# PLOS ONE

RESEARCH ARTICLE

Diagnosis of carbon monoxide exposure in clinical research and practice: A scoping review

Phil Moss[1], Natasha Matthews[1], Rosalie McDonald[1], Heather Jarman[1,2]*

1 St Georges' Emergency Department Clinical Research Group, Emergency Department, St Georges' Hospital, London, United Kingdom, 2 Population Health Research Institute, St George's University of London, London, United Kingdom

* hjarman@sgul.ac.uk
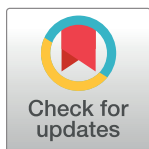
Abstract

Objective

To undertake a scoping review to identify methods and diagnostic levels used in determining unintentional, non-fire related carbon monoxide exposure.

Design

Online databases and grey literature were searched from 1946 to 2023 identifying 80 papers where carbon monoxide levels were reported.

Results

80 papers were included; 71 research studies and 9 clinical guidelines. Four methods were described: blood carboxyhaemoglobin (arterial or venous blood analysis), carbon monoxide oximetry (SpO2), expired carbon monoxide, and ambient carbon monoxide sampling. Blood analysis methods predominated (60.0% of the papers). Multiple methods of measurement were used in 26 (32.5%) of the papers. Diagnostic levels for carboxyhaemoglobin were described in 54 (67.5%) papers, ranging between 2% and 15%. 26 (32.5%) papers reported diagnostic levels that were adjusted for the smoking status of the patient.

Conclusions

Four methods were found for use in different settings. Variability in diagnostic thresholds impairs diagnostic accuracy. Agreement on standardised diagnostic levels is required to enable consistent diagnosis of unintentional, non-fire related carbon monoxide exposure.

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Competing interests: The authors have declared that no competing interests exist.

Introduction

Rationale

Carbon monoxide (CO) is a colourless, odourless gas produced by incomplete combustion of carbon compounds. It is reported as a significant cause of death from poisoning worldwide, leading to a population burden of 137 cases and 4.6 deaths per million in 2017 [1]. In the US data from the National Centre for Health Statistics show a reduction in death between 2015 and 2021 from 1,253 to 1,067 [2]. Exposure to CO leads to the formation of carboxyhaemoglobin (COHb) within the red blood cells, with CO binding to haemoglobin with an affinity 220 times that of oxygen. This results in a combination of tissue hypoxia from reduced oxygen delivery to the tissues and the generation of free radicals from CO-mediated damage to the cells [3–5]. Physiological breakdown of haem molecules produces endogenous CO [6]. Smokers have higher levels of endogenous CO compared to non-smokers [7]. This is why non-harmful levels of COHb are not set at zero. Exposure to CO can be both intentional and unintentional (accidental). Intentional exposure results from self-poisoning, usually through suicide using car exhaust fumes. Unintentional exposure can be further subdivided into fire-related exposure where there is a clear history of CO release, and non-fire related occurring due to exposure from outdoor or indoor sources. Outdoors it results from air pollution when CO is produced by vehicles and industry pollutants. Indoors the most common sources of CO are found in the home from incorrectly installed, poorly maintained, inappropriately used, or poorly ventilated fossil fuel and wood-burning heating and cooking appliances [8–10]. Threshold levels that cause harm are set by the World Health Organisation. Harmful exposure is defined by CO concentrations in parts per million (ppm) and duration of exposure i.e., 100 ppm for 15 minutes, 35 ppm for 1 hour and 10 ppm for 8 hours [11]. An increase in CO-related morbidity and mortality has also been found after natural disasters where power outages lead to the inappropriate placement of portable generators and the use of malfunctioning propane heaters in the home [12–14].

Diagnosis of CO exposure in clinical practice is reliant on a clinical diagnostic triad: 1. symptoms consistent with CO exposure; 2. a recent history of CO exposure; and 3. elevated levels of the biomarker carboxyhaemoglobin (COHb) [15, 16]. CO exposure can have different clinical effects depending on the severity, although in low-level exposure, patients may not be aware of the exposure and COHb levels may not be raised. Diagnosis based on symptoms alone is challenging due to the non-specific nature of the presentation. Neurological symptoms predominate, particularly headache, with other symptoms such as dizziness, chest pain, and drowsiness [15, 16]. In the paediatric population CO can present with seizures, vomiting, headache, and nausea [17]. Exposure to elevated levels, or ongoing exposure to low levels of CO, can lead to long-term cognitive issues with impaired memory loss and motor deficit [18–20].

Objectives

This scoping review aims to identify the current methods and diagnostic threshold levels used for determining exposure in unintentional, non-fire related (UNFR) CO exposure in clinical practice guidelines and research literature.

Methods

This review follows the five-stage process described by Arksey and O'Malley for conducting scoping reviews and the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [21, 22].

Stage 1—Identifying the research question

A preliminary exploration of the literature revealed differences in how CO is measured in practice, and in the diagnostic levels used to determine what constitutes harmful exposure. The research question for this review was: What are the current methods used in clinical practice guidelines and research to diagnose unintentional, non-fire related carbon monoxide exposure?

Stage 2 –identifying relevant studies / search strategy

Search strategy.   The search strategy was developed based on the expertise of the research team and a health information scientist and was used to generate the initial literature search. The search strategy was tested on a single database before being refined and replicated on other databases [S1 Table]. Searches were conducted using the MEDLINE, Cumulative Index to Nursing and Allied Health Literature [CINAHL] and Excerpta Medica [EMBASE] databases and performed by the health information scientist. Search terms were modified for each of the databases. This search was supplemented by grey literature identified through the TRIP Medical Database, NICE and TOXBASE to include published clinical guidance on CO diagnosis. References lists and citations of included studies were reviewed to identify additional articles meeting the inclusion criteria.

For search strategy see S1 Table.

Eligibility criteria.   The inclusion criteria were defined as articles reporting CO exposure meeting the following characteristics:

- Original articles or conference abstracts published between 01/1946 and 08/2023

- Clinical guidelines published since 2000.

- Inclusion of at least one method of measurement of CO

  The following exclusion criteria were applied:

- Articles where the source of exposure was intentional CO exposure or fire (where there are elevated levels of CO)

- Clinical review articles

- Written in language other than English.

- Articles not relating to human subjects.

- Articles relating to CO from tobacco smoking or outdoor air pollution.

Selection of studies for inclusion.   The study selection criteria were established during the initial review process. Search results were imported into the Rayyan web application for sorting and screening [23]. Two reviewers [xx] and [xx] independently screened titles and abstracts against the inclusion criteria. Where there was not enough information to decide on inclusion using the abstract a full text review was carried out. Disagreements between reviewers were resolved through screening or discussion with a third reviewer [xx]. Further exclusions were made at full text review following agreement from all reviewers. Rationale for excluding articles were recorded.

Stage 4 –charting the data

A data extraction form was developed, tested, and refined in Excel (Microsoft Office 365 E3, Redmond, Washington, US) to systematically list key components of the included articles.

Three overarching categories were extracted: 1. Article characteristics (country, population, number of participants, study setting and design where relevant); 2. Method of measuring CO; and 3. Diagnostic levels for determining an abnormal COHb. A single reviewer extracted all the data from the articles and the data extraction form was reviewed by the other reviewers. Any discrepancies were resolved by discussion. Following guidance on conducting a scoping review, no quality appraisal of the included papers was performed [21]. See S2 Table.

Stage 5 –assembling, summarising, and reporting the results

The identified studies were summarised, and relevant data was extracted. Content analysis was used to identify concepts within the papers. Data was presented narratively under the over-arching categories. Geographical region, study design, methods for measurement of CO (categorised by type), and diagnostic levels.

Results

Of 1615 articles, 80 articles were included. The most common reason for exclusion was the wrong population being studied including papers with fatalities as subjects, papers reporting correlations between symptoms and CO exposure, patients undergoing treatment for known exposure and papers using healthy volunteers as subjects. Fig 1 shows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram detailing the results of the search and selection process.

