

# NPIS REPORT FOR CO RESEARCH TRUST

# CARBON MONOXIDE EXPOSURES REPORTED TO THE NATIONAL POISONS INFORMATION SERVICE

# 01 July 2015 to 30 June 2023 (8 years)

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# **1 EXECUTIVE SUMMARY**

- Data are available for 5538 patients unintentionally exposed to CO (non-fire related).
- 1357 (24.5%) were male, 1865 (33.7%) were female. Gender was not specified for 2316 (41.8%) patients.
- In children, those aged 0–9 years (730; 13.2%) were involved in a significantly greater proportion of CO exposures than those aged 10–19 years (367; 6.6%; P <0.0001, Figure 2). More than two thirds of children in the 0-9 years cohort were aged 0-4 years.</li>
- In adults, the largest number of exposures occurred in patients aged 20–29 (736; 13.3%) and 30–39 years (749; 13.5%). These were significantly greater than those age ≥ 40 years (P < 0.0001).</li>
- CO exposures were most often reported during winter months.
- Faulty boilers in a domestic setting were most frequently reported as the CO source.
- Short term exposures ( $\leq$  24-hours) were reported in nearly 30% of cases.
- The majority of unintentional exposures resulted in no symptoms or mild symptoms only (70.4%).
- There were twelve unintentional fatalities reported to the NPIS during this 8.0-year study period.
- Symptoms commonly reported involved the CNS, GI or CV systems but were often non-specific in nature.
- 135 unintentional exposures involved pregnant women. The majority (91.1%) reported no symptoms or minor symptoms only. Three pregnant patients had symptoms of moderate severity whilst in 9 patients, no information about the symptoms were available.
- Where carboxyhaemoglobin concentrations were available, the data suggest a positive correlation with poisoning severity, however this was not statistically significant.
- Activation of a CO alarm was reported in 21.0% of cases. The majority of these cases were associated with mild symptoms or no symptoms at all.
- 297 exposures were reported as intentional (self-harm). The majority (60.3%) involved vehicle exhausts. Relative to unintentional exposures, a greater proportion

(13.5%) of self-harm exposures caused severe toxicity. There were 11 fatalities reported to the NPIS.

# **2** INTRODUCTION

Carbon monoxide (CO) is a colourless, odourless, non-irritant gas produced following the incomplete combustion of carbon containing compounds. Common sources include house fires, defective generators or heating appliances and vehicle exhaust emissions [1]. CO is also present in cigarette smoke and produced endogenously through the breakdown of haem [2, 3]. Exposure to CO may be acute or chronic and can occur either unintentionally or intentionally through an act of self-harm. Unintentional exposures may be further subdivided into those related to fires (where additional toxicity such as cyanide may contribute) and non-fire related CO exposures. Unintentional non-fire related CO exposures pose a serious public health challenge and as such are the primary focus of this study. Patients are often unaware of the presence of the poisonous gas even after they begin to experience symptoms. Public health policy is focused on raising awareness of this hidden danger while identifying and eliminating potential sources of CO. Intentional CO exposures are discussed separately within this document as due to the nature of the exposure, toxicity associated with this type of poisoning is often greater.

The epidemiology of CO exposures is complex and difficult to elucidate accurately. A recent global analysis of fatal unintentional CO poisoning from 2000 to 2021 [4], reported a global mortality rate in 2021 of 0.366/100000 with 28,900 deaths. They demonstrated a 53.5% decrease in age standardised mortality rate from 2000-2021. The World Health Organisation (WHO) previously reported a total of 140,490 CO-related deaths across 28 European member states between 1980-2008 (annual death rate of 2.2/100 000) [5]. A 13-year study in the US (1999-2012) reported 438 deaths per year from CO poisoning [6]. More recently, another US study an increase in accidental CO poisoning-deaths with 543 reported I 2021 [7]. In the UK, CO-related deaths have declined over recent decades with unintentional nonfire related CO deaths in England and Wales reducing from 3.34 deaths/million population in 1979 to 0.44 deaths/million population in 2012 [8]. In 2019, 53 CO-related deaths were recorded in England and Wales (ONS 2020). In Scotland, 209 CO-related deaths were reported between 2007-2016 with the highest number reported in the winter months [1]. Exposure to CO, however, results in many more presentations and admissions to hospital with an estimated 4000 Emergency Department presentations [9] and 200 hospital admissions annually in the UK [10].

