to be crucial in the control of gram negative bacteria, with IgM treatment used to attenuate endotoxin activity in sepsis patients, although reported outcomes are heterogenous in nature (Wand *et al.*, 2016; Kakoullis *et al.*, 2018). IgM facilitates the clearance of pathogens, with a key function in the promotion of apoptotic cell engulfment (Ehrenstein & Notley, 2010). Consequently, reduced levels of IgM can increase the severity of, and susceptibility to, infection (Ehrenstein & Notley, 2010).



Contaminants

Complete repeated measures pre exposure data sets across the 6 month time period were collected from 12 HBAI, 6 LBAI, 21 FF and 5 CON. There was a significant difference between groups ($p = 0.007$). Tukey follow up tests revealed HBAI had increased 1-HP in comparison to the Control group ($p = 0.007$) and a trend for an increase in comparison to FF ($p = 0.052$). There was no difference over time ($p = 0.292$) or variation over time between the groups ($p = 0.807$).

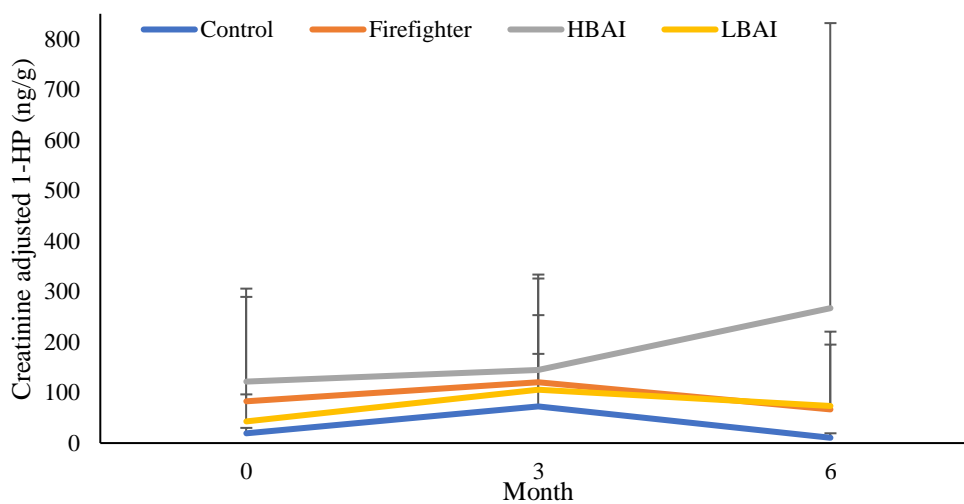


FIGURE 12: 1-HP across the 6 month collection period for each group (control, firefighter, Low exposure BAI and High exposure BAI).

At baseline 0 months 122 samples were collected. Throughout the duration of the study 276 post fire samples were collected. There was a significant increase in 1-HP from baseline samples to post fire exposures ($p = 0.012$).

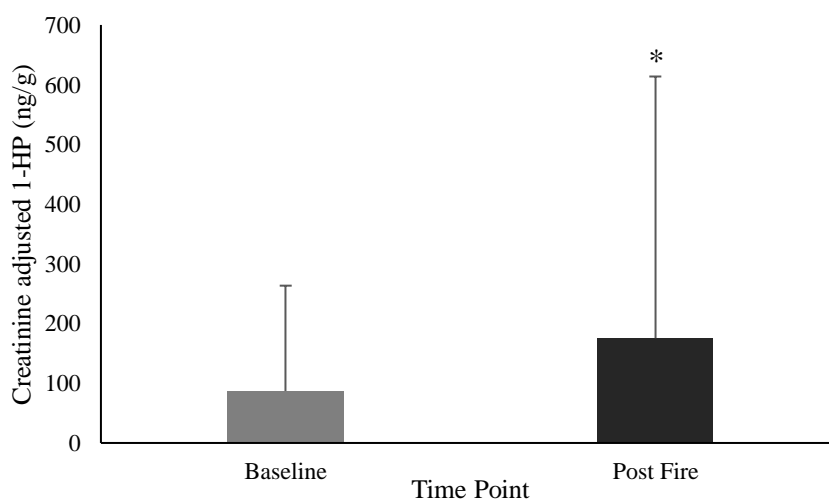


FIGURE 13: 1-HP detected in baseline ($n = 124$) compared to post fire ($n = 275$) samples. * denotes $p < 0.001$

There was a significant difference in 1-HP between exposure types ($p < 0.001$). Training ($n=75$) resulted in greater 1-HP in comparison to all fire type ($p < 0.001$) (vs dwelling ($n = 91$), industrial ($n = 27$), waste ($n=31$), vehicle ($n=26$), wildfire ($n=23$)). Dwelling fires also resulted in greater 1-HP than vehicle fires ($p = 0.023$). When compared to baseline, only training ($p < 0.001$) and dwelling ($p = 0.045$) fire resulted in increased 1-HP. Within training fires, there was no significant difference in 1-HP between single box ($n = 18$) vs multi compartment exposures ($n = 38$) ($p = 0.611$).

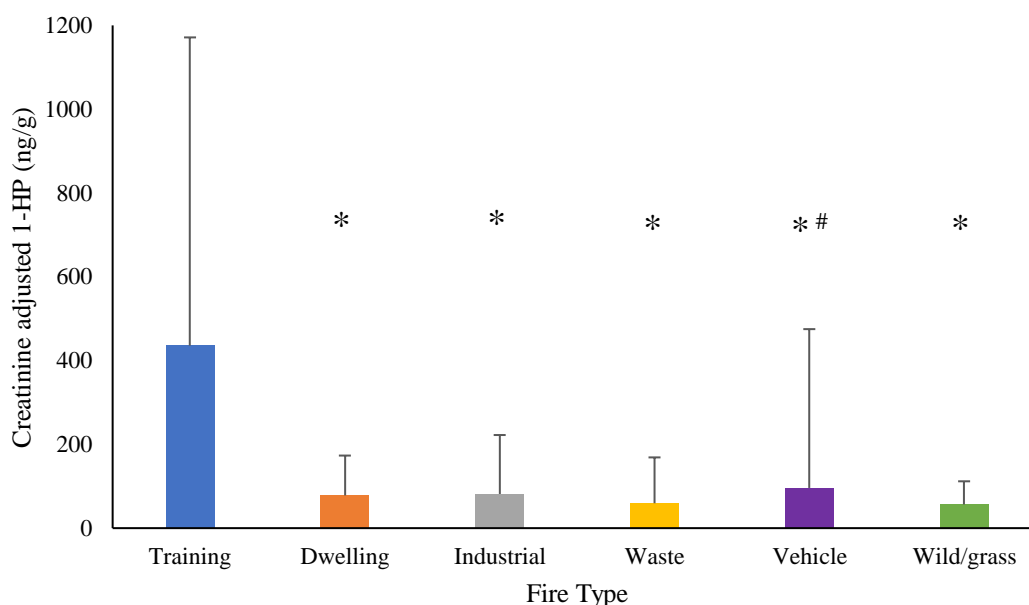


FIGURE 14: 1-HP detected post different fire exposures. * denotes significant differences from training exposure ($p < 0.05$), # denotes significant difference from dwelling fire ($p < 0.05$).

There was no significant difference in 1-HP between roles performed during operational fires ($p = 0.252$). Roles assessed included: BA wearer (70), driver (11), entry control (7), FF without BA (81), officer in charge (16), second in charge (10) and sector commander (4). However, when compared to baseline only BA wearers had a significantly increased 1-HP ($p = 0.021$). There was also no significant difference in 1-HP between instructors ($n=34$) and fire setters ($n=22$) within training scenarios ($p = 0.990$).

Participants attended fire exposures for 119 ± 104 min and there was a significant difference in duration between exposure types ($p < 0.001$). Training fires were significantly longer (139 ± 122 min) than vehicle (54 ± 34 min, $p < 0.001$) and wild fires (83 ± 117 min, $p = 0.004$), industrial fires (190 ± 124 min) were longer than dwelling (109 ± 81 min, $p = 0.009$), vehicle ($p < 0.001$) and wild



fires ($p < 0.001$), and dwelling fires were longer than vehicle fires ($p = 0.015$). Waste fires (109 ± 63 min) were also significantly longer than vehicle fires ($p = 0.008$). There was a significant weak positive correlation between duration of exposure and level of 1-HP detected ($r = 0.185$, $p = 0.003$).

Three different fuel types were used during training scenarios (OSB, wood/cardboard and pallets). However, often these fuel types were not used independently of each other, with pallets being combined with either OSB or wood/cardboard. There was no significant difference in 1-HP between fuel source ($p = 0.777$).

From the 275 post fire samples collected, 215 were accompanied with a report on decontamination protocols used. Of those, 112 scenarios of “no decontamination method” was reported. From the remaining 103 reports a variety of methods and combinations were referred to, including: brushing down PPE (33), brushing down PPE and showering (9), brushing down PPE and using wet wipes (1), brushing down PPE and using wet wipes and shower (4), hosing down PPE (7), removing PPE whilst under air (3), using wet wipes (5), showering (5), removing PPE and storing separately to appliance (31) and sending PPE for cleaning (5).

Discussion of Contaminant Data

The contamination aspect of this project aimed to investigate the level of PAH contamination detected in firefighters and instructors across a 6 month period. The study also sought to compare contaminant data collected from occupational fires. 1-hydroxypyrene (1-HP) is a strong indicator of smoke exposure. It may be readily measured in urine of many populations, including firefighters. Most carcinogenic PAHs and their DNA or protein adducts are present at extremely low concentrations in urine so determination of 1-HP may serve as a useful biomarker for many carcinogens when monitoring smoke exposure from various sources, including habitual diet (charred meats), lifestyle (tobacco smoke), urban environments (vehicle exhaust), and occupational exposures, such as firefighters and their instructors. The findings of this study highlight that 1-HP levels collected prior to fire exposure are greater amongst HBAI to that of a non-firefighting control group, and that these baseline levels persist across a 6 month period. Importantly, the study identified acute fire exposures can cause an increase in 1-HP, with greatest levels noted following training fires. Data suggests that BA wearers have a significant increase in





1-HP from baseline. A weak positive correlation indicated duration of exposure may be a small contributory factor in contamination levels.

The elevated 1-HP noted at baseline in HBAI indicates the compound may accumulate over time with high exposure frequency. Other studies have reported greater baseline 1-HP in firefighters than US general population (Adetona *et al.*, 2017) and Canadian male non-smokers and Fire Service office workers (Keir *et al.*, 2017). However, this study did not identify increased 1-HP in the FF group. There have been no previous assessments of 1-HP in UK firefighters to which this data can be compared. Differences in firefighter tactics, equipment or frequency of exposure between countries may explain the variation in findings.

Following acute fire exposure this study detected a total 2.56 fold increase in 1-HP. Previous research has reported increased 1-HP during training scenarios (Fent *et al.*, 2019; Fernando *et al.*, 2016), controlled dwelling fires (Fent *et al.*, 2020), operational fires (Keir *et al.*, 2017) and wildfires (Adetona *et al.*, 2017). Average fold increases within these scenarios ranged from 1.84 to 3.5 (Adetona *et al.*, 2017; Keir *et al.*, 2017), indicating that the acute increase in 1-HP noted in this study is consistent with that reported in other countries.

