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# HEALTH EFFECTS FROM WELDING EXPOSURES:

# 2019-2020 LITERATURE UPDATE

# CONTENTS

# ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| 8-OHdG | 8-hydroxy-2′-deoxyguanosine |
| AAS | Atomic absorption spectrometer |
| ACGIH | American Conference of Governmental Industrial Hygienists |
| AD | Alzheimer’s Disease |
| ADC | Adenocarcinoma |
| AGE | Advanced glycation end |
| ALI | Air-liquid interface |
| AOR | Adjusted odds ratio |
| As3MT | Arsenic 3-methyltransferase |
| AWS | American Welding Society |
| CAT | Catalase |
| CC | Colorectal cancer |
| Cd | Cadmium |
| CG | Control group |
| CI | Confidence interval |
| CO | Carbon monoxide |
| CPT | Continuous performance test |
| Cr | Chromium |
| Cr6+ | Hexavalent chromium |
| CRP | C-reactive protein |
| Cu | Copper |
| CuO | Copper oxide |
| DAVID | Dosimetric Aerosol in Vitro Inhalation Device |
| DNA-SB | DNA double-strand breaks |
| DTI | Diffusion tensor imaging |
| EBC | Exhaled breath condensate |
| ED | Epilepsy disease |
| epub | Electronic publication |
| ESR | Erythrocyte sedimentation rate |
| ETG | Endurance training group |
| EWT | Experimental welding test |
| FCAW | Flux-core arc welding |
| Fe | Iron |
| $FEV_1$ | Forced expiratory volume in 1 second |
| GABA | γ-amminobutyric acid |
| GC | Gastric cancer |
| GPx | Glutathione peroxidase |
| GM | Geometric mean |
| GMA-MS | Gas metal arc- mild steel |
| GMA-SS | Gas metal arc- stainless steel |
| GMAW | Gas metal arc welding |
| GPx | Glutathione peroxidase |
| GR | Glutathione reductase |
| GSD | Geometric standard deviation |

| | |
|---|---|
| GSH | Total glutathione |
| GTAW | Gas tungsten arc welding |
| HbA1c | Association-based glycated hemoglobin |
| HEPA | High-efficiency particulate air |
| HR | Hazard ratio |
| IARC | The International Agency for Research on Cancer |
| ICP-MS | Inductively coupled plasma mass spectrometry |
| IL-6 | Interleukin 6 |
| IOM | Institute of Occupational Medicine |
| JEM | Job-exposure matrix |
| LBP | Lower back pain |
| LEV | Local exhaust ventilation |
| LGD | Lou Gehrig’s disease |
| LTPA | Leisure time physical activity |
| MALDI-IMS | Matrix assisted laser desorption ionization imaging mass spectrometry |
| MET | Metabolic equivalent of task |
| MCP-1 | Monocyte chemoattractant protein 1 |
| MDA | Malondialdehyde |
| $mg/m^3$ | Milligrams per meter cubed |
| mg/s | Milligrams per second |
| MIG | Metal Inert Gas |
| MMAW | Manual metal arc welding |
| Mn | Manganese |
| MRI | Magnetic resonance imaging |
| MS | Mild steel |
| MSD | Multiple sclerosis disease/musculoskeletal disorders |
| Ni | Nickel |
| NIHL | Noise-induced hearing loss |
| NIOSH | National Institute for Occupational Safety and Health |
| nm | nanometer |
| NMNAT1 | Nicotinamide/nicotinic acid mononucleotide adenylythransferase 1 |
| NO | Nitrogen oxide |
| $NO_2$ | Nitrogen dioxide |
| NORA | National Occupational Research Agenda |
| NP | Nanoparticles |
| Nrf2 | Nuclear factor erythroid 2-related factor-2 |
| $O_3$ | Ozone |
| OR | Odds ratio |
| OSHA | Occupational Safety and Health Administration |
| Pb | Lead |
| PC | Prostate cancer |
| PD | Parkinson's disease |
| PFT | Pulmonary function test |
| PLR | Platelet-to-lymphocyte ratio |
| $PM_{2.5}$ | Particulate matter less than 2.5 micrometers in diameter |
| PPE | Personal protective equipment |

| | |
|---|---|
| ppm | Parts per million |
| PWLD | Welder’s lung disease |
| R1 | Relaxation rate |
| RAGE | Advanced glycation end receptor |
| SA1P | Sphingasine 1-phosphate |
| S1P | Sphingosine 1-phosphate |
| SAEC | Small airway epithelial cells |
| SES | Socioeconomic status |
| SIR | Standardized incidence ratio |
| SMAW | Shielded metal arc welding |
| SNEC | Sinonasal epithelial cancers |
| SOD | Superoxide dismutase |
| SSc | Systemic sclerosis |
| STG | Strength training group |
| SUS | System Usability Scale |
| SVM | Support vector machine |
| TCS | Total comet score |
| TLV | Threshold limit value |
| TNF$\alpha$ | Tumor necrosis factor alpha |
| TWA | Time weighted average |
| UPDRS | Unified Parkinson's disease rating scale |
| US | United States |
| UVR | Ultraviolet radiation |
| weldART | Welding Advanced Reach Tool |
| WHO | World Health Organization |
| Zn | Zinc |
| ZnO | Zinc oxide |

# 1 INTRODUCTION

On behalf of the American Welding Society (AWS), Ramboll conducted a comprehensive literature search and summary of studies related to the health effects of welding. In this update, we included literature published in 2019 and 2020 (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 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 years 2019-2020 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 and English language.
5. To further limit searches, we used the additional search word "health".

## 2.2 PubMed and NIOSHTIC-2 Searches

An initial search yielded 893 citations. We further refined the search to include health and this reduced the number of citations to 167. The 167 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 2019-2020.

## 2.3 Literature Review

The literature search yielded over 890 references, with 167 relevant to health effects. 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. 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

A total of 68 relevant references were identified after excluding duplicates and other non-relevant references. Some of the references were included in the 2019 review and thus not summarized in this report. The breakdown of the remaining references by category is listed in Table 2.1.

**Table 2.1. Breakdown of Abstracts Reviewed by Study Category**

| **Study Category** | **Totals from all databases** |
|---|---|
| Particle characterization and exposure | 12 |
| Epidemiology and controlled human exposure | 35 |
| Animal | 5 |
| Mechanistic/cell/*in vitro* | 9 |
| Reviews | 7 |
| **Overall Total** | **68** |

# 3 EXPOSURE STUDIES

We identified 12 exposure-related studies or studies related to regulation or health and safety in welding occupational groups published from 2019-2020 (*i.e.*, particle characterization and exposure). Some studies were published online in 2020 (*i.e.*, 2020 was the "epub date") and these were included in our summary. Articles that were not relevant or were included in prior AWS updates (*e.g.*, epub date for 2019) were excluded. A brief summary of the exposure abstracts is provided below for all the relevant studies.

Adamec et al. (2020) briefly described the results of a pilot study that measured ultrafine particulate matter associated with welding in a workplace. The authors reported that the welding process produced ultrafine particles in the size range of 300 nm and determined that inhalation exposure was the most relevant exposure route. They found that the concentrations of particulates were influenced by the welding material, type of welding, and suction (not defined but may refer to the sampling methodology). Also, they found that the particulates contained manganese, iron, and silicon, which they noted could cause neurodegenerative diseases. The authors noted that oral exposure should also be considered; however, no data or further information were provided.

Boiano et al. (2020) created a job exposure matrix (JEM) for solar and artificial ultraviolet radiation (UVR) using a United States (US) standardized coding scheme. Certified Industrial Hygienists developed separate lists for solar and artificial UVR using the US Census Bureau industry and occupational codes. Exposure ratings were assigned to industry and occupation pairs by analyzing prevalence and frequency for solar UVR exposure. Artificial UVR exposure parameters included frequency, prevalence, and intensity. Prevalence was categorized and rated by the percent of all workers employed in an exposed pair: 0 to <1, 1 to <20; 20 to <80, and ≥80. Frequency was categorized and rated by the number of hours per week workers were exposed: 0 to <5, 5 to <20, 20 to <35, and ≥35 hours per week. Intensity, used for artificial UVR only, was assigned three ratings of low, low with rare excursions, >low under normal conditions. If there were any discrepant ratings, a consensus was used to resolve them. Any ratings given a zero were excluded from the JEM, leaving 9,206 pairs rated for solar UVR and 2,010 pairs rated for artificial UVR. Welding was not a main industry or occupation for which solar UVR exposure was assessed. For artificial UVR, exposure ratings in 87 pairs (4.3% of all rated pairs) yielded maximum ratings in all three parameters for welding, soldering, and brazing workers.

Bugarski et al. (2020), researchers at National Institute for Occupational Safety and Health(NIOSH), conducted a study to characterize aerosols generated by manual metal arc welding (MMAW) in an isolated zone of an underground mine. The simulated repair of existing equipment using MMAW contributed to concentrations of nano and ultrafine aerosols measured in the mine air. The particle sizes were 140 and 480 nm, based on "electrical mobility and aerodynamic mobility" count median diameters. The particles, which were collected on filters, contained carbon, iron, manganese, calcium, and aluminum.

