# HEALTH EFFECTS FROM WELDING EXPOSURES: 2023 LITERATURE UPDATE

Prepared for: The American Welding Society 8669 NW 36th Street #130 Miami, FL 33166-6672

> Document Type: Final Report

Date: January 2025

# **TABLE OF CONTENTS**

1.0	INTRO	ODUCTION	Ν	1-1
2.0	METH	IODS		2-1
	2.1	Search	Strategy	2-1
	2.2	PubMe	ed and NIOSHTIC-2 Searches	2-1
	2.3	Literatu	ure Review	2-1
3.0	EXPO	SURE STU	IDIES	3-1
4.0	HEALTH EFFECTS STUDIES			4-4
	4.1 Studies in Humans		4-4	
		4.1.1	Neurological Effects	4-4
		4.1.2	Respiratory Effects	4-5
		4.1.3	Cancer	4-7
		4.1.4	Eye Effects	4-8
		4.1.5	Musculoskeletal Effects	4-8
		4.1.6	Other Health Effects	4-9
	4.2	1.2 Animal Studies		4-10
	4.3	Mechanistic/cell/In vitro		4-11
	4.4	4.4 Reviews and Risk Assessments		4-13
5.0	REFERENCES			4-1

# List of Acronyms and Abbreviations

AAS	Atomic Absorption Spectrometer
ACGIH	American Conference of Governmental Industrial Hygienists
AiDA	Airspace Dimension Assessment
Al	Aluminum
ALT	Alanine Aminotransferase
AWS	American Welding Society
BAL	Bronchoalveolar Lavage
BMCyt	Buccal Micronucleus Cytome
BN	Brown Norway Rat
BTEX	Benzene, Toluene, Ethylbenzene, Xylene
Cd	Cadmium
CdO	Cadmium Oxide
CI	Confidence Interval
Со	Cobalt
CO <sub>2</sub>	Carbon Dioxide
COPD	Chronic Obstructive Pulmonary Disease
COSHH	Control of Substances Hazardous to Health
Cr	Chromium
CrIV	Hexavalent Chromium
СТ	Computed Tomography
CTWD	Contact Tip to Work Distance
Cu	Copper
CuO	Copper Oxide
DA	Dimensional Allowances
DALY	Disability-adjusted Life Years
DBSI	Diffusion Basis Spectrum Imaging
DNA	Deoxyribonucleic Acid
DTI	Diffusion Tensor Imaging
EF	Emission Factor
EPA	Environmental Protection Agency
EU	European Union
FCAW	Flux-core Arc Welding
Fe	Iron
Fe2O3	Iron Oxide
FEV1	Forced Expiratory Volume in 1 second
FP-XRF	Field Portable X-ray Fluorescence
FVC	Forced Vital Capacity
GMAW	Gas Metal Arc Welding
GSH	Glutathione
GTAW	Gas Tungsten Arc Welding

HBM4EU	European Human Biomonitoring Initiative		
HF	High Fat Diet		
HQ	Hazard Quotient		
ICP-MS	Inductively Coupled Plasma Mass Spectrometry		
IL-8	Interleukin-8		
ILD	Interstitial Lung Disease		
IPD	Invasive Pneumococcal Disease		
LOQ	Limit of Quantification		
MDA	Malondialdehyde		
MEK	Methyl Ethyl Ketone		
MFF	Metal Fume Fever		
Mn	Manganese		
MN	Micronucleus		
Mn304	Manganese Oxide		
MRI	Magnetic Resonance Imaging		
MSD	Musculoskeletal Disease		
MSS	Musculoskeletal symptoms		
NBUD	Binucleated Cells		
ND	Non-detect		
NfL	Neurofilament Light Chain		
Ni	Nickel		
NIOSH	National Institute for Occupational Safety and Health		
NiO	Nickel Oxide		
NMQ	Nordic Musculoskeletal Questionnaire		
NP	Nanoparticles		
OEL	Occupational Exposure Limit		
OHRA	Occupational Health Risk Assessment		
OR	Odds Ratio		
Pb	Lead		
PBM	Peribronchiolar Metaplasia		
PbO	Lead Oxide		
PEF	Peak Expiratory Flow		
PFAS	Perfluoroalkyl Substances		
PFOS	Perfluorooctane Sulfonic Acid		
PGF1a	Phosphatidylglycerol		
PPE	Personal Protective Equipment		
PRL	Prolactin		
Reg	Regular Diet		
RN	Red Nucleus		
ROS	Reactive Oxygen Species		
RR	Relative Risk		
SAW	Submerged Arc Welding		

SD	Sprague-Dawley Rat
SeO	Selenium Oxide
SiO2	Silicon Oxide
SMAW	Shielded Metal Arc Welding
SMR	Standardized Mortality Ratio
Sn	Tin
S1P	Sphingosine-1-phosphate
SOD	Superoxide Dismutase
SWORD	Surveillance of Work Related Occupational Respiratory Diseases
TIG	Tungsten Inert Gas
TLV	Threshold Limit Value
ТР	Total Particulate Matter
TSP	Total Suspended Particulate
TWA	Time-weighted Average
UPDRS3	Unified Parkinson's Disease Rating Scale motor subsection 3
VOC	Volatile Organic Compounds
WF	Welding Fume
WMI	Working Memory Index
Zn	Zinc
ZnO	Zinc Oxide

# 1.0 INTRODUCTION

On behalf of the American Welding Society (AWS), Epsilon Associates conducted a comprehensive literature search and summary of studies related to the health effects of welding. In this update, we included literature published in 2023 (including electronic publications or epubs) but excluded any articles that have been included in previous literature updates. This report describes the literature search methods, provides a summary of the results of our searches (*e.g.*, how many articles we identified), and explains how we identified relevant articles to include in the report (Section 2). We also present summaries of the exposure-related studies in Section 3, and of relevant health effects studies in Section 4.

# 2.0 METHODS

We searched the PubMed database for articles relevant to welding exposures and health effects as described below.

#### 2.1 Search Strategy

- 1. To capture all the potentially relevant literature, the initial keyword searches included the word "welding" or "welders" or simply weld\* (where the "\*" is wild).
- 2. Searches were restricted to the year 2023 either electronically (epubs) or in print. Articles included in previous reviews were excluded from this review.
- 3. Where possible search terms were limited to searches of the titles and abstracts.
- 4. Searches were also limited to full text publications.
- 5. To further limit searches, we used the additional search word "health".

#### 2.2 PubMed and NIOSHTIC-2 Searches

An initial search yielded 1,311 citations. We further refined the search to include "health", and this reduced the number of citations to 412. The 412 citations were uploaded to excel for further screening for relevance. We also searched the NIOSHTIC-2 database using the key words "welding" or "welder" in all fields for the year 2023.

#### 2.3 Literature Review

We reviewed titles to assess the relevance to exposure and health effects from welding and identified duplicates for exclusion. We also excluded commentaries, conference abstracts, and any foreign studies that were deemed to be of little or no relevance. Some of the references were included in the 2022 review and thus not summarized in this report. The remaining citations were retained, and the article titles and abstracts were reviewed for relevance and sorted into the following categories:

- Particle characterization and exposure studies
- Epidemiology and controlled human exposure studies.
- Animal studies
- Mechanistic/cell/in vitro studies
- Reviews and risk assessments

The breakdown of the remaining references by category is listed in Table 2.1.

Study Category	Totals from all databases
Particle characterization and exposure	10
Epidemiology and controlled human exposure	21
Animal	3
Mechanistic/cell/in vitro	5
Reviews and Risk Assessments	6
Overall Total	45

# 3.0 EXPOSURE STUDIES

We identified 10 exposure-related studies or studies related to regulation or health and safety in welding occupational groups published in 2023 (*i.e.*, particle characterization and exposure). Some studies were published online in 2023 (*i.e.*, 2023 was the "epub date") and these were included in our summary. Articles that were not relevant or were included in prior AWS updates were excluded. A brief summary of the exposure abstracts is provided below for all the relevant studies.

Carey *et al.* (2023) conducted an evaluation regarding knowledge of welding health effects, current use of control measures, and interventions needed for health protection for Australian welders. The authors recruited 21 participants and used a semi-structured questionnaire, five focused on-line discussions and five individual interviews to collect information. The results indicated that the design and implementation of interventions for reducing welding exposures requires more knowledge about the barriers of control and the usage of protective equipment. A better understanding of these barriers will help improve the health of workers.