Following exposure, CO is absorbed through the lungs and combines preferentially with haemoglobin (Hb) in red blood cells to produce carboxyhaemoglobin (COHb). Carbon monoxide has 240 times higher affinity than oxygen for Hb and impairs oxygen delivery to vital tissues [11, 12]. CO also binds to myoglobin in cardiac and skeletal muscle and cytochrome oxidases, impairing cellular utilisation of oxygen [12, 13]. Additional mechanisms of toxicity can occur including platelet activation with stimulation of an inflammatory response and glutamate release in the brain leading to neurological injury [13].

The diagnosis of CO poisoning is dependent on confirming a history of CO exposure, identifying symptoms consistent with CO poisoning, and demonstrating an elevated COHb level [14]. There are challenges in making the diagnosis however as the symptoms reported, particularly in the context of chronic low-level exposure, are often varied and non-specific

and may be affected by age and co-morbidity. Individual doctors make the diagnosis CO poisoning sufficiently rarely that CO exposure may not be immediately considered at the time of presentation [2, 15]. Furthermore, COHb levels are difficult to interpret in the clinical environment and correlate poorly with symptoms [2]. The COHb level is dependent on the atmospheric concentration of CO at the scene of exposure, the level of activity of the patient following exposure, whether the patient is a smoker themselves or have been in an enclosed environment with smokers, and the timing and concentration of any supplemental oxygen administered following exposure [2, 16].

The UK National Poisons Information Service (NPIS) is a network of poisons units in Edinburgh, Birmingham, Cardiff and Newcastle, commissioned by the UK Health Security Agency (UK HSA, formally known as Public Health England) to provide management advice to healthcare professionals dealing with patients with suspected poisoning, including CO-exposure. Information is provided *via* the online database TOXBASE® and a 24-hour telephone advice line. The NPIS is therefore uniquely placed to assess the epidemiology of CO poisoning in the UK as well as the clinical course and management of patients with CO exposure. Our aim was to analyse the epidemiology of CO poisoning in the UK and the treatment provided for patients exposed. Through a greater understanding of the scale of the problem as well as the causative factors, symptoms reported and management strategies, we hope to improve our advice to future clinicians so that we can not only direct treatment towards those most in need but also prevent any unnecessary hospital presentations and admissions.

# **3 METHODS**

The NPIS provides clinical advice for the management of poisoned patients via TOXBASE and a 24-hour telephone advice line staffed by specialists in poisons information and supported by consultant clinical toxicologists. Enquiries are received from healthcare professionals from a range of clinical settings including primary and secondary care as wells as telephone advice services such as NHS Direct/NHS 111/NHS 24.

Enquiries regarding CO exposures during the period 01 July 2015 – 30 June 2023 were analysed. Telephone enquiries to the NPIS are routinely recorded in the UK Poisons Information Database. Enquiries were received from hospitals, primary care, NHS triage services (e.g. NHS 111/Direct/24) and the ambulance service. Enquiries specifically relating to CO exposure during the study period were extracted using the search terms: 'carbon monoxide', 'fire', 'fumes' or 'smoke' to ensure all potential CO exposures were identified. In addition, accesses to TOXBASE (defined as a user logging onto TOXBASE and viewing the CO page) were interrogated during the 8-year period. An online questionnaire was attached to the TOXBASE CO management page which appeared on the screen at the point of access, inviting users to anonymously provide relevant details about the exposure as they were treating the patient. Follow up questionnaires were sent to all enquirers in an order to capture as much data as possible as some information may not have been available at the time of the initial enquiry. No follow-up information was requested from NHS 111/Direct/24 users or to the ambulance service. Note: follow-up questionnaires were not sent during the period 16 March 2020 and 08 July 2020 due to the COVID pandemic.

Following collation of the data, fire–related exposures were omitted from further assessment since symptoms/outcome would likely be confounded by additional clinical effects from factors such as cyanide toxicity and thermal injury. Accidental and intentional non-fire related exposures were evaluated separately.