Paper characteristics

The characteristics of papers, including country, paper type, study design, setting for measurement of study sample, participant age (adult/child), number of participants, known or unknown exposure, source of exposure, method of measurement and diagnostic levels by smoking status and data collection method were inputted into data extraction tables (S3A and S3B Table). Overall, 32 counties published research or guidance, most were published in North America (n = 29, 35.8%). Papers identified were published between 1987 and 2023, 78.8% of which were published between 2007 and 2023. Nine clinical guidelines were identified (11.3%), [11, 16, 24–30] the remaining being research papers. Further categorisation by study methodology found observational studies predominated (65/71; 91.5%). Of these 38/71 (53.5%) were cross-sectional [17, 31–67], 17/71 (23.9%) case reports or case series [68–83], 7/71 (9.9%) cohort design [84–91]. The remaining (3/71; 4.2%) were diagnostic accuracy [92–94] Interventional studies numbered 6; 8.5% [95–100] In research papers the most frequent study setting for measurement was the emergency department (45.0%, n = 36/71) [17, 32, 34, 35, 38–41, 45, 47, 49, 51, 57–64, 70–72, 75–77, 79–82, 87, 88, 91, 93, 94]. The number of study participants ranged from 1 to 74880, with a median of 999 (IQR 34–771).

Method of CO measurement

Across all papers, four methods for measurement of CO levels were identified (Table 1).

The majority of studies (40/71; 56.3%) and all but one of the guidelines (8/9; 88.9%) used venous blood to measure COHb levels [11, 16, 24–30, 32, 33, 35, 39–41, 43, 45, 47, 49, 51, 57–64, 68, 70–72, 74, 76–83, 85, 87, 88, 91–94, 96]. Second most reported across all paper types was SpCO (25/80, 32.5%) [17, 30, 31, 34, 35, 44, 46, 51, 52, 55, 59, 60, 63, 64, 66, 69, 73, 75, 79, 84, 86, 89, 92–94]. Indoor environmental CO measurement was reported in 22 papers [33, 36, 37, 42, 44, 48, 50, 53, 54, 56, 65, 67, 70, 73, 82, 90, 95–100]. Whilst CO breath analysis was reported in 10 [38, 40, 52–54, 58, 61, 85, 86, 97]. Over half (54/80, 67.5%) used a single method
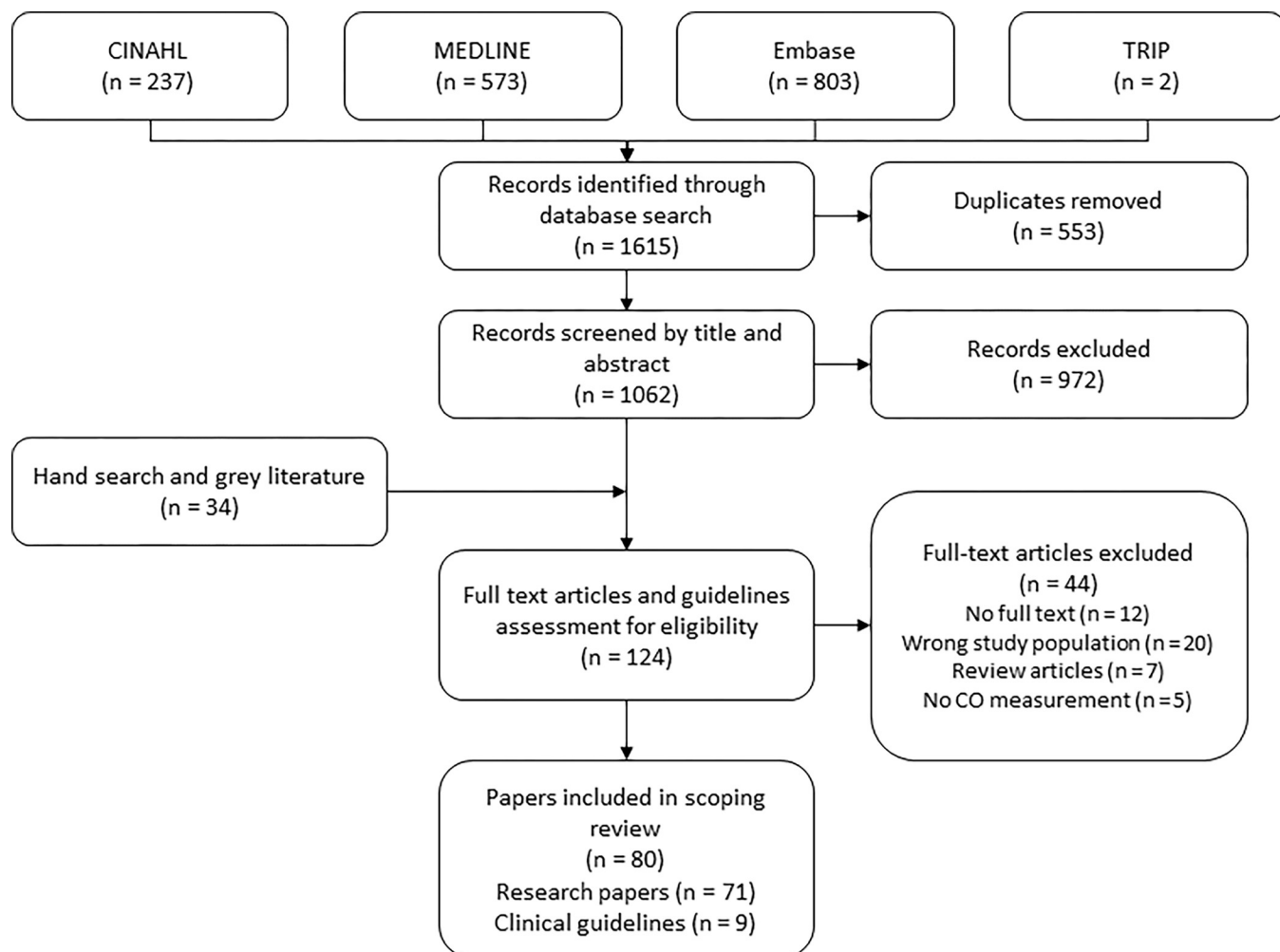
Fig 1. PRISMA flow chart.

https://doi.org/10.1371/journal.pone.0300989.g001

of measurement [11, 16, 17, 24–32, 34, 36–39, 41–43, 45–50, 55–57, 62, 65–69, 71, 72, 74–78, 80, 81, 83, 84, 87–91, 95, 99, 100], while 26 (32.5%) reported 2 methods. [33, 35, 40, 44, 51–54, 58–61, 63, 64, 70, 73, 79, 82, 85, 86, 92–94, 96–98].

Table 1. Types of CO measurement methods identified in papers.

CO measurement method	Description
Blood carboxyhaemoglobin (COHb)	Spectrophotometric measurement detects derivatives of haemoglobin by using discrete narrow bands of electromagnetic waves to differentiate the degree of light absorption by each derivative [101].
CO oximetry (SpCO)	An external skin probe using multi-wavelength photometry to detect the presence of carboxyhaemoglobin (COHb) [93]. A strong correlation between SpCO and blood COHb is shown with Bland–Altman analyses [51, 59, 60, 92–94].
CO breath analysis (end-tidal exhaled CO)	End-expiratory breath measurement in parts per million (ppm) using an electrochemical sensor. COHb% can be calculated from the ppm value and closely correlates to blood COHb concentration [102].
Environment particulates (ambient CO measurement)	CO is measured using electrochemical sensors, typically a metal oxide semiconductor [103].

https://doi.org/10.1371/journal.pone.0300989.t001

Table 2. Analysis method for all papers. Methodology, geographical setting, and setting of CO measurement for research studies.

	Total papers	COHb (blood)	COHb (oximetry)	Breath analysis	Indoor CO levels
All papers (n = 80)	80	48	25	10	22
Smoking status undifferentiated	28	15	9	2	10
Smoking levels differentiated	26	18	8	4	3
No smoking levels reported	26	15	8	4	9
Research studies (n = 71)	71	40	24	10	22
Undifferentiated	28	17	9	2	10
Differentiate	18	21	7	4	3
No levels reported	25	2	8	4	9
Guidelines	9	8	1	0	0
Undifferentiated	0	0	0	-	-
Differentiate	8	7	1	-	-
No levels reported	1	1	0	-	-
Research papers (n = 71)	Total papers	COHb (blood)	COHb (oximetry)	Breath analysis	Indoor CO levels
Study type					
Cross-sectional	38	19	14	7	12
Case report and case series	17	14	4	0	1
Diagnostic accuracy	3	3	3	0	0
Cohort	7	3	3	2	2
Interventional	6	1	0	1	7
Study geographical setting					
Africa	7	1	3	0	5
Asia	5	1	1	1	3
Europe	22	15	8	2	3
North America	25	17	9	5	7
South America	5	0	2	2	3
Middle East	4	4	1	0	0
Southeast Asia	2	2	0	0	0
Mixed	1	0	0	0	1
Study setting (location of measurement)					
Emergency Department (ED)	36	32	12	4	2
Residence	16	0	2	3	14
Workplace	5	1	2	0	4
Recreation venue	2	1	0	1	2
Pre-hospital	1	0	1	0	0
Hospital ward or outpatient clinic	9	5	5	1	0
Primary care	1	1	0	0	0
Not recorded	1	0	1	0	0

Overall papers varied by measurement method used, geographical setting, the setting in which the measurement was taken, whether they differentiated between smokers and non-smokers and research methodology. Three clinical guidelines were for use in both primary and secondary care [27, 28, 30], two in the emergency department [24, 29], one each in primary [26] and secondary care [16] and two set air quality standards [11, 25] (Table 2).

