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Paper

Welding Activities: Is EBC a Reliable Indicator for Assessing Metal Exposure or Early Biological Effects? A Systematic Review

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Abstract

Welding processes generate complex aerosols containing fine and ultrafine particulate matter, metal fumes, and gaseous by-products that may pose significant respiratory risks for exposed workers. Exhaled breath condensate (EBC) has emerged as a promising non-invasive matrix for human biomonitoring, offering the opportunity to assess exposure directly at the pulmonary target site and to evaluate early biological responses. This study systematically reviewed the scientific literature available in PubMed, Scopus, and ISI Web of Science to examine the role of EBC in exposure and effect biomonitoring among welders. Sixteen studies met the inclusion criteria. Overall, the evidence indicates that EBC is a suitable matrix for assessing occupational exposure in welding activities. Several studies reported increased concentrations of metals-including manganese, nickel, iron, and chromium in welders compared with unexposed controls, as well as higher post-shift levels compared with pre-shift samples across the workweek. Associations between cumulative exposure to inhalable dust and metal concentrations in EBC were also observed, even at low exposure levels. EBC has additionally shown potential for detecting early-effect biomarkers, such as indicators of oxidative stress, lipid peroxidation, protein and nucleic acid oxidation, and inflammatory mediators. These findings provide insight into biochemical alterations occurring in the airway lining fluid of welders. Despite encouraging findings, key methodological issues persist. The lack of standardized protocols for EBC collection, storage, and analysis hampers comparability across studies. Indeed, further research should elucidate EBC production and dilution kinetics and clarify metal toxicokinetics to fully establish EBC as a reliable biomonitoring matrix for occupational health research and practice.

1. Introduction

Welding encompasses a broad range of industrial techniques designed to join metallic components through the application of heat or mechanical pressure, with or without the addition of filler material (Chipperfield and Dunkerton 2001). Several methods are commonly employed, including Manual Metal Arc (MMA) and Submerged Arc Welding (SAW), both of which rely on striking an arc between a coated electrode and the workpiece. Other widely used processes are Tungsten Inert Gas (TIG) welding, which utilizes a non-consumable tungsten electrode to generate the weld, and techniques such as Metal Inert Gas (MIG) and Gas Metal Arc (GMA) welding, where a shielding gas is applied in combination with a consumable wire electrode to facilitate metal fusion (Shome and Tumuluru 2015; Liu *et al* 2019; Jamrozik and Gorka 2020). Despite their technical distinctions, all welding operations produce complex aerosols containing potentially harmful fumes and gases (Moroni and Viti 2009; Mehrifar *et al* 2020). The chemical composition of these emissions is influenced not only by the specific welding method but also by factors such as electrode type, filler materials, fluxes, shielding gases, the nature of the base metals, and any surface coatings present (Antonini *et al* 2003). Welding fumes are produced when metals are heated above their melting point, vaporize and condense into fumes. The fumes consist of predominantly fine solid particles with an aerodynamic diameter of less than 1 μm that primarily consist of metal oxides, silicates, and fluorides (IARC, 2018). A substantial fraction of the particulate matter generated during welding (reported to reach up to 63%) falls within the ultrafine size range (Iavicoli *et al* 2013).

Exposure to welding-related gases and aerosols has been linked to several respiratory conditions, including bronchiolitis, bronchitis, airway irritation, pneumonitis (Antonini *et al* 2003), and occupational asthma (Storaas *et al* 2015). Chronic or high-level exposure to welding fumes may also contribute to fibrogenic interstitial lung involvement. Persistent deposition of metal-rich particles in the lower respiratory tract has been associated with interstitial inflammation and fibrotic remodelling, which may lead in some cases to diffuse interstitial pneumonitis or pneumoconiosis with clinically relevant respiratory functional impairment (Cosgrove *et al* 2015; Zhou *et al* 2022; Baur and Abraham 2023).

Mechanistic studies further indicate that inflammation and oxidative stress play central roles in the development of welding-associated pulmonary disorders (Han *et al* 2005). Importantly, welding fumes themselves have been classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1) (IARC, 2018). Traditionally, the biological monitoring of metals originating from welding fumes has relied on measurements in blood or urine (Mutti *et al* 1984). However, blood sampling is invasive, and urine collection presents challenges in terms of sample integrity. Moreover, both matrices reflect overall systemic intake-including dietary sources-making them less suitable for specifically evaluating respiratory absorption and localized pulmonary effects. These limitations have stimulated growing interest in exhaled breath condensate (EBC) as an innovative biological matrix for exposure assessment and early detection of welding-related health effects.

Exhaled breath condensate can be obtained easily and non-invasively, and because it mirrors the epithelial lining fluid, it allows direct analysis of inhaled particles. Investigations suggest that EBC analysis provides a promising approach for detecting pneumotoxic metals such as chromium (Cr) (Caglieri *et al* 2006; Davis and Montpetit 2018; Goldoni *et al* 2006; Hoffmeyer *et al* 2011; Leese *et al* 2017; Ljungkvist *et al* 2022; Riccelli *et al* 2018), cobalt and tungsten (Broding *et al* 2009; Goldoni *et al* 2004), beryllium (Hulo *et al* 2016), lead (Felix *et al* 2015), and manganese (Mn) (Hulo *et al* 2014). This matrix therefore offers a means of assessing exposure at the lung target level (Corradi and Mutti 2005; Mutti and Corradi 2006), as well as associated biological responses such as inflammation and oxidative stress (Caglieri *et al* 2006; Corradi *et al* 2010; Horvath *et al* 2005; Hoffmeyer *et al* 2009; Hunt 2002, 2007). Supporting this, studies on EBC have reported trends toward increased pH in healthy workers exposed to welding fumes (Boyce *et al* 2006) and modulation of subclinical inflammatory activity depending on exposure characteristics (Fireman *et al* 2008).

The objective of the present review was to explore the potential role of EBC as a reliable biological matrix for evaluating both exposure levels and early biological effects in welders. By focusing on EBC, the review aims to provide a critical foundation for the advancement of innovative biomonitoring strategies that go beyond traditional approaches. Such strategies could significantly enhance current procedures for chemical risk assessment, offering a more precise characterization of respiratory uptake and localized lung responses. Moreover, the adoption of EBC-based monitoring may contribute to a better evaluation of the effectiveness of preventive measures already in place, while also guiding the development of new interventions. Ultimately, this perspective supports the possible implementation of EBC analysis as a complementary tool within occupational health frameworks, thereby strengthening worker protection and improving long-term risk management in welding environments.

2. Materials and Methods

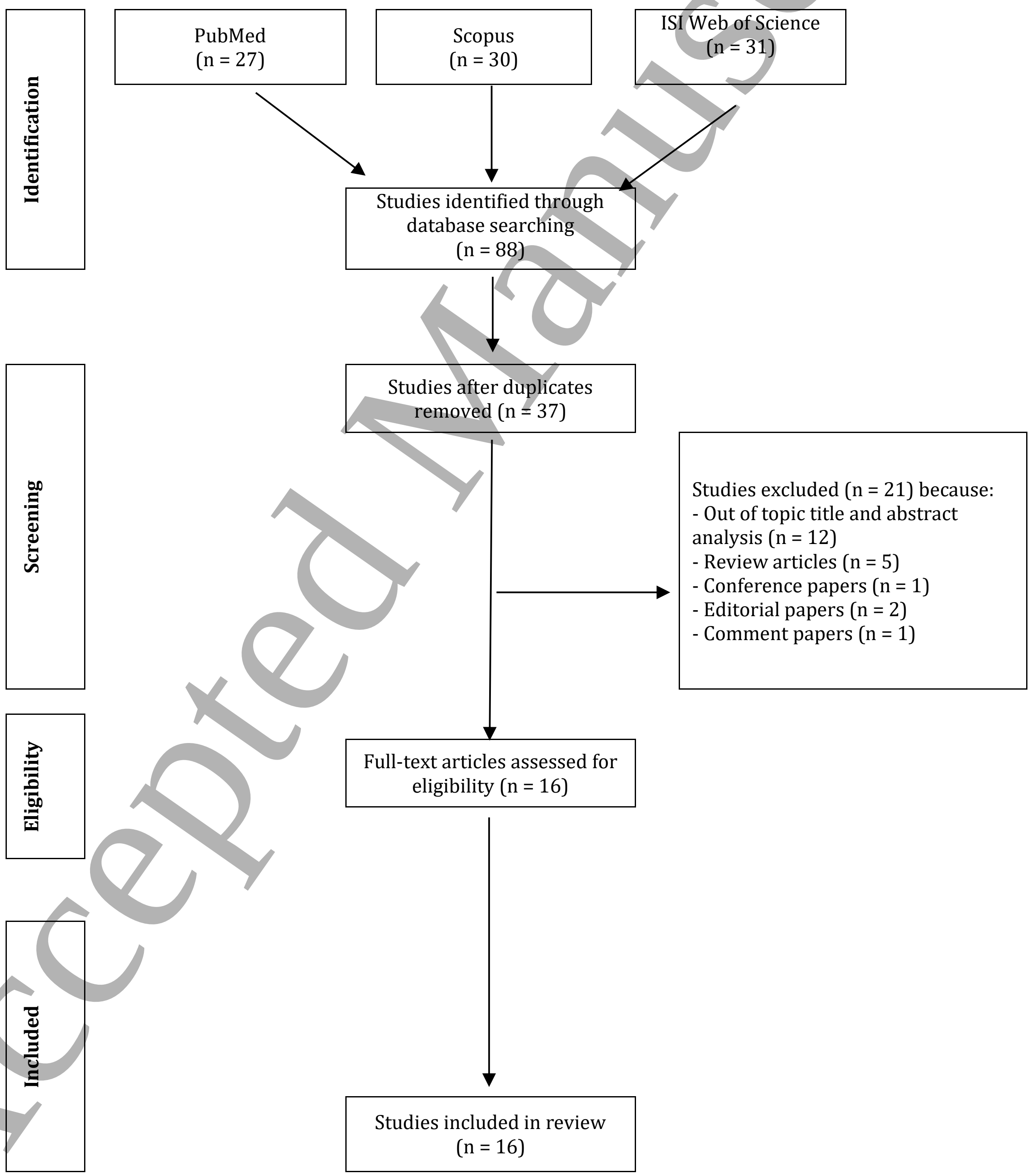
A systematic search/review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement criteria (Page *et al* 2021). Original articles that have investigated this issue and were published from April 2006 up to September 2025 were searched in principal databases of scientific literature. All titles and abstracts retrieved by the computerized librarian-assisted search were independently reviewed by two of the authors who selected the articles that appeared relevant for the aim of the review according to the inclusion criteria. These included peer-reviewed, experimental studies published in English and exploring aspects relative to the possible application of the EBC as a suitable biological matrix for the assessment of the exposure and early effects in welders. Exclusion criteria were applied for reviews, conference abstracts and for studies that did not focus on the topic of the research. We searched PubMed, Scopus, and ISI Web of Science databases from April 2006 to September 2025. The last search for all databases was performed on September 10th, 2025. The electronic search strategies included the core concepts combined terms for EBC and welding/welders (e.g., "exhaled breath condensate" OR EBC AND weld* OR welder* OR welding), adapted to each database syntax. With the aforementioned searches, we retrieved 27, 30, and 31 papers for PubMed, Scopus and ISI Web of Science, respectively. Full texts of all valuable papers were obtained, and a critical evaluation performed. A manual search of the reference list accompanying published papers was performed to supplement the citation pool of relevant publications identified in the literature search in order to include other potentially eligible articles. After excluding the duplicates, two reviewers independently screened titles and abstracts against the eligibility criteria. Full texts of potentially relevant records were retrieved and independently assessed for inclusion by the same reviewers. Disagreements were resolved by discussion; if consensus was not reached, a third reviewer arbitrated. The study selection process is reported in a PRISMA 2020 flow diagram (Figure 1). A total of 16 studies was retrieved for review.