The severity of each exposure was assessed according to the Poison Severity Score (PSS) [17]. This is a standardized scale for grading the severity of poisoning episodes according to system-based symptoms reported: no symptoms (PSS 0), mild and transient symptoms (PSS 1), moderate symptoms (PSS 2), severe or life-threatening symptoms (PSS 3) and a fatal outcome (PSS 4). A maximum PSS was applied by the poison information specialist at the time of each enquiry. For TOXBASE accesses, the PSS was applied by the lead scientist after the clinical information was provided.

Data collected from both telephone enquiries and TOXBASE access data included patient demographics (gender, age, smoking status, pregnancy), symptoms reported, location of exposure and potential source involved, investigation results including COHb level where available, and any treatment provided.

Data were analysed using Microsoft 365 Excel. Statistics were performed using GraphPad Prism Version 9. Statistical significance was taken at P<0.05.

This study did not require approval by a UK Research Ethics Committee as the UK Health Research Authority has declared that ethical approval is not needed for studies that use information collected routinely by any UK administration (England, Wales, Scotland and Northern Ireland) as part of usual clinical care, provided this information is passed to the researchers in a fully anonymised format.

# 4 **RESULTS**

During the 8-year period, there were 1660 telephone enquiries regarding CO exposures and 24331 TOXBASE accesses to the CO management page (Figure 1). TOXBASE accesses were excluded from further analysis if they were from international users or for educational purposes (3268, 13.4%), or where no clinical information was provided (17,781, 73.1%). This left 3282 patient-related TOXBASE accesses and 1660 telephone enquiries, giving a total of 4942 (19.0%) CO-related NPIS enquiries. Clinical information from follow-up questionnaires yielded information about an additional 1775 patients (e.g. where the initial enquiry was logged as a single patient but it related to a multiple occupancy household involving more than one patient exposure). Eight hundred and eighty two (3.4%) were excluded as the source was secondary to fire-exposure. Exposures reported as intentional (297, 1.1%) were excluded from the main study group and are discussed separately in this report leaving 5538 unintentional non-fire related CO exposures.

#### Figure 1 Patient-related accesses regarding carbon monoxide to the NPIS



## **Patient Demographics**

Of the 5538 unintentional non-fire related CO exposures were reported, 1865 (33.7%) were females and 1357 (24.5%) were male, gender was not reported in 2316 (41.8%) cases (Table 1).

One hundred and thirty-five patients (2.4%) were reported to be pregnant at the time of exposure.

In children, those aged 0–9 years (730; 13.2%) were involved in a significantly greater proportion of CO exposures than those aged 10–19 years (367; 6.6%; P <0.0001, Figure 2). In adults, the largest number of exposures occurred in patients aged 20–29 (736; 13.3%) and 30–39 years (749; 13.5%). These were significantly greater than those age  $\geq$  40 years (P < 0.0001, Figure 2). Interestingly, more than two thirds of children in the 0-9 years cohort were aged 0-4 years (496/730, 68.0%).

Data regarding smoking status was routinely requested since September 2017 and to date this information is available in 1932 (34.9%) patients. Where this data was available, there were 460 (8.3%) confirmed smokers and 1472 (26.6%) non-smokers.



#### Figure 2 Age distribution of patients involved in CO exposures

\* p <0.0001 (0-9 years vs 10-19; 20-29, 30-39 years vs > 40 years) Note: the paler bar in 0-9 years represents cases involving children age 0-4 years old within this cohort.

## Time and location of the exposure and source of carbon monoxide

Seasonal variation was demonstrated in the frequency of enquiries with more exposures occurring during colder winter months (Figure 3a). The highest monthly number of cases recorded (127) was during November 2016. Figure 3b demonstrates the mean exposure per year of collection (July-June). A visual assessment suggests the annual data are trending downwards since 2020 (Figure 3b).