Feldmann and Jackson (2019), researchers at National Institute for Occupational Safety and Health (NIOSH), evaluated welder's exposure to chromium, hexavalent chromium, nickel, cobalt, and noise at an aircraft powerplant parts manufacturing facility. The evaluation consisted of a review of facility health and safety practices, measurement of airborne metal and noise exposures, confidential medical interviews, medical questionnaires, nasal examinations, and measured urine nickel, chromium, and cobalt levels. Airborne nickel levels were found in one employee to be above the NIOSH recommended exposure limit; however, airborne chromium, hexavalent chromium, and cobalt were not found to exceed occupational limit. Urinary nickel levels were found to be above levels expected in the general population in one welding supervisor and four welders and urinary cobalt levels were also above the levels in the general population in one welder. The authors did not provide quantitative data or state the significance of the findings. While mobile local exhaust ventilation (LEV) was available for use, the workers reported they had not been trained to use them and none of the welding booths were outfitted with LEVs. Also, none of the welders or welding supervisors were enrolled in the company respiratory protection program. Noise levels from the use of compressed air for cooling welds or cleaning were found to be above the recommendations made by NIOSH and OSHA in six welders. Tinnitus and/or hearing issues were reported by some employees. The researchers observed earplugs being used improperly and the hearing conservation program did not include the welders or welding supervisors. The researchers recommended welding booths be fitted with LEV systems, food/drinks removed from work areas, add areas designated for changing clothes, cleaning of work areas by vacuuming with high-efficiency particulate air (HEPA) filters instead of using compressed air, adding nozzles to the air compressors to decrease noise, and enrolling employees in the company respiratory and hearing conservation programs.

Ferrreira et al. (2019) investigated the associations between blood nickel (Ni), copper (Cu), zinc (Zn), cadmium (Cd) and lead (Pb) levels found in jewelry welders in the home and informal work environment in the city of Limeira. The exposed (n=112) and control (n=53) groups consisted of 52 families (n=165). Metal air concentrations were measured from all individuals at breathing zone (n=9) and analyzed using inductively coupled plasma mass spectrometry (ICP-MS). Sociodemographic and workplace information was collected via questionnaires. Statistical analyses included principal component analysis, Mann-Whitney tests, cluster and logistic regression. Air samples results showed that Ni, Cu, Zn, Cd, and Pb concentrations were higher than occupational guidelines. Of the 80% of workers that were female, 43.5% were welders. The concentration of Pb in exposed individuals was found to be significantly increased compared to the control group ($p<0.0001$) and between sexes ($p=0.0046$). There were also significant differences in exposures between sexes for Cu ($p<0.0001$) and Sb ($p=0.0434$). The authors noted specific concerns for children in these environments as they were exposed to the same environmental conditions as the welders. The authors concluded that the working conditions were inadequate and public actions needed to be taken to protect families.

Hanley et al. (2020), researchers at National Institute for Occupational Safety and Health(NIOSH), investigated the exposure of manganese (Mn) from in flux core arc welding fume at three facilities. The objective of the exposure assessment was to evaluate different Mn fractions over 67 worker days using a sequential extraction procedure. Total or respirable Mn was monitored, and samples were analyzed to for four separate Mn fractions. These fractions were determined by chemical solubility: soluble Mn (mild ammonium acetate solution); $Mn^{0,2+}$ (25% acetic acid); $Mn^{3+,4+}$ (hydroxylamine hydrochloride in 25% acetic acid); and an insoluble Mn fraction (in hydrochloric/nitric acid). The time weighted average (TWA) concentrations were reported as the full-shift total particle size breathing zone concentrations for each fraction; these ranged from 0.51 to 43; 2.9 to 850; 1.7 to 620; and 0.56 to 331 $\mu g/m^3$, respectively. The sum of the fractions resulted in a range of 16 to 1,530 $\mu g/m^3$. The TWA concentrations for respirable particle size were 0.27 to 75; 1.6 to 690; 1.3 to 740; 0.52 to 570 $\mu g/m^3$, respectively. The sum of all the fractions for the respirable size ranged from 3.8 to 1,800 $\mu g/m^3$. For the shipyard, structural steel, and customs parts facilities, total particulate TWA geometric mean (GM) concentrations of the sum of the fractions were 56 μg/m$^3$ (geometric standard deviation (GSD)=4.0), 380 μg/m$^3$ (GSD=2.7), and 176 μg/m$^3$ (GSD=3.3), respectively. Most of the workers Mn exposure was below the NIOSH recommended exposure limit of 1000 μg/m$^3$, for 44 of the welders, exposure exceeded the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit vales (TLV) for total Mn of 100 μg/m$^3$, for 46 welders, concentrations of Mn exceeded the respirable TLV of 20 μg/m$^3$. The researchers concluded the results of this study indicated that an exposure control and management program is needed to reduce Mn exposures.

Mehrifar et al. (2020a) conducted a cross-sectional study to determine welder's exposure and risk to fumes and gases from three common types of welding. This study was carried out at a steel company where the types of welding included Shielded Metal Arc Welding (SMAW), Gas Metal Arc Welding (GMAW), and Gas Tungsten Arc Welding (GTAW). National Institute for Occupational Safety and Health (NIOSH) 7300 method was used to measure manganese (Mn), chromium (Cr), and nickel (Ni) fumes. Direct reading instruments were used to measure nitrogen oxide (NO), nitrogen dioxide ($NO_2$), carbon monoxide (CO), and ozone ($O_3$) gases. To measure level of exposure risk, a semi-quantitative chemical risk assessment method was used. The results showed Metal Inert Gas (MIG) and GTAW welding produced the highest and lowest exposures to gases, respectively. While SMAW and GTAW welding produced the highest and lowest exposure to metals, respectively. Mean exposure to gases were CO - 43.05, NO - 27.88, $NO_2$ – 4.30, and $O_3$ – 0.41 ppm. Mean exposure to metals were Mn – 2.302, Cr – 3.195, Ni – 1.241 mg/m$^3$. The risk analysis showed that $O_3$, $NO_2$, and Cr exposures yielded high and very high risk levels for all examined welding processes. The authors concluded welders performing MIG and SMAW processes have the highest occupational exposure to metal and gases. Preventative measures should be taken such as workplace air assessments, ventilation system installation, and providing respiratory protection.

Methner (2020) evaluated the potential exposure to metals during welding, grinding, and plasma cutting activities. This study was conducted after an architectural metal fabrication shop contacted National Institute for Occupational Safety and Health (NIOSH) to perform a health hazard evaluation. Employees used pneumatic grinders, performed inert gas welding, and one employee operated a plasma cutting table. In addition, facility health and safety program materials were reviewed, personal air samples were collected, and workplace conditions were observed. The metals detected included aluminum , chromium, copper, iron oxide, manganese, potassium, and zinc oxide and were found to be below occupational exposure limits for all employees. A portable fume extractor was examined at the point of fume generation and it failed to produce the minimum acceptable capture air velocity as recommended by American Conference of Governmental Industrial Hygienists (ACGIH). The emissions released when cutting plate metal steel on the plasma cutter were controlled with a water bath. The authors recommended the fume extractor either be repaired to improve air flow or to replace the unit. It was also recommended the company develop a program to conduct fume extractor filter checks and a filter replacement schedule.

Sailabaht et al. (2020) developed a model of welding fume exposure using The Welding Advanced REACH Tool (weldART). Measurements of welding fume concentrations were collected as well as other data to develop and calibrate a four-compartment mass-balance model. Measurements were obtained from welders working in a structural steel fabrication plant. Three types of welding were included in the assessment - flux-cord arc welding (FCAW), shielded metal arc welding (SMAW), and gas tungsten arc welding (GTAW). The sampling of aerosols was conducted using 13 mm diameter Swinnex sampling heads and MicroPEM direct-reading aerosol monitors. The compartments of the model included near-field, far-field, welding plume, and remaining room zone. The authors analyzed the data from the samplers and the weldART modeled estimates using fitted linear equations (forced through the origin). To obtain proportionate concentrations in each compartment, flow rates between the compartments were adjusted by trial and error. The results showed that the FCAW process generated more welding fume particulates than the other welding methods. In addition, the authors found that the MicroPEM monitors were unreliable as they underestimated concentrations and did not correlate well with the data from the Swinnex samplers. A strong association between personal exposures and the weldART model values (R2 = 0.94) were demonstrated, with an average estimated value to be 1.3 times the measured exposures. The near field (R = 0.37) and far field modeled estimates yielded poor correlations with exposure measurements (R = 0.35). However, the model estimates were, on average, close to the measured exposures (ratio modelled to measured of about 1). The authors concluded that the weldART model does an adequate job of predicting welding fume particulate exposures.

Shaw et al. (2020) assessed the relationship between inhalable and "total" hexavalent chromium exposure to determine if previous total data can be converted to inhalable exposures. Air sampling was conducted at a stainless-steel welding operation, a steel passivation operation, and at two hard chrome electroplaters. Side-by-side samples were taken for total dust and inhalable dust using a closed-face 37-mm diameter cassette samplers and Institute of Occupational Medicine (IOM) inhalable samplers, respectively. A total of 40 pairs of total and inhalable samples were collected. The range of total and inhalable dust measured at the steel passivation operation was 30-410 mg/m$^3$ and 0.2-740 mg/m$^3$; 260-1520 mg/m$^3$ and 477-6970 mg/m$^3$ for welding; and 0.01-1500 mg/m$^3$ and 204-2130 mg/m$^3$ for electroplaters, respectively. The range hexavalent chromium in total and inhalable dust samples measured at the steel passivation operation was 0.02-89 and 0.02 mg/m$^3$; 4.1-4.9 mg/m$^3$ and 2.2-6.9 mg/m$^3$ for welding; and 0.01-9.3 mg/m$^3$ and 0.01-21 mg/m$^3$ for electroplaters. A linear relationship was found between inhalable and total hexavalent chromium exposure with a slope of 1.4 (confidence interval (CI):1.3, 1.5) and 0 offset. Based on these findings, the authors concluded that a ratio of 1.4 can be used as a conversion factor to determine inhalable hexavalent chromium from previous studies that only reported total hexavalent chromium.