Cortes *et al.* (2023) evaluated welding fume exposures, including of metals absorbed by apprentice welders. Eighty-six apprentice welders from three schools in Montreal, Canada were recruited to participate in the study and measurements were taken while welders performed shield metal arc welding (SMAW). Metals were measured in urine, hair, fingernail and toenail samples that were collected before and after the SMAW training. In a subset of 19 apprentice welders, personal air samples were collected. The results showed elevated levels of manganese (Mn) in urine of geometric mean [GM] =0.31 [0.032-2.84, 5<sup>th</sup> and 95<sup>th</sup> percentiles, respectively]  $\mu g/g$  creat. and in hair of 0.37 [0.46-6.4]  $\mu g$  Mn/g hair in post-shift samples. Post-shift samples of urine also contained higher levels of iron (Fe) and nickel (Ni), 9.4 [3.1-51] and 0.87 [0.35-3.1]  $\mu g/g$  create., respectively. Air samples resulted in median concentrations [5th-95th percentiles] of 29 [4.6-1200], 120 [27-3100] and 0.31 [<LOQ-0.92]  $\mu g/m^3$  for Mn, Fe and Ni, respectively. The results show that short-term exposures in a controlled environment can still result in elevated internal concentrations of metals in welders. The authors will continue the work to assess the impact of longer term exposures.

Freire de Carvalho *et al.* (2024) evaluated 10 years of personal exposure data, including for total particulate matter (TP), hexavalent chromium (CrVI), and manganese (Mn), which were collected from an oil refinery for two welding processes Shielded Metal Arc Welding (SMAW) and Stick and Tungsten Inert Gas welding (TIG). The work environment included ventilation and use of personal protective equipment (PPE), depending on the process used. The goal of the analysis was to determine the effectiveness of these control measures and to obtain quantitative data that could be used to develop exposure models. The results showed that average concentrations of TP, CrVI and Mn were 2.01 mg/m<sup>3</sup> (n = 94), 13.86 µg/m<sup>3</sup> (n = 160), and 0.024 mg/m<sup>3</sup> (n = 95), respectively. The authors found that control measures were adequate for reducing exposures. However, multiple regression analyses indicated that confined spaces contributed to elevated exposures regardless of ventilation used, although local exhaust ventilation was more effective than natural ventilation. Elevated TP concentrations were associated with use of a carbon arc (used for gouging and grinding). A 50-fold higher CrVI concentration and a 2.5 fold higher Mn concentration was observed for stick welding compared to TIG welding. The authors concluded that the results of the analysis would be useful for understanding welding fume exposures in an oil refinery.

Göen *et al.* (2023) determined exposures to perfluoroalkyl substances (PFAS), including 8 perfluoroalkyl carboxylic acids and 4 perfluoroalkyl sulfonic acids in plasma, from workers that are also occupationally exposed to hexavalent chromium (CrVI). A total of 172 workers from four countries were recruited, spanning chrome platers (52), welders (43), surface treatment workers (3), and controls with no CrVI exposure (74). The authors reported significantly different PFAS exposures, specifically for perfluorooctane sulfonic acid (PFOS) across the different occupational groups. The median and maximum concentrations of PFOS were 4.83 and 789  $\mu$ g/l for chrome plating workers, 4.97 and 1513  $\mu$ g/l for welders, and 3.65 and 13.9  $\mu$ g/l for controls. The authors hypothesized that the significantly higher levels of PFOS in chrome platers and welders were likely due to application of PFOS as a mist suppressant in electroplating baths or for other purposes in facilities where welders conduct maintenance or do repair work.

Khan et al. (2023) evaluated exposures to heavy metals, including lead (Pb), cadmium (Cd), and chromium (Cr) in automobile workers in Pakistan. Forty blood samples were collected from three different automobile groups (battery recyclers, spray painters and mechanics) and 10 samples from controls. Samples were analyzed using atomic absorption spectrometer (AAS). Results found that the battery recycling group had the highest Pb levels ( $5.45 \pm 2.11 \mu g/dL$ ), compared to spray painters' group ( $5.12 \pm 1.98 \mu g/dL$ ) and the mechanics' group ( $3.79 \pm 2.21 \mu g/dL$ ). Similarly, Cr concentrations were higher in the battery recycling group, followed by spray painters and mechanics. The authors hypothesized that this was due to the dismantling, griding, and crushing of batteries. However, the mechanics had significantly higher Cd concentrations ( $4.45 \pm 0.65 \mu g/dL$ ), compared to the battery recycling group ( $1.17 \pm 0.45 \mu g/dL$ ) and the spray painters' group ( $1.35 \pm 0.69 \mu g/dL$ ). This is likely due to exposures to welding fumes. The authors concluded that the results would help to develop regulatory measures to protect automobile workers, and future studies should focus on assessing the health impacts of these exposures.

Lee *et al.* (2023) evaluated exposures to total suspended particulate (TSP) and volatile organic compounds (VOCs) in facilities manufacturing welding materials. TSP and respirable particles were measured using a scanning mobility particle sizer and optical particle sizer and using filters to obtain mass concentrations. VOCs were also determined using a gas chromatography mass spectrometer and heavy metals using inductively coupled plasma mass spectrometer. The results showed that average TSP concentrations were  $683.1 \pm 677.4 \,\mu\text{g/m}^3$  with 39% composed of respirable particles. Average concentrations of particles less than 10 um ranged from 11.2 to 22.8 ×  $10^4$  particles/cm<sup>3</sup>, with the majority of the particles (78-86%) with diameters of 10-100 nm. Heavy metals accounted for about 33% of the particulate concentrations. VOC concentrations were greater during the heat treatment combustions compared to the cooling process. Heavy metal concentrations depended on the materials being manufactured. The authors concluded that results indicated increased exposures to particulate matter during the heat treatment process and a higher ratio of heavy metals in dust after completion of the heat treatment process. These results could aid in further protection of workers during these processes.

Newton *et al.* (2023) evaluated the use of a field portable X-ray fluorescence spectrometer (FP-XRF) as a viable option for a more cost-effective and accurate method for assessing welding fume exposures in occupational settings. The method is far easier to use than more conventional methods. The authors compared samples analyzed using FP-XRF and the more common inductively coupled plasma mass spectrometry (ICP-MS). Results showed that there was a strong linear relationship between the two methods (0.72 < r < 0.96), although the FP-XRF method

appeared to overestimate heavy metal concentrations. The authors noted that appropriate correction factors could be calculated for this method to account for the overestimation.

Peng *et al.* (2023) evaluated the use of a screening methodology to determine if certain enrichment of metabolites in blood and urine could be used as markers of welding fume exposure. The authors recruited 49 workers from a machinery manufacturing facility. The authors evaluated statistical relationships between metabolites and metal concentrations from welding fume exposure. The results showed that 30 metabolites increased significantly with exposures to welding fume, and five decreased. Two specific metabolites lysophosphatidylcholine and phosphatidylglycerol (PGF1 $\alpha$ ) were highly correlated with molybdenum in blood and copper in urine, respectively, and could potentially be good biomarkers of welding fume exposures.

Szkudlarek *et al.* (2023) evaluated the use of 3D scans to determine the anthropometric dimensions of 200 workers (151 men and 49 women). The scans were used to determine the dimensional allowances (DAs) for personal protective equipment (PPE) designed for firefighters, mine rescue workers, and welders. The authors were interested in whether the DA was affected by sex, age or body dimensions. The results showed that they are not affected by these features, but remain constant for the type of PPE required for the job. Furthermore, the analysis provided insights into interactions between workers wearing PPE and their environment. DA results were included in an anthropometric atlas of human measurements published in 2023 by CIOP-PIB.

Tsuji *et al.* (2023a) tested whether applying mask fit tests impacted the association between personal time-weighted average (TWA) exposure measurements and metal concentration in blood and urine from welding fumes. The authors obtained blood and urine samples from 94 male welders, and measured 8-hour TWA personal exposures of respirable dust and respirable manganese (Mn). A mask fit test was also conducted using the Japanese Industrial Standard method (T8150:2021). Of the 94 welders, only 54 (57%) passed the mask fit test. The authors reported that only the workers that failed the fit test had blood Mn concentrations that were positively associated with the personal TWA air exposures (8-h TWA of respirable dust; coefficient, 0.066; standard error (SE), 0.028; P = 0.018, TWA of respirable Mn: coefficient, 0.048; SE, 0.020; P = 0.019, 8 h-TWA of respirable Mn: coefficient, 0.041; SE, 0.020; P = 0.041). The authors concluded that the study shows the importance of conducting a mask fit test to ensure that protective equipment is in good working order and will be useful in protecting exposed workers.

# 4.0 HEALTH EFFECTS STUDIES

#### 4.1 Studies in Humans

We identified studies in humans that assessed various health effects related to welding fume exposures. These health effects included neurological effects (5 studies), respiratory effects (7 studies), cancer (2 studies), eye effects (2 studies), musculoskeletal effects (1 study), and other health effects (4 studies). Summaries of these studies are provided below.

