CARBON MONOXIDE (CO) PRE-HOSPITAL SCREENING STUDY (COPS STUDY)

FINAL REPORT

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1.0 Executive Summary

Background

Carbon monoxide (CO) is the commonest type of accidental poisoning, often leading to damaging neuropsychological, breathing and cardiovascular problems and potentially death. Annual estimates suggest about 4,000 people attend United Kingdom (UK) Emergency Departments (ED) following CO poisoning (All-Parliamentary Gas Safety Group, 2011). However, accurate numbers regarding CO exposure are difficult to determine because the signs and symptoms of low-level CO poisoning may resemble viral infections or tiredness, leading to frequent misdiagnosis by health professionals. Frontline 999 ambulance clinicians frequently attend patients in the home environment so are ideally placed to screen for CO in situ, but the ability for them to measure CO exposure is not common place. The Carbon Monoxide Prehospital Screening Study (COPS study) aimed to evidence whether such CO screening should form part of routine observations within UK ambulance services.

Methods

Using ambient air CO monitors worn by ambulance clinicians for every shift, this research aimed to identify the number of patients exposed to CO (>5 parts per million) in a 999 emergency ambulance population, and to inform the social and clinical presentation of CO exposed patients (particularly those that have experienced low-level exposure). COPS subsequently intended to explore the experiences of CO exposed patients, to explore ambulance clinician views about pre-hospital screening for CO, and ultimately to inform whether CO screening should be part of routine observations in the UK ambulance setting.

Results

There were six CO monitor activations at patient incidents, in a population comprising about 15,000 incidents. None of these were suspected CO incidents at the point of the 999 ambulance call. This gives an incidence density of 4 patients per 10,000 incidents attended. The activations occurred during the winter period November to April. The environments included homes, a multi-occupancy care home and the workplace. All had more people present than solely the patient for whom the 999 call was made.

COPS findings indicated that ambulance clinicians were more frequently exposed to CO, apparently from vehicle exhaust fumes during the course of their working day. No COPS patients exposed to CO consented to be interviewed, but staff interviews were conducted, which revealed views about CO training, and CO monitor usage.

Conclusion

An incidence density of 4 patients per 10,000 incidents attended, had been exposed to CO at levels which would not have been suspected at the point of the 999 ambulance call. Ambulance clinicians would appreciate greater awareness of CO, and supported the case for prehospital CO monitoring.

2.0 Introduction

Carbon monoxide is a life threatening gas arising from the incomplete combustion of carbon fuels such as from faulty domestic gas appliances (Prockop, 2007). The Department of Health (DH, 2011) expressed concern regarding this 'silent killer' as CO poisoning can be difficult to detect because the symptoms may be very similar to those for influenza and food poisoning, including persistent headaches, sickness and tiredness. Many people are advised to go home, wrap-up warmly and turn up the heating, with potentially fatal consequence.

Weaver (2009) reported on a 37-year-old female with a history of fatigue, headache and memory lapse over several months and who remained undiagnosed despite numerous investigations. Emergency services found her semi-comatose in her home and administered supplemental oxygen, and on investigation she had a COHb level of 18%. Randomized clinical trials did not show efficacy of hyperbaric-oxygen therapy, and Weaver advocated a rigorous clinical trial.

In another study, 120 homes in Liverpool and Coventry were found to have high CO levels yet the occupiers were unaware of the threat (Liverpool John Moores University, 2012). More recently, unrecognised CO exposure during the treatment of a patient led to the hospitalisation of 11 emergency medical services (EMS) personnel as well as the initial patient (Roth et al., 2013).

CO toxicity arises following absorption of the products of incomplete combustion of carbon fuels into the blood through the alveoli. CO competes with oxygen for binding to haemoglobin having 240 times its affinity, and subsequent oxygen displacement leads to the production of COHb leading to hypoxaemia (Greaves, Porter and Garner, 2008). This is explained diagrammatically as a left shift of the oxyhaemoglobin dissociation curve (see figure 1 below).

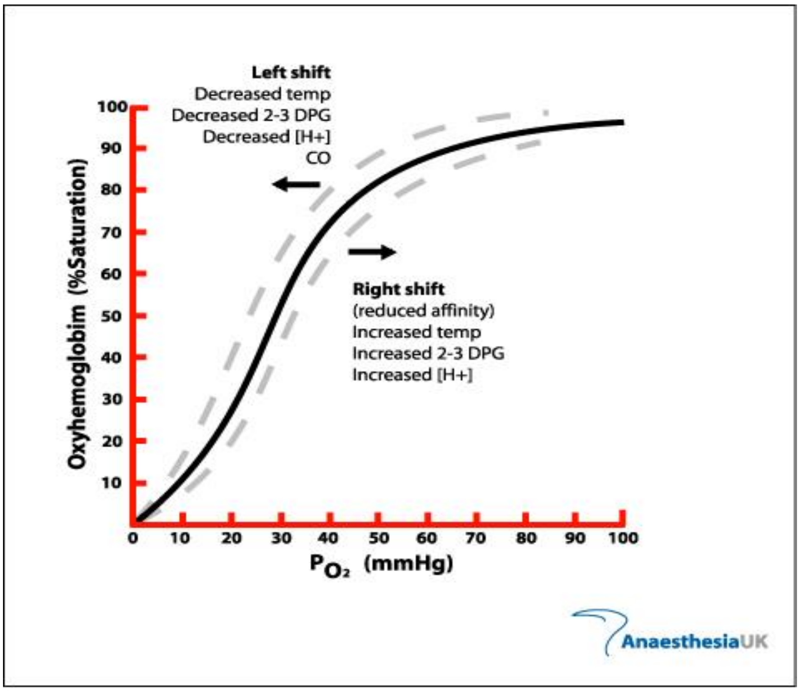

Figure 1 Oxygen Dissociation Curve (Anaesthesia UK, 2005)

Most people have a base level of less than 5% COHb in their exhaled air, however smokers generally have higher levels and a COHb level of up to 10% may cause no symptoms. The World Health Organisation (2000) recommends lower threshold levels for concern, i.e. greater than 2.5% in non-smokers and greater than 5% for smokers. Baum (2008) and Roth et al. (2009) urged clinicians to have a high index of suspicion if a patient presents even with vague symptoms and signs that are consistent with CO poisoning. This is significant because COHb has a half-life of 250 minutes in a patient breathing room air, which reduces to 40 minutes when 100% oxygen is administered (Greaves, Porter and Garner, 2008), so treatment options are important and any delay in treatment may compound neuropsychological sequelae. Weaver (2009) explained the physiological effects of CO in some detail. CO increases cystolic haem levels, leading to oxidative stress (Cronje et al., 2004), binding to platelet haem protein and cytochrome c oxidase (Thom, 2008) interrupting cellular respiration (Alonso, 2003), and causing the production of reactive oxygen species (Thom et al., 2006) which in turn leads to neuronal necrosis (Thom et al., 2006) and apoptosis (Piandatosi et al., 1997). Neurological and cardiac injury results from the development of multiple inflammatory pathways.