Given the limited number of studies per outcome and high heterogeneity, formal assessment of small-study effects/publication bias was not performed; the risk of missing results was considered qualitatively in the interpretation. Furthermore, we did not apply a validated risk-of-bias tool because the included studies were highly heterogeneous in design, exposure characterization, and EBC analytical approaches. However, to support interpretation, we conducted a structured methodological appraisal using predefined domains relevant to occupational EBC studies. Two reviewers assessed each study across the following domains: (1) participant selection and comparability of control group; (2) exposure characterization (welding process, intensity/duration, personal/environmental monitoring, personal protective equipment (PPE), respiratory protective equipment (RPE); (3) EBC collection quality (device/materials, contamination control, timing pre/post shift/week, handling/storage); (4) outcome measurement quality (analytical technique, Quality Assurance (QA)/ quality control (QC), Limit of Detection (LOD)/Limit of Quantification (LOQ) and handling of <LOD values); (5) confounding control (smoking and other co-exposures); and (6) completeness and transparency of reporting (missing data, selective outcome reporting). Each domain was judged as low/some concerns/high concern. Appraisal results were not used to exclude studies but were used to qualify the certainty of conclusions.

Data were extracted using a piloted standardized extraction form. Extracted variables included: country/year, study design, population characteristics (sample size, controls, smoking status when available), welding process [e.g., Shielded Metal Arc Welding (SMAW),TIG, MIG, Metal Active Gas Welding (MAG), GMA, Flux-Cored Arc Welding (FCAW)]), EBC collection device and timing (pre-/post-shift/week), analytical methods, environmental exposure metrics (airborne PM/metals, sampling method), and outcomes. Outcomes of interest were grouped into:

(i) EBC biomarkers of exposure (metal concentrations/speciation where available), and (ii) EBC biomarkers of early biological effects (pH, oxidative stress/nitrosative stress markers, inflammatory mediators, fractional exhaled nitric oxide (FeNO) where relevant). When multiple results were available within the same outcome domain, we preferentially extracted post-shift (or the most exposure-proximal) measurements and, where reported, pre–post-differences. Due to substantial heterogeneity in study designs, exposure metrics, EBC collection devices, analytical methods, and outcome definitions, a quantitative meta-analysis was not planned. We therefore conducted a structured narrative synthesis, grouping studies by outcome domain (exposure vs effect biomarkers) and by welding process when available. Results are presented in a structured table and summarized by direction and consistency of effects across studies.

Figure 1. PRISMA-based flowchart of the article selection process



3. Results

3.1 Overview of the revised studies and methodological approaches

A total of sixteen studies were included in this review, conducted across Europe, the United States, and Israel between 2006 and 2023 (Table 1). Most investigations focused on occupationally exposed welders, either alone or compared with controls. Nine studies adopted a welders-versus-controls design (56.3%) (Boyce *et al* 2006; Fireman *et al* 2008; Gube *et al* 2010; Hoffmeyer *et al* 2011; Hulo *et al* 2014; Dierschke *et al* 2017; Pelclova *et al* 2018; Leese *et al* 2023; Bocca *et al* 2023), four studies included welders only (25.0%) (Hoffmeyer *et al* 2012a, 2012b; Graczyk *et al* 2016; Riccelli *et al* 2018), and three studies involved controlled exposures in healthy volunteers (18.8%) (Brand et al., 2010; Brand et al., 2013; Hartmann et al., 2014). Welding processes varied widely, including SMAW, TIG, MIG, MAG, GMAW, FCAW, and submerged arc welding, reflecting the heterogeneity of occupational exposure scenarios and welding-fume composition. Collective and environmental control measures were differently described across studies. Some investigations were conducted in workplaces equipped with general and local exhaust ventilation, as reported by Bocca *et al* (2023), while others involved naturally ventilated halls (Hulo *et al* 2014) or indoor halls and confined spaces, including ship hulls, with variable availability of local exhaust ventilation (Hoffmeyer *et al* 2012a). In other cases, exposure conditions were more heterogeneous, including semi-enclosed or open working areas and different welding-, cutting-, and fitting-related tasks (Fireman *et al* 2008), whereas Brand *et al* (2010) used an enclosed welding booth with fume extraction. Individual respiratory protection was also inconsistently reported: supplied-air or air-fed respirators were used in some studies (Fireman *et al* 2008; Hulo *et al* 2014), particulate respirators were used by subsets of welders in Hoffmeyer et al (2012a, 2012b), respiratory masks were reported by Bocca *et et al* (2023), whereas Leese *et al* (2023) reported the use of respiratory protective equipment without providing detailed information on the specific device type. Conversely, other studies described only general welding PPE, such as helmets, gloves, aprons, or protective clothing (Pelclova *et al* 2018), or referred more generally to protection equipment without specifying the exact respiratory device used, as in Gube *et al* (2010) and Riccelli *et al* (2018). Boyce *et al* (2006) and Hoffmeyer *et al* (2011) did not clearly specify respiratory protection. By contrast, several studies were conducted under controlled exposure conditions or in dedicated exposure facilities rather than in routine workplace settings (Brand *et al* 2013; Hartmann *et al* 2014; Graczyk *et al* 2016; Dierschke *et al* 2017). This variability in engineering controls, workplace ventilation, and RPE use is relevant for interpreting EBC biomarkers, since similar airborne concentrations may correspond to different airway doses depending on the effectiveness and consistency of exposure-control measures.

Marked methodological variability was observed in EBC collection procedures. The included studies used ECoScreen-family condensers, Turbo-DECCS systems, RTube devices, and custom ice-cooled condensers. ECoScreen-family condensers, including ECoScreen, ECoScreen2, and ECoScreen Turbo, were the most frequently used devices (9/16; 56.3%) (Gube *et al* 2010; Brand *et al* 2010; Hoffmeyer *et al* 2011; Hoffmeyer *et al* 2012a, 2012b; Brand *et al* 2013; Hartmann *et al* 2014; Hulo *et al* 2014; Pelclova *et al* 2018). Turbo-DECCS systems were used in three studies (3/16; 18.8%) (Riccelli *et al* 2018; Leese *et al* 2023; Bocca *et al* 2023), RTube devices in two studies (2/16; 12.5%) (Graczyk *et al* 2016; Dierschke *et al* 2017), and custom ice-cooled condensers in two studies (2/16; 12.5%) (Boyce *et al* 2006; Fireman *et al* 2008). Importantly, although ECoScreen-family systems were the dominant devices in the available literature, the original ECoScreen platform is no longer commercially available or actively supported, which limits exact replication of older protocols and further complicates cross-study comparability. Condenser characteristics also differed across studies, with cooling temperatures ranging from approximately 0 °C in ice-bath systems to −25 °C in RTube devices, while ECoScreen-family units typically operated around −20 °C and Turbo-DECCS systems around −5 °C.

Standardisation of EBC collection also varied considerably. Most studies used fixed sampling times, generally 7–20 minutes of tidal breathing (12/16; 75.0%), whereas a smaller number relied on predefined exhaled air volumes of approximately 120–200 L (4/16; 25.0%) (Gube *et al* 2010; Brand *et al* 2010; Hulo *et al* 2014; Pelclova *et al* 2018). No study targeted a fixed EBC volume. Crucially, none of the included studies specified respiratory rate, respiratory pacing, metronome-guided breathing, or technician-guided standardisation of the breathing pattern, indicating that ventilation pattern was essentially uncontrolled across protocols. This represents an important source of variability, since EBC volume and biomarker concentrations may be influenced by minute ventilation, tidal volume, breathing frequency, and collection efficiency. Saliva-contamination control was also inconsistently addressed, with some studies using saliva traps, nose clips, or α-amylase testing, whereas others provided limited information on this aspect. Direct correction for water-vapour dilution was not performed in any of the included studies. No study applied established dilution-correction approaches based on urea, conductivity, total non-volatile cations, specific gravity, or comparable indicators. The absence of direct dilution correction remains a relevant methodological limitation, particularly for non-volatile biomarkers and metals, whose measured concentrations in EBC may reflect not only airway deposition or biological response, but also variable dilution by condensed water vapour, breathing pattern, collection efficiency, and device-related factors.

A separate methodological issue concerns the analysis of Cr species in EBC. In two recent studies assessing Cr(VI) and Cr(III), an aliquot of each EBC sample was diluted 10-fold with 0.5 mM EDTA, with pH adjusted to 8 using ammonia solution, immediately after collection, in order to stabilise both Cr species and prevent interconversion between oxidation states (Leese *et al* 2023; Bocca *et al* 2023). This procedure is analytically relevant for Cr speciation, as preservation of the original Cr(VI)/Cr(III) balance is essential for the interpretation of exposure biomarkers. Only Bocca *et al* (2023) performed single-particle analysis of EBC samples, using Single Particle-Inductively Coupled Plasma- Mass Spectrometry (SP-ICP-MS) to determine both number concentration and size of Cr_2O_3, Mn_3O_4, and NiO UFPs. The authors reported dilution of EBC samples with ultrapure water before analysis, followed by vortexing and sonication to promote homogeneous dispersion and prevent agglomeration. However, no specific assessment was performed to determine whether sample-preparation dilution affected particle size or agglomeration state. None of the included studies investigated the anatomical origin of EBC within the respiratory tract. Specifically, no study used lipidomic profiling of surfactant phospholipids or other endogenous airway-lining-fluid markers to determine whether the collected EBC predominantly reflected proximal airways, small airways, or distal/alveolar compartments (Larsson *et al* 2023; Leite *et al* 2025). This is relevant because exhaled breath-derived particles and condensates may differ in their site of origin depending on breathing pattern, airway closure and reopening, particle generation mechanisms, and collection technique. Accordingly, the biomarkers measured in the included welding studies should be interpreted as reflecting the EBC sample as a whole, rather than a defined anatomical region of the respiratory tract.