#### 4.1.1 Neurological Effects

Alikunju *et al.* (2023) summarized results from a case study of a 40 year old welder that presented with slurred speech and left facial weakness. The patient had worked as a welder in a steel factory for seven years and did not use any personal protective equipment (PPE). A brain computed tomography (CT) scan and magnetic resonance imaging (MRI) scan were taken. The CT scan did not show any hemorrhage indicating a potential stroke, but the MRI showed manganese (Mn) deposition that indicated Mn-induced cerebral toxicity despite normal blood levels of Mn. The patient was treated with intravenous rehydration and counseled regarding proper use of PPE. A follow-up indicated improvement of symptoms with adherence to the use of PPE.

Criswell *et al.* (2023) evaluated neuroinflammation in workers occupationally exposed to manganese (Mn), including 26 welders, 17 non-welders, and 26 controls with no Mn exposure. The participants' exposures were determined using work histories and a specialist completed the Unified Parkinson's Disease Rating Scale motor subsection 3 (UPDRS3) test. The authors also used Diffusion Basis Spectrum Imaging (DBSI) of the brain white matter and basal ganglia to determine if there were differences between Mn-exposed and non-exposed workers. Results showed significantly different DBSI metrics, associated with neurological inflammation in white matter between the exposed and non-exposed workers. DBSI metrics in the basal ganglia were higher in welders compared to controls. Some measures were also significantly associated with higher cumulative Mn exposures and higher UPRDS3 scores, which the authors noted could account for a dose-dependent effect of inflammation associated with motor effects (*i.e.,* clinical parkinsonism). The authors concluded that Mn-exposed workers had clear biomarkers associated with neural inflammation, and that these results could indicate that neural inflammation is part of the pathophysiology of Mn toxicity.

Lee *et al.* (2023) assessed the effects of welding fume exposures on brain structures and associations between exposures to metals and neurobehavioral test scores. A total of 42 welders and 31 control were included in the study. The authors determined metals exposures using work histories and whole blood metal levels. Volume and diffusion tensor imaging (DTI) were used to assess structural changes in the basal ganglia, red nucleus (RN), and hippocampus, and brain metal concentrations were assessed using R1 (as a marker for manganese) and R2\* (as a marker for iron). Neuropsychological testing was also conducted to determine neurobehavioral scores. Results indicated that welders had higher DTI metrics in the hippocampus compared to controls, but not in other regions evaluated. These higher metrics were associated with higher RN R2\*, higher blood lead levels, and lower scores on processing/psychomotor speed, executive function, and visuospatial processing tasks. The authors concluded that future studies should be conducted to specifically investigate the role of lead in the neurobehavioral and hippocampus diffusivity findings in this study.

Tsuji *et al.* (2023b) examined the association between manganese (Mn) exposure and neurological disease in 94 male welders and 95 male controls that worked in Japanese factories. Personal exposure measurements were taken for welders, and all participants provided blood and urine samples that were analyzed for Mn. The authors also conducted neurological function tests. The results showed that workers with lower blood Mn concentrations had higher Working Memory Index (WMI) scores compared to high blood Mn concentrations (Odds Ratio [OR] 2.77; 95% confidence interval [CI], 1.24, 6.19; P = .013). The association between WMI and blood Mn levels was statistically significant and highest in welders (OR, 3.73; 95% CI, 1.04, 13.38; P = .043) compared to non-welders (OR, 2.09; 95% CI, 0.63, 6.94; P = .227). The authors concluded that there was evidence of neurological dysfunction associated with blood Mn levels, especially in welders, but more work was needed to better understand this relationship.

Wu *et al.* (2023) investigated the association between exposures to heavy metals and neurological damage by evaluating metal concentrations in urine and biological markers of neural damage. The authors recruited 186 steel mill workers. The biomarkers evaluated included neurofilament light chain (NfL), sphingosine-1-phosphate (S1P), prolactin (PRL), and dopamine (DA). Associations between metal concentration in urine and these biomarkers were evaluated using different statistical methods. The authors found significant associations between nickel and NfL, S1P and DA, between iron and cobalt and PRL, and between lead and S1P. They also reported some interactions between the biological markers and zinc, arsenic, and strontium, although zinc appeared to be protective of neurological damage. The authors concluded that study results provided evidence of a potential link between exposures to heavy metals and neurological damage, specifically for nickel, cobalt, iron, and lead.

# 4.1.2 Respiratory Effects

Duan *et al.* (2023) evaluated factors that influence the development and survival of patients with pneumoconiosis in Jiangsu Province in China. Disease burden and survival rates were determined using life tables and statistical methods (*e.g.*, Cox model). Results showed that average survival was 16 ± 10 years, and factors that impacted survival included the age and the stage at diagnosis. The calculated disability-adjusted life years (DALYs), which is a measure of disease burden and quantifies the number of years lost due to disability or early death, was greatest for silicosis at 99,807 person-years (64.60%), followed by coal worker pneumoconiosis at 35,483 person-years (22.97%), and lastly welder's pneumoconiosis at 37,85.83 person-years (2.45%). The authors concluded that although pneumoconiosis cases are decreasing due to improvements in health policies, this remains an important health issue.

Fikayo *et al.* (2023) assessed the association between welder's exposures and respiratory illness in Nigeria. The authors recruited 142 welders and 142 controls in this cross-sectional study. Respiratory parameters were determined using lung function tests and clinical assessments. Statistical analyses were used to determine associations. The authors reported that measured levels of chromium, nickel, manganese, carbon monoxide and nitrogen dioxide in working environments exceeded health-based regulatory guidelines. In addition, respiratory parameters were statistically significantly lower in welders compared to controls, including forced expiratory volume in the first second (FEV1) [2.62±0.7 vs. 2.81±0.7, p<0.05] and the ratio of FEV1 to forced vital capacity (FVC)[ 75±13.7 vs. 80.7±8.0, p<0.001]. The authors concluded that the study found respiratory function was impaired in exposed welders, and this could be due to exposures to metals and gases that were elevated above the recommended levels as well as lack of use of

personal protective equipment and proper ventilation. Enforcement of workplace safety standards was recommended.

Fishwick *et al.* (2023) investigated the potential cause and incidence of irritant asthma among workers in the United Kingdom (UK). The authors analyzed data collected through the UK-based Surveillance of Work-related Occupational Respiratory Diseases (SWORD) initiative. Data were summarized over 5-year periods starting in 1999 and included potential exposures, job, work sector and disease incidence rates. The authors reported a total of 307 actual cases and 1066 estimated cases. Based on the actual cases the mean age was 46 years (standard deviation of 17.8), with 71% of the cases were males. Overall, the asthma incidence rates decreased from 1.98 per million cases in 1999 – 2003 to 0.56 per million cases in the most recent 5 year period. About eleven occupations were associated with six or more cases, and thirteen different exposure agents were associated with five of more cases, including welding fumes (n=7). The largest number of cases were associated with acids (n=23), smoke (n=25), and cleaning agents (n=39). The authors concluded that despite lower incidence rates of asthma in more recent years, this remains a health concern, with cleaning agents accounting for a large portion of the incidence numbers.

Jung *et al.* (2023) presented a case of peribronchiolar metaplasia (PBM) that is commonly observed in interstitial lung disease (ILD). Normally attributed to tobacco smoke, the authors present a case in a welder that had supportive clinical, radiographic and histological evidence. The authors present this case and proposed a diagnosis based on their experience and consultation with other specialists.

Petersson Sjögren et al. (2023) assessed the lung health of welders and the use of sensitive methods that could help in the early diagnosis of chronic obstructive pulmonary disease (COPD). The authors recruited 28 welders and 17 controls to participate in the study. Lung function tests were performed using standard spirometry as well as new methodology such as airspace dimension assessment (AiDA) and oscillometry. In addition, the authors collected blood samples to assess biomarkers of lung damage (club cell secretory protein 16, surfactant protein D, matrix metalloproteinases, fibroblast, hepatocyte growth factor, interleukins) and urine samples to measure a single biomarker (desmosine). Standard lung function test results did not show any differences between the welders and controls. Novel methods, however, did show significant changes, including higher respiratory system resistance based on oscillometry and higher levels of some blood biomarkers (metalloproteinases 9 and hepatocyte growth factor) compared to controls. Increased levels of certain biomarkers were also correlated with the number of welding years and airspace dimension results were also correlated with lung inflammatory markers. The authors concluded that new lung function methods and use of biomarkers of lung injury could be helpful in early detection of respiratory disease in workers, when traditional spirometry cannot detect any changes.

Riccò *et al.* (2023) investigated the occurrence of pneumococcal infection and invasive pneumococcal disease (IPD) among welders. The authors conducted a comprehensive literature search of PubMed, Embase and MedRxiv databases for any studies that evaluated pneumococcal infections or IPD in welders or workers with potential metals exposures. Of the 854 studies, 14 met the inclusion criteria for the meta-analysis. These studies included eight retrospective studies (1980-2010) and six studies of workers in the shipbuilding industry (2017-2020). The results indicate that welders are at an increased risk of developing IPD compared to non-welders (odds ratio [OR]: 2.59, 95% CI 2.00–3.35, p = 0.58) as well as increased mortality due to IPD (standardized

mortality ratio [SMR]: 2.42, 95% CI 1.96-2.99, p = 0.58). Based on results of serotyping the authors reported that of the 72 cases, 60.3% were serotype 4, 19.2% serotype 12 F, and 8.2% serotype 8. The authors concluded that given the increased risks, welders should be given the pneumococcal vaccine considering the most common serotypes in order to reduce infection among the workers.