Acute elevations in 1-HP appear to be greatest following training scenarios. However, previous research has postulated that on shift fire suppression may be associated with higher levels of PAH exposure, due to increased 1-HP reported operationally (Keir *et al.*, 2017), in comparison to in training scenarios (Fernando *et al.*, 2016). It has been considered that the fuel type utilised, scripted activities and stricter adherence to PPE protocols may reduce PAH contamination from training exposures (Keir *et al.*, 2017). Although it may be important to note that the training scenarios previously investigated by Keir *et al.*, (2017) involved firefighting tasks limited to 30min duration, not instructing tasks as assessed in this study. Comparison of ambient PAH between instructing and operational incident fires suggests that comparable exposures occur (Kirk & Logan, 2015a). One previous well controlled American study (Fent *et al.*, 2019) has distinguished between firefighter tasks and BAI in training scenarios and suggests that whilst time matched exposures result in similar changes, the extended and repeated exposure nature of instructing resulted in elevated 1-HP in BAI following an exercise day. Analysis of exposure length in relation to 1-HP in this study detected a weak positive correlation, suggesting duration of exposure may be a small contributory factor. However, the lack of significant difference in duration between training fires





and industrial and dwelling fires, when 1-HP was greatest post training, indicates that other contributory factors likely exist.

The fuel sources for each fire type may be a cause of 1-HP differences. Fuel sources varied between exposure types but with some cross over, for instance electrical appliances, soft furnishings, wood and waste were present in dwelling, industrial and waste fires. Only vehicle fires had a fuel source unique from other exposure categories, which may have contributed to the difference noted in 1-HP between dwelling and vehicle fires, The release of PAHs from vehicles fires has been reported before (Fent & Evans, 2011), however to the authors' knowledge, this is the first study to compare urinary 1-HP from vehicle fires to other exposure types. Exposure length is likely also an important contributory factor in this comparison, with vehicle fires being the shortest in duration (54 ± 34 min). Within training scenarios three different fuel sources are primarily used. This study identified no differences between 1-HP levels and fuel source in training. However, training centres often utilised multiple fuel sources simultaneously, with some variation of their use across services. Consequently, only a small number of samples were available for each fuel grouping: OSB 6, wood 22, pallets 11, pallets & OSB 7, wood & pallet 3. Isolated comparison of fuel types during training conducted by Fent *et al.*, (2019) revealed OSB burning resulted in greater 1-HP than pallet and straw burning and a simulated smoke exposure. Collectively, this evidence highlights the importance of minimising PAH exposure from all fire types and that consideration should be given to the need for OSB in training if other alternatives are available.

BA wearers exhibited an increase in 1-HP from baseline, although post sample comparison indicated no differences between roles. The increased 1-HP noted in BA wearers compared to pre exposure levels suggests contamination is occurring despite airway protection. Skin absorption has been suggested as an alternative entry route for PAHs into the body (Fent *et al.*, 2014). The similarity in 1-HP levels between all roles indicates that even those individuals not completing suppression activities may be exposed to PAHs. Fent *et al.*, (2020) also report increases in 1-HP following a range of tasks, including overhaul, fire attack, searching and outside ventilation, with BA use unclear amongst the ventilation group. The authors' comment that attack/search tasks may resulted in the largest magnitude change in 1-HP levels. Elevated 1-HP have also previously been measured in non-entry support roles (driver-operators and paramedics), with the suggestion that ambient smoke also represents a significant exposure hazard (Hoppe-Jones *et al.*, 2021). Overall, these findings suggest the importance of reducing exposure for all roles and consideration for reduce skin absorption for BA wearers specifically.





With the large variation in 1-HP levels noted post fire exposures, it may be suggested that there are several possible factors that are contributing to the variance across participants. Donning BA is common for most direct fire suppression activities, however respiratory protection use for wild fire exposures can be less consistent and those completing external tasks often wear minimal/no protection. Use of respiratory protection in wildfire scenarios may reduce inhalation of contaminants (Cherry *et al.*, 2021). Cleansing wipe cleaning of the skin (Beitel *et al.*, 2020; Fent *et al.*, 2017), dry brushing down PPE (Fent *et al.*, 2017), gross scrubbing of PPE with soap (Fent *et al.*, 2017), PPE cleaning (dry and with soap) prior to BA removal (Burgess *et al.*, 2021), immediate overhead removal of fire hoods (Kesler *et al.*, 2021), separate storage of PPE immediately from scene to transport for laundering (Hwang *et al.*, 2019), and showering as soon as possible (Cherry *et al.*, 2021; Fent *et al.*, 2017) have all been recommended as decontamination methods (Hwang *et al.*, 2022). Water only decontamination is not sufficient, likely due to the hydrophobic nature of the chemicals (Fent *et al.*, 2017; Banks *et al.*, 2021). Responses in this study indicated a range of decontamination methods are used, however implementation of methods is not consistent and techniques appear to vary. Based on the previous literature it is plausible to suggest that decontamination methods may be partially responsible for the variation in individual responses. Consequently, it appears that clear guidance on decontamination best practice is required.

Overall, this study identified firefighters and instructors are exposed to carcinogenic substances as part of their occupational role. A high frequency of exposures can result in increased baseline 1-HP. Exposure duration may also be related to severity of 1-HP accumulation, with longer exposures resulting in increased 1-HP. The association with exposure length may also be partially responsible for the increased 1-HP seen in training scenarios. An additional point of interest from the measurement of creatinine revealed many fire fighters with high concentrations, indicating either dehydration or acute kidney injury.





Key Findings

BAI complete a substantially greater number of fire exposures than FF (15 vs 5, respectively). Immediately following an acute exposure BAI typically feel worse than FF: hotter and more confused. High Expo BAI also feel more fatigued and more pain than FF. After cessation of an exposure core temperature continues to rise for 10 – 15min and it typically takes a minimum of 60 - 80min for core temperature to reduce back to within resting levels following an exposure, although in some cases it takes longer. New recruits are most at risk of high core temperatures and consequently heat illnesses. Currently there is no appropriate physiological monitoring device that can be deployed operationally.

Data collected over the 6 month duration of this study revealed that resting levels of fatigue and mood disturbances vary little over time and are not different between FF, BAI and the CON group. Mood disturbances are similar to that reported in military and athlete populations. However, High Expo BAI report a greater number of symptoms of ill health than CON. From the blood samples we collected it was observed that biomarkers naturally fluctuated in most groups over the duration of study, however markers of inflammation remained consistently elevated in High Expo BAI. Overall, BAI exhibit chronic systemic inflammation, which is associated with exposure number. This association is not affected by age, BMI, systolic and diastolic blood pressure, and mood state. This demonstrates and supports the need for Fire Service policies on maximum wear numbers to be introduced in the UK and internationally.

Assessment of contaminant levels suggests that fire exposure causes a significant increase in urinary 1-HP levels, indicating that firefighters are exposed to carcinogenic substances which are being metabolised in the body. Even when wearing BA there is evidence of 1-HP entering firefighters' circulation. The compound analysed, the glucuronide, is a metabolite manufactured by the liver to enable excretion of such poorly water-soluble compounds and so this is not an accidental contaminant arising from the sampling procedure. Instructors exhibited high levels of urinary 1-HP following training scenarios, which may be related to exposure duration. Monitoring over the 6 month period revealed that High Expo BAI had increased baseline levels of 1-HP in comparison to the control group, suggesting a cumulative effect of exposure. It is also important to note that decontamination methods were not consistently utilised and often no method was





implemented. These findings support the need for Fire Services to consider exposure frequency and decontamination methods to reduce exposure to carcinogenic substances.





Future Recommendations and Considerations

- Development of a physiological monitoring device is needed, with an implementation plan produced for effective use.
- Physiological monitoring of BAI and particularly new recruits during training wears is warranted.
- BAI exposures should ideally be kept to the no more than 9 a month recommendation, but certainly should not exceed ~20 a month.
- Training centres should ensure adequate advice and facilities regarding hydration and cooling methods. Ice slurries are recommended as a beneficial and logistically useable cooling intervention.
- Development of guidelines regarding decontamination methods is needed. Best practice needs to be established based on logistical realities and current scientific literature. For improved decontamination the chemical nature of the PAH compounds should be considered. Implementation of decontamination methods is of paramount importance to reduce contamination.
- BAI should receive more frequent and comprehensive medical checks than FF. These could include monitoring the classic BAI ill health symptoms, exposure numbers and screening for common cancers. Regular checks should be used to identify changes in health over time, so workloads can be adjust as required.
- Awareness campaigns regarding signs and symptoms of cancer to increase self-surveillance should be considered. All FF and BAI should be encouraged to attend cancer screening when offered.





References

- Adetona, O., Simpson, C. D., Li, Z., Sjodin, A., Calafat, A. M. and Naeher, L. P. (2017). Hydroxylated polycyclic aromatic hydrocarbons as biomarkers of exposure to wood smoke in wildland firefighters. *Journal of Exposure Science and Environmental Epidemiology* (on-line), 27: 78–83. <http://dx.doi.org/10.1038/jes.2015.75>.
- Åkerstedt, T. and Kecklund, G. (2017). What work schedule characteristics constitute a problem to the individual? A representative study of Swedish shift workers. *Applied Ergonomics*, 59: 320–325.
- Allart-Vorelli, P., Porro, B., Baguet, F., Michel, A. and Cousson-Gélie, F. (2015). Haematological cancer and quality of life: A systematic literature review. *Blood Cancer Journal*, 5.
- Amarasekera, M. (2011). Asia Pacific allergy Immunoglobulin E in health and disease. *Asia Pacific Allergy*, 1: 0–3.
- Bakri, I., Lee, J.-Y., Nakao, K., Wakabayashi, H. and Tochihara, Y. (2012). Effects of firefighters' self-contained breathing apparatus' weight and its harness design on the physiological and subjective responses. *Ergonomics* (on-line), 55: 782–791. <http://www.tandfonline.com/doi/abs/10.1080/00140139.2012.663506#.V6bmHT1940Q>.
- Banks, A. P. W., Wang, X., Engelsman, M., He, C., Osorio, A. F. and Mueller, J. F. (2021). Assessing decontamination and laundering processes for the removal of polycyclic aromatic hydrocarbons and flame retardants from firefighting uniforms. *Environmental Research* (on-line), 194: 110616. <https://doi.org/10.1016/j.envres.2020.110616>.
- Banks, W. A. (2005). Blood-brain barrier transport of cytokines: a mechanism for neuropathology. *Current Pharmaceutical Design* (on-line), 11: 973–84. <http://www.ncbi.nlm.nih.gov/pubmed/15777248>.
- Barr, D., Gregson, W. and Reilly, T. (2010). The thermal ergonomics of firefighting reviewed. *Applied Ergonomics* (on-line), 41: 161–172. <http://www.ncbi.nlm.nih.gov/pubmed/19664755>. Accessed 10 August 2014.
- Beitel, S. C., Flahr, L. M., Hoppe-Jones, C., Burgess, J. L., Littau, S. R., Gulotta, J., Moore, P., Wallentine, D. and Snyder, S. A. (2020). Assessment of the toxicity of firefighter exposures using the PAH CALUX bioassay. *Environment International* (on-line), 135: 105207. <https://doi.org/10.1016/j.envint.2019.105207>.
- Bentzon, J. F., Otsuka, F., Virmani, R. and Falk, E. (2014). Mechanisms of plaque formation and rupture. *Circulation Research*, 114: 1852–1866.
- Booth, C. K., Probert, B., Forbes-Ewan, C. and Coad, R. A. (2006). Australian army recruits in training display symptoms of overtraining. *Military Medicine* (on-line), 171: 1059–64. <http://www.ncbi.nlm.nih.gov/pubmed/17153542>.
- Bower, J. E. and Lamkin, D. M. (2013). Inflammation and cancer-related fatigue: Mechanisms, contributing factors, and treatment implications. *Brain, Behavior, and Immunity* (on-line), 30: S48–S57. <http://dx.doi.org/10.1016/j.bbi.2012.06.011>.
- Brydon, L., Walker, C., Wawrzyniak, A., Whitehead, D., Okamura, H., Yajima, J., Tsuda, A. and Steptoe, A. (2009). Synergistic effects of psychological and immune stressors on inflammatory cytokine and sickness responses in humans. *Brain, Behavior, and Immunity*, 23: 217–224.
- Burgess, J. L., Hoppe-Jones, C., Griffin, S. C., Zhou, J. J., Gulotta, J. J., Wallentine, D. D., Moore, P. K., Valliere, E. A., Weller, S. R., Beitel, S. C., Flahr, L. M., Littau, S. R., Dearmon-Moore, D., Zhai, J., Jung, A. M., Garavito, F. and Snyder, S. A. (2021). Evaluation of Interventions to Reduce Firefighter Exposures : *Journal of Occupational and Environmental Medicine*, 62: 279–288.