Regarding outcomes, four studies focused exclusively on exposure biomarkers (25.0%) (Hoffmeyer *et al* 2011; Hulo *et al* 2014; Leese *et al* 2023; Bocca *et al* 2023), ten studies evaluated oxidative or inflammatory biomarkers (62.5%) (Boyce *et al* 2006; Fireman *et al* 2008; Gube *et al* 2010; Brand *et al* 2010; Brand *et al* 2013; Hartmann *et al* 2014; Graczyk *et al* 2016; Dierschke *et al* 2017; Pelclova *et al* 2018;Hoffmeyer *et al* 2012b), and two studies assessed both exposure and effect markers (12.5%) (Hoffmeyer *et al* 2012a, Riccelli *et al* 2018). Analytical approaches included pH measurement, colorimetric or fluorimetric assays for H_2O_2, immunoassays for inflammatory mediators, Liquid Chromatography coupled with Tandem Mass Spectrometry (LC–MS/MS) for oxidative-stress biomarkers, and atomic absorption spectroscopy or ICP-MS for metal quantification.

Overall, the substantial methodological heterogeneity across studies-spanning device type, cooling temperature, collection duration, exhaled air volume, breathing pattern, saliva-contamination control, dilution correction, storage conditions, and analytical techniques-remains, together with the limited number of retrieved investigations, a major barrier to quantitative comparability. These findings underscore the need for harmonised EBC protocols in occupational studies of welding fumes, including systematic reporting of device model, condenser material, cooling temperature, collection time, exhaled air volume, recovered EBC volume, breathing instructions, saliva-control procedures, storage conditions, analytical methods, and dilution-correction strategy.

3.2 Exhaled breath condensate and biomarkers of exposure

Exhaled breath condensate has been demonstrated to be a suitable and informative biological matrix for assessing occupational exposure in welding activities, particularly for metals inhaled as fumes and aerosols. Across multiple studies, welders consistently showed higher concentrations of metals in EBC compared with unexposed controls, most notably Mn, nickel (Ni), iron (Fe), and Cr, supporting the ability of EBC to reflect inhalation-related exposure at the level of the respiratory tract (Hoffmeyer *et al* 2011; Hulo *et al* 2014; Leese *et al*. 2023; Bocca *et al* 2023) (Table 1). The metals detected in EBC are assumed to originate from inhaled welding fumes deposited along the airways, where particles may dissolve in the epithelial lining fluid or be incorporated into EBC droplets following disruption of the airway surface liquid.

Hoffmeyer *et al* (2011) reported increased concentrations of metals in the EBC of industrial welders compared with unexposed controls. Specifically, Ni concentrations were significantly higher in welders than in controls (2.47 μg/L vs 1.20 μg/L), as were Fe concentrations (50.02 μg/L vs 1.79 μg/L), whereas Cr concentrations remained below the LOD. Hulo *et al* (2014) extended these observations by investigating Mn, Ni, Fe, and Cr concentrations in the EBC of MIG welders and relating these measurements to urinary concentrations and cumulative exposure indices. In that study, Mn concentrations were significantly higher in welders than in controls (4.72 μg/L vs 0.32 μg/L), as were Ni concentrations (1.00 μg/L vs 0.24 μg/L), whereas Fe concentrations did not differ significantly between groups and Cr was not detectable in EBC. These findings suggest that EBC may serve as a valuable non-invasive matrix for biomarkers of occupational exposure, although metal-specific and exposure-dependent patterns in EBC metal content were observed.

Interpretation of metal concentrations in EBC requires consideration of metal-specific toxicokinetics rather than assuming a direct one-to-one correspondence with airborne levels. In welding aerosols, Fe generally represents a major mass component, whereas Cr and Ni are usually present at lower proportions but remain toxicologically relevant; therefore, differences in abundance, solubility, and particle chemistry may influence their detectability in EBC (Antonini *et al* 2011; Leese *et al* 2023). Since EBC reflects the airway lining fluid compartment, measured metal concentrations may depend not only on external exposure, but also on particle deposition, dissolution in the epithelial lining fluid, persistence, and respiratory clearance. This may help explain some of the apparently discordant findings reported across studies. For Cr, EBC results are strongly influenced by speciation, as the relative contribution of Cr(III) and Cr(VI) may depend both on the characteristics of the inhaled aerosol and on transformations occurring after deposition in the respiratory tract; this may contribute to the frequent observation of low or non-detectable Cr(VI) levels in EBC despite measurable airborne Cr exposure (Goldoni *et al* 2010; Riccelli *et al* 2020). Likewise, the absence of a clear relationship between airborne Fe exposure and Fe measured in EBC should not be interpreted as evidence against respiratory deposition, but rather as a reflection of metal-specific behaviour within the lung compartment and of the fact that EBC is a highly diluted respiratory matrix rather than a means to measure the total inhaled dose (Hulo *et al* 2014). Overall, these considerations support the interpretation of

EBC as a complementary target-organ matrix, informative for selected metals and exposure scenarios, rather than as a universal surrogate of air monitoring for every analyte.

For Mn in EBC, a significant exposure effect persisted after adjustment for smoking status and after applying both recent (cumulative index for the working week, CIW) and long-term (welding years, WY) exposure indices. In contrast, no exposure-dependent relationships were observed for urinary Mn concentrations, and no correlations were found between Mn-EBC and Mn-U or between Ni-EBC and Ni-U. These findings indicate that EBC and urine reflect different toxicokinetic compartments, with EBC providing information more closely related to pulmonary metal dose rather than systemic distribution. The lack of correlation between EBC and urinary metal concentrations, combined with the clear association between cumulative exposure in inhalable dust and EBC metal levels, indicates that EBC captures exposure-related information that is not reflected by urinary measurements. In particular, for Mn-EBC, the persistence of a significant exposure effect after adjustment for smoking status and after application of both recent and long-term exposure indices-an effect not observed for Mn in urine-strongly suggests that EBC more closely represents the Mn dose delivered to and retained within the respiratory tract. These findings underscore the ability of EBC to reflect target-organ exposure and support its added value over conventional biomonitoring matrices. Overall, this pilot study demonstrates that Mn–EBC and Ni–EBC can be considered robust and reliable indices of occupational exposure to welding fumes (Hulo *et al* 2014).

Chromium exposure has been extensively investigated in stainless steel (SS) welding because the respiratory tract is the primary target organ for inhaled Cr species. Leese *et al* (2023) reported that welders had significantly higher concentrations of Cr(III) in EBC compared with controls, with mean levels of 0.12 µg/L in pre-shift samples collected at the beginning of the working week (Monday) and 0.17 µg/L in post-shift samples collected later in the week (Thursday), while Cr(VI) remained below the LOQ at both the time points. These results suggest that EBC is sensitive to low-level Cr exposure and capable of capturing temporal patterns consistent with cumulative weekly exposure. The predominance of Cr(III) in EBC is consistent with the known chemical composition of SS welding fumes, which are typically dominated by poorly soluble metallic Cr. Oxidation to Cr(VI) is expected to occur mainly at very high temperatures and may be incomplete under many welding conditions, resulting in a larger contribution of Cr(III) to the inhaled dose (Hedberg *et al* 2010; Walter *et al* 2015; Yu *et al* 2014). Temporal variability in EBC metal concentrations was also addressed by Riccelli *et al* (2018), who analyzed EBC from SS TIG welders at different sampling times. Cr-EBC concentrations were lower on Monday pre-shift (<LOD) than on Friday pre-shift (0.06 µg/L) and post-shift (0.08 µg/L), indicating accumulation over the working week. In contrast, no significant pre-/post-shift changes were observed for Ni-EBC, with concentrations generally below the LOD (Riccelli *et al* 2018).

The frequent non-detectable Ni values are unsurprising, given that SS fumes typically contain much more Fe and Cr than Ni. This interpretation is consistent with both published compositional data on SS welding fumes and the air-monitoring results reported in the included studies. Fe is generally the dominant metal component of SS welding fumes, whereas Cr is usually present at higher levels than Ni, although the Cr/Ni difference is more modest and depends on welding process, alloy, and consumable (Mei et al 2018; Hedberg et al 2021). For example, occupational data on SS welding fumes showed that Fe accounted for approximately 78.1% of the inhalable fume metal content, followed by Cr compounds at 8.5% and Ni at 5.2%, corresponding to an approximate Fe/Ni ratio of 15:1 and Cr/Ni ratio of 1.6:1 (Stanisławska et al 2020). This pattern was also reflected in the studies included in this review: Hulo et al (2014) reported airborne Fe concentrations of 2.416 mg/m^3 compared with Ni concentrations of 0.034 mg/m^3, corresponding to an Fe/Ni ratio of approximately 71:1, while Cr was 0.060 mg/m^3, corresponding to a Cr/Ni ratio of approximately 1.8:1. Similarly, Riccelli et al (2018) reported airborne total Cr concentrations approximately twice those of Ni. Therefore, the lower detectability of Ni in EBC may partly reflect its lower airborne abundance relative to Fe and Cr, although metal-specific toxicokinetics, solubility, analytical sensitivity, and EBC dilution also contribute. Overall, these results indicate that Cr-EBC, unlike Ni-EBC, is a sensitive biomarker of SS welding exposure.

The capability of EBC to characterize exposure to particulate components of welding fumes was further demonstrated by Bocca *et al* (2023), who investigated the presence of metal oxide- UFPs in EBC collected from SS welders. EBC samples were obtained at two specific time points of the working week: pre-shift on the first day (Day 1) and post-shift on the last day (Day 5). Welding fumes are known to contain a substantial fraction of UFPs, with a large proportion of emitted particles having aerodynamic diameters below 100 nm (Iavicoli *et al* 2013), which can reach the distal airways and contribute to the condensate fraction. Bocca *et al* (2023) reported markedly increased numbers of Cr_2O_3 UFPs in welders' EBC, with 33,994 particles/mL measured in pre-shift samples and 127,358 particles/mL in post-shift samples, whereas no Cr_2O_3 particles were detected in the EBC of the unexposed control group. Because pre- and post-shift samples were collected on different days of the same week, this pattern suggests a cumulative increase of Cr-containing UFPs in the airway lining fluid over the workweek, rather than only a within-shift rise. NiO UFPs were similarly detected only after exposure, with 22,000 particles/mL measured in post-shift EBC, while concentrations were below the LOD in pre-shift samples and in controls. In contrast, Mn_3O_4 UFPs were not detected in EBC samples from welders, indicating that the particulate fraction of Mn may be less represented in the condensate or that Mn-containing particles were below the detection capability of the applied analytical method. These findings support the potential of EBC to capture ultrafine particulate fractions of welding fumes and to provide complementary information to dissolved metal measurements, highlighting its utility for characterizing both the chemical and physical nature of inhaled exposures in welders.