Saadiani et al. (2023) evaluated the pulmonary health of welders working in the automotive sector. The authors initially recruited 2400 male participants, 1200 exposed to welding fumes and 1200 administrative workers (controls). Workers with welding exposure had at least a year of exposure. After considering inclusion criteria and matching the exposed and nonexposed groups, a total of 1152 exposed and 1152 nonexposed (controls) were evaluated. A trained pulmonary technician conducted lung function tests using a calibrated spirometer to assess different lung function parameters, including Forced Vital Capacity (FVC), Forced Expiratory Volume in the first second (FEV1), FEV1/FVC, Forced Expiratory Flow at 25-75% pulmonary volume (FEF25-75, and Peak Expiratory Flow (PEF). A questionnaire was also used to collect demographic information, employment histories, smoking habits, history of respiratory disease and respiratory symptoms. Lastly, personal air samples were collected using the NIOSH 7300 method to measure levels of iron (Fe), copper (Cu) and lead (Pb). Statistical analyses were conducted to determine associations between lung function and respiratory symptoms and welding fume exposures, comparing exposed and non-exposed groups. The average age of the exposed and non-exposed workers was 38 years old. Exposed workers had average exposures of 0.11, 0.01, and 1.4 mg/m<sup>3</sup> for Cu, Pb and Fe, respectively. These levels do not exceed occupational exposure limits, which are 0.2, 0.05, and 5 mg/m<sup>3</sup> for Ci, Pb, and Fe, respectively. Results showed that exposed workers had a significantly higher percentage of respiratory symptoms than non-exposed workers, including cough (25 % vs 12%), sputum (20% vs 3%), and wheezing (2 % vs 1 %). In addition, exposed workers had significantly lower pulmonary function scores compared to non-exposed controls (e.g., FEV1 96% vs 102%). It is worth noting that exposed workers were comprised of a higher percentage of smokers than non-exposed workers (23% vs 15%), which could contribute to the pulmonary function differences. The authors, nonetheless, concluded that the study shows that there is a potential for pulmonary impacts associated with welding fume exposures even when measurements do not exceed occupational standards. Education of workers on the risks and use of personal protective equipment, therefore, was recommended for the automotive industry.

#### 4.1.3 Cancer

Chen-Xu *et al.* (2023) evaluated the current burden of lung cancer among European Union (EU) workers (excluding the United Kingdom) exposed to hexavalent chromium (CrVI) and the impact of the EU lowering the occupational exposure limit (OEL) to 5  $\mu$ g/m<sup>3</sup> from the current limits of 10  $\mu$ g/m<sup>3</sup> (general limit) and 25  $\mu$ g/m<sup>3</sup> (welding industry limit). The authors collected data from the Global Burden of Disease (2019 study) and Eurostat to estimate the lung cancer cases that are attributed to CrVI exposures, and calculated disability-adjusted life years (DALYs) and associated health care costs under different scenarios based on different OELs. The authors reported a total of 253 lung cancer cases and 4,684 DALYs that could be attributed to CrVI exposures in the EU under current OEL standards. If the standard was lowered to 10  $\mu$ g/m<sup>3</sup> across all industries, this would yield a decrease of 43 cases and 797 DALYs. Lastly if the new OEL was applied, this would result in a reduction on 148 lung cancer cases and 2,746 DALYs. Current health care costs associated with CrVI lung cancer cases were estimated to be about 12.5 million euros/year and up to 40 million when considering DALYs, which would be reduced to 5.2 million and up to 16.6 million

considering DALYs with the adoption of the new OEL. The authors concluded that the analysis presents what the potential impacts could be given different OELs and makes a case for reducing these limits.

Soltanpour *et al.* (2023a) assessed the cancer risks from welding fumes and how they differ depending on the welding process. Personal samples of air were collected from 31 welders to measure concentrations of iron (Fe), chromium (Cr), and nickel (Ni) during arc, argon, and carbon dioxide (CO<sub>2</sub>) welding. Measured air concentrations were compared against the American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour Time-Weighted Average Threshold Limit Value (TLV). The authors reported that  $CO_2$  welding resulted in lower Ni, Cr, and Fe concentrations compared to TLVs. However, levels of Cr and Fe were higher than TLVs for argon welding and levels of Ni and Fe were higher than TLVs with arc welding. The authors also found high non-cancer risks (hazard quotient >1) from exposures to Ni and Fe. No risk results were reported. Authors noted that results indicate potential health risks and the need for preventive measures to reduce exposures.

#### 4.1.4 Eye Effects

Belete *et al.* (2023) assessed the risks of eye injuries and the practices of using eye protection in welders in Gondar city, Ethiopia. The authors recruited 403 welders in this cross-sectional study in July 2021. A questionnaire was used to collect information on the knowledge, use, and attitudes regarding personal protective equipment (PPE) as well as on any reported eye injuries. Statistical analyses were used to calculate odds ratios. The authors reported that out of 396 welders that participated in the study, 82% had no job training and 33% reported eye injuries. Most of the welders (86%) had access to PPE, but good knowledge of PPE use and a positive attitude were found in only 48% and 61% of workers, respectively. Adequate PPE use was found in 57% of the workers, and the factors that contributed to the proper use of PPE included work experience, job training, and history of eye disease. The authors concluded that use of PPE among welders in Ethiopia was fair, and more could be done to increase use of PPE, including job training.

Nakashima *et al.* (2023) evaluated the risk of developing photoretinopathy from blue light exposure during gas metal arc welding of mild steel under different conditions. The authors measured the spectral radiance of the arcs to quantify exposures to blue light (based on American Conference of Governmental Industrial Hygienists [ACGIH] methods). The authors reported a range of blue light levels between 5.0 and 118 W/cm<sup>2</sup>/sr, which are considered to be hazardous based on ACGIH guidelines. Increased blue light was found with higher welding currents and with the use of pulsed currents compared to a steady current. The type of shielding gas was also found to influence the level of blue light. The authors concluded that study results confirm the hazards associated with exposures to blue light during arc welding and stress the need to ensure proper eye protection and safety procedures to reduce risks of eye injury.

# 4.1.5 Musculoskeletal Effects

Bamidele *et al.* (2023) assessed the prevalence of musculoskeletal disease (MSD) and most impacted parts of the body in a group of 142 welders compared to 136 security officers that served as the control group in Nigeria. The authors used the Nordic Musculoskeletal Questionnaire (NMQ). The mean age of both groups was 37 years old. With regards to welding histories, about 41% of the welders had less than 10 years of experience, 50% worked six days a week, and more

than half (55%) worked over 8 hours a day. Among the MSD symptoms, back pain was significantly higher in welders compared to controls (75% vs. 34%) followed by knee pain (32% vs 16%). The authors concluded that MSD was more prevalent in welders, with the back being the most affected area of the body. MSD can be prevented with proper training and education.

### 4.1.6 Other Health Effects

Bagheri Toolaroud *et al.* (2023) evaluated data on work-related burn injuries. The authors collected records from a burn center in Iran between 2011 and 2020. Work-related burns accounted for about 5% of the 9,220 cases that were investigated, with work-related burn cases increasing every year. The mean age of the cases was 38 years old and most of the cases were male (88%). Burn injuries to the upper body were most common (29%) and the most common cause was fire (62%). The average length of stay at the hospital was 10 days and the mortality rate was 11%. The top three occupations that resulted in burn cases included food preparation (25%), welding (17%) and electrical work (14%). The authors concluded that this study would help to develop preventive programs for specific industrial sectors to minimize burn risks.

Onyeso *et al.* (2024) assessed whether there was a correlation between aluminum (Al) concentrations in blood and various measurements of physical and mental health. The authors recruited 50 welders and 50 non-welders that were age and location matched. Blood levels of Al were collected and analyzed using atomic absorption spectrometry. The authors also collected blood pressure, body mass index data, and applied questionnaires to assess pain, cognition (General Practitioner Assessment of Cognition), quality of life (WHOQoL-BREF), and musculoskeletal symptoms (MSS, Nordic musculoskeletal symptoms questionnaire). The authors reported significantly higher blood Al levels, significantly lower quality of life scores, and higher prevalence of MSS of the neck, shoulder, upper back and knees in welders compared to non-welders. Of specific interest was a significant association between high blood Al levels and higher systolic blood pressure. The authors recommended that workers be screened regularly for blood Al levels and any adverse health conditions.