- Buyukyazi, G., Kutukculer, N., Kutlu, N., F, G., Karadeniz, G. and Ozkutuk, N. (2004). Differences in the cellular and humoral immune system between middle-aged men with different intensity and duration of physically training. *Immunology*, 44: 207–214.
- Caligiuri, G., Rudling, M., Ollivier, V., Jacob, M. P., Michel, J. B., Hansson, G. K. and Nicoletti, A. (2003). Interleukin- 10 deficiency increases atherosclerosis, thrombosis, and low-density lipoproteins in apolipoprotein E knockout mice. *Molecular Medicine*, 9: 10–17.
- Cherry, N., Aklilu, Y. A., Beach, J., Britz-Mckibbin, P., Elbourne, R., Galarneau, J. M., Gill, B., Kinniburgh, D. and Zhang, X. (2019). Urinary 1-hydroxypyrene and Skin Contamination in Firefighters Deployed to the Fort McMurray Fire. *Annals of Work Exposures and Health*, 63: 448–458.
- Cherry, N., Galarneau, J. M., Kinniburgh, D., Quemerais, B., Tiu, S. and Zhang, X. (2021). Exposure and Absorption of PAHs in Wildland Firefighters: A Field Study with Pilot Interventions. *Annals of Work Exposures and Health*, 65: 148–161.
- Cheung, S. S., McLellan, T. M. and Tenaglia, S. (2000). The thermophysiology of uncompensable heat stress. Physiological manipulations and individual characteristics. *Sports Medicine* (on-line), 29: 329–59. <http://www.ncbi.nlm.nih.gov/pubmed/10840867>. Accessed 12 November 2014.
- Cheung, S. S., Petersen, S. R. and McLellan, T. M. (2010). Physiological strain and countermeasures with firefighting. *Scandinavian Journal of Medicine & Science in Sports* (on-line), 20: 103–16. <http://www.ncbi.nlm.nih.gov/pubmed/21029197>. Accessed 24 July 2014.
- Cho, J. H. J., Irwin, M. R., Eisenberger, N. I., Lamkin, D. M. and Cole, S. W. (2019). Transcriptomic predictors of inflammation-induced depressed mood. *Neuropsychopharmacology* (on-line), 44: 923–929. <http://dx.doi.org/10.1038/s41386-019-0316-9>.
- Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W. and Kelley, K. W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. *Nature reviews. Neuroscience*, 9: 46–56.
- Das, A. (2016). Psychosocial distress and inflammation: Which way does causality flow? *Social Science and Medicine*, 170: 1–8.
- Demers, P. A., DeMarini, D. M., Fent, K. W., Glass, D. C., Hansen, J., Adetona, O., Andersen, M. H., Beane Freeman, L. E., Caban-Martinez, A. J., Daniels, R. D., Driscoll, T. R., Goodrich, J. M., Graber, J. M., Kirkham, T. L., Kjaerheim, K., Kriebel, D., Long, A. S., Main, L. C., Oliveira, M., Peters, S., Teras, L. R., Watkins, E. R., Burgess, J. L., Stec, A. A., White, P. A., DeBono, N. L., Benbrahim-Tallaa, L., de Conti, A., El Ghissassi, F., Grosse, Y., Stayner, L. T., Suonio, E., Viegas, S., Wedekind, R., Boucheron, P., Hosseini, B., Kim, J., Zahed, H., Mattock, H., Madia, F. and Schubauer-Berigan, M. K. (2022). Carcinogenicity of occupational exposure as a firefighter. *Lancet Oncology* (on-line), 23: 985–986. <https://doi.org/10.1016/S1470-2045>.
- Dorman, L. E. and Havenith, G. (2009). The effects of protective clothing on energy consumption during different activities. *European Journal of Applied Physiology*, 105: 463–470.
- Dreger, R. W., Jones, R. L. and Petersen, S. R. (2006). Effects of the self-contained breathing apparatus and fire protective clothing on maximal oxygen uptake. *Ergonomics*, 49: 911–920.
- Eglin, C. M., Coles, S. and Tipton, M. J. (2004). Physiological responses of fire-fighter instructors during training exercises. *Ergonomics* (on-line), 47: 483–494. <http://www.ncbi.nlm.nih.gov/pubmed/15204300>. Accessed 10 August 2014.
- Eglin, C. M. and Tipton, M. J. (2005). Can firefighter instructors perform a simulated rescue after a live fire training exercise? *European Journal of Applied Physiology* (on-line), 95:





- 327–334. <http://www.ncbi.nlm.nih.gov/pubmed/16096842>. Accessed 10 August 2014.
- Ehrenstein, M. R. and Notley, C. A. (2010). The importance of natural IgM: Scavenger, protector and regulator. *Nature Reviews Immunology*, 10: 778–786.
- Elbers, R. G., van Wegen, E. E. H., Verhoef, J. and Kwakkel, G. (2012). Reliability and structural validity of the Multidimensional Fatigue Inventory (MFI) in patients with idiopathic Parkinson's disease. *Parkinsonism and Related Disorders*, 18: 532–536.
- Fahy, R. F., Leblanc, P. and Molis, J. L. (2015). Firefighter Fatalities in the United States -2014. *National Fire Protection Association Journal*.
- Felger, J. C. and Lotrich, F. E. (2013). Inflammatory Cytokines in Depression: Neurobiological Mechanisms and Therapeutic Implications. *Neuroscience*, 29: 199–229.
- Fent, K. W., Alexander, B., Roberts, J., Robertson, S., Toennis, C., Sammons, D., Bertke, S., Kerber, S., Smith, D. and Horn, G. (2017). Contamination of firefighter personal protective equipment and skin and the effectiveness of decontamination procedures. *Journal of Occupational and Environmental Hygiene* (on-line), 14: 801–814. <https://doi.org/10.1080/15459624.2017.1334904>.
- Fent, K. W., Eisenberg, J., Snawder, J., Sammons, D., Pleil, J. D., Stiegel, M. A., Mueller, C., Horn, G. P. and Dalton, J. (2014). Systemic exposure to pahn and benzene in firefighters suppressing controlled structure fires. *Annals of Occupational Hygiene*, 58: 830–845.
- Fent, K. W. and Evans, D. (2011). Assessing the risk to firefighters from chemical vapors and gases during vehicle fire suppression. *Journal of Environmental Monitoring*, 13: 536–643.
- Fent, K. W., Toennis, C., Sammons, D., Robertson, S., Bertke, S., Calafat, A. M., Pleil, J. D., Geer Wallace, M. A., Kerber, S., Smith, D. L. and Horn, G. P. (2019). Firefighters' and instructors' absorption of PAHs and benzene during training exercises. *International Journal of Hygiene and Environmental Health* (on-line), 222: 991–1000. <https://doi.org/10.1016/j.ijheh.2019.06.006>.
- Fent, K. W., Toennis, C., Sammons, D., Robertson, S., Bertke, S., Calafat, A. M., Pleil, J. D., Wallace, M. A. G., Kerber, S., Smith, D. and Horn, G. P. (2020). Firefighters' absorption of PAHs and VOCs during controlled residential fires by job assignment and fire attack tactic. *Journal of Exposure Science and Environmental Epidemiology* (on-line), 30: 338–349. <http://dx.doi.org/10.1038/s41370-019-0145-2>.
- Fernando, S., Shaw, L., Shaw, D., Gallea, M., Vandenenden, L., House, R., Verma, D. K., Britz-Mckibbin, P. and McCarry, B. E. (2016). Evaluation of Firefighter Exposure to Wood Smoke during Training Exercises at Burn Houses. *Environmental Science and Technology*, 50: 1536–1543.
- Fry, R. W., Grovet, J. R., Edd, A. R. M., Hons, P. M. Z., Hons, S. G. and Keast, D. (1994). Psychological and immunological correlates of acute overtraining. *Br J Sp Med*, 28: 241–246.
- Fuggle, S. (2017). Clinical Biochemistry Reference Ranges. *East Sussex Healthcare NHS Handbook*, 9: 1–20.
- Givoni, B. and Goldman, R. (1971). Predicting metabolic energy cost. *Journal of Applied Physiology*, 30: 429–433.
- Glimcher, L. H. and Murphy, K. M. (2000). Lineage commitment in the immune system: The T helper lymphocyte grows up. *Genes and Development*, 14: 1693–1711.
- Goldwater, D., Karlamangla, A., Merkin, S. S., Watson, K. and Seeman, T. (2019). Interleukin-10 as a predictor of major adverse cardiovascular events in a racially and ethnically diverse population: Multi-Ethnic Study of Atherosclerosis. *Annals of Epidemiology* (on-line), 30: 9-14.e1. <https://doi.org/10.1016/j.annepidem.2018.08.013>.
- Gomez-Merino, D., Chennaoui, M., Burnat, P., Drogou, C. and Guezennec, C. Y. (2003). Immune and Hormonal Changes following Intense Military Training. *Military Medicine*, 168: 1034–1038.