CO toxicity is the most common type of accidental poisoning in the modern world, often leading to fatalities and/or debilitating neuropsychological and cardiovascular morbidity (Chee et al., 2008). Whilst mode of entry into the body, physiological consequences and treatment options are well documented (Bledsoe et al., 2010; Touger et al., 2010; Coulange et al., 2008; Hampson, Scott and Zmaeff, 2005; Barker et al., 2006), little is known about the extent to which the United Kingdom (UK) population is affected. Treatment for CO toxicity may involve removing the patient from the CO source, administration of 100% normobaric oxygen therapy (NBOT), and/or transfer to a hyperbaric chamber (HBOT) to receive pressurised oxygen if necessary.

Annually, it is estimated that 4,000 people are diagnosed in UK emergency departments (ED) as having been poisoned by CO (All-Party Parliamentary Gas Safety Group, 2011), and there are approximately 50 deaths related to CO toxicity in England and Wales (Liverpool John Moores University, 2012). The Health and Safety Executive (2006) examined the scale of CO problems in domestic gas appliances in the home, and expressed concern about the under-reporting of cases of exposure that could lead to misdiagnosis of illness.

Clarke et al. (2012) sought to determine the incidence of CO exposure in patients attending three EDs in England. Inclusion criteria were a primary presentation of at least one of the following symptoms:

- Chest pain characteristic of cardiac disease
- Exacerbation of chronic obstructive pulmonary disease (COPD)
- Seizures
- Flu-like symptoms
- Non-traumatic headache

From 1,758 patients there were 76 positive cases (incidence density 4.3 per 100 patients) when either blood or CO-oximeter measurements were analysed. The highest median COHb level was found in the headache group, providing a useful trigger to alert clinicians to the possibility of CO exposure. However, COHb is a relatively poor biomarker because it is difficult to interpret in clinical practice. The study confirms that a proportion of patients presenting to EDs have been exposed to CO, who may otherwise have been misdiagnosed. The UK Health Protection Agency (HPA) Action Card for CO has been amended to incorporate an awareness of non-gas sources of CO (e.g. shisha pipes) and less reassurance of a normal COHb level as a marker of lack of exposure. Also, improved liaison between HPA and local authorities is advocated.

Suner et al. (2008) conducted a prospective observational study to screen 14,818 adult patients presenting to an ED to identify those patients with unsuspected CO toxicity. The total population comprised 10,856 (75%) patients who received pulse CO-oximetry (SpCO) at triage. Venous COHb concentration was also included in the data set when available. Eleven patients with presenting signs and symptoms not consistent with CO toxicity were identified using venous and arterial SpCO screening. There was good correlation between SpCO and COHb levels in all patients who had both tests. Universal screening of patients who present to EDs for SpCO can be achieved. Further, screening for SpCO can lead to the identification of CO toxicity in patients who would otherwise have gone undetected.

Roth et al. (2014) similarly screened 32,396 consecutive ED patients using non-invasive CO-oximetry, and a pragmatic diagnosis of CO poisoning was made by attending physicians in 32 cases, representing 99/100,000 ED patients. However, 3 different definitions of poisoning were developed based on physicians' decision criteria, resulting in 9, 12, and 48 cases respectively. A clear consensus on which patients have to be regarded as 'poisoned' was recommended, to allow comparison across studies.

A further study by Roth et al. (2013) equipped an entire city EMS system with handheld CO detectors, to be carried to the patient at all times. The study again reported a similar CO incidence density (one out of 1,000 total EMS patients), with alarms occurring during the whole year of data collection, albeit a peak during the winter months. CO poisoning was concluded to be a significant matter for a high-volume EMS system.

Chee et al. (2008) declared that the ED standard test for suspected CO poisoning was venous or arterial COHb levels. A case series pulse CO-oximetry measured COHb levels on all ED patients, and elevated levels were identified on retrospective chart review. Of 74,880 patients triaged, 7 who presented with vague complaints were diagnosed with occult CO poisoning. Plante et al. (2007) advocated the use of pulse CO-oximetry to aid rapid diagnosis and early treatment of CO poisoning by emergency personnel. This is because signs and symptoms of mild to moderate CO poisoning can be confused with flu-like symptoms, particularly during the winter months, so there is justification in screening every patient in ED triage for occult CO poisoning. Crawford and Hampson (2008) reported the use of CO-oximetry to confirm a suspected diagnosis of CO poisoning following an explosion on a British Navy submarine operating under the Polar ice cap. Fifteen crewmembers potentially exposed to CO poisoning were subsequently declared as having normal measures. One was diagnosed as having a COHb level of 28% and was treated with 100% oxygen, providing an example of the use of CO-oximetry in remote, austere conditions. It should be noted that Petterson, Begnoche and Graybeal (2007) considered the clinical significance of motion artefact when monitoring patients during transfer and the need to use motion-tolerant technologies to ensure robust readings.

Coulange et al. (2008) evaluated the reliability of non-invasive real-time measurement of COHb using a pulse CO-oximeter in victims of CO poisoning. Concomitant sampling of blood and pulse CO-oximetry of 12 non-smoker ED patients revealed no difference in the two COHb assessment techniques though a slight CO overestimation was observed by the pulse oximeter. Precision of correlation between readings obtained with the non-invasive pulse CO-oximeter and COHb measurements from blood samples demonstrates that this simple rapid non-invasive technology could be useful before and after ED arrival.

Piatkowski et al. (2009) highlighted the difficulty of using invasive blood gas analysis to determine COHb levels in pre-hospital rescue conditions. In 2008, 20 patients received SpCO blood gas analysis on day one of hospital admission following CO intoxication by burn injury. Simultaneous RAD-57 co-oximetry testing occurred. Inhalation oxygen was administered according to the blood gas analysis results or hyperbaric oxygen was administered where the COHb was above 10%. Five young healthy volunteers provided the control. Pulse CO oximeter mean error was 3.15% compared to blood gas analysis concluding that the pulse CO-oximeter represents a reliable measurement technique that is easy to handle and could facilitate the early diagnosis of CO intoxication in pre-hospital rescue conditions.