Su *et al.* (2023) assessed the health of workers in an automobile manufacturing facility in Guangzhou City, China. The study included 636 welders and 757 assembly workers. The authors assessed pulmonary function, evidence of hearing loss, conducted digital radiography chest x-rays, and tested for blood biomarkers of disease (*e.g.*, alanine aminotransferase or ALT to test for liver damage). Statistical analyses were conducted to test differences between welders and assembly workers and to evaluate associations between health and number of years of work. The authors reported that noise levels were similar among welders and assembly workers, but welders had higher rates of hearing loss, chest x-ray abnormalities, reduced pulmonary function, as well as higher blood biomarkers of disease compared to assembly workers. The rate of chest x-ray abnormalities increased with the number of years of welding work, and the authors also found positive associations between rates of hearing loss and reduced pulmonary function as well as chest x-ray abnormalities in welders. The authors concluded that welders were at increased risk of both hearing loss and pulmonary disease in the automobile industry.

Kang *et al.* (2023) assessed associations between occupational exposures and metabolic syndrome, which is a group of conditions occurring together that can lead to heart disease, stroke or diabetes and include insulin resistance, obesity, high blood pressure, and high serum triglycerides. The authors conducted a retrospective evaluation of over 31,000 patients from a

National hospital in Korea from 2012-2021. Data collected included demographics, life style factors, and occupational exposures to 19 volatile organic compounds, 13 metals and dust. Hazard ratios were calculated using Cox regression analysis. The authors found that risks factors that contributed to increased metabolic syndrome included exposures to several metals (copper, antimony, lead, manganese, and iron) and welding fume. In addition, risks were higher in night shift workers and workers exposed to noise. The authors concluded that working conditions should be evaluated to assess whether exposures could be reduced in order to prevent disease development.

#### 4.2 Animal Studies

We identified three studies in animals that assessed health effects related to welding fume exposures.

Roach et al. (2023) conducted an animal study to determine the impact of multiple factors (genetics, lifestyle factors and occupational exposures) on pulmonary inflammation and systemic immunity. Two different strains of rats were used – male Sprague-Dawley (SD) and Brown Norway (BN) and fed a regular (Reg) or high-fat (HF) diet for 24 weeks. At 7 weeks (baseline period), some of the rats were euthanized and baseline samples were collected. The remaining rats were exposed to stainless steel welding fume (WF) or filtered air (control) until week 12 (exposure period). At week 12, additional rats were euthanized to collect "exposure" samples. The remaining rats were allowed to recover for 12 weeks (recovery period) and were then euthanized to obtain "recovery" samples. At each of the timepoints, blood and serum samples, bronchoalveolar lavage (BAL) samples, and lymphoid tissue samples were collected for analysis. Welding fume was characterized by inductively coupled plasma-atomic emission spectroscopy (NIOSH Method 7300) and was composed of Fe (53%), Cr (17%), Mn (24%), Ni (6%), and Cu (0.4%) [metals by % weight]. The mass median diameter of the particles was 0.26 um with a geometric standard deviation of 1.5 um. The WF exposure concentrations were set to represent 2-4 times the Threshold Limit Value (TLV, 5 mg/m3) for a welder over an 8 hr shift or were 1200 mg/m3 (20 mg/m<sup>3</sup> x 3 hr/day x 4 days/week x 5 weeks). Actual measured average concentrations were about 20 mg/m<sup>3</sup>. White blood cell counts were determined from blood samples, markers of inflammation and immune cells were determined from the BAL, and from harvested lymph nodes and spleens. Statistical analyses were performed to assess associations between inflammatory and immune parameters and exposures at the various time-points and for the different strains and diets. The authors reported the expected weight gain for rats on the HF diet, however in SD rats, WF appeared to suppress weight gain, particularly in the rats on the Reg diet. Overall, the study demonstrated that strain (*i.e.*, genetics) predominantly influenced inflammation and immune response, followed by a combination of exposure (with a slight increase for the rats on the HF diet), and a combination of strain and diet with recovery. Diet alone had a significant impact on inflammatory parameters at week 7 of the study, particularly in SD rats. In both rat strains, WF exposure resulted in acute airway inflammation as observed by an increase in several inflammatory markers (e.g., increased BAL cell and neutrophil number), with HF diet impacting the inflammatory response more in exposed SD rats. Specifically, SD rats were generally more susceptible to WF exposures and this was related to enhanced immune response in these rats from diet alone. Recovery from exposure, however, differed between the two strains, with BN rats showing a slower recovery, particularly in the HF diet group. The authors concluded that the study highlights the impacts of both genetics and diet on the severity of WF-induced lung injury and systemic inflammatory response as well as recovery and that a better understanding of these interactions can lead to a better capacity to identify individuals and populations that might be at increased risks of disease.

Sutunkova *et al.* (2023) evaluated the toxicity of different metal suspensions by exposing female albino rats to doses of 0.25 to 0.5 mg *via* intratracheal instillation and measuring different biomarkers of disease in bronchoalveolar lavage (BAL) samples taken 24 hours after exposure. The suspensions evaluated included copper oxide (CuO), lead oxide (PbO), cadmium oxide (CdO), iron oxide (Fe2O3), nickel oxide (NiO), silicon oxide (SiO2), manganese oxide (Mn3O4), and selenium oxide (SeO) nanoparticles (NP) that were obtained from laser ablation. The authors reported differential toxicity depending on the nanoparticulate composition at the two dose levels. The cytotoxicity of the suspension was as follows : CuO NPs > PbO NPs > CdO NPs > NiO NPs > SiO<sub>2</sub> NPs > Fe<sub>2</sub>O<sub>3</sub> NPs at 0.5 mg, with CuO NPs showing the greatest toxicity and Fe2O3 NPs showing the least toxicity. The pattern was different at 0.25 mg : NiO NPs > Mn<sub>3</sub>O<sub>4</sub> NPs > CuO NPs > SeO NPs, with NiO NPs having greater toxicity and selenium oxide having the least toxicity. In addition, the authors found that toxicity increased in a non-linear fashion with dose. Overall, the authors concluded that biomarkers of disease in BAL samples can be used to assess the differential toxicity of metals exposures.

Szűcs-Somlyó *et al.* (2023) assessed potential immunological pathways related to development of metal fume fever (MFF) from inhalation of metal particles, in this case specifically zinc oxide particles (ZnO). The authors exposed BALB/c mice to ZnO particles at an average concentration of 0.53 ppm or 1.76 mg/m<sup>3</sup> for 4 hours a day for 3 days. The authors collected samples from the lungs and lymph nodes 3 and 12 hours post-exposure and analyzed them for a number of inflammation-related biomarkers and genes. The authors reported a large increase in inflammatory biomarkers after exposures at the two time points. Overall, the authors concluded that the data contribute to insights regarding the immunological response to exposures that can contribute to MFF and the potential for development of allergic asthma, but more research is needed to gain a better understanding of these mechanisms.

#### 4.3 Mechanistic/cell/*In vitro*

We identified 5 mechanistic/cell/*in vitro* study that evaluated the potential health effects of welding fume exposures.

Akram *et al.* (2023) analyzed blood samples collected from workers in different industrial sectors (n=50 per industry) including brick kiln, welding, furniture and paint industries, along with controls matched by age and gender. Blood lead levels were determined along with levels of different genes related to DNA repair (XRCC1, PARP1) and lead toxicity (*i.e.*, reduced ALAD), as well as biomarkers of oxidative stress which can damage DNA. The authors reported increased expression of DNA repair genes and decreased ALAD expression (indicating lead toxicity) in exposed workers compared to controls. Similarly, increased oxidative stress biomarkers were found in exposed workers. The authors did not specify which industries had the highest effects, although exposed workers had even higher levels of DNA repair gene expression. Gene expression was highly correlated with age, exposure duration, exposure per day, and lead concentrations. The authors concluded that results show increased risk of DNA damage in exposed workers, with both increased concentrations of biomarkers of oxidative stress and deregulation of DNA repair enzymes.

Nwogueze *et al.* (2024) evaluated the effects of welding fume (WF) exposures, specifically levels of zinc (Zn) and copper (Cu) in blood and oxidative stress biomarkers (glutathione S-transferase [GSH], malondialdehyde [MDA], superoxide dismutase [SOD]), considering smoking as a potential related risk factor. The authors recruited 20 welders and 20 non-welders, with each group

comprised of 10 smokers and 10 nonsmokers. The authors found that the combination of smoking and WF exposure was associated with a significant increase in zinc and copper levels in blood, compared to the respective controls. Some of the oxidative stress markers were also significantly increased in welders that smoked including GSH compared to all other groups and SOD compared to nonsmoking welders. The authors concluded that the combination of smoking and exposures to WF can result in increased oxidative stress and contribute to adverse health effects.