Takahashi et al. (2020) examined fume particle characteristics during arc welding of cast iron. Fume particle size distribution, fume generation rate, ≤0.3um particle generation, and respirable dust generation rate were measured. In this experiment, gas metal arc welding and shielded arc welding were used on three types of filler materials (mild steel wire, stainless steel wire, and mild steel covered electrodes) with the main constituents including iron (Fe) or iron-chromium-nickel (Fe-Cr-Ni). The fumes generated contained 73-91% respirable dust and were generated at rates ranging from 1.96 to 12.2 mg/s. The authors state the results demonstrated that the welding current affects how much respirable dust is generated; the higher the fume generation rate, the more dust is generated. Respirable dust generation was low when using mild steel covered electrodes and high when using stainless steel wire. Stainless steel wire produced the highest generation rate of particles with a ≤0.3um diameter.

Wippich et al. (2020) investigated the possibility of converting inhalable dust to respirable dust from retrospective occupational exposure studies. To determine the conversion functions, 15,120 parallel measurements were obtained from the MEGA exposure database (a database that is maintained at the Institute for Occupational Safety and Health of the German Social Accident Insurance), then estimated using regression analysis. The dataset was split into two factors: working activity and material. The most important predictor variable was determined to be inhalable dust (adjusted coefficient of determination = 0.585 R2 adjusted for sample size). The model was improved by splitting the dataset into six working activities and three material groups. For example, high temperature processing showed an adjusted for sample size R2 value of 0.668. While this example helps explain the whole dataset better, it was not possible to systematically refine groups. By trial and error, seven new groups were formed: soldering, casting, welding, high temperature cutting, blasting, chiseling/embossing, and wire drawing (adjusted for sample size R2 value range of 0.733-0.835). The use of these groups is appropriate for the purposes of data reconstruction and retrospective exposure assessment, but must be carefully analyzed for working conditions. Additionally, the conversion functions are power functions with exponents ranging from 0.454 to 0.946. The authors concluded this model does not support the assumption of a general linear relationship between respirable and inhalable dust.

# 4 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 (9 studies), respiratory effects (5 studies), cardiovascular effects (2 studies), cancer (6 studies), eye effects (2 studies), and multiple or other health effects (11 studies). Summaries of these studies are provided below.

### 4.1.1 Neurological Effects

Edmondson et al. (2019) examined manganese (Mn) accumulation and changes in the brains of welders using magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS), respectively. MRI relaxation rate (R1) and thalamic y-aminobutyric acid (GABA) were measured as markers of changes in the brain. Seventeen welders were recruited to participate in this prospective cohort and images were taken 2 years apart. The thalamic and striatal regions of the brain were examined for GABA using MRS. Personal air sampling and reviews of work history were conducted to measure air Mn exposure and estimate cumulative exposure indexes of Mn, exposure for the previous 3 months, year, and for a lifetime. Also, toenails were collected from participants to assess Mn body burden. Finally, motor function was examined using the Unified Parkinson's Disease Rating Scale (UPDRS). The results demonstrated a decrease in all exposure measures between the first and second MRI scan. Significant correlations were found between GABA and changes in exposure indexes over the previous 3 months ($p=0.66$, adjusted $p=0.02$), the past year ($p=0.70$, adjusted $p=0.006$), and Mn exposure in air ($p=0.77$, adjusted $p=0.002$). Changes in GABA were found to significantly decrease linearly in the previous 3 months ($p=0.02$) and with changes in Mn exposure in air ($p=0.04$). Finally, MN exposure over lifetime was associated with in Mn concentrations in the substantia nigra (F-test, $p=0.005$). The authors concluded UPDRS was unaffected even though R1 and GABA changed with Mn exposure. This demonstrated changes in the brain after Mn exposure can be measured by GABA and R1 in most brain regions.

Edmondson et al. (2020) used support vector machines (SVM) to determine manganese (Mn) accumulation based on brain scans from welders. Mn accumulation can be seen on an MRI because it functions as a T1 contrast agent. Whole brain relaxation rate or R1 ($R1=1/T1$) maps from 57 welders and 32 controls were used to predict exposure to air Mn concentrations ([MN]air), brain accumulation (ExMnBrain), gross motor dysfunction (UPDRS), thalamic y-aminobutyric acid (GABA) concentration, and total number of welding years. The results showed R1 was 88.8% (recall 88.9%) accurate in predicting [Mn]air above a threshold of 0.20 $mg/m^3$. With 82% accuracy (recall 78.9%), R1 predicted GABA was ≤2.6 mM in subjects. Finally, SVM age prediction was used to verify that the results could be applied to Mn exposure. The predictive age was <48 years of age and accuracy was 75-82% (recall 94.7%-76.9%), but not for those >48 years of age. The authors concluded that significant changes in R1 could not be observed at lower levels of exposure (<0.20 $mg/m^3$) and with less than 18 years of welding experience. Higher levels of exposure and more years of experience were readily identifiable using SVM.

Ellingsen et al. (2019) conducted a study to determine the differences in neurobehavioral performance in patients diagnosed with manganism and idiopathic Parkinson Disease (PD) compared to a control group. The study consisted of 34 patients with manganism (17 previously tested), 13 with PD, and 43 healthy turners/fitters (control group). Compared to controls, patients with manganism scored more poorly on motor speed, manual dexterity, and balance. Compared to patients with PD, manganism patients also scored more poorly on the postural sway test. However, PD patients experienced higher postural tremor intensity with narrower frequency dispersion than those with manganism. Tests resulted in patients with PD displayed a more asymmetrical pattern in neurobehavioral performance (tremor intensity, grooved pegboard, and static steadiness). Slower movements (bradykinesia) did not differ between manganism and PD patients. After reassessing the 17 previously tested manganism patients, a slight increase in neurobehavioral deterioration was observed compared to the age-related decline of the controls.

Gliga et al. (2020) evaluated the associations between exposure to metal particles during welding and the expression of 87 putative neurology-related proteins in serum. First, a longitudinal approach was taken using the study cohort from southern Sweden, which included non-smoking, male, welders who worked with mild steel (n=56) and controls (n=89). The welders were sampled at two time points (T1, T2) six years apart. Second, a onetime cross-sectional sample was taken which included 102 welders and 89 control subjects. Any associations observed in the longitudinal analysis were then further evaluated after including the cross-sectional sample. After adjusting for respiratory protection, median respirable dust levels were 0.6 mg/m$^3$ at T1 (5-95 percentile: 0.2-4.2 mg/m$^3$) and 0.5 mg/m$^3$ (0.1-1.8 mg/m$^3$) at T2. The adjusted median respirable mmanganese (Mn) concentration at T2 was 0.049 (0.003-0.314) mg/m$^3$. The Spearman correlation between respirable Mn and adjusted respirable dust was 0.88. Five neurological proteins were expressed differently in welders compared to control subjects in the longitudinal sample. Nicotinamide/nicotinic acid mononucleotide adenylythransferase 1 (NMNAT1) was identified in both the longitudinal and cross-sectional sample to be upregulated in welders compared to controls. This axon-protective protein has been linked to Alzheimer’s disease. However, an association between degree of exposure and NMNAT1 was not found. Additional proteins associated with years welding in both studies included GCSF, EFNA4, CTSS, CLM, and VWC2. Other proteins identified were more strongly associated with age and body mass index. The results demonstrated low to moderate exposure to metal particulates in welding fumes is associated with changes in levels of key neurological proteins.

Lotz et al. (2021) investigated alterations in fine motor function in welders after exposure to manganese (Mn). Welders (n=48) and unexposed workers (n=30) underwent a battery of motor function tests, questionnaires, and blood examinations. Personal air samplers were used to measure Mn during shifts. Accumulation of Mn in the brain was measured using MRI relaxation rates. Motor function tests were measured using the Movement Disorder Society-Sponsored Revision of the UPDRS part III and found to be normal in welders. Welders demonstrated better results than controls on the steadiness test; however, the opposite was observed for slowness. An association between the motor test results and relaxations rates in the globus pallidus and substantia nigra were not found.

Mehrifar et al. (2020b) measured the concentrations of manganese (Mn) in welding fumes in the breathing zone and blood of welders to identify potential alterations in neurocognitive and neurobehavioral function. The participants in this study consisted of 38 welders and 27 administrative employees (controls). Neurobehavioral problems were evaluated using a questionnaire. Neurocognitive function was assessed using the computerized Stroop test and Continuous Performance Test (CPT). Breathing zone samples were performed according to NIOSH-7300 and blood samples according to NIOSH-8005. The average Mn concentration found in the breathing zone and blood of welders was 0.81±0.21 mg/m$^3$ and 18.33±5.84 ug/l, respectively. The frequency of neurobehavioral symptoms in welders was significantly higher compared to controls. A moderate correlation between Mn in the breathing zone and blood Mn levels was observed (Spearman correlation test, rs=0.352). A moderate correlation between frequency of neurobehavioral symptoms and Mn in the breathing zone was observed (r=0.504), with a stronger correlation with Mn in blood (r=0.643). Finally, a moderate correlation between the Stroop and CPT test results and Mn in the welders breathing zone and blood was observed (Person correlation coefficient, r=0.433-0.690). The authors concluded that results confirmed the effect of Mn inhalation exposure on induction of neurobehavioral and neurocognitive alterations in welders.