Diagnostic level used to determine CO exposure

Across all papers there were two units of measurement described. Parts per million were used to describe concentration of CO in the environment and COHb to describe levels of CO in

participants' blood. Regardless of method of measurement (blood, CO oximetry, expired or environmental) the diagnostic levels used to determine CO exposure were not stated in 32.5% (26) of papers [27, 28, 33, 36, 43, 49, 52, 53, 55, 66, 67, 69–73, 76, 80, 81, 83, 85, 86, 88, 92, 95, 98]. Of the 54 papers remaining 26 (32.5%) differentiated between CO levels in smokers and non-smokers [11, 16, 24, 26–30, 34, 40, 41, 46, 47, 51, 54, 59, 61, 68, 74, 77, 82, 84, 87, 89, 94, 97] and 28 (35.0%) did not [17, 31, 32, 35, 36, 38, 39, 42, 44, 45, 48, 50, 56–58, 60, 62–65, 75, 78, 79, 90, 91, 93, 96, 100].

In papers reporting COHb levels, using either blood or CO oximetry measurement, (42,52.5%) [11, 16, 17, 24, 26–32, 34, 35, 39, 41, 44–47, 51, 57–64, 68, 74, 75, 77–79, 82, 84, 87, 89, 91, 93, 94, 96] the most frequently used level was reported as >/ = 10% (24/80; 30.0%) [11, 16, 17, 26, 29–32, 39, 41, 45, 51, 61, 63, 64, 74, 75, 77, 79, 82, 84, 87, 89, 94]. Papers differentiating between smoker and non-smokers (24,30.0%) [11, 16, 24, 26–30, 34, 40, 41, 46, 47, 51, 59, 61, 68, 74, 77, 82, 84, 87, 89, 94], the lowest level of COHb in non-smokers was >1% [77] the highest reported was a COHb >9% [59]. In smokers the lowest value given was COHb >5% [24, 34, 46, 68] and the highest COHb >15% [28]. In papers where smokers and non-smokers were not differentiated 22.5% (18/80) [17, 31, 32, 35, 39, 45, 57, 58, 60, 62–64, 75, 78, 79, 91, 93, 96] the lowest diagnostic level reported was 2% [62] and the highest 12% [60] (Figs 2 and 3). None of the studies reported the time between exposure and COHb measurement.

Fourteen papers reported in ppm using either ambient monitoring, [37, 42, 44, 48, 50, 56, 65, 90, 100] breath analysis [38, 58, 61] or both [54, 97]. Levels were wither reported as a discrete value at a single time point or as a level present for x number of hours.

Diagnostic threshold levels using blood COHb measurement. Blood COHb was reported in 48 papers [11, 16, 24–30, 32, 33, 35, 39–41, 43, 45, 47, 49, 51, 57, 58, 60–64, 68, 70–72, 74, 76–83, 85, 87, 88, 91–94, 96] of which 33 reported threshold levels [11, 16, 24, 26–29, 32, 35, 39–41, 45, 47, 51, 57, 58, 60–64, 68, 74, 77–79, 82, 87, 91, 93, 94, 96], 15 of which, did not differentiate between levels in smokers and non-smokers [32, 35, 39, 45, 57, 58, 60, 62–64, 78, 79, 91, 93, 96], with threshold levels between 2% [62] and 12% [60] in these papers.

Where papers reported values of both smokers and non-smokers (n = 18) [11, 16, 24, 26, 27, 29, 40, 41, 47, 51, 61, 68, 70, 74, 77, 82, 87, 94] these ranged from >5% [24, 58, 68] to >15% [28] in smokers and >1% [77] to >5% [24, 51, 74, 82, 94] in non-smokers.

SpCO diagnostic threshold levels. SpCO was used by 25 (31.3%) papers [17, 30, 31, 34, 35, 44, 46, 51, 52, 55, 59, 60, 63, 64, 66, 69, 73, 75, 79, 84, 86, 89, 92–94] of which 17 reported SpCO diagnostic threshold levels [17, 30, 31, 34, 35, 46, 51, 59, 60, 63, 64, 75, 79, 84, 89, 93, 94]. Nine papers did not differentiate between smokers and non-smokers [17, 31, 35, 60, 63, 64, 75, 79, 93] and used values of >4% [35] to >12% [60]. In the 8 studies differentiating smoking status [30, 34, 46, 51, 59, 84, 89, 94], non-smoker levels ranged from >2% [46] to >9% [59] and smoker values ranged from >5% [34, 46] to >13% [59]. The single guideline recommending SpCO measurement gave a diagnostic threshold of >4% for non-smokers and > 10% for smokers [30].

In the review agreement between SpCO and blood COHb was compared in 6 studies using Bland–Altman analysis, five of which reported small mean differences and clinically acceptable limits of agreement [51, 59, 60, 92–94], with a single paper reporting clinically unacceptable limits of agreement [60]. There was, however, a tendency for CO-oximetry to overestimate the SpCO relative to the COHb reported in all 6 studies [59, 93, 94]. A single paper suggested that the overestimate was due to the SpCO measurement being taken an average of 67 minutes before the blood COHb given the short half-life of COHb [59].

Breath analysis. Studies using end-tidal CO measurement breath analysers reported diagnostic threshold levels in 7 [38, 40, 52, 54, 58, 61, 97] of 10 papers [38, 40, 52–54, 58, 61, 85, 86, 97]. Smoking status was not differentiated in two studies that used diagnostic threshold levels
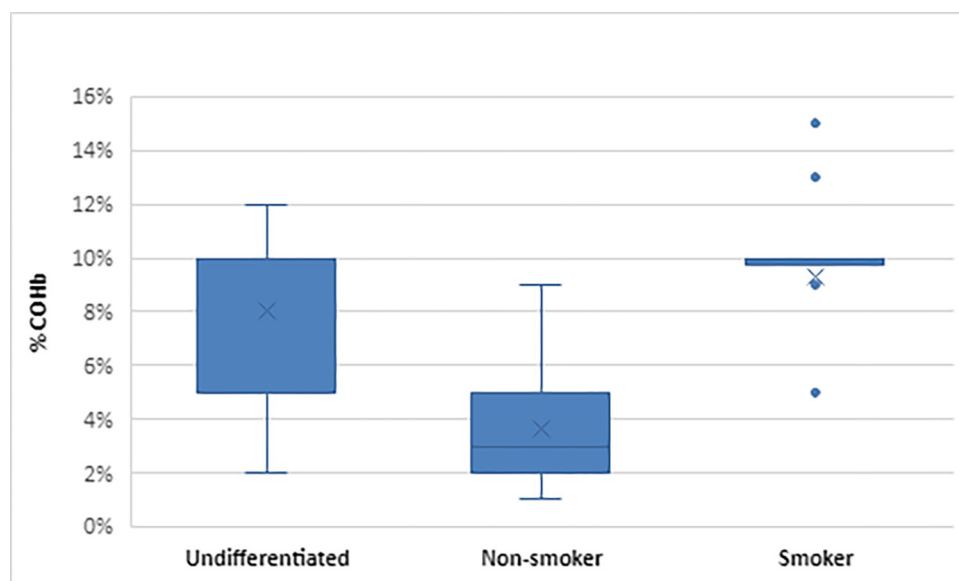
Fig 2. Box plot of COHb diagnostic levels reported in all papers (studies and guidelines).