Soltanpour *et al.* (2023b) conducted a case-control study including 34 welders and 34 controls to evaluate associations between welding fume (WF) exposures and DNA damage. DNA damage was assessed using the buccal micronucleus cytome (BMCyt) assay to measure concentrations of different markers of DNA damage including differentiated cells with micronucleus (MN), and binucleated cells (NBUD). The authors reported higher levels of MN and NBUD levels, indicating higher levels of DNA damage in welders compared to controls. The highest levels were found in arc welders, followed by argon and lastly CO<sub>2</sub> welders. The authors concluded that measures were needed to reduce exposures to WF in order to prevent potential adverse health outcomes.

Wu et al. (2023b) determined the association between personal exposures to metals, metal concentrations in urine, and serum levels of adiponectin in male workers from a shipyard in northern Taiwan. Lower levels of adiponectin, an adipose-derived hormone, have been correlated with an increased risk of metabolic syndrome, including obesity and insulin resistance. A total of 100 welders and 31 controls were recruited over a period of 2 years. The authors used questionnaires to obtain demographic information, information on lifestyle factors, and a work history (including use of personal protective equipment [PPE]). Urine and fasting blood samples were collected after one day of exposure. Personal air measurements were conducted over an 8hour period. Statistical analyses were applied to determine associations between exposed workers and controls. Air metal concentrations were higher in exposed workers, with iron (Fe) concentrations over 130 fold higher in welders than controls, followed by manganese (Mn, 82 – fold higher in welders), copper (Cu) and chromium (Cr) about 20 times higher, and other metals 17 times higher or less. With regards to concentrations of metals in urine, although levels were higher in welders, the differences were not statistically significant. Of note, all welders selfreported using PPE. The authors reported significantly lower concentrations of serum adiponectin associated with urine metal concentrations in welders, specifically Cr, Mn, cobalt (Co), nickel (Ni), zinc (Zn), cadmium (Cd) and lead (Pb), but not in office workers. Of all the metals, the authors found that Pb had the greatest impact on adiponectin, although Co and Cr also contributed a significant amount in analyses that included all metals. The authors concluded that there was a significant link between occupational exposures and an important biomarker (adiponectin) associated with metabolic disorders, and that Pb was a significant contributor.

Xia *et al.* (2023) conducted a study using human alveolar lung A459 epithelial cells exposed to nanosized particles of iron (Fe) and manganese (Mn) at concentrations of  $100 \mu g/m^3$  for 6 hr. The authors assessed cell cytotoxicity, generation of reactive oxygen species (ROS), and expression of genes related to inflammation and oxidative stress after exposure. Results showed that exposure to the nanoparticles decreased cell viability and increased formation of ROS. In addition, exposures resulted in increased expression of genes involved in inflammatory responses and oxidative stress. In particular, interleukin-8 (IL-8) was found to be significantly increased. IL-8 is a key cytokine involved in the inflammatory response in the lungs. The authors concluded that the results provide further insight into mechanisms of lung toxicity associated with metals exposures.

#### 4.4 Reviews and Risk Assessments

We identified six reviews or risk assessments that summarized the potential health effects of welding fume exposures.

Evans and Masullo (2024) reviewed the benefits of manganese (Mn) as well as the toxic effects. The authors noted that Mn is an essential element that is involved in various functions in the human body, including immune function, regulations of energy consumption, coagulation and mechanisms of removal of oxidative stress byproducts. Trace amounts of Mn that the body needs typically come from plants and drinking water, although sometimes from vitamins. For infants, breast milk is a source of Mn. Toxic levels of Mn occur from contaminated drinking water, occupational exposures (*e.g.*, from welding, smelting and mining), accidental exposures, including from medical therapy. The toxic effects of Mn result in manganism, symptoms of which resemble Parkinson's disease. The metal is well absorbed through the intestinal tract, and depend on dietary intakes and modulated by biliary and pancreatic metabolisms.

Khalili *et al.* (2023) assessed the cancer and noncancer risks associated with exposures to heavy metals including cobalt (Co), cadmium (Cd), nickel (Ni), lead (Pb), manganese (Mn) and hexavalent chromium (CrVI), volatile organic compounds (VOCs) including benzene, toluene, ethylbenzene, xylene (BTEX), and methyl ethyl ketone (MEK) from aircraft maintenance, repair, and overhaul. The authors measured concentrations of metals and VOCs at 51 workstations. The results showed that concentrations of Cd, Pb and VOCs were below occupational exposure limits (OEL). Concentrations of Co, Ni, Mn and CrVI exceeded OELs. Cancer risks associated with CrVI were highest in the plating workshop, and lowest based on Pb exposures in the electronic workshop. Co exposures in the welding workshop were associated with highest noncancer risks, and the lowest noncancer risk were associated with toluene exposures in the fabrication workshop. The authors concluded that given the measured concentrations that exceeded OELs and increased health risks, preventive measures should be implemented to reduce exposures.

Pourhassan et al. (2024) conducted a human health risk assessment of welding fume exposures in a cross-sectional evaluation of welders in a gas refinery in Iran. Air samples were collected using the National Institute for Occupational Safety and Health (NIOSH) method 7300 and analysis for heavy metals including tin (Sn), zinc (Zn), aluminum (Al), iron (Fe), cadmium (Cd), lead (Pb), copper (Cu), manganese (Mn), nickel (Ni), chromium (Cr), and arsenic (As) using inductively coupled plasma mass spectroscopy (ICP-MS). The authors applied different risk assessment methods to evaluate health risks (Malaysia's method, Control of Substances Hazardous to Health Essentials (COSHH model), Chinese OHRA standard (GBZ/T 298-2017), US EPA method). Monte Carlo simulations were used to evaluate uncertainty associated with model inputs. To compare the results across the different risk assessment methods, all results were converted to a risk ratio (RR) which was determined based on the risk level and the total number of levels for each risk assessment method. The authors reported that the highest concentrations were for Fe (1.04 mg/m<sup>3</sup>) and the lowest metal concentrations were for As (2.17  $\mu$ g/m<sup>3</sup>). All metal concentrations except for CrVI were below American Conference of Governmental Industrial Hygienists (ACGIH) occupational exposure limits (OELs). With regards to carcinogenic risks, CrVI was associated with the highest cancer risks overall across all risk assessment methods. Other heavy metals identified as having increased health risks include Al and Ni, with high noncancer risks based on the US EPA methods. Overall, the authors noted that implementation of good ventilation and reducing exposure time would help to reduce health risks associated with welding fume exposures.

Quecke et al. (2023) reviewed the development of emission factors (EFs) used to characterize welding fume formation for different processes. The review includes research that was used to develop the US EPA AP-42 EFs for welding emission from 1995 and more recent research. The authors found that fume formation is complex and the development of EFs is complicated by the multiple factors that affect fume composition including the welding process (over 80 types), the welding rod, filler metal, base metal, coating composition, as well as the experience level of the welder. In particular, the welding consumables can be quite variable and significantly influence the composition of the fume. US EPA AP-42 EFs are available covering 20 different shielded metal arc welding (SMAW) electrodes, seven gas metal arc welding (GMAW) electrodes, six flux core arc welding (FCAW) electrodes and one submerged arc welding (SAW) for PM<sub>10</sub> and six metal constituents (chromium, hexavalent chromium, cobalt, manganese, nickel and lead). The authors found additional summaries of comprehensive studies that provided EFs for GMAW processes, specifically focused on the influence of operating parameters (current, voltage, shielding gas, Contact Tip to Work Distance (CTWD) and welding speed) and using both stainless and mild steel. Similarly, the authors summarize work conducted to develop additional EFs for SMAW. The authors noted a lack of much additional data for FCAW and Gas Tungsten Arc Welding (GTAW). Specifically, they noted that FCAW tends to generate significantly higher fume emissions compared to other processes, including higher emissions of hazardous metals such as manganese, chromium and nickel. Overall, the authors summarized key research on EFs available since the publication of US EPA AP-42 factors, although research gaps remain. Reliable and relevant EFs are needed in order to support exposure assessment efforts when measurement data are not available.

Soltanpour *et al.* (2023c) conducted a systematic review and risk assessment evaluation of welding fume exposures based on studies conducted in Iran from 1900 to 2020. The authors applied the US EPA risk assessment methodology and conducted simulations using Monte Carlo methods. The authors reported average concentrations of metal fumes from gas welding to range from 1.8 to 1,060  $\mu$ g/m<sup>3</sup> and from arc welding 55 to 4,880  $\mu$ g/m<sup>3</sup>. Heavy metal concentrations from gas welding were all below the American Conference of Governmental Industrial Hygienists (ACGIH) occupational exposure limits except for manganese (Mn), and for all metals for arc welding. Excess noncancer risks were associated with Mn and nickel for both gas and arc welding, and cadmium for gas welding only. Excess cancer risks were found for nickel in both gas and arc welding. To reduce these health risks, the authors concluded that preventive measures were needed.