Hampson, Scott and Zmaeff (2005) reviewed the ability of hospitals in the Pacific Northwest to measure COHb levels suggesting that an inability to measure blood COHb could lead to delayed or missed diagnosis or treatment. In the four states: Alaska, Idaho, Montana and Washington only 44% of acute care hospitals had the capability to measure COHb. The remaining 56% sent blood samples to other laboratories and hospitals with CO-oximetry capability. Over 90% of CO-poisoned patients referred for hyperbaric treatment came from hospitals with COHb capability. Lack of availability of laboratory CO-oximetry to measure COHb is likely to contribute to missed and delayed diagnosis of CO-poisoned patients. The newly available hand-held CO-oximeter is likely to reduce this problem significantly.

Barker et al. (2006) examined the ability of the RAD-57 to measure dyshemoglobins in 10 human volunteers following induced methemoglobin and COHb levels. All were instrumented with arterial cannulae and RAD-57 pulse oximeters for comparison between the readings. The RAD-57 represents an expansion of oxygenation monitoring capability. Clinical studies are needed to evaluate the performance of the RAD-57 in seriously ill patients and at higher levels of dyshemoglobins.

In contrast, Touger et al. (2010) assessed agreement between COHb levels measured by the RAD-57 pulse oximeter and standard laboratory arterial or venous measurement in ED patients with suspected CO poisoning. Although the measurements were made in the ED as opposed to the out-of-hospital setting, the results suggested that the RAD-57 device might misclassify more than half of patients with laboratory values above the 15% CO levels cited in the (US) CO algorithm, potentially leading to a delay in hyperbaric treatment. Accordingly, these results do not support the use of the RAD-57 device to replace standard laboratory measurement or as an out-of-hospital triage tool.

Non-invasive CO monitoring devices are available to calculate CO levels, providing accurate and immediate assessment of blood and/or exhaled air gases. Although monitors are available to emergency practitioners and general practitioners, as yet there is insufficient uptake by ambulance personnel to have any real impact on detection of abnormal CO levels in the pre-hospital setting (Humber, 2010). The main reasons for the lack of monitoring were the cost of the finger-probe and leads, and a lack of drive for increased monitoring and definitive diagnosis.

In the last decade UK government policy was reinforced to heighten awareness of CO toxicity among health practitioners, and promote early detection to reduce unnecessary mortality, morbidity and financial burden on the health service associated with this poison (DH, 2010). The Chief Medical Officer and Chief Nursing Officer called for *"...increased vigilance amongst health professionals of the signs and symptoms of exposure in their patients."* Scott and Foster (2012; 2013) alerted emergency practitioners to the need for assessment of patients in the emergency setting.

Accurate numbers regarding CO exposure are difficult to determine because the signs and symptoms of low-level CO poisoning may resemble viral infections or tiredness, leading to frequent misdiagnosis by health professionals. Frontline 999 ambulance clinicians frequently attend patients in the home or work environment, so are ideally placed to screen for CO in situ, but the ability for them to measure CO exposure is not common place. Ambient air CO screening is a safe, non-invasive, easily applied tool that can identify cases of unsuspected elevated CO levels in the environment. This research aimed to evidence whether such CO screening should form part of routine observations within UK ambulance services.

3.0 Methods

3.1 Research Ethics Committee (REC) Review

The study sought proportionate REC review, and was granted a favourable ethical opinion by the Wales REC 4 Committee on 30th April 2015. In line with current legislation, an annual progress report was submitted to the main Committee in June 2016, and a declaration of the end of the study was made in July 2017.

3.2 Ambient Air CO Monitors

The ToxiRAE 3 personal CO gas monitor was chosen for the COPS study. It is a single-gas monitor with rugged stainless steel housing for harsh environments, changeable alarm settings, easy clip attachment, extended operating temperature of -20° to +60° C, calibration reminders, 2-year battery life, and fast instrument response time for better protection and safety. It therefore appeared to be fit-for-purpose for COPS in the demanding prehospital ambulance setting.

Twenty-five CO monitors and one calibration kit were purchased, and a calibration training event was scheduled with the providers in September 2015. This enabled the Trust Clinical Engineering Department to become familiar with the calibration procedure, and for the research team to gain in-depth knowledge of monitor usage in readiness for COPS ambulance clinician training.

The CO monitors were calibrated to alarm at low (5ppm) and higher (10ppm) levels of CO exposure specifically for the COPS study, and in line with the WHO recommendations, and the calibration interval was set at 6-monthly intervals. Given the 12-month data collection period, it was anticipated that the CO monitors would require just one calibration during the life of the COPS study. However, for unexplained reasons, all the CO monitors reverted to factory setting date, and therefore needed two calibration checks before data collection was completed. This meant downtime from data collection increased, since the monitors needed to be returned to Clinical Engineering for re-calibration, a round-trip of about 100 miles and hence reliant on usual Trust courier movements to keep costs within budget.

3.3 COPS Ambulance Clinicians

It was intended that 25 ambulance clinicians would be trained to use the ambient air CO monitors for participation in the study. The research team advertised the study throughout the East of England Ambulance Service NHS Trust (the Trust), with the aim of recruiting a maximum of 2 volunteer ambulance stations, dependent on the level of interest.

Two ambulance stations, Basildon and Ipswich, were subsequently chosen to host the COPS study, and training events commenced at both sites in October 2015. In total, 23 ambulance clinicians expressed interest and were trained, 15 at Ipswich and 8 at Basildon ambulance stations. Each clinician received a personal issue CO monitor following their training, and one CO monitor was available as a spare at each site.

Group training was scheduled for a maximum of 2-hours face-to-face, and topics included background to the study, plan of investigation, study management, and practical introduction to the CO monitor. Attendance was logged, and clinicians were made aware of their delegated responsibilities for delivery of the COPS study. All COPS clinicians retained a training pack, comprising a summary of training topics, an aide-memoire of the ToxiRAE 3 functionality, and an initial supply of at least 10 National Grid 'Protecting yourself from Carbon Monoxide' leaflets. Further supplies of the CO leaflet were held at both ambulance stations for clinicians to re-stock as necessary.

3.4 Study Design

Using ambient air CO monitors worn by COPS trained ambulance clinicians, this study used prospective cohort design to determine the incidence density of unsuspected CO exposure (greater than 5ppm) in two localities served by the Trust throughout a twelve-month period. Data collection commenced in October 2015 and completed in September 2016. The environments of all patients attended by a COPS trained clinician were monitored for CO exposure, and National Grid CO awareness leaflets were available for distribution. There were no exclusion criteria.