To further assess the relevance of EBC as a complementary matrix for occupational exposure assessment, available data on metals measured in EBC were summarised by analyte and compared with the corresponding workplace-air measurements where reported (Table 2). Across the included studies, EBC metal concentrations varied substantially according to analyte, chemical form, study design, and analytical method. Mn-EBC was reported at a median concentration of 4.72 μg/L, with an IQR of 2.99–17.13 μg/L, and showed a positive association with cumulative exposure indices based on duration of welding activity and atmospheric metal measurements (Hulo *et al* 2014). Ni-EBC showed median concentrations around 1.00–1.12 μg/L, with reported intervals extending from <1 to 2.47 μg/L (Hulo *et al* 2014; Hoffmeyer *et al* 2012a); a positive association with cumulative exposure indices was reported in one study (Hulo *et al* 2014), whereas Ni was below the limit of detection in another SS TIG welding study despite low but measurable airborne Ni (Riccelli *et al* 2018). Fe-EBC showed the highest reported concentrations among dissolved metals, with medians ranging from 1.48 to 12.02 μg/L and reported IQR values extending up to 44.96 μg/L (Hulo *et al* 2014; Hoffmeyer *et al* 2012a); however, available studies did not demonstrate consistent associations between airborne Fe and Fe-EBC. Cr showed the greatest heterogeneity, ranging from non-quantifiable or <LOD/<LOQ values to measurable total Cr, Cr(III), or Cr(VI) concentrations. Reported total Cr medians were generally below 0.25 μg/L (Hoffmeyer *et al* 2012a) or within the 0.06–0.08 μg/L range (Riccelli *et al* 2018), depending on the study and sampling time. In studies assessing Cr species, Cr(III) medians ranged from 0.12 to 0.17 μg/L, with reported ranges from <LOQ to 0.72 μg/L, while Cr(VI) was generally below the LOQ, although in the subset of quantifiable samples reported values ranged from 0.53 to 0.92 μg/L (Leese *et al* 2023). For Cr, a study reported measurable workplace-air concentrations but non-quantifiable EBC levels (Hulo *et al* 2014), whereas Hoffmeyer et al (2012a) demonstrated a significant association between Cr in respirable welding fumes and Cr levels in EBC. In SS welding settings, total Cr and Cr species were measurable in EBC at low airborne exposure levels, although direct air–EBC correlations were not consistently demonstrated (Riccelli *et al* 2018, Leese *et al* 2023). Finally, Bocca et al (2023) extended this approach to the ultrafine fraction, showing that Cr_2O_3 and, to a lesser extent, NiO- UFPs were detectable in EBC alongside their presence in inhalable particulate matter, whereas Mn_3O_4- UFPs were detected in air but not in EBC. As above mentioned, taken together, these findings further

support the use of EBC as a complementary matrix reflecting airway-level exposure, rather than as a direct substitute for workplace-air monitoring or urinary biomonitoring. The available evidence suggests that EBC may be particularly informative for selected metals and metal species that are deposited or retained at the respiratory tract level, thereby providing information closer to the presumed target organ of inhalation exposure. However, its performance appears to be metal- and species-dependent and is influenced by chemical form, analytical sensitivity, sampling design, and the lack of standardised dilution correction. Therefore, EBC should be interpreted within an integrated exposure-assessment framework, combining environmental monitoring, conventional biological matrices, and detailed information on welding process, exposure intensity, and sampling methodology.

Respiratory protective equipment use represents an important but inconsistently addressed factor in the interpretation of EBC biomarkers. Among the studies evaluating exposure biomarkers in EBC, several reported some form of RPE, including respiratory masks or supplied-air respirators, whereas others provided limited or no information on RPE use (see paragraph 3.1). However, Hoffmeyer et al (2012a) was the only study that explicitly examined how respiratory protection modified the relationship between workplace-air exposure and EBC metal levels. In this study, welders were stratified according to RPE use on the study day, allowing the authors to evaluate whether respiratory protection influenced the relationship between airborne metal exposure and EBC metal levels. Among the 31 welders who did not use RPE during the monitored shift, Cr concentrations in respirable fumes were positively correlated with Cr detected in EBC, indicating that EBC metal levels reflected inhaled exposure when respiratory protection was absent. This association supports the concept that EBC can capture target-organ exposure and that the use of PPE can substantially alter the internal dose reaching the airways. Furthermore, a significant association between cumulative Fe exposure and Fe-EBC concentrations was observed specifically in welders who typically did not use PPE. This finding suggests that the effectiveness of RPE is a critical determinant of EBC metal concentrations and that lack of respiratory protection leads to higher airway deposition and greater metal presence in the condensate. Conversely, in welders who consistently used respiratory protection, the relationship between airborne metal levels and EBC metal content was weaker or absent, implying that RPE may reduce the inhaled dose to a level below the detection sensitivity of EBC-based assessment. Overall, these results emphasize that behavioral factors such as RPE use can strongly influence the interpretation of EBC biomarkers and underline the importance of considering protective practices when using EBC for occupational exposure assessment (Hoffmeyer *et al* 2012a).

The impact of sampling device characteristics is also relevant when interpreting differences in detectability across studies. Among studies focused on the analysis of metal concentrations in EBC, 3 out of 6 (Hoffmeyer *et al* 2011; Hoffmeyer *et al* 2012a; Hulo *et al* 2014), employed the ECoScreen-family bench-top systems (ECoScreen and ECoScreen 2), while the other three (Riccelli *et al* 2018; Leese *et al* 2023, Bocca *et al* 2023) adopted the Turbo DECCS. Variability in condensation efficiency and in the potential adsorption or loss of trace elements on condenser surfaces may also contribute to inter-study differences. For instance, Cr was undetectable in the study by Hoffmeyer *et al* (2011) and Hulo *et al* (2014), whereas Cr(III) was measurable in welders' EBC in more recent studies performed with different devices and operative protocols (Leese *et al* 2023; Riccelli *et al* 2018). Such discrepancies may partly reflect improvements in analytical sensitivity and differences in sampling methodology, including the condenser used and the reporting LOD/LOQ. Riccelli *et al* (2018) reported Ni-EBC concentrations generally below the LOD, while Cr-EBC was detectable and showed a weekly accumulation pattern. These findings underscore that both device-related factors and analytical performance influence whether specific metals are measurable in EBC and highlight the need for consistent reporting of LOD/LOQ and standardized sampling procedures.

The physical characteristics of EBC condensing devices can substantially affect both the efficiency of EBC collection and the accuracy of biomarker detection, particularly for metals that may adhere to or leach from sampling surfaces. Evidence suggests that the condenser itself may introduce measurement errors, either through contamination from device materials or through differences in collection efficiency and sample dilution. Hoffmeyer *et al* (2011) explicitly addressed this issue by comparing metal concentrations in EBC collected from welders using two different condensers, ECoScreen and ECoScreen2. The ECoScreen device employs a reusable Teflon-coated surface that must be washed and wiped before each test, whereas ECoScreen2 collects EBC directly into disposable polyethylene bags, reducing the risk of carryover contamination and simplifying sample handling. Welders included in the study processed varying amounts of SS and mild steel, resulting in different exposure levels. When EBC was collected with ECoScreen2, welders showed significantly higher concentrations of Fe (50.02 mg/L) and Ni (2.47 mg/L) compared with controls, indicating that this device may provide a more reliable assessment of metal exposure. In contrast, the repeated use of ECoScreen may lead to contamination from metallic components, potentially masking true exposure differences or generating false-positive signals. Cr was not detectable in EBC in this study regardless of the condenser used (Hoffmeyer *et al* 2011).

3.3 Exhaled breath condensate and biomarkers of effect

Exhaled breath condensate has been increasingly used as a non-invasive matrix for the investigation of early biological effects associated with occupational exposure to welding fumes (Table 1). Because inflammatory and oxidative processes in the airways may occur before the development of clinically detectable respiratory disease, EBC allows the assessment of subclinical alterations in the airway lining fluid. A wide range of biomarkers have been measured in welders' EBC, reflecting oxidative stress, lipid peroxidation, protein and nucleic acid oxidation, nitrosative stress, and inflammatory responses (Hoffmeyer *et al* 2009).

3.3.1 Oxidative stress biomarkers

Markers of oxidative stress, including hydrogen peroxide (H_2O_2), 8-hydroxy-2′-deoxyguanosine (8-OHdG), 8-hydroxyguanosine (8-OHG), and 5-hydroxymethyluracil (5-OHMeU), have been widely applied to evaluate airway alterations related to welding fume exposure. Fireman *et al* (2008) analyzed EBC from welders exposed to different metallic combinations and reported significantly higher concentrations of H_2O_2 in exposed workers compared with controls, suggesting the presence of subclinical airway inflammation associated with welding fume inhalation. The same study also highlighted the potential of EBC to detect early oxidative alterations in the respiratory tract, even in the absence of overt clinical symptoms.

However, subsequent studies demonstrated that H_2O_2 concentrations are strongly influenced by cigarette smoking, which may act as a major confounder when interpreting this biomarker in occupational settings. Gube *et al* (2010) reported that smoking status had a greater effect on H_2O_2 levels than welding exposure, indicating that H_2O_2 may be more reflective of smoking-related oxidative burden than of welding-related airway changes. This finding underscores the need to account for smoking habits and to adjust analyses accordingly when using H_2O_2 as an effect biomarker. Additionally, the high dilution of EBC and the variability of collection and analytical procedures can further affect the sensitivity of H_2O_2 detection, potentially limiting its usefulness for distinguishing welding-related effects in heterogeneous worker populations.

Graczyk *et al* (2016) reported that short-term exposure to TIG welding fumes did not result in measurable changes in H_2O_2 or 8-OHdG levels, highlighting analytical limitations related to the high dilution of EBC samples and the relatively low intensity and duration of controlled exposures. In contrast, Pelclova *et al* (2018) detected elevated concentrations of 8-OHG, 8-OHdG, and 5-OHMeU in pre-shift samples from workers exposed to nanocomposite processing, suggesting the presence of persistent oxidative stress likely related to chronic exposure rather than acute effects.