- Grove, R. and Prapavessis, H. (1992). Abbreviated POMS Questionnaire (items and scoring key). *International Journal of Sport Psychology*, 23: 93-109.
- Haslam, C. and Mallon, K. (2003). A preliminary investigation of post-traumatic stress symptoms among firefighters. *Work and Stress*, 17: 277–285.
- Heinegård, D. and Tiderström, G. (1973). Determination of serum creatinine by a direct colorimetric method. *Clinica Chimica Acta*, 43: 305–310.
- Heiskanen, M., Kähönen, M., Hurme, M., Lehtimäki, T., Mononen, N., Juonala, M., Hutri-Kähönen, N., Viikari, J., Raitakari, O. and Hulkkonen, J. (2010). Polymorphism in the IL10 promoter region and early markers of atherosclerosis: The Cardiovascular Risk in Young Finns Study. *Atherosclerosis*, 208: 190–196.
- Hennø, L. T., Storjord, E., Christiansen, D., Bergseth, G., Ludviksen, J. K., Fure, H., Barene, S., Waage-Nielsen, E., Mollnes, T. E. and Brekke, O. L. (2017). Effect of the anticoagulant, storage time and temperature of blood samples on the concentrations of 27 multiplex assayed cytokines – Consequences for defining reference values in healthy humans. *Cytokine* (on-line), 97: 86–95. <http://dx.doi.org/10.1016/j.cyto.2017.05.014>.
- Hoppe-Jones, C., Griffin, S. C., Gulotta, J. J., Wallentine, D. D., Moore, P. K., Beitel, S. C., Flahr, L. M., Zhai, J., Zhou, J. J., Littau, S. R., Dearmon-Moore, D., Jung, A. M., Garavito, F., Snyder, S. A. and Burgess, J. L. (2021). Evaluation of fireground exposures using urinary PAH metabolites. *Journal of Exposure Science and Environmental Epidemiology*, 31: 913–922.
- Howren, M. B., Lamkin, D. M. and Suls, J. (2009). Associations of depression with c-reactive protein, IL-1, and IL-6: A meta-analysis. *Psychosomatic Medicine*, 71: 171–186.
- Huang, M., Su, S., Goldberg, J., Miller, A. H., Levantsevych, O. M., Shallenberger, L., Pimple, P., Pearce, B., Bremner, J. D. and Vaccarino, V. (2019). Longitudinal association of inflammation with depressive symptoms: A 7-year cross-lagged twin difference study. *Brain, Behavior, and Immunity*, 75: 200–207.
- Hwang, J., Taylor, R., Cann, C., Norris, P. and Golla, V. (2019). Evaluation of Accumulated Polycyclic Aromatic Hydrocarbons and Asbestiform Fibers on Firefighter Vehicles: Pilot Study. *Fire Technology* (on-line), 55: 2195–2213. <https://doi.org/10.1007/s10694-019-00851-7>.
- Hwang, J., Xu, C., Thompson, K., Grunsted, P., Malone, T., Clifton, S., Agnew, R. and Xu, X. (2022). Urinary Metabolites of Polycyclic Aromatic Hydrocarbons in Firefighters: A Systematic Review and Meta-Analysis (In preparation for submission). : 1–14.
- Ide, C. W. (2014). Cancer incidence and mortality in serving wholetime Scottish firefighters 1984-2005. *Occupational Medicine*, 64: 421–427.
- International Agency for Research on Cancer (2010). *Monographs on the Evaluation of Carcinogenic Risks to Humans: Painting, Firefighting and Shiftwork*. Lyon, France: World Health Organization.
- Di Iorio, A., Ferrucci, L., Sparvieri, E., Cherubini, A., Volpato, S., Corsi, A., Bonafè, M., Franceschi, C., Abate, G. and Paganelli, R. (2003). Serum IL-1 β levels in health and disease: A population-based study. ‘The InCHIANTI study’. *Cytokine*, 22: 198–205.
- Irwin, M. R., Cole, S., Olmstead, R., Breen, E. C., Cho, J. J., Moieni, M. and Eisenberger, N. I. (2019). Moderators for depressed mood and systemic and transcriptional inflammatory responses: a randomized controlled trial of endotoxin. *Neuropsychopharmacology* (on-line), 44: 635–641. <http://dx.doi.org/10.1038/s41386-018-0259-6>.
- Jin Shin, K., Jin Lee, Y., Ryoul Yang, Y., Park, S., Suh, P.-G., Yung Follo, M., Cocco, L. and Ho Ryu, S. (2016). Molecular Mechanisms Underlying Psychological Stress and Cancer. *Current Pharmaceutical Design* (on-line), 22: 2389–2402. <https://www.ingentaconnect.com/contentone/ben/cpd/2016/00000022/00000016/art00009>.
- Johnson, R. W. (2002). The concept of sickness behavior: A brief chronological account of four





- key discoveries. *Veterinary Immunology and Immunopathology*, 87: 443–450.
- Kakanis, M., Peake, J., Brenu, E., Simmonds, M., Gray, B. and Marshall-Gradisnik, S. (2014). T helper cell cytokine profiles following endurance exercise. *Journal of Interferon & Cytokine Research*, 34: 699–706.
- Kakoullis, L., Pantzaris, N. D., Platanaki, C., Lagadinou, M., Papachristodoulou, E. and Velissaris, D. (2018). The use of IgM-enriched immunoglobulin in adult patients with sepsis. *Journal of Critical Care* (on-line), 47: 30–35.
<https://doi.org/10.1016/j.jcrc.2018.06.005>.
- Keir, J. L. A., Akhtar, U. S., Matschke, D. M. J., Kirkham, T. L., Chan, H. M., Ayotte, P., White, P. A. and Blais, J. M. (2017). Elevated Exposures to Polycyclic Aromatic Hydrocarbons and Other Organic Mutagens in Ottawa Firefighters Participating in Emergency, On-Shift Fire Suppression. *Environmental Science and Technology*, 51: 12745–12755.
- Kesler, R. M., Mayer, A., Fent, K. W., Chen, I. C., Deaton, A. S., Ormond, R. B., Smith, D. L., Wilkinson, A., Kerber, S. and Horn, G. P. (2021). Effects of firefighting hood design, laundering and doffing on smoke protection, heat stress and wearability. *Ergonomics* (on-line), 64: 755–767. <https://doi.org/10.1080/00140139.2020.1867241>.
- Kidd, P. (2003). Th1 / Th2 Balance Th1 / Th2 Balance : The Hypothesis , its Limitations , and Implications for Health and Disease. *Alternative Medicine Review* (on-line), 8: 223–242.
https://www.researchgate.net/profile/Parris_Kidd2/publication/10591467_Th1Th2_Balance_The_Hypothesis_its_Limitations_and_Implications_for_Health_and_Disease/links/56f9fe5e08ae7c1fda311e3c/Th1-Th2-Balance-The-Hypothesis-its-Limitations-and-Implications-for.
- Kim, M., Kim, K.-S., Ryoo, J.-H. and Yoo, S.-W. (2013). Relationship between Occupational Stress and Work-related Musculoskeletal Disorders in Korean Male Firefighters. *Annals of Occupational and Environmental Medicine* (on-line), 25: 9.
<http://aoemj.biomedcentral.com/articles/10.1186/2052-4374-25-9>.
- Kirk, K. M. and Logan, M. B. (2015a). Firefighting instructors exposures to polycyclic aromatic hydrocarbons during live fire training scenarios. *Journal of Occupational and Environmental Hygiene*, 12: 227–234.
- Kirk, K. M. and Logan, M. B. (2015b). Structural fire fighting ensembles: Accumulation and off-gassing of combustion products. *Journal of Occupational and Environmental Hygiene*, 12: 376–383.
- Kleiner, G., Marcuzzi, A., Zanin, V., Monasta, L. and Zauli, G. (2013). Cytokine levels in the serum of healthy subjects. *Mediators Inflamm* (on-line), 2013: 434010.
<http://www.ncbi.nlm.nih.gov/pubmed/23533306>.
- Konsman, J. P., Parnet, P. and Dantzer, R. (2002). Cytokine-induced sickness behaviour: Mechanisms and implications. *Trends in Neurosciences*, 25: 154–159.
- Kyröläinen, H., Häkkinen, K., Kautiainen, H., Santtila, M., Pihlainen, K. and Häkkinen, A. (2008). Physical fitness, BMI and sickness absence in male military personnel. *Occupational Medicine*, 58: 251–256.
- Lakoski, S. G., Liu, Y., Brosnihan, K. B. and Herrington, D. M. (2008). Interleukin-10 concentration and coronary heart disease (CHD) event risk in the estrogen replacement and atherosclerosis (ERA) study. *Atherosclerosis*, 197: 443–447.
- LeMasters, G. K., Genaidy, A. M., Succop, P., Deddens, J., Sobeih, T., Barriera-Viruet, H., Dunning, K. and Lockey, J. (2006). Cancer risk among firefighters: A review and meta-analysis of 32 studies. *Journal of Occupational and Environmental Medicine*, 48: 1189–1202.
- Lewis, E. F., Li, Y., Pfeffer, M. A., Solomon, S. D., Weinfurt, K. P., Velazquez, E. J., Califf, R. M., Rouleau, J. L., Kober, L., White, H. D., Schulman, K. A. and Reed, S. D. (2014). Impact of cardiovascular events on change in quality of life and utilities in patients after





- myocardial infarction. A VALIANT Study (Valsartan in acute myocardial infarction). *JACC: Heart Failure*, 2: 159–165.
- Lin, J. M. S., Brimmer, D. J., Maloney, E. M., Nyarko, E., BeLue, R. and Reeves, W. C. (2009). Further validation of the Multidimensional Fatigue Inventory in a US adult population sample. *Population Health Metrics*, 7: 1–12.
- Lusa, S., Miranda, H., Luukkonen, R. and Punakallio, A. (2015). Sleep disturbances predict long-term changes in low back pain among Finnish firefighters: 13-year follow-up study. *International Archives of Occupational and Environmental Health*, 88: 369–379.
- Ma, F., Fleming, L. E., Lee, D. J., Trapido, E. and Gerace, T. A. (2006). Cancer incidence in Florida professional firefighters, 1981 to 1999. *Journal of Occupational and Environmental Medicine*, 48: 883–888.
- Martins, T. B., Bandhauer, M. E., Bunker, A. M., Roberts, W. L. and Hill, H. R. (2014). New childhood and adult reference intervals for total IgE. *Journal of Allergy and Clinical Immunology* (on-line), 133: 589–591. <http://dx.doi.org/10.1016/j.jaci.2013.08.037>.
- Mastrangelo, Giuseppe, Clonfero, E., Pavanello, S., Fedeli, U., Fadda, E., Turato, A., Piccinni, S., Montagnani, R. and Marcer, G. (2003). Exposure to diesel exhaust enhances total IgE in non-atopic dockers. *International Archives of Occupational and Environmental Health*, 76: 63–68.
- Mastrangelo, Giuseppe., Fornasa, C. V., Pavanello, S., Marcer, G., Lazzaro, M., Milan, G., Fadda, E., Fedeli, U. and Clonfero, E. (2003). Polyaromatic hydrocarbons administered in humans by dermal route increase total IgE. *International Journal of Immunopathology and Pharmacology*, 16: 145–150.
- McNair, L. D., Lorr, M. and Droppleman, L. . (1971). *POMS Manual for Profile of Mood States*. San Diego, CA: Educational and Industrial Testing Service.
- Montain, S. J., Sawka, M. N., Cadarette, B. S., Quigley, M. D. and McKay, J. M. (1994). Physiological tolerance to uncompensable heat stress: Effects of exercise intensity, protective clothing, and climate. *Journal of Applied Physiology*, 77: 216–222.
- Navinés-Ferrer, A., Serrano-candelas, E. and Martín, M. (2016). IgE-Related Chronic Diseases and Anti-IgE-Based Treatments. , 2016.
- Negm, A., MacDermid, J., Sinden, K., D’Amico, R., Lomotan, M. and MacIntyre, N. J. (2017). Prevalence and distribution of musculoskeletal disorders in firefighters are influenced by age and length of service. *Journal of Military, Veteran and Family Health* (on-line), 3: 33–41. <https://jmvfh.utpjournals.press/doi/10.3138/jmvfh.2017-0002>.
- Oliveira, M., Slezakova, K., Alves, M. J., Fernandes, A., Teixeira, J. P., Delerue-Matos, C., Pereira, M. do C. and Morais, S. (2016). Firefighters’ exposure biomonitoring: Impact of firefighting activities on levels of urinary monohydroxyl metabolites. *International Journal of Hygiene and Environmental Health* (on-line), 219: 857–866. <http://dx.doi.org/10.1016/j.ijheh.2016.07.011>.
- Oliveira, M., Slezakova, K., Fernandes, A., Teixeira, J. P., Delerue-Matos, C., Pereira, M. do C. and Morais, S. (2017). Occupational exposure of firefighters to polycyclic aromatic hydrocarbons in non-fire work environments. *Science of the Total Environment* (on-line), 592: 277–287. <http://dx.doi.org/10.1016/j.scitotenv.2017.03.081>.
- Orr, R., Simas, V., Canetti, E. and Schram, B. (2019). A profile of injuries sustained by firefighters: A critical review. *International Journal of Environmental Research and Public Health*, 16.
- Perroni, F., Tessitore, A., Cibelli, G., Lupo, C., D’Artibale, E., Cortis, C., Cignitti, L., De Rosas, M. and Capranica, L. (2009). Effects of simulated firefighting on the responses of salivary cortisol, alpha-amylase and psychological variables. *Ergonomics* (on-line), 52: 484–91. <http://www.ncbi.nlm.nih.gov/pubmed/19401900>. Accessed 10 August 2014.
- Petersen, K., Pedersen, J. E., Bonde, J. P., Ebbelhoej, N. E. and Hansen, J. (2018). Long-term