Figure 3a Mean CO exposure according to month (± standard deviation)

Figure 3b Mean monthly CO exposure according to year (± standard deviation)



The location of exposures was recorded in 4002 (72.3%) cases, with the vast majority in the home (3046; 55.0%; P < 0.0001 compared to other locations, Table 1). The CO source was

identified in 3702 (66.8%) cases. Faulty boilers were significantly more common than other identified sources (1566; 28.3%; P < 0.0001 compared to all other identified sources, Table 2).

| Location              | Ν     | %    |
|-----------------------|-------|------|
| Home                  | 3046* | 55.0 |
| Car                   | 273   | 4.9  |
| Business – non-office | 231   | 4.2  |
| Business - office     | 115   | 2.1  |
| Caravan               | 66    | 1.2  |
| Garage                | 47    | 0.9  |
| Leisure accommodation | 46    | 0.8  |
| Public space          | 35    | 0.6  |
| Tent                  | 20    | 0.4  |
| Boat                  | 8     | 0.1  |
| School                | 6     | 0.1  |
| Other <sup>a</sup>    | 109   | 1.9  |
| unknown               | 1536  | 27.7 |
| TOTAL                 | 5538  | -    |

## Table 1Location of CO exposure

\* p < 0.0001 compared to other variables in the group.  $^{a}$  - e.g. restaurant kitchen, industrial site

| Source                                | Ν     | %    |
|---------------------------------------|-------|------|
| Boiler                                | 1566* | 28.3 |
| Exhaust (vehicle)                     | 383   | 6.9  |
| Gas appliance (other)                 | 360   | 6.5  |
| Wood/coal fire burner                 | 286   | 5.2  |
| Cooker (domestic)                     | 246   | 4.4  |
| Gas fire                              | 127   | 2.3  |
| Exhaust (generator)                   | 123   | 2.2  |
| Gas heater (portable)                 | 109   | 2.0  |
| BBQ                                   | 69    | 1.3  |
| Industrial/work appliances            | 68    | 1.2  |
| Exhaust (other)                       | 32    | 0.6  |
| Camping stove                         | 28    | 0.5  |
| Cooker (commercial)                   | 32    | 0.6  |
| Fire pit                              | 13    | 0.3  |
| Aga                                   | 14    | 0.3  |
| Chiminea                              | 5     | 0.1  |
| Patio heater                          | 5     | 0.1  |
| Biomass heating system (wood pellets) | 3     | 0.1  |
| Other⁵                                | 233   | 4.2  |
| Unknown                               | 1836  | 33.2 |
| TOTAL                                 | 5538  | -    |

#### Table 2Source of unintentional CO exposure

\* p < 0.0001 compared to other variables in the group.

<sup>a</sup> – e.g. scuba diving tank, paint stripper, shisha

# **Duration of exposure**

The duration of CO exposure was reported in 2730 (49.3%) of cases (Table 3). Short term exposures ( $\leq$  24 hours) were reported in 1511 (27.3%) of cases and longer-term exposures were reported in 696 (12.6%) cases ( $\leq$  1month) and 523 (9.4%) cases (> 1 month). In 2808 (50.47of cases, duration of exposure was unknown.

#### Table 3Duration of exposure

| Exposure Duration     | Ν    | %    |
|-----------------------|------|------|
| Short term (≤ 24 hrs) | 1511 | 27.3 |
| Sub-Acute (<1 month)  | 696  | 12.6 |
| Chronic (>1 month)    | 523  | 9.4  |
| Unknown/Not reported  | 2808 | 50.7 |
| Total                 | 5538 | -    |

### Symptoms reported and poisoning severity score

There were 1629 (29.3%) asymptomatic patients. A wide range of clinical features were reported with many patients reporting multiple symptoms (Table 4). Clinical features involving the CNS were most common with headache being the most frequently reported system (p<0.0001).

The majority of patients (3901, 70.4%) experienced no symptoms (PSS 0) or minor symptoms (PSS 1) only, with 311 (5.6%) exposures being recorded as moderate (PSS 2) and 61 (1.1%) being recorded as severe (PSS 3) (Table 5).

Twelve fatalities (0.2%, PSS 4, Table 5) related to unintentional non-fire related COexposures were reported. Five of these occurred in a domestic setting, one in a commercial premises, one in a garage, one in a caravan and four fatalities occurred in an unreported location. Three patients suffered a cardiac arrest, two pre-hospital and one in hospital soon after presentation. While CO was considered the causative factor, no confirmatory evidence was ever established.