Lipid peroxidation biomarkers, particularly malondialdehyde (MDA), showed heterogeneous results across studies. Brand *et al* (2013) and Hartmann *et al* (2014) did not observe significant changes in MDA concentrations following short-term exposure to different welding techniques, findings that were confirmed under controlled TIG welding conditions by Graczyk *et al* (2016). Conversely, Riccelli *et al* (2018) reported increased concentrations of both H_2O_2 and MDA during the work shift, with a return to baseline levels after the weekend, indicating an acute and reversible oxidative response associated with welding activity.

The influence of welding technique and fume composition on oxidative stress markers was further demonstrated by Hoffmeyer *et al* (2012a,b). These authors reported significantly higher concentrations of 8-iso-prostaglandin $F_2\alpha$ (8-iso-PGF$_2\alpha$) in welders exposed to Fe-, Ni-, and Cr-rich fumes, with higher levels observed in FCAW compared with gas metal arc welding (GMAW). While these findings suggest that both welding process and metal composition contribute to enhanced lipid peroxidation, the extent to which individual metals, particle size distribution, or co-exposures drive this response remains uncertain, given the complexity of welding fumes and the limited ability to disentangle correlated exposure factors. In line with these results, Pelclova *et al* (2018) similarly observed post-shift increases in MDA, aldehydes C6–C13, and 8-iso-PGF$_2\alpha$, whereas 4-hydroxyhexenal (HHE) remained unchanged. This pattern indicates a selective activation of lipid peroxidation pathways rather than a uniform oxidative response. However, inter-individual variability, relatively small sample sizes, and differences in analytical sensitivity across biomarkers may partially account for the heterogeneous responses observed. Moreover, the short-term, cross-shift design of these studies limits inference on the temporal persistence and clinical relevance of these alterations.

Protein oxidation biomarkers have also been explored as indicators of airway oxidative damage. Brand *et al* (2010) reported increased hydroxyproline concentrations during welding, suggesting inflammatory processes potentially affecting connective tissue. Similarly, Pelclova *et al* (2018) found elevated levels of o-tyrosine and 3-nitrotyrosine both before and after the work shift, consistent with sustained oxidative and nitrosative stress. Nonetheless, the presence of elevated baseline levels complicates interpretation, as it is difficult to distinguish cumulative occupational effects from other sources of oxidative stress, such as smoking, diet, or environmental exposures. Overall, while these biomarkers appear sensitive to welding-related exposures, further longitudinal studies with improved exposure characterization are needed to clarify their specificity and predictive value for adverse respiratory outcomes (Table 1). Additionally, available studies on welders have mainly focused on biomarkers of oxidative damage, such as H_2O_2, MDA, 8-OHdG, 8-OHG, and 8-iso-PGF$_2\alpha$, whereas the antioxidant response in EBC has been poorly explored. To date, markers of antioxidant defence, such as glutathione, total antioxidant capacity, superoxide dismutase, or catalase, have not been systematically investigated in EBC from welders. This represents an important research gap, as the balance between oxidative injury and antioxidant defence may provide a more complete interpretation of welding-related airway effects than oxidative damage markers alone. Future studies in welders should therefore expand EBC-based assessment beyond oxidative damage biomarkers alone, incorporating markers of endogenous antioxidant defence to better characterize the balance between pro-oxidant injury and respiratory redox adaptation.

3.3.2 Inflammatory and nitrosative stress biomarkers

Inflammatory mediators measured in EBC may provide additional evidence of airway responses associated with welding fume exposure. Hoffmeyer *et al* (2012a) reported increased concentrations of leukotriene B_4 (LTB_4) and prostaglandin E_2 (PGE_2) in welders exposed to Fe- and Ni-rich fumes, suggesting activation of inflammatory pathways in the airways. In a subsequent study, Hoffmeyer *et al* (2012b) observed higher concentrations of 8-iso-prostaglandin $F_2\alpha$ (8-iso-PGF$_2\alpha$) and less acidic EBC pH values in FCAW welders compared with GMAW welders, whereas PGE_2 concentrations did not differ significantly between groups. While these findings point to potential technique-related differences in airway responses, the extent to which these changes reflect inflammation per se, rather than concomitant oxidative processes or methodological variability, remains uncertain. Dierschke *et al* (2017) reported a decrease in LTB_4 concentrations following exposure, despite markedly higher baseline levels among welders reporting respiratory symptoms. This pattern suggests that EBC inflammatory markers may be influenced by pre-existing airway conditions and baseline inflammatory status, complicating the interpretation of short-term exposure-related changes. Moreover, substantial inter-individual variability and limited sample sizes may partly account for the divergent findings across studies.

Nitric oxide–related metabolites, including nitrate, nitrite, and 3-nitrotyrosine, have been explored as indicators of nitrosative stress in the airways. Brand *et al* (2010) observed elevated concentrations of these metabolites during welding, particularly during manual metal arc welding with alternating current (MAW-a). Gube *et al* (2010) similarly reported that the nitrite/tyrosine ratio depended on the predominant welding technique ($p = 0.043$), with the highest values in MMA welders. They also found that PPE use modulated acute EBC responses, as welders without protection showed significant increases in nitrite/tyrosine, nitrate/tyrosine, and MDA/tyrosine ratios, compared to PPE users. These observations are consistent with a possible exposure-related effect, although differences in exposure intensity, protective equipment use, and analytical approaches limit direct comparability.

In contrast, no significant post-exposure changes were reported by Brand *et al* (2013) or Hartmann *et al* (2014), whereas Pelclova *et al* (2018) identified 3-nitrotyrosine as a potentially sensitive post-shift biomarker of nitrosative stress. Nonetheless, nitric oxide–related markers in EBC are subject to multiple sources of uncertainty, including dilution effects, smoking status, and transient respiratory conditions. Overall, while these markers appear responsive in some exposure scenarios, their specificity and reliability as indicators of welding-related airway inflammation require further confirmation in standardized, longitudinal studies (Table 1).

In contrast to oxidative and inflammatory biomarkers, the anti-inflammatory or resolution-related response in EBC has received little attention in studies on welders. Most available investigations have assessed markers reflecting airway inflammation or irritation, such as leukotrienes, prostaglandins, nitric oxide-related products, pH, or nitrotyrosine, while anti-inflammatory mediators have not been systematically evaluated. In particular, cytokines with regulatory or anti-inflammatory activity, such as IL-10 and IL-4, as well as specialized pro-resolving lipid mediators, remain largely unexplored in this occupational setting. This represents a relevant gap, since the balance between pro-inflammatory activation and anti-inflammatory or resolution pathways may be important for understanding the persistence, reversibility, and potential clinical relevance of welding-related airway responses. Future research should also investigate anti-inflammatory and resolution-related mediators in EBC, in order to clarify whether welding-related airway inflammation is accompanied by compensatory regulatory responses or by impaired resolution mechanisms.

3.3.3 EBC pH as an integrative biomarker

EBC pH has been widely proposed as a simple and integrative indicator of airway inflammation and oxidative stress. Boyce *et al* (2006) reported acute alkalinization of EBC pH following exposure to SMAW and TIG welding. Fireman *et al* (2008) observed more alkaline EBC pH values in Al/Fe welders and more acidic values in workers exposed to Cd/Cr/Fe/Pb/Ni, suggesting metal-specific effects on airway acid–base balance. Gube *et al* (2010) reported higher EBC pH in welders compared with controls, while Hoffmeyer *et al* (2012b) found less acidic pH values in FCAW welders compared with GMAW welders. Lower EBC pH values have been associated with higher concentrations of pro-inflammatory cytokines, supporting the interpretation of EBC pH as an integrated marker of airway inflammation (Kostikas *et al* 2002). Taken together, these findings indicate that EBC biomarkers capture a broad spectrum of early biological responses to welding fume exposure, ranging from transient oxidative changes to markers suggestive of sustained inflammatory and nitrosative stress (Table 1).

4. Conclusions

Exhaled breath condensate is increasingly supported as an informative, non-invasive matrix for assessing exposure and early airway effects in welders, because it samples the respiratory tract lining environment where inhaled welding fume constituents deposit and initiate biological responses.

Across studies, welders generally show higher EBC concentrations of inhaled metals than unexposed controls-most consistently Mn, Ni, Fe and Cr-indicating that EBC can reflect inhalation-related, target-organ exposure and, more specifically, the lung dose of pneumotoxic substances. This is biologically plausible given the substantial fine and ultrafine particle fraction in welding fumes that can reach the distal airways; deposited particles may dissolve in epithelial lining fluid, persist within the respiratory tract, undergo clearance, or be incorporated into exhaled droplets collected as EBC. However, interpretation of EBC metal concentrations requires a deeper understanding of metal-specific toxicokinetics and toxicodynamics. Differences in solubility, oxidation state, particle size, pulmonary deposition, dissolution, macrophage uptake, epithelial translocation, and clearance may explain why individual metals are not equally detectable in EBC and why EBC concentrations do not always correlate directly with airborne levels or systemic biomarkers.

A recurring observation is that EBC and traditional matrices such as urine (and, where available, blood) capture different toxicokinetic compartments: exposure indices correlate with Mn or Ni in EBC even when urinary measures show weak or absent exposure–response patterns and do not correlate with EBC levels, supporting EBC as a complementary indicator of local airway burden rather than systemic distribution. In this perspective, the integrated use of EBC with classic biological matrices that reflect systemic exposure could meaningfully complete biological monitoring of pneumotoxic compounds by jointly addressing both target-organ and whole-body compartments. In SS welding, Cr in EBC-especially Cr(III)-can be measurable at low exposure levels and may increase over the workweek, whereas Cr(VI) often remains below quantification, consistent with typical fume chemistry dominated by poorly soluble Cr species. Emerging evidence that EBC can capture ultrafine particulate fractions (e.g. Cr_2O_3 and NiO particles) suggests added value for characterising the physical as well as chemical nature of welding aerosols. The application of single-particle techniques such as SP-ICP-MS opens a promising perspective for EBC-based biomonitoring, as it allows not only the quantification of metal content but also the characterization of particle number concentration and size. Future studies could further strengthen this approach by systematically reporting and optimising sample dilution, dispersion procedures, sonication conditions, matrix effects, size-detection limits, and particle recovery, thereby improving the comparability and interpretation of UFP measurements in EBC. Exhaled breath condensate has also been applied to investigate early biological effects relevant to allergic, inflammatory and potentially carcinogenic respiratory pathways, including oxidative stress, lipid peroxidation, nitrosative stress and inflammatory mediators. Overall, the literature supports the concept that welding fumes can induce subclinical airway alterations detectable in EBC, but findings remain heterogeneous across biomarkers and study designs. Some endpoints vary within shifts or across the workweek, consistent with transient oxidative responses, while others may indicate more sustained stress; interpretation is complicated by strong confounding-most notably cigarette smoking-by differences in welding technique and fume composition, and by sensitivity constraints in highly diluted EBC. Future studies should move beyond isolated oxidative-damage markers and adopt more balanced multi-marker panels. In addition to H_2O_2, MDA, 8-OHdG, 8-OHG, 8-iso-PGF$_2\alpha$, nitrite/nitrate, and inflammatory mediators, EBC research in welders should incorporate markers of antioxidant defence, such as glutathione, total antioxidant capacity, superoxide dismutase, or catalase, as well as anti-inflammatory and resolution-related mediators, including regulatory cytokines or specialised pro-resolving lipid mediators. Such panels may better capture the balance between airway injury, adaptation, and resolution.