- follow-up for cancer incidence in a cohort of Danish firefighters. *Occupational and Environmental Medicine*, 75: 263–269.
- Pitman, A., Suleman, S., Hyde, N. and Hodgkiss, A. (2018). Depression and anxiety in patients with cancer. *BMJ* (on-line), 361: 1–6. <http://dx.doi.org/doi:10.1136/bmj.k1415>.
- Pukkala, E., Martinsen, J. I., Weiderpass, E., Kjaerheim, K., Lynge, E., Tryggvadottir, L., Sparén, P. and Demers, P. A. (2014). Cancer incidence among firefighters: 45 years of follow-up in five Nordic countries. *Occupational and Environmental Medicine*, 71: 398–404.
- Purcell, A., Fleming, J., Bennett, S., Burmeister, B. and Haines, T. (2010). Determining the minimal clinically important difference criteria for the multidimensional fatigue inventory in a radiotherapy population. *Supportive Care in Cancer*, 18: 307–315.
- Ridker, P. M. (2003). Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation*, 107: 363–369.
- Ridker, P. M. (2016). From C-Reactive Protein to Interleukin-6 to Interleukin-1: Moving Upstream to Identify Novel Targets for Atheroprotection. *Circulation Research*, 118: 145–156.
- Ridker, P. M., Rifai, N., Stampfer, M. J. and Hennekens, C. H. (2000). Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation*, 101: 1767–1772.
- Ridker, P. M., Rifai, N., Stampfer, M. J. and Hennekens, C. H. (2000). Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation*, 101: 1767–1772.
- Robson-Ansley, P., Barwood, M., Canavan, J., Hack, S., Eglin, C., Davey, S., Hewitt, J., Hull, J. and Ansley, L. (2009). The effect of repeated endurance exercise on IL-6 and sIL-6R and their relationship with sensations of fatigue at rest. *Cytokine* (on-line), 45: 111–116. <http://dx.doi.org/10.1016/j.cyto.2008.11.006>.
- Siddall, A. G., Stevenson, R. D. M., Turner, P. F. J., Stokes, K. A. and Bilzon, J. L. J. (2016). Development of role-related minimum cardiorespiratory fitness standards for firefighters and commanders. *Ergonomics* (on-line), 59: 1335–1343. <http://dx.doi.org/10.1080/00140139.2015.1135997>.
- Smets, E. M. A., Garssen, B., Bonke, B. and De Haes, J. C. J. M. (1995). The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*.
- Smets, E. M. A., Garssen, B., Cull, A. and De Haes, J. C. J. M. (1996). Application of the multidimensional fatigue inventory (MFI-20) in cancer patients receiving radiotherapy. *British Journal of Cancer*, 73: 241–245.
- Smith, D. L. and Petruzzello, S. J. (1998). Selected physiological and psychological responses to live-fire drills in different configurations of firefighting gear. *Ergonomics* (on-line), 41: 1141–1154. <http://www.ncbi.nlm.nih.gov/pubmed/9715673>.
- Smith, D. L., Petruzzello, S. J., Chludzinski, M. A., Reed, J. J. and Woods, J. A. (2005). Selected hormonal and immunological responses to strenuous live-fire firefighting drills. *Ergonomics*, 48: 55–65.
- Smith, D. L., Petruzzello, S. J., Kramer, J. M. and Misner, J. E. (1996). Physiological, psychophysical, and psychological responses of firefighters to firefighting training drills. *Aviation, Space, and Environmental Medicine* (on-line), 67: 1063–8. <http://www.ncbi.nlm.nih.gov/pubmed/8908345>. Accessed 5 December 2014.
- Smith, L. J., Bartlett, B. A., Tran, J. K., Gallagher, M. W., Alfano, C. and Vujanovic, A. A. (2019). Sleep Disturbance Among Firefighters: Understanding Associations with Alcohol Use and Distress Tolerance. *Cognitive Therapy and Research* (on-line), 43: 66–77. <http://dx.doi.org/10.1007/s10608-018-9955-0>.





- Smith, L. L. (2000). Cytokine hypothesis of overtraining : a physiological adaptation to. *Medicine & Science in Sports & Exercise*, 32: 317–331.
- Smith, L. L. (2003). Overtraining , Excessive Exercise , and Altered Immunity Is This a T Helper-1 Versus T Helper-2 Lymphocyte Response ? *Sports Medicine*, 33: 347–364.
- Stec, A. A., Dickens, K. E., Salden, M., Hewitt, F. E., Watts, D. P., Houldsworth, P. E. and Martin, F. L. (2018). Occupational Exposure to Polycyclic Aromatic Hydrocarbons and Elevated Cancer Incidence in Firefighters. *Scientific Reports*, 8.
- Strawbridge, R., Sartor, M. L., Scott, F. and Cleare, A. J. (2019). Inflammatory proteins are altered in chronic fatigue syndrome—A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews* (on-line), 107: 69–83.
<https://doi.org/10.1016/j.neubiorev.2019.08.011>.
- Taylor, N. A. S., Lewis, M. C., Notley, S. R. and Peoples, G. E. (2012). A fractionation of the physiological burden of the personal protective equipment worn by firefighters. *European Journal of Applied Physiology*, 112: 2913–2921.
- Tsimikas, S., Duff, G. W., Berger, P. B., Rogus, J., Huttner, K., Clopton, P., Brilakis, E., Kornman, K. S. and Witztum, J. L. (2014). Pro-inflammatory interleukin-1 genotypes potentiate the risk of coronary artery disease and cardiovascular events mediated by oxidized phospholipids and lipoprotein(a). *Journal of the American College of Cardiology*, 63: 1724–1734.
- Vidarsson, G., Dekkers, G. and Rispen, T. (2014). IgG subclasses and allotypes: From structure to effector functions. *Frontiers in Immunology*, 5: 1–17.
- Walker, A., Keene, T., Argus, C., Driller, M., Guy, J. H. and Rattray, B. (2015). Immune and inflammatory responses of Australian firefighters after repeated exposures to the heat. *Ergonomics* (on-line), 58: 2032–2039.
<http://www.tandfonline.com/doi/full/10.1080/00140139.2015.1051596>.
- Walker, A., McKune, A., Ferguson, S., Pyne, D. B. and Rattray, B. (2016). Chronic occupational exposures can influence the rate of PTSD and depressive disorders in first responders and military personnel. *Extreme Physiology & Medicine* (on-line), 5: 1–12.
<http://extremephysiolmed.biomedcentral.com/articles/10.1186/s13728-016-0049-x>.
- Wand, S., Klages, M., Kirbach, C., Warszawska, J., Meybohm, P., Zacharowski, K. and Koch, A. (2016). IgM-enriched immunoglobulin attenuates systemic endotoxin activity in early severe sepsis: A before-after cohort study. *PLoS ONE*, 11: 1–13.
- Watkins, E. R., Hayes, M., Watt, P. and Richardson, A. J. (2018). Fire service instructors ' working practices : A UK survey. *Archives of Environmental & Occupational Health* (on-line): 1–9. <https://doi.org/10.1080/19338244.2018.1461601>.
- Watkins, E. R., Hayes, M., Watt, P. and Richardson, A. J. (2019a). Heat tolerance of Fire Service Instructors. *Journal of Thermal Biology* (on-line), 82: 1–9.
<https://linkinghub.elsevier.com/retrieve/pii/S0306456519300142>.
- Watkins, E. R., Hayes, M., Watt, P. and Richardson, A. J. (2019b). The acute effect of training fire exercises on fire service instructors. *Journal of Occupational and Environmental Hygiene* (on-line), 16: 27–40. <http://dx.doi.org/10.1080/15459624.2018.1531132>.
- Watkins, E. R., Richardson, A. J., Hayes, M., Watt, P. and Renshaw, D. (2020). Extreme occupational heat exposure is associated with elevated haematological and inflammatory markers in Fire Service Instructors. : 1–11.
- Watt, P. W., Willmott, A. G. B., Maxwell, N. S., Smeeton, N. J., Watt, E. and Richardson, A. J. (2016). Physiological and psychological responses in Fire Instructors to heat exposures. *Journal of Thermal Biology* (on-line), 58: 106–114.
<http://www.sciencedirect.com/science/article/pii/S0306456516300316>.
- Welsh, P., Murray, H. M., Ford, I., Trompet, S., De Craen, A. J. M., Jukema, J. W., Stott, D. J., McInnes, I. B., Packard, C. J., Westendorp, R. G. J. and Sattar, N. (2011). Circulating





- interleukin-10 and risk of cardiovascular events: A prospective study in the elderly at risk. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 31: 2338–2344.
- Williams, D. A. and Arnold, L. M. (2011). Measures Applied to the Assessment of Fibromyalgia. *Arthritis Care and Research*, 63: 1487–1495.
- Williamson, A. and Friswell, R. (2013). Fatigue in the workplace: causes and countermeasures. *Fatigue: Biomedicine, Health and Behavior*, 1: 81–98.
- Wingfors, H., Nyholm, J. R., Magnusson, R. and Wijkmark, C. H. (2018). Impact of fire suit ensembles on firefighter pah exposures as assessed by skin deposition and urinary biomarkers. *Annals of Work Exposures and Health*, 62: 221–231.
- Wolkow, A., Aisbett, B., Reynolds, J., Ferguson, S. A. and Main, L. C. (2016). Acute Psychophysiological Relationships Between Mood, Inflammatory and Cortisol Changes in Response to Simulated Physical Firefighting Work and Sleep Restriction. *Applied Psychophysiology Biofeedback*, 41: 165–180.
- Wright-Beatty, H. E., McLellan, T. M., Larose, J., Sigal, R. J., Boulay, P. and Kenny, G. P. (2014). Inflammatory responses of older firefighters to intermittent exercise in the heat. *European Journal of Applied Physiology* (on-line), 114: 1163–74. <http://www.ncbi.nlm.nih.gov/pubmed/24563092>. Accessed 22 January 2015.
- Wright, C. E., Strike, P. C., Brydon, L. and Steptoe, A. (2005). Acute inflammation and negative mood: Mediation by cytokine activation. *Brain, Behavior, and Immunity*, 19: 345–350.
- Wu, M. T., Pan, C. H., Wu, T. N., Huang, Y. L., Chen, C. Y., Huang, L. H. and Ho, C. K. (2003). Immunological Findings in a Group of Coke-Oven Workers Exposed to Polycyclic Aromatic Hydrocarbons. *Journal of Occupational and Environmental Medicine*, 45: 1034–1039.
- Zhao, G., Zhou, S., Davie, A. and Su, Q. (2012). Effects of moderate and high intensity exercise on T1/T2 balance. *Exercise Immunology Review*, 18: 97–113.