Of the 135 pregnant patients, the majority (123, 91.1%) reported no symptoms or minor symptoms only. Three pregnant patients had symptoms of moderate severity (including palpitations, dyspnoea, general feeling of being unwell and headache), while for the remaining 9 patients, no information about the symptoms was available.

| Body System     | Feature  | Ν    | %    |
|-----------------|--|------|------|
|                 | Asymptomatic   | 1526 | 29.7 |
| CNS             | Headache   | 1290 | 23.3 |
|                 | Nausea   | 575  | 10.4 |
|                 | Lethargy/fatigue/malaise                               | 513  | 9.3  |
|                 | Dizzy, faint, lightheaded                              | 511  | 9.2  |
|                 | Somnolence, drowsy                                     | 163  | 2.9  |
|                 | Confusion/concentration impaired                       | 133  | 2.4  |
|                 | Coma, unconsciousness                                  | 37   | 0.7  |
|                 | Syncope  | 32   | 0.6  |
|                 | Memory impairment, amnesia                             | 30   | 0.5  |
|                 | Anxiety  | 20   | 0.4  |
|                 | Flushing   | 18   | 0.3  |
|                 | Agitation/irritable mood                               | 17   | 0.3  |
|                 | Vertigo  | 17   | 0.3  |
|                 | Pyrexia  | 17   | 0.3  |
|                 | Ataxia (un-coordination)                               | 14   | 0.3  |
|                 | Tremor, shaking  | 15   | 0.3  |
|                 | Stupor, consciousness decreased                        | 16   | 0.3  |
|                 | Convulsions  | 14   | 0.3  |
| GI              | Vomiting   | 207  | 3.7  |
|                 | GI upset   | 130  | 2.3  |
|                 | Mouth/throat sore, pharyngitis                         | 59   | 1.1  |
|                 | Taste perversion, unpleasant                           | 17   | 0.3  |
|                 | Dry mouth  | 12   | 0.2  |
| Respiratory     | Cough  | 114  | 2.1  |
|                 | Dyspnoea   | 114  | 2.1  |
|                 | Chest Pain   | 69   | 1.3  |
|                 | Flu like symptoms                                      | 50   | 0.9  |
|                 | Wheeze   | 42   | 0.8  |
| Eye             | Eye Abnormal vision/irritation                         | 47   | 0.9  |
| Cardiovascular  | Palpitations/tachycardia                               | 48   | 0.9  |
| Musculoskeletal | Muscle weakness  | 37   | 0.7  |
|                 | Muscle aching, myalgia                                 | 16   | 0.3  |
| Skin            | Skin irritation, erythema, dermatitis, rash, urticaria | 11   | 0.2  |
|                 | Paraesthesia   | 11   | 0.2  |

#### Table 4Clinical features

Note: clinical features reported where frequency was > 10.

Since patients may have had multiple symptoms, the sum of the percentages in the table will be > 100% when asymptomatic and unknown cases are included.

| DCC                 |      |      |
|---------------------|------|------|
| P35                 | Ν    | %    |
| None<br>(PSS 0)     | 1522 | 27.5 |
| Minor<br>(PSS 1)    | 2379 | 43.0 |
| Moderate<br>(PSS 2) | 311  | 5.6  |
| Severe<br>(PSS 3)   | 61   | 1.1  |
| Fatal<br>(PSS 4)    | 12   | 0.2  |
| Uncertain           | 1253 | 22.6 |
| Total               | 5538 | -    |

### Table 5Poisoning Severity Scores

## Carboxyhaemoglobin concentration

Carboxyhaemoglobin concentration was reported in 1614 (29.1%) cases (1388 blood, 135 CO pulse oximetry, 91 CO exhaled air). Our analysis focused on blood sampling (as the gold standard method) which was reported in 1388 patients (25.1%). Analysis of Severity PSS according to median COHb% values indicates a positive correlation (r = 0.9, Spearman; Figure 4), however, this was not found to be statistically significant (p = 0.08).