Prasad et al. (2019) reported on a case study of a 27-year-old welder experiencing upper limb tremor for the previous two years. The man had nine years of experience welding, but did not use respiratory protection. Welding was performed in various environmental conditions (inside and outside). The upper limb tremor was present in his right arm and only when the elbow was flexed. The tremor was observed to be a jerky movement when the elbow joint was flexed. Surface electromyography showed the tremor at 4-5 Hz while the right forearm, biceps and triceps muscles contracted. Results from an MRI scan showed the globus pallidus and substantia nigra to have bilateral, symmetric T1-weighted hyperintensities. There were no other physical or neurological symptoms and medical and family history were not remarkable. Serum manganese (Mn) levels were measured and found to be elevated (2.68 ng/ml). Transporter gene defects were tested and ruled out. A diagnosis of Mn neurotoxicity was considered as there were no other clinical signs of Parkinson’s disease. The authors were not able to follow-up with the patient, but recommended a change in occupation. The direct link between the tremor and Mn neurotoxicity is uncertain; however, this could be a presenting symptom of Mn toxicity.

Rana et al. (2019) developed a quantitative framework to identify a link between welding fume exposure and neurodegenerative disease. Gene expression microarray data from fume-exposed tissues and neurodegenerative diseases was analysed. Neurodegenerative diseases included Parkinson’s disease (PD), Alzheimer’s disease (AD), Lou Gehrig’s disease (LGD), Epilepsy disease (ED), and multiple sclerosis disease (MSD). Disease-gene relationship networks were constructed and the authors used multilayer network topology and neighbourhood-based benchmarking to identify dysregulated pathways, ontological pathways, and protein-protein interaction sub-networks. The results showed that there was an association between welding fume and 18 PD, 16 AD, 19 LGD, and 19 MSD differentially expressed genes. Welding fume may be associated with the progression of the noted neurodegenerative diseases based on the gene expression dysregulation, relationship networks, pathways, and ontologic analysis. The authors concluded this approach could be a useful way to understand the causal influences of welding fume exposure in the progression of neurodegenerative diseases.

Rechtman et al. (2020) investigated the associations between respirator use and neurological health outcomes in welders. Diffusion tensor imaging (DTI) was used to determine the effectiveness of workers using respirators to protect white brain matter from welding fume exposure. White matter microstructural integrity was marked using fractional anisotropy, a common DTI measurement of water diffusion. Participants for this pilot cohort included 19 welders from New York City area unions. Questionnaires were completed to assess occupational health and work history and a DTI was conducted on a 3T Siemens scanner. A bioinformatic analytical strategy (partial least squares discriminant analysis) was used to model 48 regions of white matter microstructures and the results between welders who used respirators and those who did not were compared. Brain regions were defined using the ICBM-DTI-81 atlas. A clear difference between white matter microstructure in the uncinate fasciculus, cerebellar peduncle, and superior longitudinal fasciculus regions of the brain were observed between respirator users and non-users. These are all areas involved in motor and cognitive functions. The results suggest wearing respirators may protect white matter in welders exposed to welding fume. The authors suggested more studies should be conducted to confirm these results.

#### 4.1.2 Respiratory Effects

Ahmad et al. (2020) assessed respiratory symptoms and alterations in pulmonary function in workers of multiple industries including welding, painting, and vehicle repair. This cross-sectional study was conducted by enlisting occupationally exposed and non-exposed small scale industry workers with matching demographic and anthropometric parameters To determine currently present respiratory ailments, a Medical Research Council (MRC) questionnaire was completed. Pulmonary function tests (PFT) were administered using a Micro Direct computerized automated spirometer. Welding specific results were not provided, results were only given between "exposed" and "non-exposed" workers, which consisted of 40.9% mechanics, 31.8% welders, and 27.3% painters. Chest tightness and whistling in exposed (22.7%) and non-exposed (10%) was the most common respiratory symptom reported. In exposed cases, exposure incidence was reported as often (22.7%), sometimes (68.2%), and never (9.1%). The use of any respiratory protection, such as masks, was reported to be low. Overall respiratory health was compared between exposed and non-exposed and authors reported that it was excellent (54.5% vs 73.4%), good (27.3% vs 23.8%), and average (18.2% vs 3.3%). PFTs conducted in the exposed group revealed decreased mean values in the following parameters compared to controls: forced expiratory volume in one second ($FEV_1$) (3.12 vs 3.50), forced vital capacity (FVC) (4.12 vs 4.43), $FEV_1$/FVC (79.60% vs 80.79%), and peak expiratory flow (PEF) (414.7 vs 523.2). The authors concluded that the study results indicated that workers are at an increased risk of decreased pulmonary function and developing respiratory symptoms.

Karataş et al. (2020) examined the neutrophil- and platelet-to-lymphocyte ratio (NLR and PLR) in patients diagnosed with welders' lung disease (PWLD) and how this could relate to changes in pulmonary function parameters. There were 116 male PWLD and 118 healthy, non-exposed controls recruited for this study. Individuals participated in pulmonary function tests (PFTs) and complete blood count, erythrocyte sedimentation rate (ESR), c-reactive protein (CRP) were also measured. For both groups, NLR and PLR were analyzed retrospectively. White blood cells, NLR, PLR, ESR, and CRP measurements in PWLD were significantly higher compared to controls (p=<0.001 for all). In PWLD, all PFTs were significantly decreased compared to controls, except for FEV1/FVC. A positive correlation was observed between NLR and ESR (r=0.241 and p=<0.001). The authors concluded that NLR and PLR could be considered new inflammatory markers of PWLD and could be measured routinely due to the cheap, fast, and easily measurable nature of the test.

Lindström et al. (2020) reported on two cases of asthma initiation shortly after exposure to fluorinated hydrocarbon-based cooling agents while welding or smoking cigarettes in a confined space. These chemicals thermally degrade into hydrofluoric acid and are present in refrigerators and air conditioning units. Respiratory symptoms, headache, and nonspecific bronchial hyperresponsiveness were found in both patients. After a follow-up, asthma was persistent in both patients and neither responded positively to asthma medication. The authors theorized that the low toxicity of fluorinated hydrocarbons did not lead to the effects observed in the patients, but it was more likely due to exposure to the degradation product: hydrofluoric acid. In the environmental condition of a confined space, the patients presented typical clinical irritant-induced asthma onset and acute symptoms resembling hydrofluoric acid poisoning. The authors concluded welding, smoking, and other potential sources of combustion in confined spaces could be a risk when fluorinated hydrocarbons are used in the workplace.

Stanton and Nett (2019) evaluated health concerns regarding lung disease and air quality at a paper tissue converting equipment manufacturing facility. Potential exposures included coolants, oils, solvents, paper dust, exhaust fumes, welding and plasma cutting fumes, and lacquer thinner. An assessment was conducted in June 2012, which consisted of a tour of the facility, employee interviews, employee observations, inspection of some of the mist collectors and vacuum pumps, and collection of bulk samples of unused and in-use process fuels. A medical survey and a full industrial hygiene survey were conducted of employees with lung disease. In addition, a health questionnaire and breathing tests were administered to employees. The industrial hygiene survey involved the collection of personal and area air samples for metals and particulate matter, real time measurements of size-selective particulate matter, and an examination of airflow. For the welding activities, airborne exposures to steel (85-90%), aluminum (10-15%), and cast iron (<1%) were generated by using saws, pressurized water, or plasma cutting. Exposure levels to metals were found to be below occupational exposure limits with higher levels in the production areas. The ventilation assessment demonstrated air contaminants could migrate from the machine shop to the assembly area. Based on the medical survey and examinations, current employees displayed symptoms of lung disease, but spirometry abnormalities were not in excess. The causes of severe lung diseases in four employees were not definitively concluded; however, engineering and administrative controls were recommended to decrease airborne exposures and provide voluntary respiratory protection along with a routine medical monitoring program.

Torén et al. (2020) investigated the risk of invasive pneumococcal disease (IPD) associated with occupational exposure to metal fumes. Cases of Streptococcus pneumonia (4,438 aged 20-65) were gathered from a Swedish registry of invasive infection caused by this bacterium. The Swedish population registry was used to identify six controls for each case of infection and were matched for gender, age, and region of residency. The study observation period was defined by assigning the index date for each control to their corresponding case. The Swedish registries for socioeconomic status (SES) was used to link cases and controls by occupational history and hospital discharge. Conditional logistic analysis, adjusted for comorbidities and SES, was used to estimate the odds ratio (OR) of IPD and pneumonia-IPD and associations with exposure and occupations in the year before the index date. The results showed welders were at an increased risk of IPD (OR 2.99, 95% confidence interval (CI) 2.09-4.30). Elevated odds of IPD were associated with occupational exposures to fumes (OR 1.11, 95% CI 1.01-1.21) and silica dust (OR 1.33, 95% CI 1.11-1.58). Welders and those exposed to silica dust were also associated with the highest increased risk of IPD with pneumonia. The authors concluded working as a welder increase the odds of developing IPD. The authors suggested those at risk should be vaccinated.