Appendices

Appendix A: Working history form

PARTICIPANT NUMBER



University of Brighton

PARTICIPANT DETAILS

NAME

EMAIL

DOB

HEIGHT WEIGHT

BLOOD PRESSURE

ARE YOU A SMOKER? YES NO

DO YOU USE E CIGERATES? YES NO

WORK HISTORY

TIME IN FIRE SERVICE

JOB TITLE

TIME IN THIS ROLE

NUMBER OF FIRE INCIDENTS ATTENDED IN PREVIOUS MONTH

AVERAGE NUMBER OF FIRE INCIDENTS ATTENDED PER MONTH

HAVE YOU ATTENDED A FIRE INCIDENT IN THE LAST 24 HOURS? YES NO

HAVE YOU COMPLETED HEAVY EXERCISE IN THE LAST 24 HOURS? YES NO



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Appendix B: Health Questions and Illness Symptoms

PARTICIPANT NUMBER



University of Brighton

HEALTH QUESTIONS

HAVE YOU PREVIOUSLY SUFFERED FROM ANY MAJOR ILLNESS OR INJURIES? If yes please detail. (eg. diabetes, high blood pressure, cancer, heat illnesses)

ARE YOU CURRENTLY TAKING ANY MEDICATIONS? If yes please detail.

DO YOU POSSIBLY EXPERIENCE HIGH CONTAMINATION OR PHYSIOLOGICAL STRESS LEVELS FROM WORK/HOBBIES OUTSIDE OF FIREFIGHTING? If yes please detail (eg. motor racing, manual labour)

HAVE YOU HAD A BBQ IN THE PREVIOUS 3 MONTHS? IF YES HOW MANY?

HAVE YOU ATTENDED A FIRE INCIDENT IN THE LAST 24 HOURS? YES NO

HAVE YOU COMPLETED HEAVY EXERCISE IN THE LAST 24 HOURS? YES NO

BELOW IS A LIST OF SYMPTOMS, PLEASE TICK IF YOU HAVE EXPERIENCED ANY OF THESE IN THE PREVIOUS MONTH (DURING A NORMAL DAY NOT JUST AS A RESULT FROM EXERCISE).

	How often did you experience this in the last month?					
	None	Once	2-3 times	once a week	2-3 times a week	continuously
Broken sleep	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heavy sweating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Extreme fatigue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Headaches	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Mood swings	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cold	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Persistent coughing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heart palpitations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Back pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lower limb muscle/joint pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Upper limb muscle/joint pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Appendix C: Multidimensional Fatigue Inventory

FATIGUE INVENTORY

To get an indication of how you have been feeling over the last month, please rate each of the following statements.

For example if the statement was "I feel relaxed" and you think that this is entirely true, that lately you have been feeling relaxed, you would select the extreme left box "yes,that is true".

The more you disagree with the statement the further towards "no, that is not true" you should select.

	1, Yes that is true	2	3	4	5, No that is not true
I feel fit	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Physically, I feel only able to do a little	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel very active	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel like doing all sorts of nice things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel tired	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I think I do a lot in a day	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
When I am doing something, I can keep my thoughts on it	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Physically I can take on a lot	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I dread having to do things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I think I do very little in a day	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I can concentrate well	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I am rested	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
It takes a lot of effort to concentrate on things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Physically I feel I am in a bad condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I have a lot of plans	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I tire easily	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I get little done	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I don't feel like doing anything	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My thoughts easily wander	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Physically I feel I am in an excellent condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Appendix D: Abbreviated POMS questionnaire and its scoring criteria

Abbreviated POMS (Revised Version)

Name: _____

Date: _____

Below is a list of words that describe feelings people have. Please **CIRCLE THE NUMBER THAT BEST DESCRIBES HOW YOU FEEL RIGHT NOW.**

	Not At All	A Little	Moderately	Quite a lot	Extremely
Tense	0	1	2	3	4
Angry	0	1	2	3	4
Worn Out	0	1	2	3	4
Unhappy	0	1	2	3	4
Proud	0	1	2	3	4
Lively	0	1	2	3	4
Confused	0	1	2	3	4
Sad	0	1	2	3	4
Active	0	1	2	3	4
On-edge	0	1	2	3	4
Grouchy	0	1	2	3	4
Ashamed	0	1	2	3	4
Energetic	0	1	2	3	4
Hopeless	0	1	2	3	4
Uneasy	0	1	2	3	4
Restless	0	1	2	3	4
Unable to concentrate	0	1	2	3	4
Fatigued	0	1	2	3	4
Competent	0	1	2	3	4
Annoyed	0	1	2	3	4
Discouraged	0	1	2	3	4
Resentful	0	1	2	3	4
Nervous	0	1	2	3	4
Miserable	0	1	2	3	4

PLEASE CONTINUE WITH THE ITEMS ON THE NEXT PAGE





	Not At All	A Little	Moderately	Quite a lot	Extremely
Confident	0	1	2	3	4
Bitter	0	1	2	3	4
Exhausted	0	1	2	3	4
Anxious	0	1	2	3	4
Helpless	0	1	2	3	4
Weary	0	1	2	3	4
Satisfied	0	1	2	3	4
Bewildered	0	1	2	3	4
Furious	0	1	2	3	4
Full of Pep	0	1	2	3	4
Worthless	0	1	2	3	4
Forgetful	0	1	2	3	4
Vigorous	0	1	2	3	4
Uncertain about things	0	1	2	3	4
Bushed	0	1	2	3	4
Embarrassed	0	1	2	3	4

THANK YOU FOR YOUR COOPERATION

PLEASE BE SURE YOU HAVE ANSWERED EVERY ITEM

Citation:

Grove, J.R., & Prapavessis, H. (1992). Preliminary evidence for the reliability and validity of an abbreviated Profile of Mood States. *International Journal of Sport Psychology*, 23, 93-109.

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Abbreviated POMS (Revised Version)

*** SCORING KEY ***

Scores for the seven subscales in the abbreviated POMS are calculated by summing the numerical ratings for items that contribute to each subscale. The correspondence between items and subscales is shown below.

Item	Scale	Not At All	A Little	Moderate	Quite a lot	Extremely
Tense	TEN	0	1	2	3	4
Angry	ANG	0	1	2	3	4
Worn Out	FAT	0	1	2	3	4
Unhappy	DEP	0	1	2	3	4
Proud	ERA	0	1	2	3	4
Lively	VIG	0	1	2	3	4
Confused	CON	0	1	2	3	4
Sad	DEP	0	1	2	3	4
Active	VIG	0	1	2	3	4
On-edge	TEN	0	1	2	3	4
Grouchy	ANG	0	1	2	3	4
Ashamed	ERA	Reverse-score this item [0 = 4, 1 = 3, 2 = 2, 3 = 1, 4 = 0]				
Energetic	VIG	0	1	2	3	4
Hopeless	DEP	0	1	2	3	4
Uneasy	TEN	0	1	2	3	4
Restless	TEN	0	1	2	3	4
Can't concentrate	CON	0	1	2	3	4
Fatigued	FAT	0	1	2	3	4
Competent	ERA	0	1	2	3	4
Annoyed	ANG	0	1	2	3	4
Discouraged	DEP	0	1	2	3	4
Resentful	ANG	0	1	2	3	4
Nervous	TEN	0	1	2	3	4
Miserable	DEP	0	1	2	3	4





Item	Scale	Not At All	A Little	Moderate	Quite a lot	Extremely
Confident	ERA	0	1	2	3	4
Bitter	ANG	0	1	2	3	4
Exhausted	FAT	0	1	2	3	4
Anxious	TEN	0	1	2	3	4
Helpless	DEP	0	1	2	3	4
Weary	FAT	0	1	2	3	4
Satisfied	ERA	0	1	2	3	4
Bewildered	CON	0	1	2	3	4
Furious	ANG	0	1	2	3	4
Full of Pep	VIG	0	1	2	3	4
Worthless	DEP	0	1	2	3	4
Forgetful	CON	0	1	2	3	4
Vigorous	VIG	0	1	2	3	4
Uncertain...	CON	0	1	2	3	4
Bushed	FAT	0	1	2	3	4
Embarrassed	ERA	Reverse-score this item [0 = 4, 1 = 3, 2 = 2, 3 = 1, 4 = 0]				

TEN = Tension	<p>Note that 2 of the items on the Esteem-related Affect (ERA) subscale are reverse-scored prior to being combined with the other items.</p> <p>Total Mood Disturbance (TMD) is calculated by summing the totals for the negative subscales and then subtracting the totals for the positive subscales:</p> $\text{TMD} = [\text{TEN} + \text{DEP} + \text{ANG} + \text{FAT} + \text{CON}] - [\text{VIG} + \text{ERA}]$ <p>A constant (e.g., 100) can be added to the TMD formula in order to eliminate negative scores.</p>
ANG = Anger	
FAT = Fatigue	
DEP = Depression	
ERA = Esteem-related Affect	
VIG = Vigour	
CON = Confusion	

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Appendix E: Online Fire Exposure Log

Fire Exposure Log

0% complete

Page 1: Page 1

This is the exposure log for the UK firefighter and instructor physiological and contamination study. Please complete this log after every real or training based fire incident.

If you have any questions or issues with the log, or wish for something to be added or amended for ease of use, please email Alan Richardson and Emily Watkins (firehealthresearch@gmail.com).

1. Participant Code * *Required*

2. Role at the start of the shift * *Required*

- BA Instructor
- Firefighter
- Firefighter in development
- Acting Crew Manager
- Crew Manager
- Acting Watch Manager
- Watch Manager
- Other - please specify





- a. If you selected Other, please specify:

3. Start message / Training Start - Date & Time * Required

Please enter a date and time in the format 'DD/MM/YYYY HH:MM', for example 27/03/1980 15:43.

(dd/mm/yyyy hh:mm)

- a. Stop Message / Training End - Date & Time * Required

Please enter a date and time in the format 'DD/MM/YYYY HH:MM', for example 27/03/1980 15:43.