The data is also reported in a Box and Whiskers plot to demonstrate the range of values (minimum, interquartiles, median and maximum values) reported (Figure 5). Statistics performed in the course of generating this plot (Kruskal-Wallis test) indicate the median values vary significantly (p < 0.0001).

The greatest range of reported COHb% values was observed in patients with minor symptoms. Note: the highest level reported was at 62.5% in a patient with minor symptoms. Unfortunately, there was no response from the follow-up request to confirm whether this was an accurate value or an anomaly.

#### Figure 4 Correlation (Spearman) of Severity (PSS) and Median COHb Concentrations



Figure 5 Poisoning Severity (PSS) versus COHb%



## Carbon monoxide detector

Information about activation of CO detectors during each exposure was not specifically collected until January 2022. Nevertheless, in 1165 cases (21.0% of the total study group), it was reported that activation of a CO detector prompted the patient to seek medical attention. In the majority of these cases (995; 85.4%), the patients had no symptoms or minor symptoms, whilst 11 patients (0.9%) experienced symptoms of moderate severity and one patient experienced symptoms of severe severity (0.1%). Symptoms were unknown in 157 patients (13.5%).

In 119 cases (since January 2022), a CO release was confirmed by either a gas engineer or the FRS. In 62.2% (74/119) of these exposures, the patients did not have a CO detector. These are insufficient data to analyse any further at this stage.

## Intentional CO Exposures

Two hundred and ninety-seven patients were exposed to CO as a result of self-harm during the 8-year study period. There were 160 male (53.9%), 25 female (9.4%) and 109 (36.7%) cases where gender was unknown.

When compared to unintentional exposures (Table 5), a higher proportion of moderate, severe or fatal outcomes were observed (15.2%, 13.5% and 3.7%, respectively, Table 6). Eleven patients died as a result of intentional CO exposure.

The source of these exposures is detailed in Table 7. The majority involved vehicle exhausts (179; 60.3%), followed by BBQs (45; 15.2%).

#### Table 6Poisoning Severity Scores for Intentional CO Exposures

| DCC                 |     |      |
|---------------------|-----|------|
| P33                 | N   | %    |
| <b>None</b> (PSS 0) | 79  | 26.6 |
| Minor (PSS 1)       | 78  | 26.3 |
| Moderate (PSS 2)    | 45  | 15.2 |
| Severe (PSS 3)      | 40  | 13.5 |
| Fatal (PSS 4)       | 11  | 3.7  |
| Uncertain           | 44  | 14.8 |
| Total               | 297 | -    |

#### Table 7Intentional exposures: source of CO

| Source                | N   | %    |
|-----------------------|-----|------|
| Exhaust (vehicle)     | 179 | 60.3 |
| BBQ                   | 45  | 15.2 |
| Exhaust (generator)   | 13  | 4.4  |
| Cooker (domestic)     | 5   | 1.7  |
| Boiler                | 3   | 1.0  |
| Gas heater (portable) | 2   | 0.7  |
| Wood/coal fire        | 2   | 0.7  |
| Gas appliance (other) | 2   | 0.7  |
| Camping Stove         | 1   | 0.3  |
| Gas fire              | 1   | 0.3  |
| Exhaust (other)       | 1   | 0.3  |
| Other*                | 23  | 7.7  |
| Unknown               | 20  | 6.7  |
| Total                 | 297 | -    |

\* e.g. mixing formic and sulphuric acid to liberate CO

# 5 DISCUSSION

### **Main Findings**

This study presents data on a total of 5538 enquiries to the NPIS related to unintentional non-fire related CO exposures between July 2015 and June 2023. These were most often reported during winter months, involved all age groups but most frequently children and adults aged 20–39 years, and commonly occurred in the home as a result of faulty boilers. While the majority of cases were of low severity, there were eleven fatalities were reported.