#### 4.1.3 Cardiovascular Effects

Baloch et al. (2020) investigated potential accumulation of cadmium (Cd) and lead (Pb) in adolescents and adults from occupational exposures. Blood and scalp hair samples were collected from subjects working in battery recycling and welding workshops and reference/control subjects (number of workers and controls not provided). Reference/control subjects were matched by age and lived in nonindustrial areas. Graphite furnace atomic absorption spectrometry was used to analyze the blood and scalp hair samples. The concentration of Cd and Pb in workers was found to be three-fold higher compared to controls. The authors also measured Cd and Pb in the drinking water of both workshops and determined concentrations of both metals were five- to thirteen-fold higher than the permissible exposure limits recommended by the World Health Organization. A significant, negative correlation was observed between blood lead levels and hemoglobin percentage in adolescent workers (r = -0.78). In adult workers, a positive correlation was observed between blood pressure and Pb and Cd concentrations found in blood and hair samples (r = 0.65-0.83), however, the significance of this correlation was not stated. Also, the authors don't provide any information regarding the differences in exposures between the battery recycling and the welding workshops. The authors concluded that occupational exposure to metals could be improved by implementation of an adequate workplace management program.

Taj et al. (2021) assessed if there could be an association between low-to-moderate exposure to welding fumes and adverse effects on the cardiovascular system. A longitudinal analysis was performed with 78 male, non-smoking mild steel workers and 96 controls with measurements taken twice over six years (time points 1 and 2). Questionnaires on health, work history, and lifestyle were completed as well as measurements for blood pressure and endothelial function (by EndoPAT). Risk factors for cardiovascular disease (low-density lipoprotein homocysteine, C-reactive protein) were also measured. The questionnaires were also used to assess exposure to welding fumes in addition to personal measurements of respirable dust in the breathing zone (adjusted for respiratory protection). Median respirable dust concentrations in welders were 0.7 mg/m$^3$ (5-95 percentile range 0.2-4.2 mg/m$^3$) at time point 1 and 0.5 (0.1-1.9) mg/m$^3$ at time point 2. Blood pressure was observed to significantly increase in welders compared to controls over the six-year study period (systolic 5.11 mm Hg, 95% confidence interval (CI) 1.92-8.31; diastolic 3.12 mm Hg, 95% CI 0.74-5.5). An increase in diastolic blood pressure was observed with each additional year of welding; however, this was not significant (0.22 mm Hg, 95% CI -0.02-0.45). Associations between welding and endothelial function were not found. The authors concluded that an increase in blood pressure is associated with low-to-moderate exposure to welding fumes and that the occupational exposure limit in Sweden should be decreased from 2.5 mg/m$^3$ in order to protect cardiovascular health.

#### 4.1.4 Cancer

Barul et al. (2020) conducted a case-control study (the Investigation of Occupational and Environmental Causes of Respiratory Cancers Study) in a French population to determine the potential association of occupational exposure to welding and the risk of head and neck cancer. Male participants in this study included 2703 controls and 1588 cases of squamous-cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx. Questionnaires were used to assess welding activity and any confounding factors. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional logistic regression. Potential confounders included occupational exposure to asbestos, alcohol consumption, age, area of residence, and tobacco smoking. The results showed welding was associated with an increased risk of head and neck cancer overall (OR=1.31, 95% CI 1.03-1.67) and laryngeal cancer (OR=1.66, 95% CI 1.15-2.38). A significant increase in the risk of laryngeal cancer was observed as cumulative and weighted duration of welding increased (p=<0.01). A significant association was observed for oral cancer in those exposed to welding for more than 10 years (cumulative OR=1.82, 95% CI 1.09-3.04; weighted OR=2.10, 95% CI 0.99-4.45). Long duration of different types of welding were associated with different cancers. Arc welding was found to be associated with laryngeal cancer and pot welding was associated with oral cancer. No associations were found between welding and the risk of oropharyngeal and hypopharyngeal cancer. The authors concluded the risk of laryngeal cancer and to a lesser extent oral cancer were increased by exposure to welding and several welding-related tasks.

An important limitation of this study is that the authors only collected exposure information via interview with participants and not based on actual or estimated exposure concentrations

d'Errico et al. (2020) evaluated the risk of sinonasal epithelial cancers (SNEC), mainly adenocarcinoma (ADC) and squamous cell carcinoma (SCC), and exposure to occupational hazards such as welding fumes. The study population, which was followed from 1996 to 2014, included 375 SNEC cases throughout the Piedmont region of Italy and identified by the regional Sinonasal Cancer Registry along with 408 controls. Exposure was determined by examining interviews on the subject's work history. Unconditional logistic regression models were developed to assess the relationship between SNEC and occupational exposure (models were adjusted for age, sex, area of residence, smoking habit, year of enrolment and co-exposures). SSC, but not ADC, significantly increased by ever occupational exposure to metals (nickel and cchromium) and with ever of cumulative exposures to welding fumes. The authors concluded exposure to occupational hazards, including exposures to welding fume, were associated with SNEC. As with similar studies, a major limitation of this study is that the authors only collected exposure information via work history examination and not based on actual or estimated exposure concentrations.

Lynge et al. (2020) investigated the association of rare cancers and occupational exposures. A multi-center case-control study (The Rare Cancer Study) was conducted in a European population for the risks of cancers in the small intestine, bone sarcoma, uveal melanoma, mycosis fungoides, thymus, male biliary tract, and breast cancer from occupational exposures. Participants were 35-69 years old with incidence of rare cancers (n=1053). Age and sex matched population (n=2062)/colon cancer controls (n=1084) were also included in the analysis. Interviews were conducted and a complete list of jobs was compiled. To assess any associations between occupational exposure and cancer the authors used unconditional logistic regression controlled for age, sex, confounders, and country. The results were reported as odds ratios (OR) and 95% confidence intervals (CI). Multiple occupational exposures were associated with different rare cancers. Specifically for welding, uveal melanoma was associated with those who worked as a welder/sheet metal worker (OR 1.95; 95% CI 1.08-3.52). The authors concluded the results provided evidence of welding being a human carcinogen; however, across nine countries, some cancers only had about 100 interviewed cases. In addition, like other similar studies this study was limited because exposure information was derived only from questionnaires and work histories and not actual measured levels of exposure.

Michalek et al. (2019) examined the incidence of kidney cancer in a Nordic population and occupation. The cohort population consisted of individuals included in the census from 1960-1990 (14.9 million). For each occupational group, standardized incidence ratios (SIRs) were calculated. Specifically for welding, the authors calculated a significantly increased SIR for kidney cancer among welders (1.24, 95% confidence interval (CI) 1.14-1.35). Overall, however, the authors concluded there was little variability in kidney cancer incidence across occupations and more studies should be conducted to support the study results.

Rana et al. (2020) assessed if welding fumes could influence the development of cancer by evaluating gene expression changes using a quantitative analytical framework. Datasets of studies focusing on tissues exposed to welding fumes and colorectal cancer (CC), prostate cancer (PC), lung cancer (LC), and gastric cancer (GC). First, gene-disease association networks were constructed. Then, any signalling and ontological pathways were identified. A clustered protein-protein interaction network using multilayer network topology was developed. Finally, the Cox proportional hazards (Cox PH) model and product-limit (PL) estimator were used to determine the significant genes that were associated with the cancer types. The results demonstrated alterations in the expression of multiple genes with the investigated cancer types. Welding fumes altered the expression of 36 genes for CC, 13 for PC, 25 for LC, and 17 for GC. Overall, the results suggest that welding fume exposure may influence the progression of these four cancer types. The authors concluded that the framework they used could be a novel mechanism for assessing how gene expression changes caused by exposure to welding fumes could affect cancer development.

Reed et al. (2020) investigated whether different phenotypes of cancers could be linked to different occupational exposures. Participants (352 men and 102 women) with bladder cancer completed a questionnaire outlining employment, tasks, potential exposures, smoking, family history, and lifestyle. The authors included multiple types of exposures, but only results regarding exposure to welding were included in the summary. Those who welded (hazard ratio (HR) 1.85, confidence interval (CI) 1.24-2.77; $p=0.003$) or were exposed to welding materials (HR 1.92, CI 1.27-2.91; $p=0.002$) were found to be more likely to experience disease progression and undergo extreme treatment compared to others. High-grade cancers were more common in workers from steel, foundry, and metal industries compared to low-grade diseases ($p<0.05$). Chromium was commonly found in those with high-grade and higher stage cancers ($p<0.05$). While the authors noted their study needs a stronger assessment, there were some associations in phenotype between occupational tasks related to welding and bladder cancer.

#### 4.1.5 Eye Effects

AlMahmoud et al. (2020) investigated eye injuries and risk factors among small-scale industrial workers. The cross-sectional study consisted of 500 workers in Al-Ain City, United Arab Emirates. A questionnaire was used to collect information on self-reported eye injuries, risk factors, and outcomes in the previous 12 months. Interviews were conducted between October 2018 – June 2019. Eye injuries were reported by 175 of the workers interviewed and 25 experienced recurrent injuries. Another 25 received treatment for an injury and five percent had to be hospitalized. The only welding specific information that was reported was that arc welding was associated with a higher risk for injury, which included 76 of the workers. The authors concluded arc welding posed a significant risk for eye injury and the information gained form this study could be used to increase safety among small-scale industrial enterprises.

Kwaku Tetteh et al. (2020) examined the prevalence and factors influencing eye injuries among welders in Accra, Ghana. A cross-sectional study was conducted with 382 welders from two welding sites. A questionnaire was used to gather information on eye injury history, ownership, eye personal protective equipment (PPE) use, and workplace environmental characteristics. To determine potential factors influencing eye injury incidence, bivariate and multivariate logistic regressions at 5% level of significance were conducted using the Stata statistical package. The results showed the percentage of welders working with arc welding and gas welding to be 59.7 and 40.3%, respectively. Eye injury prevalence was 47.9% higher in those participating arc welding compared to gas welding. Adjusted odds ratios (AOR) were calculated for risk factors determined to be associated with eye injuries such as gas welding (AOR 0.08, confidence interval (CI) 0.04-0.16), higher monthly income (AOR 5.26, CI 1.72-16.09), nonuse of eye PPE during work (AOR 1.86, CI 1.02-3.43), and a lack of training on how to use eye PPE (AOR 2.17, CI 1.07-4.38). The authors concluded the listed factors were significantly associated with eye injuries and health policies need to be implemented to protect workers.