(dd/mm/yyyy hh:mm)

- b. How long did you carry out operational activities at the incident? * Required

- 0-10 minutes
- 10-20 minutes
- 20-30 minutes
- 30-40 minutes
- 40-50 minutes
- 50-60 minutes
- 60+ minutes

- c. If wearing BA please specify time in BA

- 1-5 mins
- 5-10 mins
- 10-15 mins
- 15-20 mins
- 20-25 mins
- 25-30 mins
- 30-35 mins
- 35-40 mins
- 45+ mins
- Multiple BA wears - Please describe in comments





4. What was your role during the incident? * *Required*

- Officer in charge
- Second in charge
- Sector commander (or other specialist role)
- Entry control officer
- Safety officer
- BA wearer
- Gas tight suit / LTS wearer
- Firefighting without BA
- Casualty carrier
- Rescue tool operator
- Line rescue
- Driver
- BA Training - Fire Setter
- BA Training - Vents
- BA Training - BA Control Officer
- BA Training - BA Instructor
- Other - please specify

a. If you selected Other, please specify:





5. What was the type of fire exposure? * *Required*

- Dwelling Fire
- Industrial Building Fire
- Waste or rubbish fire in open ground
- Vehicle Fire
- High Rise Fire
- Basement Fire
- Educational / sports / entertainment building fire
- Road Traffic Collision
- Technical or line rescue
- Wild / grass fire
- Large waste Fire
- Hazmat Incident
- Skip Fire
- Emergency Medical Response
- BA Training - Demo
- BA Training - Attack
- BA Training - Compartment Fire
- BA Training - Vehicle Fire
- BA Training - Hazmat
- Other - Please describe

a. If you selected Other, please specify:



6. Type of material involved in the fire

- Electrical appliance etc.
- Modern soft furnishing (sofa, bed, chairs etc.)
- Older soft furnishing (sofa, bed, chairs etc.)
- Household waste
- Industrial waste
- Hazardous materials - please provide further details in comments
- Modern vehicle related materials <15 years old
- Older vehicle related materials > 15 years old
- Wood /timber / cardboard
- Grass / trees
- Peat
- Petroleum based
- Training - Pallets
- Training - Supplied product (specify in comments)
- Other - please describe

a. If you selected Other, please specify:

7. Did you use any form of decontamination technique?

Please select





Appendix F: Results from the MFI at 0, 3 and 6 months.

Data presented as Median \pm IQR.

		General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation
0 months	FF (n=92)	9 \pm 3	6 \pm 3	8 \pm 5	6 \pm 3	6 \pm 3
	BAI (n=44)	9 \pm 6	8 \pm 3	9 \pm 5	7 \pm 2	8 \pm 4
	High Expo BAI (n=21)	10 \pm 4	7 \pm 3	8 \pm 5	6 \pm 1	7 \pm 3
	Low Expo BAI (n=23)	9 \pm 6	8 \pm 4	9 \pm 6	7 \pm 3	9 \pm 4
	CON (n=14)	7 \pm 5	5 \pm 3	7 \pm 5	5 \pm 2	6 \pm 4
3 months	FF (n=62)	9 \pm 5	7 \pm 6	9 \pm 6	7 \pm 5	7 \pm 5
	BAI (n=33)	10 \pm 3	6 \pm 4	7 \pm 6	6 \pm 3	7 \pm 3
	High Expo BAI (n=17)	10 \pm 3	7 \pm 2	7 \pm 7.5	6 \pm 3	8 \pm 2
	Low Expo BAI (n=16)	10 \pm 3	6 \pm 4	7 \pm 6	5 \pm 3	7 \pm 4
	CON (n=14)	9 \pm 6	7 \pm 4	8 \pm 6	5 \pm 3	7 \pm 5
6 months	FF (n=56)	10 \pm 5	8 \pm 5	8 \pm 6	7 \pm 4	8 \pm 3
	BAI (n=34)	10 \pm 5	8 \pm 4	10 \pm 6	6 \pm 4	9 \pm 5
	High Expo BAI (n=16)	11 \pm 4	7 \pm 4	8 \pm 4	6 \pm 3	9 \pm 5
	Low Expo BAI (n=18)	11 \pm 5	9 \pm 5	10 \pm 7	8 \pm 6	11 \pm 4
	CON (n=14)	11 \pm 3	7 \pm 5	11 \pm 10	6 \pm 4	8 \pm 5





Appendix G: Results from the POMS at 0, 3 and 6 months.

Data presented as Median \pm IQR. TMD = Total Mood Disturbance. * significantly different to 0 months within same group ($p < 0.05$).

		Tension	Anger	Fatigue	Depression	Esteem	Vigour	Confusion	TMD
0 months	FF (n=92)	2 \pm 4	1 \pm 3	3 \pm 5	0 \pm 2	18 \pm 4	10 \pm 6	2 \pm 3	83 \pm 17
	BAI (n=44)	2 \pm 5	0 \pm 3	3 \pm 4	0 \pm 3	18 \pm 4	10 \pm 6	2 \pm 3	84 \pm 21
	High Expo BAI (n=21)	2 \pm 4	0 \pm 2	3 \pm 3	0 \pm 4	18 \pm 3	11 \pm 7	2 \pm 3	81 \pm 16
	Low Expo BAI (n=23)	1 \pm 4	0 \pm 3	4 \pm 5	1 \pm 3	17 \pm 5	9 \pm 5	2 \pm 4	85 \pm 23
	CON (n=14)	2 \pm 3	9 \pm 1	3 \pm 4	0 \pm 1	17 \pm 6	10 \pm 6	1 \pm 2	79 \pm 13
3 months	FF (n=62)	2 \pm 3	1 \pm 4	4 \pm 5	1 \pm 3	17 \pm 5	11 \pm 5	2 \pm 4	84 \pm 20
	BAI (n=33)	2 \pm 6	1 \pm 4	4 \pm 5	1 \pm 4	19 \pm 3	12 \pm 3	2 \pm 4	80 \pm 28
	High Expo BAI (n=17)	2 \pm 5	1 \pm 4	4 \pm 5	1 \pm 6	19 \pm 2	11 \pm 3	3 \pm 4	83 \pm 30
	Low Expo BAI (n=16)	2 \pm 3	1 \pm 4	4 \pm 5	1 \pm 2	18 \pm 4	12 \pm 6	2 \pm 4	79 \pm 27
	CON (n=14)	2 \pm 5	1 \pm 2	4 \pm 4	0 \pm 2	17 \pm 6	11 \pm 5	1 \pm 4	82 \pm 19
6 months	FF (n=56)	2 \pm 4	1 \pm 3	4 \pm 13	1 \pm 3	18 \pm 3	11 \pm 6	2 \pm 3	81 \pm 24
	BAI (n=34)	4 \pm 6	1 \pm 3	5 \pm 9	1 \pm 4	18 \pm 4	11 \pm 6	3 \pm 4	85 \pm 32
	High Expo BAI (n=16)	3 \pm 7	1 \pm 3	5 \pm 9	1 \pm 8	19 \pm 5	11 \pm 5	3 \pm 3	85 \pm 33
	Low Expo BAI (n=18)	4 \pm 5*	1 \pm 3	5 \pm 6*	1 \pm 3*	18 \pm 3	11 \pm 6	3 \pm 4	86 \pm 18
	CON (n=14)	1 \pm 5	1 \pm 3	5 \pm 6	1 \pm 6	16 \pm 10	11 \pm 8	1 \pm 6	90 \pm 33





Appendix H: Responses to the illness symptoms questionnaire at 0, 3 and 6 months
(presented as a percentage of each group)

0 months	BROKEN SLEEP	HEAVY SWEATING	EXTREME FATIGUE	HEADACHES	MOOD SWINGS	COLD	PERSISTENT COUGHING	HEART PALPITATIONS	BACK PAIN	LOWER LIMB/JOINT PAIN	UPPER LIMB/JOINT PAIN
BAI											
"None"	23%	52%	48%	41%	61%	66%	77%	86%	55%	61%	66%
"Once"	7%	9%	11%	30%	0%	20%	14%	5%	16%	11%	11%
"2-3 times"	32%	18%	14%	20%	25%	7%	7%	5%	16%	14%	11%
"Once a week"	11%	9%	5%	5%	5%	2%	0%	2%	0%	5%	5%
"2-3 times a week"	16%	7%	20%	5%	9%	5%	2%	2%	14%	7%	5%
"Continuously"	11%	5%	2%	0%	0%	0%	0%	0%	0%	2%	2%
High Expo BAI											
"None"	19%	43%	43%	33%	71%	62%	67%	81%	43%	67%	71%
"Once"	10%	5%	10%	33%	0%	14%	19%	10%	19%	0%	5%
"2-3 times"	38%	24%	14%	19%	19%	10%	14%	5%	14%	19%	19%
"Once a week"	14%	5%	10%	5%	0%	5%	0%	0%	0%	0%	0%
"2-3 times a week"	5%	14%	24%	10%	10%	10%	0%	5%	24%	14%	5%
"Continuously"	14%	10%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Low Expo BAI											
"None"	26%	61%	52%	48%	52%	70%	87%	91%	65%	57%	61%
"Once"	4%	13%	13%	26%	0%	26%	9%	0%	13%	22%	17%
"2-3 times"	26%	13%	13%	22%	30%	4%	0%	4%	17%	9%	4%
"Once a week"	9%	13%	0%	4%	9%	0%	0%	4%	0%	9%	9%
"2-3 times a week"	26%	0%	17%	0%	9%	0%	4%	0%	4%	0%	4%
"Continuously"	9%	0%	4%	0%	0%	0%	0%	0%	0%	4%	4%
FF											
"None"	15%	60%	53%	58%	63%	74%	82%	90%	51%	56%	75%
"Once"	2%	2%	16%	19%	14%	21%	13%	4%	20%	15%	11%
"2-3 times"	15%	7%	14%	14%	10%	3%	4%	3%	15%	15%	8%





"Once a week"	18%	11%	9%	5%	5%	0%	0%	2%	4%	4%	0%
"2-3 times a week"	37%	16%	5%	3%	5%	2%	0%	0%	7%	7%	4%
"Continuously"	12%	3%	2%	0%	2%	0%	0%	0%	3%	2%	2%
CONTROL											
"None"	43%	93%	86%	64%	64%	71%	100%	100%	86%	64%	86%
"Once"	29%	7%	0%	21%	7%	29%	0%	0%	0%	7%	0%
"2-3 times"	7%	0%	7%	0%	21%	0%	0%	0%	7%	14%	7%
"Once a week"	0%	0%	7%	0%	0%	0%	0%	0%	7%	7%	7%
"2-3 times a week"	14%	0%	0%	14%	7%	0%	0%	0%	0%	7%	0%
"Continuously"	7%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%





3 months	BROKEN SLEEP	HEAVY SWEATING	EXTREME FATIGUE	HEADACHES	MOOD SWINGS	COLD	PERSISTENT COUGHING	HEART PALPITATIONS	BACK PAIN	LOWER LIMB/ JOINT PAIN	UPPER LIMB/ JOINT PAIN
BAI											
"None"	6%	48%	33%	39%	52%	76%	88%	85%	55%	55%	64%
"Once"	12%	12%	21%	36%	6%	15%	0%	9%	12%	6%	6%
"2-3 times"	18%	12%	33%	15%	27%	3%	3%	3%	9%	18%	15%
"Once a week"	21%	15%	9%	6%	9%	3%	6%	0%	18%	6%	0%
"2-3 times a week"	33%	9%	3%	3%	6%	3%	0%	3%	3%	9%	12%
"Continuously"	9%	3%	0%	0%	0%	0%	3%	0%	3%	6%	3%
High Expo BAI											
"None"	6%	29%	29%	24%	53%	76%	88%	71%	29%	59%	53%
"Once"	18%	12%	24%	47%	0%	18%	0%	18%	12%	12%	12%
"2-3 times"	0%	12%	29%	18%	29%	0%	6%	6%	18%	12%	18%
"Once a week"	29%	24%	12%	6%	12%	0%	6%	0%	29%	0%	0%
"2-3 times a week"	41%	18%	6%	6%	6%	6%	0%	6%	6%	12%	12%
"Continuously"	6%	6%	0%	0%	0%	0%	0%	0%	6%	6%	6%
Low Expo BAI											
"None"	6%	69%	38%	56%	50%	75%	88%	100%	81%	50%	75%
"Once"	6%	13%	19%	25%	13%	13%	0%	0%	13%	0%	0%
"2-3 times"	38%	13%	38%	13%	25%	6%	0%	0%	0%	25%	13%
"Once a week"	13%	6%	6%	6%	6%	6%	6%	0%	6%	13%	0%
"2-3 times a week"	25%	0%	0%	0%	6%	0%	0%	0%	0%	6%	13%
"Continuously"	13%	0%	0%	0%	0%	0%	6%	0%	0%	6%	0%
FF											
"None"	13%	52%	42%	61%	66%	84%	87%	89%	56%	63%	82%
"Once"	8%	8%	16%	16%	2%	15%	6%	3%	19%	10%	5%
"2-3 times"	32%	18%	24%	15%	21%	0%	5%	8%	13%	18%	6%
"Once a week"	11%	3%	10%	8%	3%	0%	0%	0%	5%	5%	2%