Defining the true epidemiology of CO exposures continues to be challenging with variation in how data is collected, categorised, recorded and reported. Hospital Episode Statistics (HES) data (2015-2018) reported 208 admissions/year due to accidental CO exposures in the UK [18-21], while McCann et al [9] reported an estimated 4000 ED presentations annually. We have presented data on 5538 NPIS enquiries (approximately 692/year) which represents information from healthcare professionals treating CO poisoned patients in all four UK nations. Importantly, the data presented here includes information on clinical parameters including biomarkers, poisoning severity and the source and location of the exposure, not traditionally included in other epidemiological studies using coded hospital data. Furthermore, in addition to admitted patients, the current study includes patients presenting to EDs who are discharged without admission and those assessed in the community who do not always attend a hospital.

We have reported twelve fatalities over the 8-year study period. This is lower than expected when compared to national mortality data which demonstrated 18 deaths from unintentional CO exposures in 2018 (note, more recent mortality data for England and Wales is available showing 23, 21 and 20 deaths for 2019, 2020 and 2021, respectively), overall, a reduction from 32 deaths reported in 2015 [22-33]. We recognize that our data may underestimate mortality figures as it only represents those cases where health professionals contacted the NPIS for clinical management advice. Exposures managed without NPIS involvement and out-of-hospital deaths are not included.

The seasonal variation in exposures supports previous studies and is likely due to an increased use of gas appliances during colder temperatures [34-36]. Children and the elderly have previously been reported to be more commonly implicated [34]. While it is possible that these patient groups are at a particular risk from CO, they are also more likely to spend longer periods of time indoors, particularly in the winter and, should a CO leak occur, be less able to recognise and seek help to reduce exposure. In the current study we demonstrated a significantly greater number of CO exposures in younger children (<10 years) compared to their older counterparts (10-19 years). We have also shown that nearly 70% of children in the 0-9 years cohort were  $\leq$  4-years old which is in keeping with younger patients likely being exposed due to their time spent within a domestic setting. In contrast, fewer exposures were reported in patients over the age of 60 years. It is unclear why fewer exposures were reported in older patients in our study but may reflect the methodology. Older patients are perhaps more likely to be admitted to hospital following an episode of CO exposure and therefore in studies reporting hospital admission data, they may demonstrate a greater proportion of elderly patients compared to our data which include exposures not requiring admission. In addition, Mattiuzzi and Lippi (2020) and Close et al. (2022) reported

that death rates were highest amongst the over 70s therefore it is also possible that these patients in this elderly cohort may have succumbed to the effects of CO without ever attending hospital [37, 38].

The majority of exposures reported were of low severity and associated with no symptoms or mild symptoms only. Where clinical features were reported these were often varied and non-specific, highlighting the diagnostic challenge facing health professionals. As previously shown, symptoms reported most often involved the CNS with headache being most common [13, 39].

A raised COHb% is the current gold-standard biomarker necessary to confirm exposure so that appropriate treatment may be instigated, and the source of CO investigated. Clinical interpretation of the COHb% concentration is complex since as it can be affected by patientrelated factors such as smoking status and co-morbidity. Cigarette smoking can significantly impact COHb% with baseline concentrations considered to be ≥2.5% in non-smokers and ≥5% in smokers [14]. Environmental factors (e.g. atmospheric concentration of CO at the scene, duration of exposure, time since removal from CO source and any oxygen administration) also influence COHb% [16]. In the current study, blood COHb% concentration was reported in only 25.1 % of patients. The low reporting of this biomarker may be related to the large proportion of asymptomatic patients as clinicians may have felt an invasive confirmatory test in an otherwise well patient was unnecessary. It should also be noted that smoking status was only available in 34.9% of patients making it difficult to determine any effects of this variable. Furthermore, limited information was available about the specific timing of the COHb% measurement with respect to the time of exposure and indeed whether supplemental oxygen was administered pre- or in hospital. In our study, COHb% values of greater than 10% and 20% were reported in 5.4% and 1.1% of asymptomatic patients respectively, while 39.4% of patients with moderate toxicity demonstrated a COHb% of <5%. This highlights the challenge of interpreting COHb% as a marker of severity as opposed to simply confirmation of exposure. It is important that clinicians are aware of this as a low COHb% could be falsely reassuring and result in patients being sent home, potentially to be re exposed to CO.

