

Construction and validation of a matrix for the estimation of exposures in the welding trades: a
three-part series

by

Jean-Michel François Galarneau

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Department of Medicine
University of Alberta

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Abstract

Introduction:

This three-part series of papers aimed to construct and validate an exposure matrix that would be used to estimate personal airborne exposures to total dust, manganese, nickel, chromium and aluminum for welders in the What-me cohort. The *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* study established a cohort of both women and men welders for the purposes of investigating pregnancy and other birth outcomes along with general health issues related to welding. To achieve this, data were extracted and assembled from the literature and later analyzed to produce exposure models. Final models derived in this first step were then validated through the use of external data gathered under controlled conditions. Finally, exposure estimates were made for all welders in the cohort and using the exposure matrix developed an investigation of the relation between exposures and urinary metals analysis was undertaken.

Methods:

A systematic literature search was first conducted to identify and extract all relevant data from published journal articles appearing in selected databases. Summary data were extracted that represented airborne personal exposures to total, inhalable and respirable dusts along with metal concentrations for manganese, nickel, chromium and aluminum. Mathematical exposure models were derived from these data and a validation of the models undertaken in the second part of this study. To do this, the most common welding combinations of welding process, base metal and consumable (welding scenarios) for welders taking part in the What-me study were identified through detailed welding questionnaires. These were replicated under controlled conditions with a welder equipped with a personal air sampling pump to gather samples. A

gravimetric analysis was later performed to determine total dust exposures followed by a metals analysis using ICP-MS. Predictions were made for these scenarios using the exposure models derived in the first step of this study and correlated against the results from the welding scenario replication. Lastly, exposures to manganese, nickel, chromium and aluminum were estimated using the welding exposure matrix described above and analysed against spot urine samples taken from welders between 2011 and 2016. The estimated exposures were correlated against urinary metal concentrations followed by linear regressions of urinary metal concentrations including exposure estimates as a predictor of urinary metals.

Results:

The systematic review process yielded 92 published articles from which 737 summary statistics were extracted representing 4620 personal samples of total dust, 4762 of manganese, 4679 of nickel, 3972 of chromium and 676 of aluminum. The highest total dust exposures were for flux-core arc welding (FCAW) while the highest manganese producing base metal was for mild steel. For nickel, the highest emissions were from high alloyed steel using gas metal arc welding (GMAW) while chromium emissions were most abundant in manual metal arc welding (MMAW) on stainless steel. Aluminum exposures were highest in FCAW welding and on aluminum as a base metal. The scenario replication part of this study identified 21 scenarios covering more than 90% of the scenarios in the What-me study. Sixty-one welding sessions took place with a minimum of two replicates per scenario. Spearman rank correlations between predicted exposures and mean measured exposures resulting from the scenario replications yielded a rho of 0.93 ($p < 0.001$) for total dust, 0.87 ($p < 0.001$) for manganese, 0.54 ($p < 0.024$) for nickel, 0.43 ($p = 0.055$) for chromium and 0.29 ($p = 0.210$) for aluminum. Spot urine samples were gathered from welders and linked to an exposure estimate resulting in 204 samples from women

and 225 samples from men. Spearman rank correlations between urinary metal concentrations and estimated metal exposures yield a rho of 0.08 ($p=0.181$) for manganese, 0.081 ($p=0.093$) for nickel, 0.14 ($p<0.005$) for chromium and 0.13 ($p<0.01$) for aluminum. Linear regression showed chromium and aluminum as having strong positive log linear relations between estimated exposures and urinary metal concentrations while manganese and nickel showed weaker ones.

Conclusion:

This study produced the first validated welding exposure matrix composed of process, base metal and consumable. This matrix was able to accurately predict exposures observed under controlled conditions while also predicting urinary metal concentrations in an existing cohort providing additional validity to the matrix developed here. This matrix can be used by any researcher to estimate welding exposures in a multitude of occupational contexts.

Preface

This thesis is an original work by Jean-Michel François Galarneau. No part of this thesis has been previously published.

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Chapter 1

1.1 Introduction

The study of welding exposures and their effects on welders' health outcomes has been the subject of scientific inquiry for the past several decades. The process of metal joining through various welding techniques is one that exposes welders, and others that are in proximity of welding activities, to hazardous fumes, dusts, gases, heat, ultraviolet light and radiation (Antonini, 2003). Variations in exposures to these hazards resulting from different combinations of welding factors also lead to variations in the risk to human health. One of these welding factors, welding process, can be summarized into three main categories that cover most welding activities in Canada; Manual Metal-Arc Welding (MMAW), Semi-Automatic Arc Welding (Flux-Cored Arc-Welding (FCAW), Gas Metal-Arc Welding (GMAW), Metal Core Arc-Welding (MCAW)) and Gas Tungsten Arc Welding GTAW (Table 1.1). Paired with the welding processes are different base metals that are selected to satisfy various properties and could broadly be described as low alloy steels, high alloy steels and aluminum. These base metals are the most commonly seen in the industry but specifically, mild steel and galvanized steel are the main low alloy steels of interest in this study while high alloy steel is divided into stainless steel and other high alloy steel. These base metals are generally matched with a welding rod or filler metal that both matches the steels being welded and the desired welding properties. A variety of fluxes and shielding gases (often argon, carbon dioxide or combinations of both) can also be used to create a micro atmosphere which protects the weld from outside elements during the arc activity. All of these attributes contribute to variations in welding fume exposure (Antonini, 2003; Method for sampling airborne particulates generated by welding and allied processes, 2006). It is with this in mind that this three-part study was undertaken such that a welding exposure matrix could be constructed from studying and quantifying exposures based on these three aspects of welding (i.e., process, base-metal, consumable).