Where CO exposure was confirmed by monitor alarm, all such patients would receive normal prehospital care in accordance with their clinical condition and CO level, and with permission would be referred to the National Gas Emergency Service using the Freephone 0800 number to make safe the environment. COPS clinicians subsequently notified the research team of the date and job number, and non-patient identifiable demographic data was then gathered from the Trust Patient Care Record, to inform the social and clinical presentation of CO exposed cases. This cohort was then sent information by the research team about the COPS study in the post, i.e. the Participant Information Sheet (PIS), consent form, and a pre-paid envelope. On receipt of a completed consent form, the research team would then contact to invite them to participate in a confidential digitally-recorded, semi-structured interview or focus group about their experience of CO exposure and prehospital screening. A £20 gift voucher would be given as a thank you for participation.

Similarly, all COPS study trained ambulance clinicians were sent the PIS and invited to consent to participate in a confidential interview or focus group, in order to explore their views about CO monitoring. Once again, a £20 gift voucher would be given for participation.

The intention was to employ an inductive and systematic approach to analysing verbal data to identify patterns and themes emerging from within the data. The computerised assisted qualitative data analysis software NVivo was originally selected for this purpose; however its application was dependent upon a higher response rate. Because there were so few participants, manual data analysis of the interviews was carried out, and the broad issues raised have been presented.

4.0 Results

4.1 Quantitative Analysis

It was beyond the scope of this study to describe in detail, the total number and type of incidents that COPS clinicians attended during the 12-month data collection period. However, taking into account the usual shift pattern of Trust ambulance clinicians, and attendances per day averaging 5 per clinician (range of 1-8 incidents attended per shift), it has been determined that the frequency of CO exposure in a sample of around 15,000 incidents attended is reported.

The research team were notified by COPS clinicians, of 6 incidents where the CO alarm activated during patient attendance (a rate of 4 patients per 10,000 incidents). Given the relatively low frequency of CO exposure encountered, these incidents are presented as case studies in the section below.

Although not routinely notified to the research team, there were other times when the CO alarms activated, which became apparent whilst the monitors were with the Trust Clinical Engineering Department for re-calibration checks. Since the monitors were only capable of storing the 10 most recent events, it is likely that information about such activations was not entirely captured. However, the research team subsequently undertook additional investigation of CO events against ambulance shift information to determine any emerging themes. For example, there were at least 25 occasions when COPS clinicians were moving around the outside of the ambulance vehicle, either clearing at a scene or at the ambulance station. Also, road traffic accident incidents where multiple emergency vehicles were on scene would cause the CO alarms to activate. It was presumed that exhaust fumes were the cause in both these types of cases. Whilst it was of interest to understand that CO exposure was occurring in such incidents, it was deemed inappropriate to include any patients involved in COPS follow-up activity.

The COPS study was proposed in order to capture CO incidents at low levels of exposure (>5ppm), that would not likely be identified at the point of 999 call by the Trust Computer Aided Dispatch (CAD) system. Within the Trust CAD system, incidents where there is suspicion of CO / smoke or other inhalation / contact with hazardous material / or chemical, biological, radiation contact at the point of 999 call would be coded 'Code 8' in accordance with the Advanced Medical Priority Dispatch System. Such calls would trigger dispatch of the Trust specialist Hazardous Area Response Team (HART) in addition to usual frontline clinicians.

Due to the relatively low frequency of CO incidents reported, the COPS research team undertook additional interrogation of the CAD for information about 'Code 8' records. During the same 12-month timeframe as COPS data collection, there were 223 such incidents. It was beyond the scope of this study to review these cases in more detail, but suffice to say none of the COPS incidents were 'Code 8' calls, so CO had not been suspected at the point of the 999 call.

4.2 CO Incident Case Studies

As mentioned above, there were 6 incidents where the CO monitor alarmed during patient attendance by COPS clinicians, and the case studies are summarised in Table 1 below:

Table 1 Summary of CO Incident Cases

Case Study Demographics	Incident Details and Outcome
Case study 1 – November 2015 in Ipswich, 71-year old male in own home with wife present. CO monitor registered 10ppm.	Patient reported as having fallen three times. Ambulance clinicians noted that the patient was alert, but appeared drowsy on questioning. National Grid contacted for attendance, and boiler turned off in the meantime. Patient transported to hospital.

Case study 2 – December 2015 at 15:30 in Shenfield, 80-year old male in family members' home. CO monitor showed persistent levels of 8-19ppm.	Patient collapsed suddenly and suffered cardiac arrest. On arrival, the ambulance clinicians noted that the heating, oven and a fire were all on. Return of spontaneous circulation achieved, and the patient was transported to hospital. When the clinicians returned to the scene after conveyance, the family had ventilated by opening all windows, and the CO monitor registered 0ppm. The family were given information about ensuring the environment was safe.
Case study 3 – February 2016 at 20:00 in Basildon, 27-year old male in own home with family. CO monitor registered persistent levels of 5-7ppm.	Patient reported feeling weak and lethargic since previous day, and suffering heart palpitations. The family were given the CO information leaflet by the ambulance clinicians and advised to call, and the patient was transported to hospital.
Case study 4 – February 2016 at 15:30 in Billericay, 40-year old male at work in an industrial unit. CO monitor registered 5-6ppm.	Patient reported sharp and intermittent abdominal pains, and the ambulance clinicians noted previous history of similar health events over course of 12-months. The most recent such event was a month prior to this 999 call, and had resulted in a GP referral for further exploration. Within the workshop there were many machines cutting material. The CO monitor alarmed whilst the ambulance clinicians were in the adjacent office with the patient and his manager. There was a boiler within a cupboard in this office, which was due to be serviced the following day. The manager was given the CO information leaflet and advised to discuss with the boiler engineer, and the patient was transported to hospital.
Case study 5 – March 2016 at 03:00 in Ipswich. 41-year old female member of care home staff. CO monitor registered 12ppm.	The ambulance clinicians were dispatched to a care home for an unrelated call. Whilst there, a member of staff complained of feeling dizzy with a headache and nausea. The ambulance clinicians contacted the Trust HART for assistance testing others in the care home. They also contacted the National Grid as per the information leaflet, and the care home was advised to turn off the boiler pending further investigations. The member of staff was transported to hospital.

Case study 6 – April 2016 in Basildon. Elderly patient in own home with family member on scene. CO monitor registered 14ppm.	Patient reported as confused. The ambulance clinicians noted that the CO monitor registered 14ppm whilst in the downstairs toilet beside a newly fitted boiler (fitted approximately 3-weeks previously), and that the CO monitor ceased alarming when they walked away from the boiler back to the kitchen. The information leaflet was discussed and left with the family to call.