#### 4.1.6 Multiple or Other Health Effects

Damtie and Siraj (2020) assessed the risk factors and prevalence of occupational injury in Bahir Dar Textile SC, Northwest Ethiopia. In 2019, the cross-sectional study consisted of 195 male and 105 female employees of the textile facility. Employees were selected randomly from the spinning, weaving, finishing, engineering, and administration sections. Occupational prevalence for the year was 42.7% and consisted of multiple types of injuries, but none were noted to be specific to welding. A statistically significant ($p<0.05$) difference in injuries was found due to exposure to rays/welding sparks, as well as other factors which include gender, job category, exposure to vibration, and labor-intensive work. The authors concluded the major causes for injury in this facility were mostly due to machines and falling/slipping. The authors suggest occupational safety and health training.

Kazi et al. (2021) conducted a health risk assessment to determine the potential health disorders caused by welding. The groups selected for this study were age-matched into adolescents and adults, then age-matched to nonindustrial controls. Scalp hair was collected from all subjects and analyzed for chromium (Cr) and manganese (Mn), which can be found welding fumes. Clinical and biological parameters were also measured to evaluate any potential health effects from occupational exposure to welding. The authors reported that there were significantly greater concentrations of both metals in the hair of welders compared to controls. Anemia and stomach disorders were highly prevalent in adolescent workers compared to adult workers, while asthma and respiratory disorders were more prevalent in adults. Neurological alterations were observed mostly in welders over 50 years old.

Meo et al. (2020) investigated the connection between multiple industries (wood, welding, motor mechanic, and oil refinery) and the prevalence of diabetes (prediabetes and type 2 diabetes mellitus). The authors included 560 welders and 201 controls based on a review of potential participant's demographics and medical histories. Participants average body mass index was $26.14 \pm 0.11$ kg/m$^2$, median age was $36.59 \pm 0.29$ years, and exposure occurred for 8 hours per day, 6 days per week. To diagnose prediabetes and type 2 diabetes mellitus, the American Diabetic Association-based glycated hemoglobin (HbA1c) criterion was used. An HbA1c of <5.7% was considered non-diabetic, 5.7-6.4% was considered prediabetic, and > 6.4% was considered type 2 diabetic. In welders, a prediabetic value was found in 261 participants (46.60%) and a type 2 diabetic value was found in 90 participants (16.07%). The prevalence of both types of diabetes was observed to increase with the duration of working exposure and a noted increase in HbA1c (0.03%) was observed within one year of working. The authors concluded that working in the welding industry increased the risk of developing prediabetes and type 2 diabetes mellitus.

Novotna et al. (2020) researched DNA damage in leukocytes to determine the potential health risks of exposure to nanoparticles (NP) during welding and smelting of metals. This study consisted of 20 workers who were occupationally exposed to NP long-term ($18 \pm 10$ years). Blood samples were taken from the participants before and after a shift to assess acute (after shift) and chronic (before shift) effects on DNA. The blood was heparinized, and leukocytes were isolated on a Ficoll gradient. Compared to controls, increases in single- and double-strand breaks in DNA (DNA-SB), as well as oxidized bases (2.4x and 2x, respectively) were measured by the enzyme-modified comet assay. Further DNA-SB were observed after acute exposure. Welders are at a higher risk of genotoxicity after exposure to NP compared to other occupations. Other risk factors included obesity (increased risk to genotoxicity) and being male because males were more likely to be exposed than females. This study was conducted in 2016 and repeated in 2017. The trend of DNA damage was similar; however, levels were found to be lower in the second study. The authors estimated exposure decreased due to changes in nanomaterial composition and working operations. The authors concluded that more studies need to be conducted to identify the genotoxic constituents in the aerosol and the reasons for the observed gender differences.

Oginawati et al. (2021) analyzed urinary concentrations of chromium (Cr) in Indonesian blacksmiths. A cross-sectional study consisted of 30 blacksmiths and 10 non-exposed controls. Inhalation exposure to hexavalent chromium (Cr6+) was measured using personal air sampling pumps and analyzed using a UV-visible spectrophotometer. Urinary Cr was collected, then measured with a graphite furnace atomic absorption spectrophotometer. The results from the personal air sample analysis showed that the Cr6+ exposure ranged from 0.03-0.63 mg/m$^3$ in workers and 0.02-0.04 mg/m$^3$ in controls. The urinary Cr6+ concentration results showed 16 out of the 30 workers were over the biological exposure index value and 21 were above the threshold limit value (TLV). A hazard index value of above 1 was calculated for 22 out of 30 workers, indicating potentially higher hazard for these workers. Results also showed a significant difference ($p=0.0001$) in TLV, chronic daily intake, and urinary Cr between exposed and controls. The authors concluded that these results show that exposure to Cr6+ in this worker population indicated a potential hazard to their health and hoped to bring awareness to potential risks in the workplace.

Ouchene et al. (2021) presented a comprehensive review of the potential external risk factors for systemic sclerosis (SSc). The literature search was conducted in PubMed and EMBASE databases. All studies published before January 1, 2020 were reviewed. The results showed an association between exposure to silica and organic solvents (occupational and/or environmental) with severity and incidence of SSc. However, not enough evidence was available to establish an association between SSc development and other occupations such as welding. The authors concluded that patients at risk of developing SSc or have been diagnosed should avoid potential exposures to silica, organic solvents, and other substances (not associated with welding).

Shahriyari et al. (2020) examined the potential musculoskeletal effects in the back, neck, and shoulders of welders. This study consisted of 15 welders who completed the Nordic questionnaire. Inclinometry was used to measure the physical workload (range of motion in relation to gravity) of the neck, back, and upper arms during welding for one year. Most of the musculoskeletal issues observed were in the lower back and shoulders. A statistically significant association ($p<0.05$) between median trunk and neck flexion with back and neck pain was found in welders during the study period. The pain experienced by welders was linked to a higher incidence of awkward postures and time spent with the trunk and neck flexed >20°. The authors concluded the type of work welders perform and how workstations are designed could be the cause of the observed musculoskeletal effects.

Tahmasebi et al. (2020) designed an ergonomic chair for near-ground welders to decrease the incidence of work-related musculoskeletal disorders. The impact of this chair was evaluated using electromyography activity to examine lower limb muscles in eight postures. Three postures were chosen by observing welders performing normal work activities and the other five postures were suggested for using the chair during welding. The System Usability Scale (SUS) was used to evaluate the proposed chair. The eight on-chair postures significantly ($p<0.001$) decreased muscle activity compared to the three normal postures. While kneeling had the lowest mean muscle activity ($p<0.01$) of the normal postures, it was still significantly higher than those using the chair ($p<0.001$). The SUS increased and muscle activity decreased when the slope of the seat pad increased 15°. One posture (KCC-90) was observed to not be acceptable. The authors concluded that a more ergonomic chair could prevent incidences of work-related musculoskeletal disorders due to awkward postures.

Tokaç et al. (2020) investigated how welding fume exposure could affect oxidative stress parameters in 48 Turkish workers. Superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), total glutathione (GSH), glutathione peroxidase (GPx), malondialdehyde (MDA), and 8-hydroxy-2′-deoxyguanosine (8-OHdG) were measured. Confounders were also analyzed, such as age, smoking habits, alcohol consumption and duration of exposure. The results in workers compared to control showed a significant decrease in the level of GSH and activities of CAT, SOD, and GPX, indicating increased oxidative stress in workers. Also, significant increases were observed in levels of MDA and 8-OHdG and GR activity. Alcohol usage and GSH were negatively correlated and GR in older workers was significantly higher compared to younger workers (<35 years old). No significant effects were observed from exposure to welding fumes and confounding factors. The authors concluded that exposure to welding fumes may cause oxidative stress and oxidative DNA damage.

Weyh et al. (2020a) examined the effects of a 24-week exercise program on the prevalence of work-related musculoskeletal disorders in welders. Employees were divided into a control group (CG), an endurance training group (ETG), or a strength training group (STG) to assess workload, physical performance, and overall health. The training groups participated in a focused 24-week standardized and progressive exercise training program. To determine if training would reduce the relative workload in eight muscles which were measured by surface electromyography, an experimental welding test (EWT) was conducted before (TP1) and after training (TP2). Further EWT-induced stress parameters and health-related outcome measures were also investigated. The results showed significant decreases in muscle load of the trapezius, rate of perceived exertion, visual analog scale, and body fat percentage after training ($p<0.05$) compared to CG. Significant increases in physical performance (bicycle exercise test and isometric core strength) and maximum EWT duration ($p<0.05$) was observed compared to CG. The authors concluded that an improvement in physical activity, endurance and strength, could reduce workload and prevent injury.