"2-3 times a week"	23%	15%	6%	0%	5%	0%	0%	0%	3%	5%	3%
"Continuously"	13%	5%	2%	0%	3%	2%	2%	0%	3%	0%	2%

CONTROL											
"None"	29%	86%	79%	50%	57%	86%	100%	100%	43%	79%	86%
"Once"	14%	0%	7%	36%	7%	7%	0%	0%	21%	7%	7%
"2-3 times"	29%	7%	7%	7%	14%	0%	0%	0%	29%	7%	0%
"Once a week"	14%	0%	0%	7%	21%	7%	0%	0%	7%	0%	7%
"2-3 times a week"	14%	7%	7%	0%	0%	0%	0%	0%	0%	7%	0%
"Continuously"	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%





6 months	BROKEN SLEEP	HEAVY SWEATING	EXTREME FATIGUE	HEADACHES	MOOD SWINGS	COLD	PERSISTENT COUGHING	HEART PALPITATIONS	BACK PAIN	LOWER LIMB/ JOINT PAIN	UPPER LIMB/ JOINT PAIN
INSTRUCTORS											
"None"	21%	32%	38%	56%	47%	68%	88%	91%	62%	38%	56%
"Once"	12%	3%	15%	26%	12%	29%	9%	3%	9%	3%	9%
"2-3 times"	21%	15%	15%	6%	21%	0%	0%	0%	9%	32%	21%
"Once a week"	15%	15%	15%	6%	9%	0%	3%	3%	6%	9%	12%
"2-3 times a week"	24%	32%	15%	6%	12%	3%	0%	3%	6%	15%	0%
"Continuously"	9%	3%	3%	0%	0%	0%	0%	0%	9%	3%	3%
High Expo BAI											
"None"	22%	17%	39%	50%	50%	61%	83%	83%	50%	39%	39%
"Once"	11%	6%	11%	17%	11%	33%	11%	6%	11%	6%	11%
"2-3 times"	11%	17%	17%	11%	11%	0%	0%	0%	6%	39%	33%
"Once a week"	17%	11%	17%	11%	11%	0%	6%	6%	11%	6%	17%
"2-3 times a week"	28%	44%	17%	11%	17%	6%	0%	6%	11%	11%	0%
"Continuously"	11%	6%	0%	0%	0%	0%	0%	0%	11%	0%	0%
Low Expo BAI											
"None"	19%	50%	38%	63%	44%	75%	94%	100%	75%	38%	75%
"Once"	13%	0%	19%	38%	13%	25%	6%	0%	6%	0%	6%
"2-3 times"	31%	13%	13%	0%	31%	0%	0%	0%	13%	25%	6%
"Once a week"	13%	19%	13%	0%	6%	0%	0%	0%	0%	13%	6%
"2-3 times a week"	19%	19%	13%	0%	6%	0%	0%	0%	0%	19%	0%
"Continuously"	6%	0%	6%	0%	0%	0%	0%	0%	6%	6%	6%
FIREFIGHTERS											
"None"	14%	48%	55%	64%	59%	63%	82%	91%	55%	63%	70%
"Once"	11%	9%	16%	23%	16%	18%	13%	5%	23%	9%	16%
"2-3 times"	23%	18%	14%	7%	13%	13%	5%	4%	11%	7%	5%
"Once a week"	13%	5%	13%	4%	5%	0%	0%	0%	2%	9%	5%
"2-3 times a week"	27%	20%	0%	2%	5%	7%	0%	0%	4%	4%	4%





"Continuously"	13%	0%	2%	0%	2%	0%	0%	0%	5%	9%	0%
CONTROL											
"None"	21%	79%	79%	57%	64%	86%	100%	86%	50%	64%	79%
"Once"	7%	14%	7%	7%	7%	14%	0%	7%	14%	7%	7%
"2-3 times"	50%	0%	7%	36%	14%	0%	0%	7%	21%	14%	14%
"Once a week"	14%	0%	0%	0%	14%	0%	0%	0%	0%	0%	0%
"2-3 times a week"	0%	7%	7%	0%	0%	0%	0%	0%	14%	7%	0%
"Continuously"	7%	0%	0%	0%	0%	0%	0%	0%	0%	7%	0%





Appendix I: Bloods results at 0, 3 and 6 months

* Vs. 6 months

vs. 3 months

\$ vs. 0 months

		<i>C-RP</i> (<i>mg.L-1</i>)	<i>IL-6</i> (<i>pg.mL-1</i>)	<i>IL-1β</i> (<i>pg.mL-1</i>)	<i>IgG</i> (<i>g.mL-1</i>)	<i>IgM</i> (<i>g.L-1</i>)	<i>IgA</i> (<i>g.L-1</i>)	<i>IgE</i> (<i>ng.mL-1</i>)	<i>IL-10</i> (<i>pg.mL-1</i>)	<i>IL-4</i> (<i>pg.mL-1</i>)	<i>IFN-γ</i> (<i>pg.mL-1</i>)
0 months	FF (n=92)	0.41±0.25 (2/2%)	2.24±2.89 ^{#*} (26/28%)	3.74±5.84 [#] (43/47%)	10.03±3.04 ^{#*} (64/70%)	1.21±0.77 ^{#*} (8/9%)	1.11±1.00 (5/5%)	50.61±62.68 ^{#*} (5/5%)	40.86±69.54 ^{#*} (5/5%)		76.12±6.62 (2/2%)
	BAI (n=44)	0.50±0.33 (2/5%)	5.08±12.5 (26/59%)	3.68±10.20 (28/64%)	9.39±2.69 (42/95%)	0.99±0.34 (1/2%)	1.14±0.97 (2/5) %	87.34±95.39 (5/11%)	94.45±227.77 (15/34%)		73.90±7.50 (5/11%)
	High Expo BAI (n=21)	0.49±0.29* (1/5%)	5.50±13.88 (11/52%)	3.68±6.24 (14/67%)	9.45±3.08 (20/95%)	0.99±0.29 (0/0%)	1.17±0.74 (1/5%)	90.79±92.63* (3/14%)	109.59±405.3 0 (10/48%)		75.04±22.01 (6/29%)
	Low Expo BAI (n=23)	0.51±0.30 (1/5%)	3.39±9.97* (15/68%)	9.41±11.32 (14/64%)	9.60±2.33 (22/100%)	0.99±0.30* (1/5%)	1.29±1.00* (1/5%)	85.94±102.46 ** (2/9%)	81.21±198.74 * (5/23%)		72.93±4.31 (3/14%)
	CON (n=14)	0.46±0.10* (0/0%)	0.73±0.85* (1/7%)	0.00±1.84 (3/21%)	7.10±1.88 (9/64%)	1.78±0.95 (2/14%)	1.18±0.90 (2/14%)	38.41±30.45 (0/0%)	7.75±10.00 (0/0%)		78.87±3.79 (0/0%)
3 months	FF (n=)	0.36±0.56 (0/0%)	1.39±1.55\$ (10/16%)	1.87±3.39\$ (23/37%)	7.28±2.46\$ (45/49%)	1.09±0.51\$ (3/5%)	1.05±0.67 (3/5%)	73.45±102.51 \$ (6/10%)	7.55±42.77\$ (3/5%)		75.74±7.05 (3/5%)
	BAI (n=)	0.75±1.68 (7/21%)	3.21±9.00 (17/52%)	10.26±24.68 (27/82%)	12.60±4.73 (31/70%)	1.02±0.26 (1/3%)	1.04±0.94 (3/9%)	123.48±130.2 5 (4/12%)	93.16±124.06 (9/27%)		75.14±5.85 (4/12%)
	High Expo BAI (n=)	0.73±1.05 (4/24%)	3.23±27.48 (10/59%)	5.25 ±57.47 (13/76%)	11.80 ± 6.18 (16/76%)	0.95±0.21 (0/0%)	1.09±0.81 (0/0%)	132.43±115.7 0 (2/12%)	90.80 ± 332.56 (7/41%)		76.02 ± 34.35 (6/35%)
	Low Expo	0.85±2.17 (3/19%)	3.04±3.90 (8/50%)	11.32±23.46 (15/94%)	13.63±3.45* (16/73%)	1.12±0.15* (1/6%)	0.96±0.68 (1/6%)	107.20±159.0 6\$* (2/13%)	91.02±102.10 * (2/13%)		74.52±3.44 (2/13%)





	BAI (n=)									
	CON (n=)	0.52±0.29* (0/0%)	2.12±1.29* (1/7%)*	1.97±4.41 (5/36%)	8.50±10.33 (10/71%)	1.57±1.32* (3/21%)	1.29±0.82 (1/7%)	43.12±23.55 (0/0%)	13.12±20.24* (0/0%)	79.72±4.88 (0/0%)
6 months	FF (n=)	0.40±0.42 ^{\$} (1/2)	1.67±1.24 ^{\$} (8/14)	1.95±1.89 (20/36)	6.98±2.16 ^{\$} (47/51)	1.03±0.53 ^{\$} (1/2)	1.02±0.58 (2/4)	63.42±62.19 ^{\$} (6/11)	5.90±25.35 ^{\$} (1/2)	76.54±11.29 (5/9)
	BAI (n=)	0.54±1.54 (7/21)	1.61±3.44 (8/24)	5.34±12.79 (20/59)	7.26±2.02 (31/70)	0.97±0.21 (1/3)	1.19±0.70 (2/6)	73.49±125.40 (1/3)	15.59±122.19 (7/21)	76.74±16.39 (4/12)
	High Expo BAI (n=)	0.66±0.99 ^{\$} (5±31)	3.00±40.04 ^{\$} (9/56)	13.62±115.41 (13/81)	7.25±4.93 (16/76)	0.99±0.18 (0/0)	1.16±0.61 (1/6)	101.96±203.3 4\$ (1/6)	108.92±521.2 3 (7/44)	78.65±46.70 (7/44)
	Low Expo BAI (n=)	0.30±2.38 (2/13)	1.16±0.98 (0/0)	2.66±3.88 (8/50)	7.49±1.47 [#] (16/73)	0.97±0.17 ^{\$#} (1/6)	1.23±0.66 ^{\$} (1/6)	66.16±81.74 [#] (0/0)	4.93±15.09 ^{\$#} (0/0)	75.54±4.21 (3/19)
	CON (n=)	0.14±0.11 ^{#\$} (0/0)	0.58±0.65 ^{#\$} (0/0)	1.31±0.78 (3/21)	7.63±1.53 (11/79)	1.56±1.07 [#] (3/21)	1.12±0.64 (0/0)	44.92±23.64 (0/0)	2.75±5.69 [#] (0/0)	78.43±2.94 (0/0)