Despite these encouraging findings, methodological variability remains the main barrier to the routine use of EBC in occupational biomonitoring. The included studies differed in collection device, condenser material, cooling temperature, sampling duration, exhaled air volume, breathing pattern, saliva-contamination control, storage conditions, analytical technique, and reporting of LOD/LOQ. These limitations substantially restrict quantitative comparability and make between-study synthesis difficult. Greater harmonisation is therefore essential. Future occupational EBC studies should follow and explicitly report the methodological domains recommended by the American Thoracic Society and European Respiratory Society task force (Horvath *et al* 2005, 2017), including device type and material, condenser temperature, collection duration, exhaled air volume, recovered EBC volume, breathing instructions, saliva-control procedures, sample handling and storage, analytical methods, LOD/LOQ, and dilution-correction strategy. Where multicentre studies are performed, protocols should be aligned as closely as possible, as attempted in the HBM4EU chromates study, to reduce pre-analytical variability and improve comparability across settings. The development of consensus procedures specific to occupational biomonitoring is particularly needed, because welders are exposed to complex mixtures of metals, gases, and particles under highly variable working conditions.

In particular, the need to normalise EBC results for dilution-i.e., to account for the variable dilution of expiratory droplets by condensed water-has not been definitively resolved and represents a major barrier to quantitative interpretation and between-study synthesis. Further work is required to standardise sampling and reporting, to clarify the kinetics of EBC production and collection (including determinants of sample dilution), and to characterise the toxicokinetics of metals and other constituents within EBC. Prospective validation studies linking EBC exposure and effect biomarkers-ideally as multi-marker panels-to exposure metrics, use of respiratory protective equipment, key confounders and clinically meaningful respiratory outcomes are needed before EBC-based approaches can be widely implemented in occupational settings.

In conclusion, EBC is a promising and biologically meaningful matrix for assessing airway-level exposure and early effects in welders, but it should currently be regarded as a complementary tool within an integrated occupational exposure-assessment framework. Its greatest value may lie in combination with workplace-air monitoring, conventional biological matrices, detailed exposure reconstruction, and carefully selected panels of exposure, oxidative, antioxidant, inflammatory, anti-inflammatory, and particle-related biomarkers. Before EBC can be widely implemented in occupational health practice, prospective validation studies are needed to clarify EBC production and dilution kinetics, metal toxicokinetics and toxicodynamics, regional airway origin, the influence of PPE/RPE, and the relationship between EBC biomarkers and clinically meaningful respiratory outcomes.

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Table 1. Studies retrieved for review

STUDY LOCATION AND YEAR	STUDY POPULATION	TYPE OF WELDING	STUDY DESIGN	RESULTS	ENVIRONMENTAL MONITORING	REFERENCE
United States of America 2006	**Welding apprentices** (14) **Controls** (8)	Shielded metal arc welding (**SMAW**) Tungsten inert gas welding (**TIG**)	**EBC collection time:** pre-shift and post-shift. **EBC collection device:** disposable collection system consisting of a mouthpiece with one-way valves, inspiratory filter, expiratory saliva trap, and disposable corrugated plastic respiratory tubing coiled in an ice bath and used as condensate trap **Cooling chamber temperature:** ~ 0°C (ice bath) **Duration of collection:** 7 min **Sample volume:** ~ 3–5 mL **Dilution correction:** N/A **Saliva contamination:** expiratory one-way valve served as a saliva trap; subjects were instructed to swallow saliva if present **Sample storage:** condensate was immediately transferred to Eppendorf tubes and stored at −80°C until further processing **EBC analysis:** pH measurement using the Orion Pure Water pH Test Kit with addition of potassium chloride, argon deaeration, and standard pH microelectrode	**pH**: welders 7.39 and control 7.21; $p = 0.86$	**Collection method:** KTL cyclone with a Vortex Timer 2 personal sampling pump **$PM_{2.5}$**: 1.17 ± 0.18 mg/m³ for welders; 0.03 ± 0.01 mg/m³ for controls	Boyce *et al* 2006
Israel 2008	**Welders** (46) *Group 1* (30) *Group 2* (16) **Controls** (27)	Not specified	**EBC collection time**: N/A **EBC collection device:** perfluoroalkoxy Teflon tubing (890 FEP 3/16 × 1/4 × 1/32; Nalgene Dupont) immersed in an ice-filled bucket of a specially designed double-wall plastic condenser system; EBC collected into a 10-mL polypropylene tube **Cooling chamber temperature:** ice-filled bucket; exact temperature N/A **Duration of collection:** ~ 20 min **Sample volume:** N/A **Dilution correction:** N/A **Saliva contamination:** N/A **Sample storage:** sample was kept on ice and analyzed within 30 min of collection **EBC analysis:** H_2O_2 measured by colorimetric phenol red/horseradish peroxidase assay; pH measured after argon deaeration using a sensitive electrode	**H_2O_2**: Group 1 (0.19 ± 0.11 μM) and Group 2 (0.19 ± 0.16 μM) showed higher concentrations than controls (0.03 ± 0.04 μM); $p < 0.0001$ **pH**: was significantly alkaline in Group 1 (8.0 ± 0.64) than in Group 2 (7.52 ± 0.48) and controls (7.7 ± 0.74); $p < 0.001$	Not specified	Fireman *et al* 2008
Germany 2009	**Welders** (45)	Metal inert gas welding (**MIG**)	**EBC collection time**: friday pre-shift (T1) (baseline) and after 8 h of work at the end of the shift (T2)	**Nitrate**: welders (0.71 ± 0.13 nM) showed higher concentrations than	**Collection method:** fibre glass filters for inhalable and respirable dust	Gube *et al* 2010

	Controls (24)	**TIG** Gas metal arc welding with gas mixture (**MAG-M**) Gas metal arc welding with CO_2 (**MAG-C**) Shielded manual metal arc welding (**MMA**)	**EBC collection device:** ECOSCREEN condenser (Jaeger, Höchberg, Germany) **Cooling chamber temperature:** −20°C **Duration of collection:** N/A **Sample volume:** collection was completed when 200 L of exhaled air had been achieved (measured by EcoVent flow meter) **Dilution correction:** N/A **Saliva contamination:** N/A **Sample storage:** aliquoted and stored at −80°C until analysis **EBC analysis:** • MDA: HPLC-MS/MS after DNPH derivatization • Nitrite/nitrate: photometric Griess reaction • 3-nitrotyrosine, tyrosine, hydroxyproline, proline: HILIC-MS/MS • H_2O_2 and pH: measured immediately after sample collection using ECoCheck (VIASYS-HealthCare).	controls (0.22 ± 0.04 nM); $p < 0.05$ **H_2O_2**: welders (56 ± 19 pM) showed a higher concentration than controls (6.6 ± 2.2 pM); $p < 0.05$ **Cotinine**: welders (751 ± 157 µg/l) showed a higher cotinine concentration than controls (343 ± 170 µg/l); $p < 0.05$ **Nitrite, MDA, Nitrotyrosine**, **Hydroxyproline**, **pH**: no significant differences between welders and controls **Respiratory protective equipment (RPE):** Subjects who did not use RPE showed signifiantly increased nitrite/tyrosine ratios (p = 0.004), increased nitrate/tyrosine ratios (p < 0.001) and increased MDA/tyrosine ratios (p = 0.002) compared to those whoe employed RPE	Concentrations of NO_2, CO_2, CO and O_3 were assessed using Dräger tubes **Inhalable dust**: 4.9 mg/m^3 **Respirable dust**: 0.7 mg/m^3 **O_3**: 0.32 mg/m^3 **NO_2**: 1.0 mg/m^3 **CO_2**: 0,03% **CO**: < 2.5 mg/m^3	
Germany 2010	**Healthy subjects** (6)	Shielded manual metal arc welding with alloyed material (**MAW-a**) Metal active gas welding with alloyed material (**MAG-a**)	**EBC collection time**: baseline (0 h), 3 h, 6 h, and 24 h after welding start **EBC collection device:** EcoScreen condenser (Jaeger, Höchberg, Germany) **Cooling chamber temperature:** −20°C **Duration of collection:** N/A **Sample volume:** collection was completed when 200 L of exhaled air had been achieved (measured by EcoVent flow meter) **Dilution correction:** N/A **Saliva contamination:** N/A **Sample storage:** aliquoted and stored at −80°C until analysis; nitrate and nitrite were measured directly after	**Nitrate:** increased for all time points (ϱY_{3-0} = 0.011; ϱY_{6-0} = 0.035; ϱY_{24-0} = 0.02) **Hydroxyproline:** increased after 3 hours (ϱY_{3-0} = 0.034) ϱY is the difference between each time point	Not specified	Brand *et al* 2010