Weyh et al. (2020b) analyzed the prevalence of musculoskeletal disorders (MSDs) and leisure time physical activity (LTPA) in welders. Risk factors for low back pain (LBP) were also investigated. This study consisted of 145 welders from 34 companies in the German steel industry. Data collected from workers included individual factors (demographics and health behavior), job-related factors (welding process and hours worked per day, year of employment, shift work, and ergonomic tools used), and MSD (Nordic questionnaire). The International Physical Activity Questionnaire was completed to assess LTPA. After LTPA was calculated, Metabolic equivalent of task (MET) per week was determined to measure energy expenditure. Odds ratios (OR) were determined by prevalence and multivariate regression analysis. The prevalence of LBP was 71%, neck pain was 61% and shoulder pain was 55% in the previous 12-months. Participants (42%) accumulated less than 600 MET per week. The multivariate regression model showed LBP to be significantly associated with LTPA <600 MET/week (OR 3.4, confidence interval (CI) 1.05-10.85) and neck pain (OR 5.2, CI 2.02-13.56) in the previous 12 months. The authors concluded that LTPA should be prioritized by employers due to the high prevalence of MSDs.

## 4.2 Animal Studies

We identified 5 animal studies that evaluated the potential health effects of welding fume exposures.

Antonini et al. (2020) investigated an experimental animal model of the exposome during critical life stages that could be applied to similar exposure stages in worker populations. Three strains of male rats were used to account for genetic differences (Fischer-344, Sprague Dawley, and Brown-Norway). Animals were given a regular or high-fat diet for 24 weeks, then from week 7 to 12, rats were exposed to air or stainless-steel welding fumes (20 mg/m$^3$ for 3 hours/day for 4 days per week for 5 weeks). At the end of week 12, some animals were euthanized, and some were allowed to recover until the end of the study period. Serum and bronchoalveolar lavage fluid were collected at 7, 12, and 24 weeks. Kidney toxicity was the most severe in animals exposed welding fume and given a high-fat diet. Several serum enzymes and proteins were also altered in this group. Pulmonary toxicity was significantly influenced by welding fume exposure, but was not significantly associated with diet. The authors concluded that both diet and exposure were important risk factors for different health comes, exposure alone was important for respiratory outcomes, and rat strain was the most significant contributor to health outcomes other than respiratory, indicating and important genetic component to health outcomes.

Boyce et al. (2020) examined lipid changed in Sprague-Dawley rat liver after inhalation exposure to welding fumes and a high fat diet to replicate occupational exposure and a Western diet. To analyze lipid changes in the rat liver, matrix assisted laser desorption ionization imaging mass spectrometry (MALDI-IMS) was used. Animals were given a high fat or regular diet and/or exposed to welding fume via inhalation. The results of the MALDI-IMS analysis showed that each treatment group had a unique hepatic lipid profile. In the high fat diet group, triglycerides and phosphatidylinositol lipids were significantly increased. Also, lysophosphatidic lipids and cardiolipin were significantly decreased in the high fat group. The regular diet group had a higher amount of cerimide-1-phosphate, which has been shown to regulate pro-inflammatory responses via the eicosanoid pathway. The authors concluded welding fumes and a high fat diet caused significant alterations in the hepatic lipidome and welding fumes alone increased lipid markers of inflammation.

Kodali et al. (2020) evaluated if pulmonary exposure to welding fumes could lead to alterations in circulating factors which affect endothelial function. Sprague Dawley rats were exposed intratracheally to 2 mg/rat of metal-rich welding particulates. Manual metal arc welding using stainless steel electrodes (MMA-SS) or gas metal arc welding using mild steel electrodes (GMA-MS) were used for the exposure groups along with a saline treated control group. Molecular and functional effects were measured in *in vitro* primary cardiac microvascular endothelial cells cultured with serum from exposed animals. Results observed *in vivo* were significant for pulmonary injury and inflammation after exposure to welding fumes with minor changes in antioxidant and cytokine levels in the serum. Results observed from the *in vitro* study showed that of the 84 genes related to endothelial function analysed, MMA-SS influenced several aspects including cell migration, angiogenesis, inflammation, and vascular function. Exposure to GMA-MS or saline did not have an effect on any genes analysed. This was confirmed by using the scratch assay (an *in vitro* functional assay) and the aortic ring angiogenesis assay (an *ex vivo* functional assay). The authors concluded endothelial cells can be an effective screening tool when determining bioactivity of altered circulatory factors in exposed workers and results of their study showed that exposure to MMA-SS fume altered endothelial function.

Skovmand et al. (2020) assessed male reproductive effects after exposure to gas metal arc-stainless steel welding fumes (GMA-SS) in two strains of rats. Brown Norway and Sprague Dawley rats were used to determine the influence of strain on the detection of toxicity. A high fat or regular diet was fed to animals for 24 weeks. During weeks 7 to 12, animals were exposed to air or GMA-SS (20 mg/m$^3$ for four days per week). Health outcomes were measured or observed at the end of exposure (week 12) or the end of the recovery period (week 24). The results at week 12 showed pulmonary inflammation after exposure to GMA-SS; however, consistent changes in systemic inflammation markers (CRP, MCP-1, IL-6, and TNFα) were not observed. Daily sperm production was lowered after exposure to GMA-SS in Sprague Dawley rats fed both diets compared to controls and in Brown Norway rats fed the high fat diet. An increase of metal content in the testes was not found in Brown Norway rats. The results at the end of the study period showed bronchoalveolar lavage cell counts in Sprague Dawley rats exposed to GMA-SS returned to background levels but remained elevated in Brown Norway rats. While daily sperm production was not significantly affected, testicular weights and serum testosterone were lower in exposed Sprague Dawley rats. The authors concluded the changes in sperm count were unlikely to be caused by inflammation or lowered testosterone levels. Also, Sprague Dawley rats seemed more prone to reproductive effects compared to Brown Norway rats.

Zeidler-Erdely et al. (2020) examined the potential for initiation of lung tumors by a common components of welding fume, iron (III) oxide ($Fe_2O_3$), in A/J mice, which is a tumor susceptible strain. Male A/J mice were exposed to suspensions containing 1 mg $Fe_2O_3$ (exposed), calcium chromate (positive control), or 50 µL phosphate buffered saline (negative control) by oropharyngeal aspiration one time per week for 26 weeks. All mice were euthanized 70 weeks after the first exposure and lung nodules were examined. The results showed a significant increase in gross-observed lung tumor multiplicity in both the exposed (9.63±0.55) and positive control (3.35±0.30) animals compared to the negative control group (2.31±0.19). Histopathological analysis demonstrated bronchiolo-alveolar carcinomas were significantly increased in the positive control group (146%) and almost significantly increased in the exposed group (100%, p=0.085). Bronchiolo-alveolar adenomas followed the same pattern as the carcinomas. The authors concluded inhalation of iron alone may be a potential risk factor for lung carcinogenesis.

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

We identified 9 mechanistic/cell/*in vitro* study that evaluated the potential health effects of welding fume exposures.

Gao et al. (2021) investigated how welding fume exposure could affect the human metabolome. The metabolic profiles from 74 participants were identified from blood samples on a non-welding day and on a welding day, before and after working a six-hour shift. Blood samples (n=509) were collected in 2006 and 2010-2012 at a training center in Quincy, MA and analyzed using liquid chromatography-mass spectrometry. Of the 665 metabolites identified, some were found to interact significantly with the time of day (afternoon vs morning) and day (welding vs non-welding) by two-way analysis of variance. Overnight changes were also evaluated. The results showed a significant interaction for sphingosine 1-phosphate (S1P) and sphingasine 1-phosphate (SA1P) between day and time (p=0.03, <0.01, respectively). In addition, higher levels of both metabolites were observed in the morning of a non-welding day, then declined by the afternoon. However, on a welding day, levels were lower at the beginning of the day and remained low. Smoking status was not found to be related to the patterns observed. The authors concluded the levels of metabolites were altered between the welding and non-welding days and because S1P is a vital protein with many roles in the body, the underlying mechanism for changes with welding exposure should be investigated.

Khalid et al. (2020) evaluated the expression of arsenic 3-methyltransferase (As3MT) and superoxide dismutase (SOD) genes in the blood of industrial workers. A total of 250 blood samples were taken from workers in multiple industries (brick, kiln, paint, welding, pesticide, and furniture) along with age- and gender-matched controls. Genes were assessed using quantitative real-time polymerase chain reaction. The results showed the relative expression of both genes were significantly downregulated in exposed workers compared to matched controls as well as in smoking workers compared to smoking controls (As3MT p=<0.05, SOD p=<0.01 for both comparisons). Expressions of As3MT and SOD were lower in those working in the paint and pesticide industry compared to workers in other industries. As3MT expression was decreased in workers that worked longer than 10 years compared to workers with less than 10 years of exposure. A positive Spearman correlation was found between As3MT and SOD in workers (r=0.742, p=<0.0001). No results specific to welding were provided. The authors concluded arsenic may bioaccumulate due to the downregulation of the two genes evaluated leading to an increase in oxidative stress which could potentially induce DNA damage.

Khisroon et al. (2021) examined heavy metal exposure and DNA damage in welders. This study consisted of 59 welders and 59 controls. The comet assay was used to assess for DNA damage in lymphocytes and atomic absorption spectroscopy (AAS) was used to evaluate heavy metals (lead, iron, nickel, manganese, chromium, and cadmium) in scalp hair. The results revealed DNA damage was significantly increased in the lymphocytes of welders (121.8±10.7) compared to controls (56.5±17.6). Similarly, the concentration of all metals tested were significantly higher in welders compared to controls (p=<0.0001). A prominent association was identified between the heavy metals and total comet score (TCS) by regression analysis. Also, age and exposure duration significantly affected TSC (p=<0.05). The authors concluded DNA damage may be caused by occupational exposure to welding fumes and could lead to adverse health effects in workers.