https://doi.org/10.1371/journal.pone.0300989.g002

of 6ppm and 9ppm [38, 58] respectively. One study converted ppm to COHb% and reported diagnostic threshold levels as 2% and 5% for non-smokers and smokers [40]. The remaining 3 studies that differentiated reported in ppm with values for non-smokers of 5.4, 6.91 and 15ppm and for smokers 16.2, 17 and 48ppm [54, 61, 97]. Breath analysis correlated well with blood COHb when measured contemporaneously, reporting r values > 0.7 in both children [58] adults [61] presenting to the ED. A single study measuring both SpCO and breath CO reported a high correlation; r = 0.79 [52]. In contrast, correlation between breath analysis and ambient monitoring was reported as poor (r = 0.17) [53].
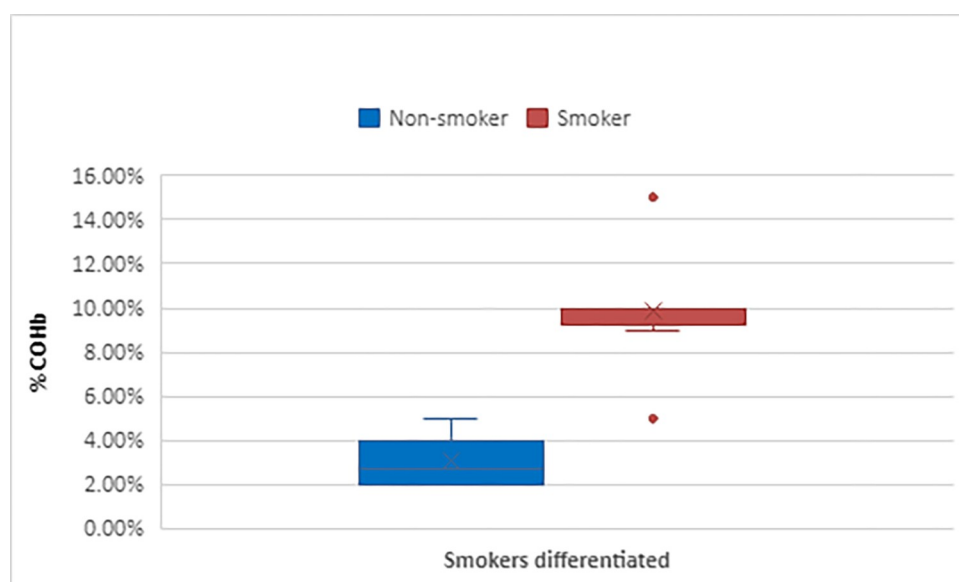

Fig 3. Box plot of COHb diagnostic levels reported in guidelines.

https://doi.org/10.1371/journal.pone.0300989.g003

Ambient CO measurement.   22 studies measured ambient CO levels [28, 33, 36, 37, 42, 44, 48, 50, 53, 54, 56, 65, 67, 70, 73, 82, 90, 95–98, 100] of which 12 gave diagnostic cut off levels. The WHO guidance [11] was used in 7 studies [44, 54, 56, 90, 96, 97, 100] whilst 5 papers gave ranges from > 1.0ppm to > 9.4 ppm [37, 42, 48, 50, 65].

Discussion

This scoping review presents a summary of the available research and clinical practice guidance of the current methods and diagnostic levels used to determine unintentional, non-fire-related CO exposure. We chose to carry out a scoping review to ensure a broad range of both research and clinical guidance was captured. We found four methods used to detect abnormal levels of CO (blood COHb, CO oximetry, breath analysis and ambient monitoring) but with variation in the stipulated levels used to determine exposure. We identified two principal areas for discussion, first the levels used to diagnose CO exposure and second, the method of CO measurement employed. The levels used in determining exposure varied widely across papers. This was true for papers using both COHb and CO concentration in ppm. The greatest variation was shown across research studies. Those reporting COHb ranged from 2–12% for undifferentiated studies, 1–9% for non-smokers, and 5–13% for smokers. Studies reporting ppm ranged from 1-25ppm for undifferentiated, 5.4-15ppm for non-smokers, 16.2-48ppm for smokers while clinical guidance ranging from 2.5–5% for non-smokers and 5–15% for smokers. This disparity in diagnostic threshold levels leads to variation in the diagnosis rates for CO exposure, either under-diagnosis or over-diagnosis depending on where the level is set. Whilst lower cut-off points may lead to over-diagnosis, this presents no impact on patient safety but may lead to an overutilisation of healthcare resources in the treatment of CO exposure. Using a higher threshold for determining if exposure has occurred could lead to under-diagnosis and the risk that the patient may be falsely reassured and discharged back to an environment where they are continually exposed to low levels of CO. Ongoing CO exposure can lead to long term health effects including delayed neurological sequalae and neuropsychological issues [104]. Guidelines were focused on diagnosis and treatment of patients with known CO exposure, with the implicit assumption that the clinician had already determined CO as a cause for the patient's symptoms. The difficulty in diagnosing occult, low-level exposure is well documented as clinicians frequently mistake the vague symptoms for another cause [104–107]. We found no evidence of how levels of CO in ongoing exposure might differ from levels in acute exposure or be detected through the commonly used methods of screening in healthcare setting (blood or breath analysis and CO oximetry). Variance in levels used to determine exposure to CO in research papers has the potential to lead to heterogeneity in reporting of prevalence and lack of comparable data across studies. The predominant method reported for CO measurement was blood COHb. COHb is known to have deficiencies in its' utility due to its short half-life of 137 to 240 minutes [108, 109] which is further reduced to 74 minutes when treated with high-flow oxygen at atmospheric pressure [110]. Patients may have levels of COHb that do not exceed the diagnostic threshold when measured if sufficient time has passed since exposure and this becomes more likely if oxygen is administered [110]. It is known that COHb levels correlate poorly with the patients' clinical picture and degree of severity of exposure [111]. Despite these deficiencies blood COHb is still widely used in the hospital setting and was the recommended analytical method in eight of the nine clinical guideline documents. No studies reported the time between exposure and COHb measurement. This may lead to under-diagnosis of CO exposure in clinical practice as COHb may not be raised when measured at the time of clinical consultation. CO-oximetry was the second most common method used to measure CO levels. All studies used the Masimo Rad-57Ⓡ Pulse CO-OximeterⓇ, a

handheld battery-operated portable device that does not require regular calibration [112]. The majority of studies comparing CO-oximetry with blood COHb, Bland-Altman analysis reported small mean differences and moderate limits of agreement but with a tendency to overestimate the SpCO relative to the COHb reported. A recently published systematic review concluded that SpCO was "probably" not accurate enough to either confirm or exclude a diagnosis of CO exposure with certainty [113 (P233)]. However, the findings were limited by conducting a Bland Altman analysis of the complete data set. Despite these limitations, SpCO can be deployed in settings where blood COHb is not available such as in primary and prehospital care. CO breath analysis correlated well with blood COHb and SpCO but poorly with ambient monitoring. The utility of CO breath analysis in clinical practice is reduced by both device and individual patient factors. Devices require a breath hold of 15–20 seconds before measurement to ensure equilibrium between alveolar CO and COHb [114]. This can be challenging for patients with dyspnoea [115]. One of the clinical guidelines recommend its use. Ambient CO levels were recorded using either personal 'wearable' or static environmental monitoring devices. In research it has been used to confirm the source of CO. Harmful CO exposure depends both on CO level and duration of exposure. Safe exposure limits are defined in the WHO and the National Research Council guidance [11, 25]. Ambient CO detection in isolation is not enough to detect harmful exposure, and forms one part of the triad for diagnosis [16]. For patients presenting with symptoms that could be related to CO exposure but in whom COHb is normal ambient monitoring may provide an indication of the cause of symptoms as it overcomes the limitation of delayed COHb measurement by measuring CO levels at source. Currently this analytical method is not readily available to clinicians in practice and is only used in research.

Strengths and limitations

Our review followed the methodology described by Arksey and O'Malley and included both online databases and the grey literature. The reference lists of all included papers were hand searched to ensure as wide a coverage of the topic area as possible. The review does have some limitations. We did not undertake a quality appraisal of the literature in the review which could have introduced bias into our findings. The search was current up to August 2023 and therefore we may have missed subsequent relevant papers published of in press. Finally, we chose to exclude papers written in languages other than English which also may have missed relevant papers.