4.3 Qualitative Interview Findings

None of the six CO exposed patients consented to be contacted for interview. As reported previously, there were a total of 23 ambulance clinicians that participated in the COPS study; 13 were male, and 10 were female clinicians. All were invited to consent to take part in a confidential audio-recorded interview about their experience of COPS. Four agreed to be interviewed over the telephone, providing contact details (3 males and 1 female). On receipt, the qualitative researcher made an initial phone call to establish a convenient time to record the interview confidentially. Immediately prior to interview consent was re-established and the recorded interview took place for approximately 15-20 minutes duration. Verbatim transcription was manually analysed to establish emerging patterns. In line with good clinical research practice, the transcribed recordings were subsequently deleted. The findings are presented below:

Themes

Emerging themes comprised: a description of the CO events, the locations involved, patient safety concerns, safety of colleagues, giving advice, crew CO awareness, CO training received, the case for CO monitoring, and considerations of which was the most appropriate CO device.

The CO events

Two of the four practitioners interviewed reported a low level CO alarm during the study. One practitioner recalled that the people involved were due to have the boiler serviced within the next seven days. Although this was not a case of suspected CO poisoning, it was a positive activation during a routine 999 call to a workplace, for a middle aged gentleman with chest pain complicated by intense anxiety.

"I think I had one activation of it and it was a very low reading and it wasn't for anything carbon monoxide related. I think it was for chest pain or something like that…it was like a chest pain combined with a bit of an anxiety thing. I remember it was an ongoing problem. I remember it was in a workplace and the CO alarm went off. It was quite a low level but I don't know what it was". P1

Another spoke of an incident when the alarm sounded in a patient's house but the symptoms they had were not consistent with CO poisoning. This patient was symptomatic of a stroke and the alarm activated at 6 parts per million, so the practitioner assumed that it was unlikely to be related to CO.

"I think once it went off I sort of looked at the alarm first and saw the reading which it was giving me which was I think, 6 parts per million and I think I left it for a second or so because I think the alarms I found to be very sort of temperamental so I wanted to make sure it was alarming for a genuine reason…and I let my crewmate know about the reading and I think we sort of treated our patient as normal and that's the long and the short of it really". P4

The location

Two locations visited were deemed problematic and created cause for concern. When the emergency crew first stepped into the workplace, the alarm sounded within about five or ten seconds and led to further investigation.

"So while my crewmate was seeing to the patient I walked around the different spots in the room just to see if the CO^2 (meant CO reading) would go up or go down. I walked into the other room and the alarm stopped and I walked back into that room and it went off again and whatever door I went out of and closed it, the alarm would stop. So, it was probably something to do with that boiler although it was kind of an industrial workplace and when I walked into the industrial area it didn't go off! It just seemed to be in the office. I guess there could have been a risk". P1

During a different visit to a couple who lived in quite an old house, the smell emanating from the gas fire was fairly strong and activated the alarm so the patient was moved outside.

"He lived with his wife, I mean I was quite suspicious because it was a very old house and I thought the whole house was a bit rickety but yeah, if I hadn't had the alarm I would have been more suspicious of it but as the alarm went off at such a low level that sort of eased some of my concerns you see". P4

Patient safety concerns

Regarding patient risk the emergency crew seemed on one occasion to be able to arrive at a decision based on the fact that the reading was very low (5-6ppm).

> *"I didn't think so no 'cos it's an ongoing chest pain problem which he had had outside of the workplace as well. So I don't think it was related to it and it was a very low reading on the alarm. Not that that matters because any CO^2 is CO^2 (participant meant CO) isn't it?"* P1

On another occasion a different crew were readily able to ventilate the room even though the alarm showed a very low reading.

> *"I think because it was such a low reading and because we were easily able to ventilate the room and he was the only person working in that room that had the issue you know it was not like the other people working there that felt unwell".* P1

These actions demonstrate that the emergency crew were aware of the dangers of gas leakage and acted upon it.

Personal safety concerns

The crew did not seem overly concerned that there could be a risk to personal safety in the following quotation.

> *"No 'cos I kept the doors open. It was a very low reading and we kept the doors open. I don't think it concerned me that much really".*P1

Although not too concerned, one crew member ensured that she did not forget to put her alarm on but was surprised to find that it triggered in her own car.

> *"So I didn't forget to turn my monitor on I would, I've got my little box of bits 'n' bobs that I attach to my uniform like my pens and my stethoscope and stuff and I would turn my alarm on in my house and clip it on and from that moment I would leave the house and go to work. My alarm would actually go off in my car, which is a bit worrying! The reading in my car was higher than what it was when it triggered off at the job".* P1

When attending an incident another crew participant said,

> *"Well I was a little bit (concerned) but as the levels were so low and we were not there for very long it wasn't much of a factor for me to be honest".* P4

Safety of colleagues

When asked whether the alarm activated Participant 3 said,

> *"No it didn't go off at all actually, not with a patient anyway…but it did go off a number of times when I was in the garage at the (ambulance) station 'cos often the ambulances would be kept running so, when I went round the back of it the alarm was something like as high as 90…and when I went back round to the front or in the general area it would be about 10 or a bit higher…I guess it's an issue for the guys who work in there all day, in the closed area of the (ambulance station) garage".* P3

This comment raises an important health and safety issue in relation to the workplace which NHS Trusts may need to examine more closely to assess whether there is a need to monitor long-term low-level CO exposure in the garage workplace.

Giving advice

It was helpful that crew gave information to people where warranted.

> *"I spoke to the manager who was there because obviously he (the patient) was one of his members of staff and he was the one that said that…I think it was the Friday or something and he was getting it (the boiler) seen to on the Monday to get a check on it but I gave him a leaflet that you'd issued to us anyway and advised him to keep the door open".* P1

Another participant said that they had,

> *"…left a leaflet with his (patient's) wife to sort of let them know to have it looked at. Then I got this chap into hospital and it was confirmed that he'd had a stroke".* P4

Crew CO awareness

Practitioners indicated their awareness of CO risk, though one incident revealed that a team member had no idea what their colleague was doing with the ambient air measurement device.

> *"It's really curious because my crewmate was looking at me and going, 'What on earth are you doing?' They weren't on the study and had never heard of it and we go to different hospitals and stuff around [location]…and we'd have crews thinking that we were like doing like a part of a BBC production 'cos they thought*

it was a camera. 'Well no, it's not a camera it's like a carbon monoxide machine!…'cos they did look quite curious about it yeah". P1

CO training received

Prior to COPS study preparation, the time devoted to CO training and the nature of any training was quite revealing among the four participants, and all said that they could not recall any solid formal CO training.