Lai et al. (2020) assessed the relationships of occupational exposure to metal fumes and inflammatory biomarker levels, specifically advanced glycation end products (AGE) and its receptor (RAGE). Participants of this study consisted of 53 shipyard welders and 29 control workers (office jobs) and lasted from September 1 – December 31, 2017. The demographics and clinical information were gathered from participants as well as AGE, RAGE, IL-6, TNFα, and urinary metal concentrations. Flow cytometric analysis was used to measured RAGE levels. Metals and particulate matter (PM2.5) were measured using personal air samplers. The results showed welders had significantly higher exposure to PM2.5 ($p=0.015$) and an elevated exposure to metals compared to control workers. A significant increase in inflammatory biomarkers RAGE ($p=0.02$) and IL-6 ($p=0.008$) was observed in welders compared to control workers. RAGE was also significantly associated with increased levels of IL-6 levels (adjusted: $\beta=0.294$, confidence interval (CI) 0.083-0.732). Relationships between biomarkers and metal were identified. A significant positive association was found between AGE and nickel levels (adjusted: $\beta=0.101$, CI 0.031-0.172), RAGE and chromium levels (adjusted: $\beta=0.173$, CI 0.017-0.329), and RAGE and cadmium levels (adjusted: $\beta=0.084$, CI 0.011-0.157). The authors concluded urinary metal levels were associated with an increase in inflammatory biomarkers (AGE and RAGE) which could cause proinflammatory cytokine production (IL-6) and lead to further inflammatory effects.

NIOSH (2019) investigated the effects of welding fumes from mild-steel (MS) and stainless-steel (SS) welding processes during pregnancy. First-trimester placental trophoblast cells (HTR-8/SVneo) were exposed to MS fumes or SS fumes *in vitro*. The results showed cellular viability and free radical production were significantly changed by exposure to welding fumes, while invasive capabilities were negatively altered. Pro-inflammatory cytokines IL-6 and IL-8 were significantly increased in cells exposed to MS fumes. The authors concluded welding fumes to be cytotoxic to trophoblasts and further studies need to be done to examine the mechanisms leading to this effect.

Olgun et al. (2020) also investigated the effects of welding fumes from mild-steel (MS) and stainless-steel (SS) welding processes on placental trophoblast (HTR-8/SVneo) cells. Welding fume particle size and ability of the particles to enter cells was examined by electron microscopy. Endpoints analyzed included cellular viability, free radical production, cytokine production, and maintenance of invasive properties. Methods used to measure these endpoints were, respectively, WST-1, electron paramagnetic resonance, DCFH-DA, V-plex MULTI-SPOT assay system, and a matrix gel invasion assay. The average particles size of the welding fumes was <210 nm and was small enough to be internalized by trophoblasts and nuclear condensation was observed. The highest dose of tested welding fumes (100 μg/ml) caused a significant decrease in cell viability. Stainless-steel welding fumes generated the highest production of intracellular reactive oxygen species and hydroxy radicals. The production of IL-6 and IL-8 were observed after exposure, but levels of IL-1β and TNFα were not elevated. Exposure to mild and stain-less steel welding fumes decreased the invasive capability of trophoblasts. The authors concluded welding fumes are cytotoxic to the cells used in this study based on the production of oxidative stress and inflammation as well as the decline of invasive capabilities.

Samulin Erdem et al. (2020) examined the effects of mild steel welding fume (MSWF) on risk factors for cardiovascular disease. The expression of 40 genes involved in inflammation, fibrosis, and endothelial activation were measured in macrophages, pulmonary epithelial, and vascular endothelial cells. Exposure consisted of low doses (not provided) for 6 hours per day for 5 consecutive days. The results showed expression of matrix metallopeptidase 1 (MMP1) in epithelial and endothelial cells after exposure. There were no other changes in inflammation, cell proliferation, oxidative stress, or migration capacities. The authors concluded that exposure to low doses over a week did not result in increased risks for cardiovascular disease typically associated with increased cellular inflammation.

Ward et al. (2020) validated the use of a novel air-liquid interface (ALI) exposure device using welding fumes. The Dosimetric Aerosol in Vitro Inhalation Device (DAVID), based on the human respiratory system, used water condensation to efficiently deposit aerosols to the ALI culture. Welding fumes were used as a positive control to validate the ability of the device to elicit toxicological responses. The results showed a linearly dose-dependent reduction in cell viability with exposure time as well as differences in toxicity that were dependent on the welding conditions, which has not been shown by other methods. The authors note that DAVID is more efficient in delivering high doses ($>100$ μg/cm$^2$) quickly compared to other delivery methods. The authors concluded DAVID could provide a more accurate exposure assessment and one that is physiologically more relevant to human exposures for *in vitro* toxicity evaluations.

Wu et al. (2020) examined whether exposure to nanomaterials ($<100$ nm dimension) would exacerbate preexisting inflammatory respiratory diseases. Normal and TNFα-inflamed primary human small airway epithelial cells (SAEC) were exposed to reference nanomaterial species (copper oxide - CuO, zinc oxide - ZnO, and mild steel welding fume - MSWF). Inflamed SAEC cells were 15-70% more susceptible to cytotoxicity than normal SAEC cells due to higher amounts of basal reactive oxygen species. Only CuO and ZnO were able to trigger a response in normal SAEC cells, not MSWF. Normal cells developed a tolerance against subsequent oxidative insults. However, the inflamed cells were not able to adapt due to an impairment in nuclear factor erythroid 2-related factor 2 (Nrf2)-cytoprotective response. The authors concluded that pulmonary toxicity caused by nanomaterials is dependent on the type of nanomaterial and any underlying inflammation of the alveolar region of the lungs.

## 4.4 Reviews

We identified 7 reviews of welding exposure and health effects.

Cherrie and Levy (2020) focused on evaluating current health-based exposure limits for welding fumes in light of The International Agency for Research on Cancer (IARC) determination that welding fumes cause lung cancer in humans to ensure that they are protective. IARC, however, does not distinguish between effects from mild and stainless-steel welding fumes. Lung cancer risks were observed at low exposures averaged over a working lifetime (below 1 $mg/m^3$ and as low as 0.1 $mg/m^3$). Due to IARC's conclusions, fume control for welding operations has been strengthened in occupational setting in Britain.

Evans et al. (2020) discussed the multitude of human biological process that require manganese (Mn), including immune function, biochemical regulation of energy, growth, coagulation and hemostatic function, and oxidative stress byproduct removal. However, Mn toxicity has also been observed in occupational, accidental, or iatrogenic (illness caused by medical treatment) exposures. The authors describe the differences in symptoms related to Mn toxicity and Parkinson syndrome and common etiologies of Mn toxicity.

Pega et al. (2020) proposed to conduct a systematic review and meta-analysis on the effects of occupational exposure to welding fumes on the respiratory system (trachea, bronchus, and lung cancer) by applying the Navigation Guide systemic review methodology to organize the framework. The authors would search Medline, EMBASE, Web of Science, and CISDOC for relevant publications. Additional searches for grey literature, internet searches, and organization website would be conducted and review of previous systematic review reference lists along with expert consultation. The authors list inclusion and exclusion criterion which consists of age, work history, occupational exposure to welding fumes, and effects of the respiratory system. The studies would be reviewed and risk of bias using the Navigation Guide tool applied. The report would be completed using PRISMA guidelines for the systematic review and meta-analysis.

Maestrelli et al. (2020) updated a literature search conducted in 2010 which focused on the use of exhaled breath condensate (EBC) to research occupational lung diseases. The keywords "breath AND condensate AND occupational" were searched in Medline via PubMed. Eleven relevant articles were found between January 2018 and October 2019 with one focused on occupational allergies. The allergy study concluded EBC hydrogen peroxide is not a useful marker to identify allergies in animals. The authors found most of the biomarkers studied were related to oxidative stress after exposure to occupational agents including welding fumes. The authors concluded that the use of EBC remained a useful approach but was specific to the study of occupational diseases. Also, the issue of dilution needed to be addressed in future research.

Memarian et al. (2020) analyzed the mortality reports of United States workers in the construction industry. The authors noted that the majority of fatalities were due to chronic occupational illnesses (95,000), not job site accidents, with 50% of occupational cancers originating from this industry. The National Occupational Research Agenda (NORA) Construction Sector Council identified silica, welding, noise, and lead as research priorities. The authors focused on the selection and the feasibility of appropriate engineering controls to reduce exposures, the development of the Exposure Control Database, and addressing issues associated with air sampling procedures and improvements in data collection and data sharing processes.

Riccelli et al. (2020) examined *in vivo* and *in vitro* studies to determine welding fume pathogenesis in respiratory disease. The authors conducted a literature search in PubMed, NIOSHTIC, and Web of Sciences. Epidemiological studies, toxicological studies, reviews, meta-analysis were included. The results of the literature showed a dose, time, and welding fume dependent effect on lung injury. The authors concluded that occupational lung diseases need further researched and the cause identified.

Zhou et al. (2020) performed a systematic review and meta-analysis to determine the risk of noise-induced hearing loss (NIHL) in the Chinese occupational population. A literature search was conducted for publications dated 1993-2019, and studies were analyzed for a correlation between NIHL and occupational exposure to noise. Any exposures to complex noise and co-exposures to noise and chemicals were also included. Welding fumes were only associated with high-frequency NIHL as a co-exposure to noise compared to noise exposure alone. Occupations were also analyzed, but in general terms. The authors concluded the prevalence of NIHL was aggravated by co-exposures to complex noise and chemicals and efforts need to be made to reduce occupational noise exposure in China.

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