Conclusion

This review included 80 papers discussing the diagnostic methods for detecting unintentional low-level (UNFR) CO exposure. Findings suggest there is limited international agreement on the CO levels used to determine exposure in research papers. Variation was more heterogeneous in clinical guidelines. Clinical diagnosis of UNFR CO exposure is important to reduce the effects of both acute and chronic exposure. Diagnostic measures for determining CO exposure should be used as part of the triad of 1. symptoms consistent with CO exposure; 2. a recent history of CO exposure; and 3. elevated levels of COHb. Defining what constitutes CO exposure is difficult due to the variability of levels presented in papers which may lead to over- or under-diagnosis depending on the level used. Variation leads to difficulty in determining the true prevalence of UNFR globally. We recommend that researchers consider standardising the values used to determine abnormally high CO to allow for comparability of results and enable an accurate picture of CO exposure worldwide.

Supporting information

S1 Checklist. PRISMA SCR checklist.
(DOCX)

S1 Table. Search strategy.
(DOCX)

S2 Table. Data extraction variables.
(DOCX)

S3 Table. a. Characteristics of papers. b. Analysis methods and diagnostic levels.
(ZIP)

S1 File.
(XLSX)

S2 File.
(XLSX)

Acknowledgments

Author Contributions

Conceptualization: Heather Jarman.

Formal analysis: Phil Moss.

Investigation: Phil Moss.

Methodology: Heather Jarman.

Supervision: Heather Jarman.

Writing – original draft: Phil Moss.

Writing – review & editing: Natasha Matthews, Rosalie McDonald, Heather Jarman.

References

1. Mattiuzzi C, Lippi G. Worldwide epidemiology of carbon monoxide poisoning. Human & experimental toxicology 2020 Apr; 39(4):387–392. https://doi.org/10.1177/0960327119891214 PMID: 31789062

2. Hampson NB. Carbon Monoxide poisoning mortality in the United States from 2015–2921. Clinical toxicology (Philadelphia, Pa.) 2023 Jul; 61(7):483–491.

3. Chenoweth JA, Albertson TE, Greer MR. Carbon Monoxide Poisoning. Critical care clinics 2021 Jul; 37(3):657–672. https://doi.org/10.1016/j.ccc.2021.03.010 PMID: 34053712

4. Ernst A, Zibrak JD, Eren ŞH, Korkmaz İ. Carbon Monoxide Poisoning. New England Journal of Medicine 1998 Nov 26; 339(22):1603–1608. https://doi.org/10.1056/NEJM199811263392206 PMID: 9828249

5. Bateman N. Carbon Monoxide. Medicine 2012; 35(11):604–605.

6. Wu L, Wang R. Carbon Monoxide: Endogenous Production, Physiological Functions, and Pharmacological Applications. Pharmacological reviews 2005 Dec 1; 57(4):585–630. https://doi.org/10.1124/pr.57.4.3 PMID: 16382109

7. Hart CL, Davey Smith G, Hole DJ, Hawthorne VM. Carboxyhaemoglobin concentration, smoking habit, and mortality in 25 years in the Renfrew/Paisley prospective cohort study. Heart (British Cardiac Society) 2006 Mar 1; 92(3):321–324. https://doi.org/10.1136/hrt.2005.065185 PMID: 15939724

8. QuickStats. MMWR. Morbidity and Mortality Weekly Report 2017 Mar 3;66(8):234.

9. Ashcroft J, Fraser E, Krishnamoorthy S, Westwood-Ruttledge S. Carbon monoxide poisoning. BMJ (Online) 2019 Jun 13; 365: l2299. https://doi.org/10.1136/bmj.l2299 PMID: 31197022

10. Kinoshita H, Türkan H, Vaccenic S, Naqvi S, Bedair R, Rezaee R, et al. Carbon monoxide poisoning. Toxicology Reports 2020 Jan 1; 7:169–173. https://doi.org/10.1016/j.toxrep.2020.01.005 PMID: 32015960

11. World Health Organisation. WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulphur dioxide and carbon monoxide. 2021; Available at: https://www.who.int/publications/i/item/9789240034228. Accessed Oct 5, 2023.

12. Lutterloh EC, Iqbal S, Clower JH, Spiller HA, Riggs MA, Sugg TJ, et al. Carbon Monoxide Poisoning After an Ice Storm in Kentucky, 2009. Public health reports (1974) 2011 May 1; 126(1_suppl):108–115.

13. Styles T, Przysiecki P, Archambault G, Sosa L, Toal B, Magri J, et al. Two Storm-Related Carbon Monoxide Poisoning Outbreaks-Connecticut, October 2011, and October 2012. Archives of environmental & occupational health 2015 Sep 3; 70(5):291–296.

14. Iqbal S, Clower JH, Hernandez SA, Damon SA, Yip Fuyuen Y. A Review of Disaster-Related Carbon Monoxide Poisoning: Surveillance, Epidemiology, and Opportunities for Prevention. American journal of public health (1971) 2012 Oct 1; 102(10):1957–1963.

15. Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, et al. Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy. American journal of respiratory and critical care medicine 2017 Mar 1; 195(5):596–606. https://doi.org/10.1164/rccm.201606-1275CI PMID: 27753502

16. Hampson NB, Piantadosi CA, Thom SR, Weaver LK. Practice Recommendations in the Diagnosis, Management, and Prevention of Carbon Monoxide Poisoning. American journal of respiratory and critical care medicine 2012 Dec 1; 186(11):1095–1101. https://doi.org/10.1164/rccm.201207-1284CI PMID: 23087025

17. Deniz T, Kandis H, Eroglu O, Gunes H, Saygun M, Kara IH. Carbon monoxide poisoning cases presenting with non-specific symptoms. Toxicology and industrial health 2017 Jan 1; 33(1):53–60. https://doi.org/10.1177/0748233716660641 PMID: 27495248

18. Townsend CL, Maynard RL. Effects on health of prolonged exposure to low concentrations of carbon monoxide. Occupational and environmental medicine (London, England) 2002 Oct 1; 59(10):708–711. https://doi.org/10.1136/oem.59.10.708 PMID: 12356933

19. Myers RAM, DeFazio A, Kelly MP. Chronic carbon monoxide exposure: A clinical syndrome detected by neuropsychological tests. Journal of clinical psychology 1998 Aug; 54(5):555–567. https://doi.org/10.1002/(sici)1097-4679(199808)54:5<555::aid-jclp1>3.0.co;2-k PMID: 9696105

20. Jeon S, Sohn CH, Seo D, Oh BJ, Lim KS, Kang D, et al. Acute Brain Lesions on Magnetic Resonance Imaging and Delayed Neurological Sequelae in Carbon Monoxide Poisoning. JAMA neurology 2018 Apr 1; 75(4):436–443. https://doi.org/10.1001/jamaneurol.2017.4618 PMID: 29379952

21. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International journal of social research methodology 2005 Feb 1; 8(1):19–32.

22. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Annals of internal medicine 2018 Oct 2; 169 (7):467–473. https://doi.org/10.7326/M18-0850 PMID: 30178033

23. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a Web and mobile App for Systematic Reviews. Systematic Reviews 2016 Dec 5; 5(1):210. https://doi.org/10.1186/s13643-016-0384-4 PMID: 27919275

24. Health Austin. Carbon Monoxide, Austin Clinical Toxicology Guideline V3. 2021; Available at: https://www.austin.org.au/Assets/Files/Carbon%20Monoxide%20Guideline%20Nov%202021%20FINAL.pdf. Accessed 6/6/, 2023.

25. Council NR, Studies DoEaL, Toxicology BoESa, Toxicology Co, Levels CoAEG. Acute Exposure Guideline Levels for Selected Airborne Chemicals. 1st ed. Washington, D.C: National Academies Press; 2010.

26. National Institute for Health and Care Excellence. Clinical Knowledge Summary: Carbon Monoxide Poisoning. 2023; Available at: https://cks.nice.org.uk/topics/carbon-monoxide-poisoning/. Accessed Oct 5, 2023.

27. Centers for Disease Control and Prevention. Clinical Guidance for Carbon Monoxide (CO) Poisoning. 2020; Available at: https://www.cdc.gov/disasters/co_guidance.html.

28. Alexander A. BMJ Best Practice: Carbon monoxide poisoning. BMJ; 2023. Available from https://bestpractice.bmj.com/topics/en-gb/3000169?q=Carbon%20monoxide%20poisoning&c=suggested Accessed June 2023.

29. Wolf SJ MD, Maloney GE DO, Shih RD MD, Shy BD MD, Brown, Michael D., MD, MSc. Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department with Acute Carbon Monoxide Poisoning. Annals of emergency medicine 2017 Jan 1; 69 (1):98–107.e6.