> *"Do you know I don't think I have, I don't think, I can't think off the top of my mind whether I have and if I have it would have been such a small session that I can't bring it to mind. No I can't actually, to be honest with you"*. P1

When asked about whether CO training may have been part of a session on inhalation injury another participant recalled that it may have been 'mentioned' but was uncertain that anything had been received but there may have been a suggestion that,

> *"Obviously not a regular update that CO can mess around with your SATS monitors 'cos you can get a nice full 100% SATS reading but have a really hypoxic patient in front of you.*

Whilst physiologically correct, the person was unable to say how she had learnt this information adding,

> *"It messes around with the SATS readings 'cos it's still got gas attached to the haemoglobin. I can't (remember any training) no, not with the Trust anyway. It's been mentioned with other activities I've done outside of work but I can't recall anything that's been taught to me in the Trust or anything in a great deal of depth anyway".* P1

Another participant who trained about ten years ago talked of his lack of training and was fairly pro-active, though he was also unable to recall any formal training on the clinical problem,

> *"Well, when the study started I wanted to know a bit more about carbon monoxide so I looked up some articles on the problem and learned a bit about it that way, about the symptoms and what to look out for like flu and stuff. I can't remember doing anything (training) on it particularly no I mean, they (Paramedic training) may have done but I don't remember anything. I mean I know about the need to think about flu symptoms and the problem that the GPs don't really check either".* P3

Another was more positive, highlighting how in his training he was taught to be aware of faulty gas appliances and boilers. He considered it a matter of common sense to be alert to the possible presenting symptoms such as colds or influenza, headache, nausea and sickness. His knowledge extended to the different types of available CO equipment,

> *"We've got the saturation probes that can't differentiate between carbon monoxide and oxygen when it's measuring someone's oxygen levels (SATs)". P3*
> However, at the other end of the spectrum, from what another could recall, *"It was briefly mentioned in a Powerpoint maybe, but that's about it to be honest". P4*

When asked where he had learned about CO one participant commented on how he had read relevant literature,

> *"Well I'd say that most peoples' knowledge is what they've learned outside of work, like when there has been something published about it and things like that. I can't really remember being specifically trained on it. I mean someone may have mentioned it in a classroom a couple of times but that's about it really".*

When asked about his awareness of national policy for health practitioners, he agreed that it was important that practitioners should be aware of the dangers of CO exposure, expressing concern about his perceived lack of awareness and action to take among the professional discipline,

> *"Yes, and the need to recognise the symptoms and of course, we are not, I know we are not".* P4

Case for CO monitoring

When asked about whether CO monitoring should be routine practice, one participant said,

> *"I think they're great and I know that there has been a couple of carbon monoxide incidents in other areas of the Trust where I think a crew got poorly as well. I think it was just a regular crew".* P1

Two other participants agreed that there was a case, but the inconvenience of the ambient air device was mentioned, and another device would be preferred,

> *"Well, yes, but you would need to find an easier way than on your uniform 'cos of all the things we carry". P3*

> *"I think it should be (standard equipment) although I don't think if I had the choice I would want the specific monitors that we used during the trial"* P4

Most appropriate CO device

Consideration was given to the most appropriate CO monitoring device for local use and, due to the increasing cost-limitations of the ambulance service, cost was a factor.

> *"They're useful for personal issue because of the cost, but we take the (cardiac) monitors into every job so it might be an idea. I think they'd be great on the monitors*". P1

When asked whether they meant it should be an adjunct to the multi-functional patient monitoring device such as the Lifepak, participant 1 responded,

> *"Yeah, not even a part of it but like onto the strap or something and then they're permanently on wherever you go 'cos the monitor goes in with every job…and it's just on permanently. So when the battery goes you swap it at the station for another one and clip it back onto the monitor rather than a personal issue one 'cos they (ambient air device) can actually get quite annoying, the one's that we had on".* P1

Further, regarding the convenience of attaching the ambient air device directly onto the uniform one participant said,

> *"When it was on my main shirt…on my jumper, the soft shell, I didn't notice it too much 'cos it's quite thick and it was quite bulky (the soft shell) and during the summer it was quite heavy and it would pull down on my radio clip. Other than that it's not too bad"*.

Another talked of the inconvenience of the device,

> *"Yeah, they're OK if they're on the outside of your uniform near your head otherwise they get caught up under your coats and jackets and things…and you change your jackets and high viz and such during the shift and when you're in the vehicle so you may not have it on". P3*

He then expanded on the issue demonstrating how he was aware of the availability of different types of CO devices,

> *"Of course there are different types of devices (explained the exhaled air and CO-oximetry)".* P3

Another agreed,

"So we've got saturation probes which clip onto the end of someone's finger and it reads the amount of oxygen in someone's blood so I mean your normal levels are between 95 and 100. Less than 94 is when we begin to give oxygen…and obviously you can see the levels are all over the place and I believe the way it works is it shines a light through someone's finger and it counts the amount of oxygen". P4

When asked about the availability of a co-oximeter one person responded,

"On a normal vehicle you've just got the oxygen saturation probe and in this Trust it's only in the HART (Hazardous Area Response Team) vehicles where I believe they've got the RAD57 but, where I worked previously in (location), all of the team leaders' cars carried that so that resource was much more accessible and was useful at things like house fires and things like that". P4

So with regard to the distribution of devices, he went on to explain,

"Yeah, I only know of one standard ambulance which may offer CO^2 (meant CO) monitoring and that's where we've got our big monitors for ECGs and things like that. The monitor that we've got with the SATs probe doesn't offer it but there's one that several Trusts use and it's called a Lifepack 15…and that offers it and I think you just go into a menu to sort of change the setting. As far as I know I think it's used by (location) so (location) use it and (another location) do and we were using it at (a third location) too. (A fourth location) have got it as well but I'm not sure whether it is something that you have to pay extra for". P4

This participant considered the RAD57 to be "quite useful" but that its availability was limited to HART, itself a limited resource, and thought that, due to their response timeframe, the RAD57 equipment should be more widely available,

"…and certainly where I am and for a large part of the Trust for them (HART) to come to you in sort of upwards of an hour really, well it's a bit of a shame really 'cos as I say, (location) used to get the team leader out and I think they used the TOXCO as opposed to the RAD57". P4

Concurring with Humber (2010) he went on to explain how with the TOXCO device it,