Zhang *et al.* (2023) evaluated the health risks associated with exposure to welding fume and heavy metals in five electronic manufacturing facilities in Hangzhou, China. The authors collected a total of 76 air samples across the facilities. The results showed that welding workshops had elevated levels of welding fume 8-h time weighted average (8 h-TWA) range 0.29 to 6.28 mg/m<sup>3</sup>, manganese range non-detect (ND) to 0.83 mg/m<sup>3</sup>, and iron range 0.027 to 2.23 mg/m<sup>3</sup> compared to non-welding workshops. Interestingly, the non-welding workshops had elevated copper concentrations (average of 8 h-TWA 0.41 mg/m<sup>3</sup>) compared to the welding workshop, and these levels exceed permissible occupational limits. In addition, relative risks (RR) for several metals were higher in the welding workshops, including lead (Pb, 2.4 vs 1.7), manganese (Mn, 2.0 vs 1.4), and iron (Fe. 1.4 vs 1.0), whereas for copper the RR was higher in the non-welding workshop (1.0 vs 2.2). Mean excess lifetime cancer risks were not overly elevated welding (5.59E - 06 per 1000 people) and non-welding (1.88E - 06 per 1000 people). However, the mean non-cancer risk or hazard quotient (HQ) for manganese was elevated in both the welding (HQ=164) and non-welding (HQ=11) workshops. The authors concluded that workers in this industry had elevated health risks

and would benefit from workplace controls such as more efficient ventilation and reducing working hours to reduce exposures.

- Akram Z, Mahjabeen I, Batool M, Kanwal S, Nawaz F, Kayani MA, Rizwan M. Expression deregulation of genes related to DNA repair and lead toxicity in occupationally exposed industrial workers. Int Arch Occup Environ Health. 2023 Dec;96(10):1333-1347. doi: 10.1007/s00420-023-02012-4. Epub 2023 Oct 7.
- Alikunju M, Misiriyyah N, Sayeed Iqbal S, Khan M. Manganese Neurotoxicity as a Stroke Mimic: A Case Report. Cureus. 2023 Apr 7;15(4):e37247. doi: 10.7759/cureus.37247.
- Bagheri Toolaroud P, Attarchi M, Afshari Haghdoust R, Feizkhah A, Esmailzadeh M, Rimaz S, Pirooz A, Mobayen M. Epidemiology of work-related burn injuries: A ten-year retrospective study of 429 patients at a referral burn centre in the north of Iran. Int Wound J. 2023 Nov;20(9):3599-3605. doi: 10.1111/iwj.14238. Epub 2023 May 23.
- Bamidele EF, Okebalama VC, Sodeinde JK, Ogunkoya JO, Oshinaike A, Adefala NO, Amaike C, Abiodun O, Monday OK, Obinna-Chinatu N, Mbon IC, Ndinne KW, Abaenowa CC, Nwankpa CC. The Prevalence of Musculoskeletal Symptoms among Welders and Non-Welders in Ikenne, Ogun State, Nigeria: A Comparative Cross-Sectional Study. West Afr J Med. 2023 Sep 28;40(9):943-949. PMID: 37767923.
- Belete YA, Assefa NL, Tegegn MT. Ocular Protection Practice and Associated Factors Among Ethiopian Welders: Institution-Based Cross-Sectional Study. Clin Optom (Auckl). 2023 Sep 11;15:175-184. doi: 10.2147/OPTO.S424522.
- Carey RN, Fritschi L, Nguyen H, Abdallah K, Driscoll TR. Factors Influencing the Use of Control Measures to Reduce Occupational Exposure to Welding Fume in Australia: A Qualitative Study. Saf Health Work. 2023 Dec;14(4):384-389. doi: 10.1016/j.shaw.2023.09.001. Epub 2023 Sep 7.
- Chen-Xu J, Jakobsen LS, Pires SM, Viegas S. Burden of lung cancer and predicted costs of occupational exposure to hexavalent chromium in the EU The impact of different occupational exposure limits. Environ Res. 2023 Jul 1;228:115797. doi: 10.1016/j.envres.2023.115797. Epub 2023 Mar 29.
- Cortes JB, Sarazin P, Dieme D, Côté J, Ouellet C, El Majidi N, Bouchard M. Biomonitoring of exposure to multiple metal components in urine, hair and nails of apprentice welders performing shielded metal arc welding (SMAW). Environ Res. 2023 Dec 15;239(Pt 2):117361. doi: 10.1016/j.envres.2023.117361. Epub 2023 Oct 14.
- Criswell SR, Nielsen SS, Faust IM, Shimony JS, White RL 3rd, Lenox-Krug J, Racette BA. Neuroinflammation and white matter alterations in occupational manganese exposure assessed by diffusion basis spectrum imaging. Neurotoxicology. 2023 Jul;97:25-33. doi: 10.1016/j.neuro.2023.04.013. Epub 2023 Apr 29.
- Duan Z, Zhou L, Wang T, Han L, Zhang J. Survival and Disease Burden Analysis of Occupational Pneumoconiosis From 1956 to 2021 in Jiangsu Province. J Occup Environ Med. 2023 May 1;65(5):407-412. doi: 10.1097/JOM.00000000002795.

- Evans GR, Masullo LN. Manganese Toxicity. 2023 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32809738.
- Fikayo BE, Chimezie OV, John SK, Omotola OJ, Mbon IC, Eleonu PC, Ndinne KW, Atinuke TA. Occupational Exposure to Welding Fumes and Associated Respiratory Morbidities among arc Welders in Ikenne, Nigeria. Ethiop J Health Sci. 2023 Mar;33(2):373-382. doi: 10.4314/ejhs.v33i2.23.
- Fishwick D, Carder M, Iskandar I, Fishwick BC, van Tongeren M. Irritant asthma and work: cases from the UK SWORD reporting scheme from 1999 to 2018. Occup Environ Med. 2023 Oct;80(10):553-557. doi: 10.1136/oemed-2023-108884. Epub 2023 Sep 28.
- Freire de Carvalho M, Kliebert J, Urbanus J. Levels and control of welding fume exposure to total particulate, hexavalent chromium, and manganese in contracted activities in an oil refinery setting (2008-2018). J Occup Environ Hyg. 2024 Jan;21(1):35-46. doi: 10.1080/15459624.2023.2264350. Epub 2023 Nov 1.
- Göen T, Abballe A, Bousoumah R, Godderis L, Iavicoli I, Ingelido AM, Leso V, Müller J, Ndaw S, Porras SP, Verdonck J, Santonen T; HBM4EU Chromates Study Team. HBM4EU chromates study PFAS exposure in electroplaters and bystanders. Chemosphere. 2024 Jan;346:140613. doi: 10.1016/j.chemosphere.2023.140613. Epub 2023 Nov 7.
- Jung F, Shapera S, Cabanero M, McInnis M, Fisher J. An unusual case of interstitial lung disease: Revisiting peribronchiolar metaplasia interstitial lung disease (PBM-ILD). Respirol Case Rep. 2023 Jan 4;11(2):e01081. doi: 10.1002/rcr2.1081.
- Kang D, Lee ES, Kim TK, Kim YJ, Lee S, Lee W, Sim H, Kim SY. Association with Combined Occupational Hazards Exposure and Risk of Metabolic Syndrome: A Workers' Health Examination Cohort 2012-2021. Saf Health Work. 2023 Sep;14(3):279-286. doi: 10.1016/j.shaw.2023.08.006. Epub 2023 Aug 21.
- Khalili M, Nasrabadi T. Assessment of occupational health risk due to inhalation of chemical compounds in an aircraft maintenance, repair, and overhaul company. Environ Sci Pollut Res Int. 2023 Apr;30(20):57558-57570. doi: 10.1007/s11356-023-26572-7. Epub 2023 Mar 25.
- Khan K, Room SA, Bacha AU, Nabi I, Ahmad S, Younas M, Ullah Z, Iqbal A, Alrefaei AF, Almutairi MH, Chang JW, Chi KH. Assessment of heavy metals among auto workers in metropolitan city: a case study. Front Public Health. 2023 Nov 7;11:1277182. doi: 10.3389/fpubh.2023.1277182.
- Lee EY, Kim J, Prado-Rico JM, Du G, Lewis MM, Kong L, Kim BG, Hong YS, Yanosky JD, Mailman RB, Huang X. Higher hippocampal diffusivity values in welders are associated with greater R2\* in the red nucleus and lower psychomotor performance. Neurotoxicology. 2023 May;96:53-68. doi: 10.1016/j.neuro.2023.03.005. Epub 2023 Mar 24.
- Lee M, Jung S, Do G, Yang Y, Kim J, Yoon C. Measurement of Airborne Particles and Volatile Organic Compounds Produced During the Heat Treatment Process in Manufacturing Welding Materials. Saf Health Work. 2023 Jun;14(2):215-221. doi: 10.1016/j.shaw.2023.03.005. Epub 2023 Mar 11.