30. Jüttner B, Busch H, Callies A, Dormann H, Janisch T, Kaiser G, et al. S2k Guideline Diagnosis and Treatment of Carbon Monoxide Poisoning. German medical science 2021;19: Doc13. https://doi.org/10.3205/000300 PMID: 34867135

31. Acharya SP, Purpura A, Kao L, House DR. Incidence, and risk factors for carbon monoxide poisoning in an emergency department in Nepal. Toxicology communications 2022 Dec 31; 6(1):13–19.

32. Aksu N, Akkaş M, Çoşkun F, Karakiliç E, Günalp M, Akküçük H, et al. Could Vital Signs Predict Carbon Monoxide Intoxication? Journal of international medical research 2012 Jan 1; 40(1):366–370. https://doi.org/10.1177/147323001204000138 PMID: 22429377

33. Banjoko SO, Sridhar MK, Ogunkola IO, Masheyi OO. Methylene chloride exposure and carboxyhaemoglobin levels in cabinetmakers. Indian Journal of Industrial Medicine 2007 May 1; 11(2):56–60.

34. Clarke S, Keshishian C, Murray V, Kafatos G, Ruggles R, Coultrip E, et al. Screening for carbon monoxide exposure in selected patient groups attending rural and urban emergency departments in England: a prospective observational study. BMJ Open 2012 Jan 1; 2(6): e000877. https://doi.org/10.1136/bmjopen-2012-000877 PMID: 23242237

35. Cooper JS, Miller E, Nichols H, Zeger W. 306 Carbon Monoxide-Oximetry in the Emergency Department. Annals of emergency medicine 2020 Oct; 76(4): S118.

36. Croxford B, Hutchinson E, Leonardi G, McKenna L, Riddington M, Volans G, et al. Real time carbon monoxide measurements from 56 UK (United Kingdom) homes. 2005. Proceedings of Indoor Air 2005 pp2376–2380. Available at https://discovery.ucl.ac.uk/id/eprint/2511/

37. Croxford B, Hutchinson E, Leonardi G, McKenna L, Riddington M, Volans G, et al. Real time carbon monoxide measurements from 270 UK homes. Indoor Environmental Quality: Problems, Research and Solutions Conference 2006; North Carolina, USA: Air and Waste Management Association (A&WMA) and US EPA's Office of Research and Development; Jul 2006. Available at https://discovery.ucl.ac.uk/id/eprint/5017/

38. Cunnington AJ, Hormbrey P. Breath analysis to detect recent exposure to carbon monoxide. Postgraduate medical journal 2002 Apr 1; 78(918):233–237. https://doi.org/10.1136/pmj.78.918.233 PMID: 11930027

39. Dolan MC, Haltom TL, Barrows GH, Short CS, Ferriell KM. Carboxyhaemoglobin levels in patients with flu-like symptoms. Annals of emergency medicine 1987 Jul 1; 16(7):782–786.

40. Eberhardt M, Powell A, Bonfante G, Rupp V, Guarnaccia JR, Heller M, et al. Non-invasive measurement of carbon monoxide levels in ED patients with headache. Journal of medical toxicology 2006 Sep 1; 2(3):89–92. https://doi.org/10.1007/BF03161015 PMID: 18072124

41. El Sayed MJ, Tamim H. Carbon monoxide poisoning in Beirut, Lebanon: Patient's characteristics and exposure sources. Journal of Emergencies, Trauma, and Shock 2014 Oct; 7(4):280–284.

42. Fandiño-Del-Rio M, Kephart JL, Williams KN, Moulton LH, Steenland K, Checkley W, et al. Cardiopulmonary outcomes and Household Air Pollution trial (CHAP) Trial Investigators. Household air pollution exposure and associations with household characteristics among biomass cookstove users in Puno, Peru. Environmental research 2020 Dec 1; 191:110028.

43. Hampson NB MD, Dunn SL CHRN. Carbon Monoxide Poisoning from Portable Electrical Generators. The Journal of emergency medicine 2015 Aug 1; 49(2):125–129. https://doi.org/10.1016/j.jemermed.2014.12.091 PMID: 26032763

44. Havens D, Wang D, Grigg J, Gordon SB, Balmes J, Mortimer K. The Cooking and Pneumonia Study (CAPS) in Malawi: A Cross-Sectional Assessment of Carbon Monoxide Exposure and Carboxyhaemoglobin Levels in Children under 5 Years Old. International Journal of Environmental Research and Public Health 2018 Sep 1; 15(9):1936.

45. Heckerling PS. Occult carbon monoxide poisoning: A cause of winter headache. The American journal of emergency medicine 1987 May 1; 5(3):201–204. https://doi.org/10.1016/0735-6757(87)90320-2 PMID: 3580051

46. Hubbell AM, Jareczek FJ, Vonnahme L, Hockenberry JM, Buresh C. Smoke exposure among women in Haiti: The case for improved stoves. Global public health 2013 Jan 1; 8(7):822–830. https://doi.org/10.1080/17441692.2013.815793 PMID: 23906187

47. Jarman H, Atkinson RW, Baramova D, Gant TW, Marczylo T, Myers I, et al. Screening patients for unintentional carbon monoxide exposure in the Emergency Department: a cross-sectional multi-centre study. Journal of public health 2023 Jan 31; 45(3):553–559. https://doi.org/10.1093/pubmed/fdad007 PMID: 36721987

48. Jaslow D, Ukasik J, Sananman P. Routine Carbon Monoxide Screening by Emergency Medical Technicians. Academic emergency medicine 2001 Mar; 8(3):288–291. https://doi.org/10.1111/j.1553-2712.2001.tb01309.x PMID: 11229955

49. Keleş A, Demircan A, Kurtoğlu G. Carbon monoxide poisoning: how many patients do we miss? European journal of emergency medicine 2008 Jun; 15(3):154–157. https://doi.org/10.1097/MEJ.0b013e3282efd519 PMID: 18460956

50. Kirkham TL, Koehoorn MW, Davies H, Demers PA. Characterization of Noise and Carbon Monoxide Exposures among Professional Firefighters in British Columbia. The Annals of occupational hygiene 2011 Aug 1; 55(7):764–774. https://doi.org/10.1093/annhyg/mer038 PMID: 21765005

51. Koyuncu S, Bol O, Ertan T, Günay N, Akdogan Hİ. The detection of occult CO poisoning through non-invasive measurement of carboxyhaemoglobin: A cross-sectional study. The American journal of emergency medicine 2020 Jun 1; 38(6):1110–1114.

52. Lam N, Nicas M, Ruiz-Mercado I, Thompson LM, Romero C, Smith KR. Non-invasive measurement of carbon monoxide burden in Guatemalan children and adults following wood-fired temazcal (sauna-bath) use. Journal of environmental monitoring 2011 Aug 1; 13(8):2172–2181. https://doi.org/10.1039/c1em10172b PMID: 21687856

53. Lee A, Sanchez TR, Shahriar MH, Eunus M, Perzanowski M, Graziano J. A cross-sectional study of exhaled carbon monoxide as a biomarker of recent household air pollution exposure. Environmental research 2015 Nov 1; 143(Pt A):107–111. https://doi.org/10.1016/j.envres.2015.09.017 PMID: 26457622

54. Lévesque B, Bellemare D, Sanfaçon G, Duchesne J, Gauvin D, Prud'homme H, et al. Exposure to carbon monoxide during indoor karting. International journal of environmental health research 2005 Feb 1; 15(1):41–44. https://doi.org/10.1080/09603120400018899 PMID: 16025813

55. Nilson D, Partridge R, Suner S, Jay G. Non-Invasive Carboxyhaemoglobin Monitoring: Screening Emergency Medical Services Patients for Carbon Monoxide Exposure. Prehospital and disaster medicine 2010 Jun 1; 25(3):253–256.