The majority of exposures occurred within the home and were most commonly associated with faulty boilers. This is consistent with previously published UK data [34,40]. We know that public health policy is aimed at increasing awareness of the hidden dangers associated with CO poisoning through the promotion of CO detectors [41], however, there are differences between constituent nations of the UK with respect to the installation of CO detectors [42-47]. Information about CO detectors was not routinely collected during NPIS enquiries until January 2022. Despite this, enquirers voluntarily provided information about activation of a CO detector in approximately 21.0% of cases. The vast majority of these patients reported no symptoms or minor symptoms, with only eleven patients reporting clinical features of moderate toxicity and one patient with features of severe toxicity.

As already highlighted in this discussion and frequently reported in literature, many patients may not be aware they are being exposed to the effects of CO [2]. In around 50% of cases reported to the NPIS, the duration of exposure was unknown. As noted above, an alarming CO detector alerted at least 21.0% of patients, however, in around one third of these

patients the duration of exposure was not reported/unknown. We also have very limited data collected since January 2022 indicating that in nearly 60% of confirmed CO releases, a CO detector was not present. This again emphasizes the concerns of CO poisoning being dubbed "the silent killer". In the absence of an alarming detector, it is possible that a patient was either alerted to a potential exposure following a gas engineer visit or they had experienced non-specific symptoms and CO toxicity was considered. What is not discernible from these data is how many patients have had low level CO exposures and their duration. This is an area of interest as there are reports that persistent neurological damage may occur as a result of such exposures [48], therefore it will be important to gather as much data on these poisonings as possible.

We have also collected and reported the data for intentional CO exposures. These were far fewer (297) than the unintentional exposures (5538) however the poisoning outcomes showed proportionally more serious features of toxicity. This is not unexpected if the CO is "actively contained" with no attempt to be removed from the source. In the majority of cases, vehicle exhausts were the source of exposure. There were 11 (3.7%) fatalities in the intentional cohort.

#### Limitations of this study

There are a number of limitations associated with this study. Similar to other poison centre studies, these data represent only cases where health professionals have contacted the NPIS for clinical management advice and therefore may underestimate the true incidence of CO poisoning in the UK. Minor exposures where the patient does not present for assessment, or a clinician does not require NPIS advice, are not included. Similarly, severe exposures resulting in out of hospital deaths would not be included. The quality of the data is reliant on the information provided by the treating clinicians whose primary concern at the time of the enquiry was the patient in their care. Additionally, no data was available on the long term follow up of patients. Finally, since the outbreak of the COVID-19 pandemic, daily life and working practices around the world have changed with many more people staying at home. It would be interesting to determine if the demographics of exposures are altered at all, however there are insufficient data at this stage to assess this.

# 6 CONCLUSIONS

CO poisoning is a major public health concern in the UK. Unintentional non-fire related CO exposures pose a particular public health challenge as patients are often unaware of the presence of CO even after they begin to experience symptoms.

- CO is a common and potentially serious source of unintentional poisoning in the UK.
- Twelve fatalities were recorded as a result of unintentional non-fire related CO exposure during this 8-year study period. These were typically reported to the NPIS as multiple presentations where poisoning did not result in death.
- The majority of unintentional exposures resulted in no symptoms or mild symptoms only.
- Symptoms most commonly involve the CNS, GI or CV systems but are often non-specific in nature and may often be mistaken for flu-like symptoms.
- Where blood COHb% measurements were available, the data suggest a correlation between these levels and poisoning severity, however this was not statistically significant.
- Faulty boilers, in the home, were the most reported source of CO causing unintentional poisoning.
- The NPIS was made aware of 21.0% of cases where the activation of a CO alarm prompted the patient to seek medical attention. The majority of these cases were associated with mild symptoms or no symptoms at all.
- Self-harm cases resulted in proportionally higher cases of serious poisoning. Vehicle exhausts and BBQs were the predominant source of exposure in this cohort.
- The NPIS is uniquely placed to collect and act as a central repository for national data on CO exposures across the UK.
- Public health policy needs to continue to focus on raising awareness of this hidden danger while identifying and eliminating potential sources of CO.
- Further investigations into long-term outcomes and assessment of low-level chronic exposures should be included in future work.

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