		Shielded manual metal arc welding (**MAW-u**)	collection **EBC analysis:** • Nitrite/nitrate: photometric Griess reaction • 3-nitrotyrosine, tyrosine, hydroxyproline, proline: HILIC-MS/MS • MDA: HPLC-MS/MS after DNPH derivatization			
Germany 2009	**Welders** (36) **Controls** (24)	Mild Steel (**MS**) welding Stainless Steel (**SS**) welding	**EBC collection time:** after shift (welders); control (during study session) **EBC collection device:** comparison study using new ECoScreen, old ECoScreen, and ECoScreen2 **Cooling chamber temperature:** −20°C **Duration of collection:** 10 min of tidal breathing **Sample volume:** no fixed target volume; after 10 min of tidal breathing in controls, median collected volumes were: new ECoScreen 1.20 mL; old ECoScreen 1.40 mL; ECoScreen2 1.45 mL **Dilution correction:** N/A **Saliva contamination:** subjects used a nose clip and were instructed to swallow excess saliva after removal of the mouthpiece **Sample storage:** aliquoted and immediately stored at −70°C; analyzed within 2 months **EBC analysis:** metal determination by graphite furnace atomic absorption spectrometry (GF-AAS; ZEEnit 700, Analytic Jena) for Cr, Fe, and Ni; dilute nitric acid added before analysis; Zeeman background correction used	**Fe:** welders (50.02 µg/L) showed significant increase of median concentration compared to controls (1.79 µg/L); $p < 0.0001$ **Ni:** welders (2.47 µg/L) showed higher median concentration compared to controls (1.20 µg/L); $p < 0.001$ **Cr:** median concentrations were below the LOD of the assay	Not specified	Hoffmeyer *et al* 2011
Germany 2011	**Welders** (43) *Group A* (24) *Group B* (19)	**MAG** in mild steel	**EBC collection time**: after shift **EBC collection device**: ECoScreen2 (FILT, Berlin, Germany) **Cooling chamber temperature**: −20°C **Duration of collection**: 10 min **Sample volume**: N/A **Dilution correction**: N/A **Saliva contamination**: subjects used a nose clip and were instructed to swallow excess saliva after coming off the mouthpiece **Sample storage**: aliquoted, immediately stored at −70°C, and analyzed within 2 months **EBC analysis**: • Metals (total Cr, Fe, Ni): GF-AAS (ZEEnit 700, Analytic Jena) • pH: pH meter with glass electrode after argon deaeration	**Metals (Fe, Cr, Ni)**: concentration of Fe (12.02 µg/L) was an order of magnitude higher than Cr (<0.25µg/L) or Ni (1.12 µg/L) **pH**: EBC-pH was more acid in group B (6.52) than in group A (6.82); $p < 0.05$ **8-Iso PGF2α**: group A (443.3 pg/mL) showed higher concentrations than group B (247.2 pg/mL); p = 0,001	**Collection method:** respirable fraction of welding fumes was collected by a cellulose nitrate filter in conjunction with polyurethane foam as a pre-selector for larger particles. Metals were determined by ICP-MS **Respirable fraction:** 5.55 mg/m^3 **Cr:** 1,2 µg/m^3 **Ni:** 1,5 µg/m^3 **Fe:** 1800 µg/m^3	Hoffmeyer *et al* 2012a

			• Biomarkers (8-iso PGF2α, LTB4, PGE2): specific sandwich enzyme immunoassay kits (Assay Designs, Ann Arbor, USA)	**LTB4**: group A (30.5 pg/mL) showed higher concentrations of LTB4 than group B (17.3 pg/mL); p = 0.01 **PEG2**: no significant differences between group A and group B		
Germany 2012	**Welders** (58)	Gas metal arc welding (**GMAW**) Flux-cored wire (**FCAW**)	**EBC collection time**: after shift **EBC collection device**: ECoScreen2 (FILT, Berlin, Germany) **Cooling chamber temperature**: −20°C **Duration of collection**: 10 min **Sample volume**: N/A **Dilution correction**: N/A **Saliva contamination**: subjects used a nose clip and were instructed to swallow excess saliva after removal of the mouthpiece **Sample storage**: N/A **EBC analysis**: • pH: pH meter with glass electrode after argon deaeration • LTB4, PGE2, 8-iso PGF2α: enzyme immunoassay kits	**pH:** samples derived from welders using GMAW showed significantly lower pH values (median 6.61) vs. FCAW (median 6.84); p < 0.05 **8iso-PGF2α:** markedly higher in FCAW (median 404.2 pg/ml) compared to GMAW welders (median 247.2 pg/ml); p < 0.05 **LTB4**: GMAW (median 19.24 pg/ml) versus FCAW (median 30.21pg/ml); p < 0.05 **PGE2**: GMAW (median 179 pg/ml) versus FCAW (median 174.4 pg/ml); p = 0,321	**Collection method:** respirable fraction of welding fumes was collected by a cellulose nitrate filter in conjunction with polyurethane foam as a pre-selector for larger particles. The particle-loaded filters were gravimetrically analyzed	Hoffmeyer *et al* 2012b
Germany 2013	**Healthy subjects** (12)	**MAG**	**EBC collection time**: before exposure and after the 6-h controlled exposure session to welding fumes with different exposure concentrations (0, 1, 2.5 mg/m^{-3}) **EBC collection device**: ECOSCREEN condenser (Jaeger, Höchberg, Germany) **Cooling chamber temperature**: −20°C **Duration of collection**: 20 min **Sample volume**: N/A **Dilution correction**: N/A **Saliva contamination**: N/A **Sample storage**: aliquoted and stored at −80°C until analysis **EBC analysis**:	**Nitrate, Nitrite, Nitrotyrosine**; **Hydroxyprolin, MDA:** no significant differences between the two time-points and exposure concentrations	**Collection method:** welding fume concentration was measured using a Tapered Element Oscillating Microbalance (TEOM) **Ni**: 4.81% **Cr**: 12% **Cr(VI)**: 0.3%	Brand *et al* 2013

			• Nitrite/nitrate: photometric Griess reaction • 3-nitrotyrosine, tyrosine, hydroxyproline, proline: HILIC-MS/MS • MDA: HPLC-MS/MS after DNPH derivatization			
France 2011/ 2012	**Welders** (17) **Controls** (16)	**MIG**	**EBC collection time**: after 5 days of exposure **EBC collection device:** Ecoscreen device (Jaeger™, Würzburg, Germany) **Cooling chamber temperature**: -20°C **Duration of collection**: N/A **Sample volume:** collection was completed when the total expired volume reached 200 L **Dilution correction**: N/A **Saliva contamination:** alpha-amylase activity of EBC was tested **Sample storage**: aliquoted and stored at –80°C until analysis. **EBC analysis**: Inductively coupled plasma mass spectrometry (ICP-MS)	**Mn**: median concentration was significantly higher among welders (4.72 µg/L) than controls (0.32 µg/L); p < 0,001 **Ni**: median levels were higher in welders (1.00 µg/L) than controls (0.24 µg/L); p < 0,001 **Fe**: no significant difference was detected between median concentrations welders and controls. **Cr**: not quantifiable in EBC	**Collection method:** for sampling the inhalable dust was used GilAir pumps with filter cassette and quartz microfibers filters. The concentrations of Mn, Ni, Fe and Cr were determined using an ICP atomic emission spectrometer **Inhalable dust**: 4,72 mg/m^3 **Mn:** 0,27 mg/m^3 **Ni:** 0,034 mg/m^3 **Fe:** 2,416 mg/m^3 **Cr:** 0,06 mg/m^3	Hulo *et al* 2014
Germany 2012	**Healthy subjects** (12)	**MIG**	**EBC collection time**: before exposure, directly after exposure, 24h and 7 days after the beginning of exposure (6 h) to an average concentration of 2.5 mg welding fume from MIG welding of aluminium or 2.5 mg of fume from MIG soldering of zinc coated steel using a copper containing welding wire **EBC collection device:** Ecoscreen condenser (Jaeger, Hoechberg, Germany). **Cooling chamber temperature**: -20°C **Duration of collection**: 15 min of tidal breathing without wearing a nose-clip **Sample volume**: N/A **Dilution correction**: N/A **Saliva contamination:** N/A **Sample storage**: aliquoted and stored at –80°C until analysis. **EBC analysis**: • Nitrite and nitrate: photometric Griess reaction with enzymatic nitrate reduction • Tyrosine: HILIC-MS/MS • Malondialdehyde (MDA): HPLC-MS/MS after DNPH derivatization	**Nitrate, Nitrite, MDA**: no statistical significance between sampling times	**Collection method:** Particle mass concentration during welding fume exposure was continuously monitored using a TEOM. Particle number-size distribution and total number were measured using a fast mobility particle sizer. Fumes were analysed with Atomic Absorption Spectrometry (AAS) **PM**: concentration was 6.0 × 105 cm^{-3} (during MIG soldering of Zn); 1.8 × 106 cm^{-3} (during MIG welding of Al) **Constituents of welding fumes**: fumes from MIG soldering of zinc consisted of 60.1% Zn, 16.7% Cu, 0.9% Fe and 0.3% Mn; whereas MIG welding of Al generated fumes	Hartmann *et al* 2014

					that contained 51.4% Al, 4.6% Mg and 0.1% Mn **Ozone**: concentrations below 50 μg m^{-3} (MIG soldering of Zn); 200–300 μg m^{-3} (MIG welding of Al)	
Switzerland 2014	**Welding apprentices** (20)	**TIG**	**EBC collection time**: before exposure, immediately after exposure, 1 h and 3 h post exposure **EBC collection device:** Rtube (Respiratory Research, Atlanta, USA) **Cooling chamber temperature**: –25 °C **Duration of collection**: breathing normally for 10 min into the Rtube while wearing a nose clip. **Sample volume**: up to 2 mL of EBC were recovered and weighed. Approximately 50 µL of EBC were used immediately to assess total reducing capacity **Dilution correction**: N/A **Saliva contamination**: N/A **Sample storage**: BC samples were stored at −70 °C until analysis **EBC analysis**: • Total reducing capacity: measured with an electrochemical redox sensor (EDEL sensor chip/EDELSCAN device) • H_2O_2: ferrous-ion oxidation–xylenol orange assay (FOX assay). • MDA: derivatization with thiobarbituric acid, followed by high-performance liquid chromatography (HPLC) separation and fluorescence detection. • 8-OHdG: N/A (ELISA assay used was not sensitive enough for the collected EBC samples)	**H_2O_2**: < LOD **MDA**: < LOD **8-OHdG**: the ELISA assay used was not sensitive enough to detect its concentrations	**Collection method:** particle concentration and morphology were assessed with Mini Particle Sampler with a copper mesh Transmission Electron Microscopy (TEM) grid attached to an Escort Elf personal pump; a PM_4 Parallel Particle Impactor containing PTFE filter attached to a Leland Legacy personal pump; and the inlet impactor of a DiscMini particle counter **Al:** 0.386 mg/m^3 **W:** 0.205 mg/m^3 **Si:** 0.074 mg/m^3 **Na:** 0.019 mg/m^3 **Mg:** 0.015 mg/m^3 **Ce:** 0.007 mg/m^3 **Fe:** 0.006 mg/m^3	Graczyk *et al* 2016
Sweden 2016	**Welders** (21) With *work-related symptoms* from the lower airways WS (11) With *no work-related symptoms* from the lower airways symptoms WNS (10)	**MAG**	**EBC collection time**: before, during and immediately after exposure. The participants were randomly exposed twice at different occasions either to welding fume or to filtered air respectively, in a double-blind manner in an exposure chamber. Each exposure time was 5.5 h with a lunch break for 1 h after 2.5 h of exposure **EBC collection device:** RTube (Respiratory Research, Charlottesville, VA, USA) **Cooling chamber temperature**: –25 °C **Duration of collection**: the subject took 15 deep breathes into the RTube **Sample volume**: N/A **Dilution correction**: N/A	**LT-B4**: WS (228.0 pg/mL) before exposure had a tenfold higher level of LT-B4 than WNS (29.0 pg/mL) and NWNS 27.0 (pg/mL)	**Collection method:** $PM_{2.5}$ particle mass concentration was monitored with a TEOM. **$PM_{2.5}$**: mass concentration was 1 mg/m^3	Dierschke *et al* 2017