56. Rylance S, Nightingale R, Naunje A, Mbalume F, Jewell C, Balmes JR, et al. Lung health and exposure to air pollution in Malawian children (CAPS): a cross-sectional study. Thorax 2019 Nov 1; 74(11):1070–1077. https://doi.org/10.1136/thoraxjnl-2018-212945 PMID: 31467192

57. Salameh S, Amitai Y, Antopolsky M, Rott D, Stalnicowicz R. Carbon monoxide poisoning in Jerusalem: epidemiology and risk factors. Clinical toxicology 2009 Feb; 47(2):137–141. https://doi.org/10.1080/15563650801986711 PMID: 18720104

58. Shenoi R, Stewart G, Rosenberg N. Screening for carbon monoxide in children. Pediatric emergency care 1998 Dec; 14(6):399–402. https://doi.org/10.1097/00006565-199812000-00005 PMID: 9881983

59. Suner Selim, MD MS, Partridge Robert, MD MPH, Sucov A MD, Valente J MD, Chee K MD, Hughes A BS, et al. Non-Invasive Pulse CO-oximetry Screening in the Emergency Department Identifies Occult Carbon Monoxide Toxicity. The Journal of emergency medicine 2008 May 1; 34(4):441–450. https://doi.org/10.1016/j.jemermed.2007.12.004 PMID: 18226877

60. Touger M MD, Birnbaum, Adrienne, MD, MS, Wang J, MD, Chou, Katherine, MD, MS, Pearson D, BA, Bijur P, PhD. Performance of the RAD-57 Pulse Co-Oximeter Compared with Standard Laboratory Carboxyhaemoglobin Measurement. Annals of emergency medicine 2010 Oct 1; 56(4):382–388.

61. Turnbull TL, Hart RG, Strange GR, Cooper MA, Lindblad R, Watkins JM, et al. Emergency department screening for unsuspected carbon monoxide exposure. Annals of emergency medicine 1988 May 1; 17(5):478–483. https://doi.org/10.1016/s0196-0644(88)80240-3 PMID: 3364828

62. Unsal Sac R, Taşar MA, Bostancı İ, Şimşek Y, Bilge Dallar Y. Characteristics of Children with Acute Carbon Monoxide Poisoning in Ankara: A Single Centre Experience. Journal of Korean Medical Science 2015 Dec 1; 30(12):1836–1840. https://doi.org/10.3346/jkms.2015.30.12.1836 PMID: 26713060

63. Villalba N, Osborn ZT, Derickson PR, Manning CT, Herrington RR, Kaminsky DA, et al. Diagnostic Performance of Carbon Monoxide Testing by Pulse Oximetry in the Emergency Department. Respiratory care 2019 Nov; 64(11):1351–1357. https://doi.org/10.4187/respcare.06365 PMID: 31040204

64. Zorbalar N, Yesilaras M, Aksay E. Carbon monoxide poisoning in patients presenting to the emergency department with a headache in winter months. Emergency medicine journal 2014 Oct 1; 31(e1):e66–e70. https://doi.org/10.1136/emermed-2012-201712 PMID: 24128732

65. Rabbani U, Razzaq S, Irfan M, Semple S, Nafees AA. Indoor Air Pollution and Respiratory Health in a Metropolitan City of Pakistan. Journal of occupational and environmental medicine 2022 Sep 1; 64 (9):761–765. https://doi.org/10.1097/JOM.0000000000002573 PMID: 35672913

66. Zoller T, Mfinanga EH, Zumba TB, Asilia PJ, Mutabazi EM, Wimmersberger D, et al. Symptoms and functional limitations related to respiratory health and carbon monoxide poisoning in Tanzania: a cross sectional study. Environmental health 2022 Apr 2; 21(1):38. https://doi.org/10.1186/s12940-022-00847-x PMID: 35365149

67. Silver E. The true COst of red meat. North American Congress of Clinical Toxicology; 2023; Montreal, Canada; 2023.

68. Abelsohn A, Sanborn MD, Jessiman BJ, Weir E. Identifying and managing adverse environmental health effects: 6. Carbon monoxide poisoning. Canadian Medical Association journal 2002 Jun 25; 166(13):1685–1690. PMID: 12126326

69. Ahmed N MD, Goldring R MD, Berger K MD. Diagnosis of Carbon Monoxide Poisoning: Which Oxygen Saturation Is Correct. Chest 2015 Oct; 148(4):760A–760B.

70. Audin C. Carbon Monoxide Poisoning Following a Natural Disaster: A Report on Hurricane Rita. Journal of emergency nursing 2006 Oct 1; 32(5):409–411. https://doi.org/10.1016/j.jen.2006.07.005 PMID: 16997030

71. Ayalloore S. Carbon monoxide poisoning presenting as myocardial infarction. Journal of investigative medicine 2012 Jan; 60(1):312–466.

72. Balzan MV, Cacciottolo JM, Mifsud S. Unstable angina and exposure to carbon monoxide. Postgraduate medical journal 1994 Oct 1; 70(828):699–702. https://doi.org/10.1136/pgmj.70.828.699 PMID: 7831163

73. Bledsoe BE, Nowicki K, Creel JH, Carrison D, Severance HW. Use of Pulse Co-Oximetry as a Screening and Monitoring Tool in Mass Carbon Monoxide Poisoning. Prehospital emergency care 2010 Jan 1; 14(1):131–133. https://doi.org/10.3109/10903120903349853 PMID: 19947878

74. Chan L. A 37-year-old woman found unconscious at home. Hong Kong journal of emergency medicine 2017 Jan 1; 24(1):57–59.

75. Chee KJ, Nilson D, Partridge R, Hughes A, Suner S, Sucov A, et al. Finding needles in a haystack: A case series of carbon monoxide poisoning detected using new technology in the emergency department. Clinical toxicology 2008 Jun; 46(5):461–469. https://doi.org/10.1080/15563650701725110 PMID: 18568803

76. Hol S, de Vooght KMK, van der Spoel JJI, van Solinge WW, Kemperman H. A 56-Year-Old Man with an Apparently Normal Oxygen Saturation and a Dead Canary. American journal of respiratory and critical care medicine 2012 Nov 1; 186(9):928–929. https://doi.org/10.1164/ajrccm.186.9.928 PMID: 23118086

77. McGuffie C, Wyatt JP, Kerr GW, Hislop WS. Mass carbon monoxide poisoning. Emergency medicine journal 2000 Jan; 17(1):38–39. https://doi.org/10.1136/emj.17.1.38 PMID: 10658990

78. Medhane F, Faras H, Kakkar A. Where there is a smoke there is thrombosis. Journal of general internal medicine 2018 33; Suppl 2: S665

79. Roth D, Hubmann N, Havel C, MD, Herkner, Harald, MD, MSC, Schreiber W, MD, Laggner A, MD. Victim of Carbon Monoxide Poisoning Identified by Carbon Monoxide Oximetry. The Journal of emergency medicine 2011 Jun 1; 40(6):640–642.

80. Roth D MD, Krammel M MD, Schreiber W MD, Herkner, Harald MD, MSc, Havel C, MD, Laggner AN, MD. Unrecognized Carbon Monoxide Poisoning Leads to a Multiple-Casualty Incident. The Journal of emergency medicine 2013 Oct 1; 45(4):559–561. https://doi.org/10.1016/j.jemermed.2013.05.003 PMID: 23810117

81. Tetsuka S, Suzuki T, Ogawa T, Hashimoto R, Kato H. Repeated unconsciousness due to chronic carbon monoxide poisoning in an older patient: a case report. Journal of Rural Medicine 2021; 16(4):289–292. https://doi.org/10.2185/jrm.2021-033 PMID: 34707741

82. Wilson E, Tomasallo C, Meiman J. Notes from the Field: Occupational Carbon Monoxide Exposure in an Industrial Kitchen Facility—Wisconsin, 2017. MMWR. Morbidity and mortality weekly report 2018 Jul 20; 67(28):786.

83. Turhan T. A Very Rare Complication of Carbon Monoxide Intoxication; Thrombotic Thrombocytopenic Purpura. Biyokimya dergisi 2014 39; 4:571–573.

84. Bol O, Koyuncu S, Günay N. Prevalence of hidden carbon monoxide poisoning in auto service workers; a prospective cohort study. Journal of Occupational Medicine and Toxicology 2018 Nov 6; 13 (1):35. https://doi.org/10.1186/s12995-018-0214-9 PMID: 30450122

85. Creswell PD, Meiman JG, Nehls-Lowe H, Vogt C, Wozniak RJ, Werner MA, et al. Exposure to Elevated Carbon Monoxide Levels at an Indoor Ice Arena—Wisconsin, 2014. MMWR. Morbidity and

mortality weekly report 2015 Nov 20; 64(45):1267–1270. https://doi.org/10.15585/mmwr.mm6445a3 PMID: 26583915

86. Hullin T, Aboab J, Desseaux K, Chevret S, Annane D. Correlation between clinical severity and different non-invasive measurements of carbon monoxide concentration: A population study. PLoS ONE 2017 Mar 28; 12(3): e0174672. https://doi.org/10.1371/journal.pone.0174672 PMID: 28350859

87. Liu S, Liu Y, Yang C, Xie D, Zhang X. Charcoal burning is associated with a higher risk of delayed neurological sequelae after domestic carbon monoxide poisoning in South China: A retrospective cohort study. The American journal of emergency medicine 2022 Oct 1; 60:57–61. https://doi.org/10.1016/j.ajem.2022.06.003 PMID: 35907270

88. Mortelmans L, Populaire J, Desruelles D, Sabbe M. Mass carbon monoxide poisoning at an ice-hockey game: initial approach and long-term follow-up. European Journal of Emergency Medicine 2013 Dec 20; 6:408–412.