- Nakashima H, Takahashi J, Fujii N, Okuno T. Hazards associated with blue light emitted during gas metal arc welding of mild steel using various shielding gases and currents. Ind Health. 2024 Apr 3;62(2):79-89. doi: 10.2486/indhealth.2023-0038. Epub 2023 Aug 11.
- Newton A, Rule AM, Serdar B, Koehler K. Laboratory comparison of field portable X-ray fluorescence spectrometer (FP-XRF) and inductively coupled plasma mass spectrometry (ICP-MS) for determination of airborne metals in stainless steel welding fume. J Occup Environ Hyg. 2023 Nov;20(11):536-544. doi: 10.1080/15459624.2023.2244022. Epub 2023 Sep 14.
- Nwogueze BC, Ofili MI, Uzuegbue UE, Brotobor D, Esievo NJ. Modulatory role of welding fumes on serum zinc and copper levels and oxidative stress markers among welders: Considering smoking as a possible implication. Toxicol Rep. 2023 Dec 21;12:48-55. doi: 10.1016/j.toxrep.2023.12.007.
- Onyeso OK, Ugwu AK, Adandom HC, Damag S, Onyeso KM, Abugu JO, Aruma OE, Odole AC, Awosoga OA, Ezema CI. Impact of welding occupation on serum aluminium level and its association with physical health, cognitive function, and quality of life: a cross-sectional study. Int Arch Occup Environ Health. 2024 Mar;97(2):133-144. doi: 10.1007/s00420-023-02038-8. Epub 2023 Dec 18.
- Peng F, Yu L, Zhang C, Liu Q, Yan K, Zhang K, Zheng Y, Liu W, Li Y, Fan J, Ding C. Analysis of serum metabolome of laborers exposure to welding fume. Int Arch Occup Environ Health. 2023 Sep;96(7):1029-1037. doi: 10.1007/s00420-023-01987-4. Epub 2023 May 27.
- Petersson Sjögren M, Kåredal M, Broberg K, Assarsson E, Thuresson S, Dierschke K, Hedmer M, Rissler J, Wollmer P, Löndahl J. Sensitive methods for assessment of lung health in welders and controls. Respir Med. 2023 Jun;212:107244. doi: 10.1016/j.rmed.2023.107244. Epub 2023 Apr 14.
- Pourhassan B, Beigzadeh Z, Nasirzadeh N, Karimi A. Application of Multiple Occupational Health Risk Assessment Models for Metal Fumes in Welding Process. Biol Trace Elem Res. 2024 Mar;202(3):811-823. doi: 10.1007/s12011-023-03717-w. Epub 2023 Jun 22.
- Quecke E, Quemerais B, Hashisho Z. Review of welding fume emission factor development. Ann Work Expo Health. 2023 Jul 6;67(6):675-693. doi: 10.1093/annweh/wxad024. PMID: 37191647.
- Riccò M, Ferraro P, Zaffina S, Camisa V, Marchesi F, Gori D. Vaccinating Welders against Pneumococcus: Evidence from a Systematic Review and Meta-Analysis. Vaccines (Basel). 2023 Sep 15;11(9):1495. doi: 10.3390/vaccines11091495.
- Roach KA, Kodali V, Shoeb M, Meighan T, Kashon M, Stone S, McKinney W, Erdely A, Zeidler-Erdely PC, Roberts JR, Antonini JM. Examination of the exposome in an animal model: The impact of high fat diet and rat strain on local and systemic immune markers following occupational welding fume exposure. Toxicol Appl Pharmacol. 2023 Apr 1;464:116436. doi: 10.1016/j.taap.2023.116436. Epub 2023 Feb 21.
- Saadiani E, Hosseinkhani Z, Safari-Variani A. Investigating the Effect of Welding Fume in Pulmonary Function of Welders in an Automobile Industry. Indian J Occup Environ Med. 2023 Apr-Jun;27(2):166-171. doi: 10.4103/ijoem.ijoem\_194\_21. Epub 2023 Jul 3.

- Soltanpour Z, Rasoulzadeh Y, Ansarin K, Seyedrezazadeh E, Mohammadian Y. Carcinogenic and noncarcinogenic risk of exposure to metal fume in different types of welding processes. Environ Sci Pollut Res Int. 2023a. Jul;30(35):83728-83734. doi: 10.1007/s11356-023-28258-6. Epub 2023 Jun 22.
- Soltanpour Z, Rasoulzadeh Y, Ansarin K, Seyedrezazadeh E, Jafarpour M, Mohammadian Y, Khuniqi HN. Micronucleus assay of DNA damage among welders: Effects of welding processes. Mutat Res Genet Toxicol Environ Mutagen. 2023b. Apr;887:503598. doi: 10.1016/j.mrgentox.2023.503598. Epub 2023 Feb 10.
- Soltanpour Z, Rasoulzadeh Y, Mohammadian Y. Occupational Exposure to Metal Fumes Among Iranian Welders: Systematic Review and Simulation-Based Health Risk Assessment. Biol Trace Elem Res. 2023c. Mar;201(3):1090-1100. doi: 10.1007/s12011-022-03246-y. Epub 2022 May 5.
- Su YW, Li YH, Wang JY, Zhang Y, Zhou LL, Wang Z. [Effects of electric welding on hearing loss and respiratory damage]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2023 Oct 20;41(10):832-837. Chinese. doi: 10.3760/cma.j.cn121094-20221009-00477.
- Sutunkova MP, Klinova SV, Ryabova YV, Tazhigulova AV, Minigalieva IA, Shabardina LV, Solovyeva SN, Bushueva TV, Privalova LI. Comparative Evaluation of the Cytotoxic Effects of Metal Oxide and Metalloid Oxide Nanoparticles: An Experimental Study. Int J Mol Sci. 2023 May 6;24(9):8383. doi: 10.3390/ijms24098383.
- Szkudlarek J, Owczarek G, Jachowicz M, Zagrodny B, Sencerek J. Study of The Impact of Users' Features on Dimensional Allowances Resulting from the Use of Personal Protective Equipment. Int J Environ Res Public Health. 2023 Feb 15;20(4):3380. doi: 10.3390/ijerph20043380.
- Szűcs-Somlyó É, Lehel J, Májlinger K, Tóth F, Jerzsele Á, Kővágó C. Immune response to zinc oxide inhalation in metal fume fever, and the possible role of IL-17f. Sci Rep. 2023 Dec 14;13(1):22239. doi: 10.1038/s41598-023-49430-5.
- Tsuji M, Koriyama C, Ishihara Y, Isse T, Ishizuka T, Hasegawa W, Goto M, Tanaka R, Kakiuchi N, Hori H, Yatera K, Kunugita N, Yamamoto M, Sakuragi T, Yasumura Y, Kono M, Kuwamura M, Kitagawa K, Ueno S. Associations between welding fume exposure and neurological function in Japanese male welders and non-welders. J Occup Health. 2023 Jan;65(1):e12393. doi: 10.1002/1348-9585.12393.
- Tsuji M, Hori H, Koriyama C, Tanaka R, Isse T, Ishihara Y, Ishizuka T, Hasegawa W, Goto M, Yatera K, Kunugita N, Kuwamura M, Sakuragi T, Yasumura Y, Yamamoto M, Ueno S. The effect of mask fit test on the association between the concentration of metals in biological samples and the results of time-weighted average personal exposure: A study on Japanese male welders. J Occup Health. 2023b Jan-Dec;65(1):e12399. doi: 10.1002/1348-9585.12399.
- Wu CJ, Ho AC, Chen SY, Pan CH, Chuang HC, Lai CH. Exposure to Heavy Metals and Serum Adiponectin Levels among Workers: A 2-Year Follow-Up Study. Metabolites. 2023b Jan 20;13(2):158. doi: 10.3390/metabo13020158.
- Wu L, Cui F, Zhang S, Ding X, Gao W, Chen L, Ma J, Niu P. Associations between multiple heavy metals exposure and neural damage biomarkers in welders: A cross-sectional study. Sci Total Environ. 2023a Apr 15;869:161812. doi: 10.1016/j.scitotenv.2023.161812. Epub 2023 Jan 24.

- Xia L, Park JH, Biggs K, Lee CG, Liao L, Shannahan JH. Compositional variations in metal nanoparticle components of welding fumes impact lung epithelial cell toxicity. J Toxicol Environ Health A. 2023 Oct 18;86(20):735-757. doi: 10.1080/15287394.2023.2238209. Epub 2023 Jul 24.
- Zhang L, Yu JM, Shan XY, Shao J, Ye HP. Characterization of welding fume and airborne heavy metals in electronic manufacturing workshops in Hangzhou, China: implication for occupational population exposure. Environ Sci Pollut Res Int. 2023a Apr;30(20):57398-57409. doi: 10.1007/s11356-023-26569-2. Epub 2023 Mar 25.