	Controls (11)		**Saliva contamination**: N/A **Sample storage**: condensate was allocated to tubes in amounts of 50 µl each and frozen at –80°C for later analysis **EBC analysis**: leukotriene B4 (LT-B4) by enzyme immunoassay (EIA) kit			
Czech Republic 2018	**Welders** (19) **Controls** (19)	**MAG**	**EBC collection time**: pre-shift and post-shift (welders); one sample (controls) **EBC collection device:** Ecoscreen Turbo DECCS device (Jaeger, Hochberg, Germany) **Cooling chamber temperature**: -20°C **Duration of collection**: 15 min of tidal breathing while wearing a nose-clip **Sample volume**: A minimum volume of exhaled air of 120 L was maintained (monitored via the EcoVent device) **Dilution correction**: N/A **Saliva contamination:** the alpha-amylase concentration was monitored to account for any contamination **Sample storage**: stored at –80°C until analysis **EBC analysis**: oxidative stress markers analyzed after solid-phase extraction (SPE) by liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS)	**Oxidative stress markers**: not significant differences at the two time-points **Oxidation of lipids markers**: only pre-shift MDA and aldehydes C6–C13 were significantly higher in the researchers than controls ($p < 0.5$). Post-shift MDA, aldehydes C6–C13 and 8-iso-PGF2α were elevated compared to controls ($p < 0.05$) **Oxidation of nucleic acid and protein markers**: already significantly elevated in the pre-shift compared to control (p < 0,05); no further increase was observed in post-shift	**Collection method:** Berner low-pressure impactor was used to sample aerosol particles. Particles matter was analysed with optoelectronic method **PM**: median concentration (1.3 x 105 particles/cm³)	Pelclova *et al* 2018
Italy 2015/ 2016	**Welders** (100)	**TIG**	**EBC collection time**: pre-(T0) and post-shift (T1) on a Friday, and pre-shift (T2) on the following Monday morning **EBC collection device:** Turbo-DECCS (Medivac, Parma, Italy) **Cooling chamber temperature**: -5°C **Duration of collection**: 15 min of tidal breathing **Sample volume**: ~ 1.0–1.5 mL **Dilution correction**: N/A **Saliva contamination:** excluded by means of the colorimetric detection of alpha-amylase activity **Sample storage**: stored at –80°C until analysis **EBC analysis**: • H2O2: Amplex® Red fluorimetric assay • 8-isoprostane: enzyme immunoassay • MDA and HNE: LC–MS/MS • Cr, Cr(VI) and Ni: ETAAS with Zeeman background correction	**Ni**: values were generally <LOD µg/L, with no significant differences between the three sampling times **Cr**: levels were significantly lower at T2 (< LOD) than T1 (0.08 µg/L), $p < 0.0001$; and T0 (0.06 µg/L), $p < 0.05$. Cr(VI) was never detected **H_2O_2**: concentrations were significantly higher at T1 (0.25 ± 0.14 µM) than at T0 (0.18 ± 0.10 µM) and T2 (0.16 ± 0.09 µM), but the	**Collection method:** airborne particulates were collected on a mixed cellulose ester membrane. Cr(VI) sampling was carried out using polyvinyl chloride membrane **Cr**: 0.002 mg/m³ **Cr(VI)**: < 0.002 mg/m³ **Ni**: 0.001 mg/m³	Riccelli *et al* 2018

				difference between T0 and T2 was not significant **MDA**: levels were not significantly different between T0 (2.79 nM) and T1 (2.98 nM) but significantly lower at T2 (2.43 nM), and significantly different from T0 ($p < 0,05$) and T1 ($p < 0.0001$) **8-iso**: no significant differences between time-points **HNE**: levels were significantly higher at T0 (0.53 nM) than at T2 (0.51 nM); ($p < 0.05$)		
France, Finland, Italy, Netherland United Kingdom 2019/ 2022	**Occupationally Exposed Workers** (177) **Controls** (98)	SS welding	**EBC collection time**: pre- and post-working week (welders); one sample collected during the working day (control) **EBC collection device:** Turbo-DECCS (Medivac, Parma, Italy) **Cooling chamber temperature**: -5°C **Duration of collection**: 15 min of tidal breathing **Sample volume:** an average of 1-2 ml of EBC **Sample complexation:** the aliquoted EBC sample were 10-fold diluted with 0.5 mM EDTA solution (pH adjusted to pH 8 using 10% v/v ammonia solution) **Dilution correction**: N/A **Saliva contamination**: saliva trap integrated in the collection device **Sample storage**: refrigerated at ~2-8°C **EBC analysis**: measurement of Cr(VI) and Cr(III) using Hyphenated liquid chromatography (LC), micro-LC (µLC) or ion chromatography (IC) system with ICP-MS	**Cr**: median Cr(VI) median values resulted <LOD. A significant difference was found between pre (0.12 µg/L) and post (0.17 µg/L) shift for Cr(III) median concentrations, $p = 0.004$	**Collection method:** a SKC Mini-sampler was used at a flow rate of 0.75 l/min outside the respiratory protective equipment. All the samples were collected for a representative period of the work shift. **Inhalable Cr(VI)** (median and 95th : 0.50 (4.06 µg m^{-3}) **Respirable Cr(VI)** (median and 95th : 0.11 (22.31 µg m^{-3}) (Extrapolated from Santon *et al* 2022)	Leese *et al* 2023
Italy 2019	**Welders** (18) **Controls** (15)	**TIG** **MMA** Submerged Arc welding (**SAW**)	**EBC collection time**: pre-shift on 1st day and post-shift on 5th day of the workweek; one sample in controls (time not specified) **EBC collection device:** Turbo-DECCS (Medivac, Parma, Italy) **Cooling chamber temperature**: -5°C **Duration of collection**: 15 min of tidal breathing	**Cr_2O_3**: median number was significantly higher at post-shift (127,358 particles/mL) than at pre-shift (33,994 particles/mL)	**Collection method:** inhalable particulate matter (IPM) was collected by a personal IOM sampler containing a IOM-cassette fitted with a PVC- filter	Bocca *et al* 2023

		MIG **GMAW**	**Sample volume**: an average of 1-2 ml of EBC **Sample complexation:** aliquoted EBC sample were 10-fold diluted with 0.5 mM EDTA solution (pH adjusted to pH 8 using 10% v/v ammonia solution) **Dilution correction**: N/A **Saliva contamination**: N/A **Sample storage**: refrigerated at ~2-8°C **EBC analysis**: Single Particle Inductively coupled plasma mass spectrometry (SP-ICP-MS) to determine size and particle number concentration of Cr_2O_3, Mn3O4 and NiO nanoparticles	**Mn_3O_4**: no UFPs were found in samples of welders **NiO**: UFP median number was detected only at post-shift (22,000 particles/mL). Controls and pre-shift values were <LOD	**Cr_2O_3**: 5.22 g/cm^3 **Mn_3O_4**: 4.86 g/cm^3 **NiO**: 6.67 g/cm^3	

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Table 2. Metal-specific summary of EBC concentrations and their relation to workplace-air measurements in the included welding studies

Metal	Range of concentrations in EBC	Relationship with workplace-air metal concentration	Reference
Mn	Median (IQR): 4.72 [2.99–17.13] µg/L in welders	Mn-EBC showed a positive association with cumulative exposure indices (CIW[a] and WY[b]) based on duration of welding activity and atmospheric metal measurements (0.08–0.88 mg/m^3)	Hulo *et al* 2014
Ni	Median (IQR): 1.00 [0.84–1.46] µg/L	Ni-EBC showed a positive association with cumulative exposure indices (CIW and WY) based on duration of welding activity and workplace-air metal measurements (0.01–0.07 mg/m^3)	Hulo *et al* 2014
	Median (IQR): 1.12 [<1–2.47] µg/L	Ni was detectable in a subset of respirable air and EBC samples, but no direct air–EBC correlation coefficient was reported	Hoffmeyer *et al* 2012a
	<LOD	Ni-EBC remained mostly <LOD despite low but measurable airborne Ni: median (25th–75th percentile) 0.001 (0.0003–0.006) mg/m^3	Riccelli *et al* 2018
Fe	Median (IQR): 1.48 [0.50–1.94] µg/L	No significant exposure-related difference in Fe-EBC despite higher airborne Fe (0.64–5.58 mg/m^3)	Hulo *et al* 2014
	Median (IQR): 12.02 [6.15–44.96] µg/L	No associations between the Fe concentrations in respirable welding fumes and Fe-EBC after a working shift	Hoffmeyer *et al* 2012a
Cr	Not quantifiable in EBC	Cr was measurable in air (0.01–0.02 mg/m^3) but not in EBC	Hulo *et al* 2014
	Median (IQR): <0.25 [<0.25–0.33] µg/L	An association between Cr-concentration in respirable welding fumes and levels detected in EBC was demonstrated (rs = 0.440, p = 0.013)	Hoffmeyer *et al* 2012a
	Median (25th–75th percentile): - T0: 0.06 [<LOD–0.14] µg/L - T1: 0.08 [<LOD–0.22] µg/L - T2: <LOD (<LOD–0.10) µg/	Total Cr was measurable in EBC at very low airborne total Cr (0.002 [0.0006–0.009] mg/m^3) and showed a workweek pattern, whereas Cr(VI) was never detected in EBC	Riccelli *et al* 2018
	Cr(III): median [range] - Pre-working week 0.12 [<LOQ–0.60] µg/L - Post-working week 0.17 [<LOQ–0.72] µg/L Cr(VI): median [range] - Pre-working week <LOQ [<LOQ-0.53] µg/L - Post-working week <LOQ [<LOQ-0.92] µg/L	Lack of observed correlation between the levels of Cr(VI) or Cr(III) in EBC samples and the other sample matrices collected and analysed within the HBM4EU chromates study (air samples - p < 0.5) (Santonen *et al* 2022)	Leese *et al* 2023

[a] *An individual weekly exposure index (CIW) was calculated for each welder by multiplying the self-reported hours spent welding during the working week by the concentration of atmospheric metal measurements of each matching workstation.*

[b] *An individual cumulative exposure index was also calculated for the total welding years (WY) by multiplying the years of welding by the estimated-exposure peryear (CIW × number of working weeks per year). These two exposure indices werecalculated for each metal studied here (Mn, Ni, Fe, and Cr).*