89. Suliman AK, Saleh MM, Sznajder K, King TS, Warren WS. Prospective Cohort Study on the Effect of an Intervention to Reduce Household Air Pollution Among Sudanese Women and Children. Journal of health & pollution 2021 Sep; 11(31):210905. https://doi.org/10.5696/2156-9614-11.31.210905 PMID: 34434597

90. North CM, MacNaughton P, Lai PS, Vallarino J, Okello S, Kakuhikire B, et al. Personal carbon monoxide exposure, respiratory symptoms, and the potentially modifying roles of sex and HIV infection in rural Uganda: a cohort study. Environmental Health 2019 Aug 20; 18(1):73. https://doi.org/10.1186/s12940-019-0517-z PMID: 31429759

91. Güven D, Sarıcı D. Clinical and Laboratory Characteristics Predicting the Severity of Carbon Monoxide Poisoning in Children: A Single-Center Retrospective Study. Pediatric emergency care 2023 Apr 1; 39 (4):207–215. https://doi.org/10.1097/PEC.0000000000002927 PMID: 36898143

92. Barker SJ, Curry J, Redford D, Morgan S. Measurement of carboxyhaemoglobin and methemoglobin by pulse oximetry: A human volunteer study. Anaesthesiology (Philadelphia) 2006 Nov 1; 105(5):892–897.

93. Roth D, Herkner CM, Harald MD, MSc, Schreiber W, MD, Hubmann N, MD, Gamper G, MD, Laggner AN, MD, et al. Accuracy of Noninvasive Multiwave Pulse Oximetry Compared with Carboxyhaemoglobin from Blood Gas Analysis in Unselected Emergency Department Patients. Annals of emergency medicine 2011 Jul 1; 58(1):74–79.

94. Sebbane M, Claret P, Mercier G, Lefebvre S, Théry R, Dumont R, et al. Emergency Department Management of Suspected Carbon Monoxide Poisoning: Role of Pulse CO-Oximetry. Respiratory care 2013 Oct; 58(10):1614–1620. https://doi.org/10.4187/respcare.02313 PMID: 23513247

95. Yip F, Christensen B, Sircar K, Naeher L, Bruce N, Pennise D, et al. Assessment of traditional and improved stove use on household air pollution and personal exposures in rural western Kenya. Environment International 2017 Feb 1; 99:185–191. https://doi.org/10.1016/j.envint.2016.11.015 PMID: 27923586

96. Thomassen Ø, Brattebø G, Rostrup M. Carbon monoxide poisoning while using a small cooking stove in a tent. The American journal of emergency medicine 2004 May; 22(3):204–206. https://doi.org/10.1016/j.ajem.2004.02.011 PMID: 15138958

97. Pope D, Diaz E, Smith-Sivertsen T, Lie RT, Bakke P, Balmes JR, et al. Exposure to Household Air Pollution from Wood Combustion and Association with Respiratory Symptoms and Lung Function in Non-smoking Women: Results from the RESPIRE Trial, Guatemala. Environmental Health Perspectives 2015 Apr 1; 123(4):285–292. https://doi.org/10.1289/ehp.1408200 PMID: 25398189

98. Balakrishnan K, Sambandam S, Ghosh S, Mukhopadhyay K, Vaswani M, Arora NK, et al. Household Air Pollution Exposures of Pregnant Women Receiving Advanced Combustion Cookstoves in India: Implications for Intervention. 2015 Jan 1, https://doi.org/10.1016/j.aogh.2015.08.009 PMID: 26615072

99. Alexander D, Linnes JC, Bolton S, Larson T. Ventilated cookstoves associated with improvements in respiratory health-related quality of life in rural Bolivia. Journal of public health (Oxford, England) 2014 Sep 1; 36(3):460–466. https://doi.org/10.1093/pubmed/fdt086 PMID: 23965639

100. Johnson M, Pillarisetti A, Piedrahita R, Balakrishnan K, Peel JL, Steenland K, et al. Exposure Contrasts of Pregnant Women during the Household Air Pollution Intervention Network Randomized Controlled Trial. Environmental health perspectives 2022 Sep 1; 130(9):97005. https://doi.org/10.1289/EHP10295 PMID: 36112539

101. Brunelle JA, Degtiarov AM, Moran RF, Race LA. Simultaneous measurement of total haemoglobin and its derivatives in blood using CO-oximeters: Analytical principles; Their application in selecting analytical wavelengths and reference methods; A comparison of the results of the choices made. Scandinavian journal of clinical & laboratory investigation. Supplement 1996; 56(S224):47–69.

102. Wald NJ, Idle M, Boreham J, Bailey A. Carbon monoxide in breath in relation to smoking and carboxyhaemoglobin levels. Thorax 1981 May 1; 36(5):366–369. https://doi.org/10.1136/thx.36.5.366 PMID: 7314006

103. Fine GF, Cavanagh LM, Afonja A, Binions R. Metal Oxide Semi-Conductor Gas Sensors in Environmental Monitoring. Sensors 2010 Jun 1; 10(6):5469–5502. https://doi.org/10.3390/s100605469 PMID: 22219672

104. UK Health Security Agency. Carbon Monoxide: Toxicological Review. 2022; Available at: https://www.gov.uk/government/publications/carbon-monoxide-properties-incident-management-and-toxicology/carbon-monoxide-toxicological-overview#references. Accessed 01/10/, 2023.

105. Harper A, Croft-Baker J. Carbon monoxide poisoning: undetected by both patients and their doctors. 2004 Mar 1; 33(2):105–109. https://doi.org/10.1093/ageing/afh038 PMID: 14960423

106. Eichhorn L, Thudium M, Jüttner B. The Diagnosis and Treatment of Carbon Monoxide Poisoning. 2018 Dec 24; 115(51–52):863–870. https://doi.org/10.3238/arztebl.2018.0863 PMID: 30765023

107. UK Department of Health. Carbon monoxide poisoning: recognise the symptoms and tackle the cause. 2013; Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/260211/Carbon_Monoxide_Letter_2013_FinalforPub.pdf. Accessed 01/10/, 2023.

108. Shimazu T, Ikeuchi H, Sugimoto H, Goodwin C, Mason A, Pruitt B. Half-Life of Blood Carboxyhaemoglobin after Short-Term and Long-Term Exposure to Carbon Monoxide. The Journal of trauma 2000 Jul; 49(1):126–131.

109. Burney RE, Wu S, Nemiroff MJ. Mass carbon monoxide poisoning: Clinical effects and results of treatment in 184 victims. Annals of emergency medicine 1982 Aug; 11(8):394–399. https://doi.org/10.1016/s0196-0644(82)80033-4 PMID: 7103154

110. Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxyhaemoglobin Half-life in Carbon Monoxide-Poisoned Patients Treated With 100% Oxygen at Atmospheric Pressure. Chest 2000 Mar 1; 117(3):801–808.

111. Hampson NB MD, Hauff NM BE. Carboxyhaemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture? The American journal of emergency medicine 2008 Jul 1; 26(6):665–669.

112. Masimo. Rad-57® Pulse CO-Oximeter®. Available at: https://www.masimo.com/products/continuous/rad57/. Accessed 05/10/, 2023.

113. Papin M, Latour C, Leclère B, Javaudin F. Accuracy of pulse CO-oximetry to evaluate blood carboxyhaemoglobin level: a systematic review and meta-analysis of diagnostic test accuracy studies. European journal of emergency medicine 2023 Aug 1; 30(4):233–243.

114. MicroCO Meter Operating Manual. 2021; Available at: https://mdspiro.com/image/data/manuals/MicroCO%20-%20MC02.pdf. Accessed Nov 2015.

115. Fife C, Otto G, Koch S, Nguyen M, Wilhelm G. A Noninvasive Method for Rapid Diagnosis of Carbon Monoxide Poisoning. The internet journal of emergency and intensive care medicine 2001; 5(2).