"...was fairly useful to have that resource there" and, in relation to their level of sensitivity, *"I think it is probably something that every SATS probe has the*

> *capability of doing but…" the cost of such devices were a financial barrier to their availability, "… they just whack another zero onto it don't they?"* P4

In contrast to the earlier suggestion that the ambient air device was alerting crew to the danger of colleagues working in the ambulance garage concurrently one participant noted how the alarm was too sensitive,

> *"The issue I have with those (ambient air devices) is that they give off spurious readings for no sort of reason. I mean I think the most common activation would be if you walked through the garage at the station and the vehicle had just driven out you would have it fire off with some ridiculous reading. I had one where it went off and it wouldn't stop and I actually took it back to the calibration people at (location) and the monitor had been reading for like a few days, reading as like 100 parts per million or something silly like that. I also found that whenever I went for a cigarette that would set it off. I think those (ambient air) devices, which we used, if there was an option where once it alarmed you could silence it to stop it beeping, I think that would be really good, but the fact that once it goes off it is beeping constantly for a few minutes". P4*

Indeed, this practitioner reported how he came back from leave and refrained from using the monitor for about a week as he found it to be so annoying. So, if practical issues with that particular piece of ambient air CO monitoring device could be remedied it may be considered a *"useful piece of kit"* P4.

When asked about other types of co-oximetry one respondent replied,

> *"Yeah, absolutely, I mean I've only used it (RAD57) a few times myself but I think it's a really useful piece of equipment. The main thing we use it for is house fires…but certainly, I can imagine it's got uses as far as patients with COPD to see if they are not retaining and things like that…and I think it's always good to have another tool inside your arsenal really. I mean it's almost as if for those who are running the service and if money was no object then I'd have one on every vehicle but it's about balancing the costs isn't it?"* P4

In conclusion, two locations were involved where the device had alerted crew to the potential presence of CO, albeit at what the attending crew considered to be very low readings of 5-6ppm. One was in a workplace setting with a faulty boiler and one in an old and rickety home where there was a strong smell of gas. Concern for patient safety was paramount and crew took action to address this e.g. by opening the window, checking the readings and moving the patient outside. Safety of colleagues was also a cause for concern, as crew recognised that the ambient air devices were alerting them to CO exposure in the closed environment of the ambulance garages. Offering advice to patients and their family was appropriate given the fact that two alarms alerted the crew.

Regarding crew CO awareness, one person commented on their crew member's lack of awareness of the use of the device and this ties in well to the absence of CO training received by all during formal professional education. This issue should be addressed as soon as possible, by ensuring the visibility of CO recognition and management within the pre-registration Paramedic Science Curriculum and other Continuing Professional Development courses.

Whilst the case for CO monitoring was supported, prior to adoption Trust's should consider the appropriateness of the particular device and bear in mind that the RAD57 may well be the equipment of choice.

5.0 Discussion

This research reports an incidence density less than half that of other similar populations studied (Suner et al. 2008; Roth et al. 2013/2014), but it may be important to note that the study was conducted against the backdrop of a relatively mild winter, which could have impacted on the number of CO incidents encountered.

As previously mentioned, the Chief Medical Officer and Chief Nursing Officer have called for increased vigilance towards the recognition of CO by emergency personnel. The CO exposed incidents reported here included a range of environments (homes, a multi-occupancy care home and the workplace) and clinical presentations. All incidents had more people present than solely the patient for whom the 999 call was made, and CO was not suspected at the time of the 999 call for any of them, which highlights the importance of CO monitoring capability for patient safety. A central heating boiler was considered the likely CO source in at least 3 of the 6 incidents where the CO monitor had activated.

Furthermore, COPS findings indicated that ambulance clinicians were more frequently exposed to CO during the course of their working day, apparently from vehicle exhaust fumes. Such data was not explicitly due to be captured for COPS, and therefore warrants further investigation to inform staff welfare issues for EMS staff, to include Patient Transport Services and support services personnel involved with vehicles.

Evidence of variation in CO training and awareness by clinicians in the prehospital ambulance setting could be examined to inform improvements. Further work could also consider the most appropriate means of CO monitoring for staff and patient benefit.

It was beyond the scope of COPS to explore the translation of CO alarm reading to actual COHb reading in ED, and subsequent outcome of patients. A future larger research study could consider the inclusion of such measures.

The qualitative aspects of COPS have revealed some important points regarding health and safety and education, but the volume of data was obviously weakened by the low response rate overall, and the lack of patient perspective.

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8.0 Dissemination

The research team are preparing publications for submission to peer reviewed journals, and propose to deliver the findings to the National Ambulance Research Steering Group and other suitable conference locations.

9.0 References

All-Party Parliamentary Gas Safety Group (2011) Carbon monoxide poisoning. London: Department of Health.

Alonso, JR. Cardellach, F. Lopez, S. Casademont, J. Miro, O. (2003) Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. Pharmacology and Toxicology 93: 142-146.

Anaesthesia UK (2005) Oxygen Dissociation Curve, available at http://www.frca.co.uk/article.aspx?articleid=100345 accessed 26 July 2012.

Baker, D. Karalliedde, L. Murray, V. Maynard, R. Parkinson, N. (2012) Essentials of toxicology for health protection: a handbook for field professionals. Oxford University Press.

Barker, SJ. Curry, J. Redford, D. Morgan, S. (2006) Measurement of carboxyhemoglobin and methoglobin by pulse oximetry: a human volunteer study. Anesthesiology 105(5): 892-897.

Baum, CR. (2008) What's new in Pediatric carbon monoxide poisioning? Clinical Pediatric Emergency Medicine 9: 43-46.

Bledsoe, BE. Nowicki, K. Creel, J.H. Carrison, D. Severance, HW. (2010) Use of pulse CO-oximetry as a screening and monitoring tool in mass carbon monoxide poisoning. Prehospital Emergency Care 14: 131-133.

Brierley, J. Larcher, V. (2011) Emergency research in children: options for ethical recruitment. Journal of Medical Ethics 37: 429-432.

Chee, KJ. Nilson, D. Partridge, R. Hughes, A. Suner, S. Sucov, A. Jay, G. (2008) Finding a needle in a haystack: a case series of carbon monoxide poisoning detected using new technology in the emergency department. Clinical Toxicology 46(5): 461-469.

Clarke, S. Keshishian, C. Murray, CV. Coultrip, E. Oetterli, S. Earle, D. Ward, P. Bush, S. Ruggles, R. (2012) Non-invasive screening for carbon monoxide exposure in selected patient groups attending rural and urban Emergency Department in England. Report to the Department of Health PRP: 002/0030.

Coulange, M. Barthelemy, A. Hug, F. Thierry, AL. De Haro, L. (2008) Reliability of new pulse CO-oximeter in victims of carbon monoxide poisoning. Undersea and Hyperbaric Medicine 352): 107-111.

Crawford, DM. Hampson, NB. (2008) Fire and ice: diagnosis of carbon monoxide poisoning in a remote environment. Emergency Medicine 25(4): 235-236.

Cronje, FJ. Carraway, MS. Freiberger, JJ. Suliman, HB. Piantadosi, CA. (2004) Carbon monoxide actuates O(2)-limited heme degradation in the rat brain. Free Radical Biology Medicine Journal 37: 1802-12.

Department of Health (2010) Carbon monoxide poisoning: needless deaths, unnecessary injury. PL/CMO/2010/02, PL/CNO/2010/02 at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_121501.pdf [accessed 15 November 2011].

Department of Health (2011) Carbon monoxide poisoning sends 4,000 people to A&E each year. at: http://www.dh.gov.uk/health/2011/11/co-poisoning/ [accessed 10 July 2012].

European Union Clinical Trials Directive 2004/20/EC at: www.eur-lex.europa.eu accessed 12 March 2012.

Greaves, I. Porter, K. Garner, J. (Eds.) (2008) Trauma Care Manual 2nd edition. London, Edward Arnold.

Hampson, NB. Scott, KL. Zmaeff, JL. (2005) Carboxyhemoglobin measurement by hospitals: implications for the diagnosis of carbon monoxide poisoning. The Journal of Emergency Medicine 31(1): 13-16.

Health and Safety Executive (2006) Lord Hunt calls for renewed action on gas safety. News release. 2 October 2006. E096:06 at: http://www.hse.gov.uk/ [accessed 10 July 2012].

Humber, A. (2010) Carbon Monoxide: 'The Silent Killer': Feasibility Study 2009/2010. London Ambulance Service. February 2012.

Liverpool John Moores University (2012) Carbon monoxide study saves lives: BEST Research Institute. At: http://ljmu.ac.uk/NewsUpdate/index_123350.htm [accessed 10 July 2012].

Mak, TWL. Kam, CW. Lai, JPS. Tang, CMC. (2000) Management of carbon monoxide poisoning using oxygen therapy. Hong Kong Medical Journal 6(1): 113-115.

Masimo Corporation. RAD-57 Pulse CO-oximeter: noninvasive measurement of methemoglobin, carboxyhemoglobin, oxyhemoglobin and pulse rate in the blood. Available at: http://www.masimo.com/rad-57/. Accessed 06 December 2011.

Medicines for Human Use (Clinical Trials) Regulations (2004) Version 3, 1 May 2008.

Petterson, MT. Begnoche, VL. Graybeal, JM. (2007) The effect of motion on pulse oximetry and its clinical significance. Anesthesia and Analgesia 105(6): Review article S78-S84.

Piantadosi, CA. Zhang, J. Levin, ED. Folz, RJ. Schmechel, DE. (1997) Apoptosis and delayed neuronal damage after carbon monoxide poisoning in the rat. Experimental Neurology 147: 103-114.

Piatkowski, A. Ulrich, D. Grieb, G. Pallua, N. (2009) A new tool for the early diagnosis of carbon monoxide intoxication. Inhalation Toxicology 21(13): 1144-1147.

Plante, T. Harris, D. Savitt, J. Akhlaghi, F. Monti, J. Jay, G. (2007) Carboxyhemoglobin monitored by bedside continuous CO-oximetry. Journal of Trauma Injury, Infection and Critical Care 63(5): 1187-1190.

Prockop, LD. Chichkova, RI. (2007) Carbon monoxide intoxication: an updated review. Journal of the Neurological Sciences 262: 122-130.

Roth, D. Bayer, A. Schrattenbacher, G. Malzer, R. Herkner, H. Schreiber, W. Havel, C. (2013) Exposure to carbon monoxide for patients and providers in an urban emergency medical service. Prehospital Emergency Care 17: 354-360.

Roth, D. Hubmann, N. Havel, C. Herkner, H. Schreiber, W. Laggner, A. (2009) Victim of carbon monoxide poisoning identified by carbon monoxide oximetry. The Journal of Emergency Medicine 40(6): 640-642.

Roth, D. Krammel, M. Schreiber, W. Herkner, H. Havel, C. Laggner, A. (2013) Unrecognised carbon monoxide poisoning leads to a multiple-casualty incident. Journal of Emergency Medicine 45(4): 559-561.

Roth, D. Schreiber, W. Herkner, H. Havel, C. (2014) Prevalence of carbon monoxide poisoning in patients presenting to a large emergency department. International Journal of Clinical Practice 68 (10).

Scott, T. and Foster, T. (2012) 'Assessment and management of carbon monoxide toxicity in emergency patients'. Royal College of Nursing Emergency Care Association Conference, Manchester, November 2012.

Scott, T. and Foster, T. (2013) 'Assessing carbon monoxide poisoning', Emergency Nurse 20(10): 14-19.

Suner, S. Partridge, R. Sucov, A. Valente, J. Chee, K. Hughes, A. Jay, G. (2008) Non-invasive pulse CO-oximetry screening in the emergency department identifies occult carbon monoxide toxicity. The Journal of Emergency Medicine 34(4):441-450.

Thom, SR. (2008) Carbon monoxide pathophysiology and treatment. IN: Neuman TS, and Thom SR, (eds.) Physiology and medicine of hyperbaric oxygen therapy. Philadelphia: Saunders Elsevier pp321-347.

Thom, SR. Bhopale, VM. Han, ST. Clark, JM. Hardy, KR. (2006) Intravascular neutrophil activation due to carbon monoxide poisoning. American Journal of Respiratory and Critical Care Medicine 174: 1239-1248.

Touger, M. Birnbaum, A. Wang, J. Chou, K. Pearson, D. Bijur, P. (2010) Performance of the RAD-57 pulse CO-oximeter compared with standard laboratory carboxyhemoglobin measurement. Annals of Emergency Medicine 56(4):382-388.

Weaver, LK. (2009) Carbon monoxide poisoning. The New England Journal of Medicine 360: 1217-1225.

World Health Organisation (2000) Air quality guidelines for Europe (2nd edition). WHO Regional Publications. European Series No 91. 2000 Available at: http://www.euro.who.int/__data/assets/pdf_file/0005/74732/E71922.pdf Accessed 27 February 2012.