Table 1.1: Description of most common welding processes

Manual Processes		Semi-Automatic Processes		
Manual metal arc welding - MMAW	Gas tungsten arc welding - GTAW	Gas metal arc welding - GMAW	Flux-cored arc welding - FCAW	Metal-cored arc welding - MCAW
Flux coated, no shielding gas	No flux, solid wire, requires shielding gas	No flux - solid wire, requires shielding gas	Flux centre - not solid wire, shielding gas not required but sometimes used	Not solid, includes other minerals, shielding gas is required and a wide variety of gases can be used
Stick electrode	Hand-held stick/filler metal	Wire fed from spool (higher deposition rate than manual processes)	Wire fed from spool (higher deposition rate than manual processes)	Wire fed from spool (higher deposition rate than manual processes)

These axes of welding are well represented in the *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* project (Cherry et al., 2018), a cohort study that began in 2011 to investigate the possible adverse health effects that welding exposures may have on the unborn child, while at the same time studying the effects that such exposures could have on the health of the welder (Arrandale et al., 2015). It was later expanded to include men in 2013. Participants from different parts of Canada were recruited forming a cohort of 1001 welders. As part of the study, participants completed 6-monthly questionnaires with detailed questions on past work histories, current occupation and details on welding that included questions on welding process, base metal and consumable, among others. The study was designed such that rates of miscarriages and other pregnancy outcomes could be compared between welders and a similar group of tradeswomen that were not welders (i.e., electricians) in an initial analysis followed by the addition of considering specific chemical exposures, among welders, that could lead to an increase in the risk of miscarriage and other adverse pregnancy outcomes. To do this, exposures to specific metals would need to be estimated and it was simply not possible to assess their exposures through personal monitoring in their places of work so a detailed welding questionnaire was designed. It was necessary to construct a welding exposure matrix that would provide the study with exposure estimates that could be assigned to every welder based on the welding exposure questionnaire (Appendix A). Thus, this three-part study was designed to

construct and validate a welding exposure matrix that could be used in the estimation of exposures to both total dust and specific metals for the participants of the What-me study. The first part of this study was to construct the matrix using data from published literature. The second part was to measure, under controlled conditions, exposures for key combinations of process, base metal and consumable to validate and/or calibrate the models produced in step 1. Finally, the third part of the study was to investigate and further validate the matrix by examining the relationship between exposure estimates derived from previous steps and urinary metal concentrations found in the urines of welders from the What-me cohort.

1.2 Background

1.2.1 Health effects

There have been reports of varying health effects that welding exposures have on the health of welders ranging from effects on the lungs to neurological ones (Antonini, 2003). Certain metals that are commonly found in base metals or consumables that welders work with are known to be more detrimental to the worker's health than other metals. Chromium, hexavalent chromium (Cr(VI)) and nickel have been associated with work related skin problems and lung cancer (Gerin et al., 1993; Athavale et al., 2007; Cherry and Galarneau, 2020), while other metals like manganese and aluminum were linked to diseases of the nervous system (Sjogren et al., 1996; Santamaria et al., 2007; Racette et al., 2017). The most relevant health effects to this specific study are those reported on pregnancy and birth outcomes.

It remains unclear whether or not welding during pregnancy can lead to adverse pregnancy outcomes and this prompted the creation of the What-me study. There is some evidence that shows the possibility for welding fumes and metal dusts to increase the risk of preterm births or *small for gestational age* (SGA) babies in women who are exposed to such fumes/dusts during pregnancy (Quansah and Jaakkola, 2009). In a study conducted in Finland, 68 women had been identified, through the use of a population registry, as exposed to welding/metal fumes and dusts during pregnancy who had given birth to a singleton baby and were compared to 1602 women fitting the same criteria but that had not been exposed to metal/welding fumes or dusts. The risk of preterm births in women exposed to metal dusts/fumes was indeed higher (OR=5.63) than in women not exposed in a fully adjusted model but this relation had a very wide confidence interval (1.15-27.65) and was based on a small number of

exposed women. The risk of low birthweight was also elevated in women that were exposed to metal or welding fumes/dusts during pregnancy or in the months preceding conception adding some evidence to the increased risk of adverse pregnancy outcomes in those exposed but the overall evidence from that study was weak. A recent study out of Sweden also used population registries to identify women that could possibly be exposed to welding fumes during pregnancy (Norlen et al., 2019). In this study, welding fumes were stratified into none vs. low exposure or high exposure. They found that in women working at the time of their 10-week pregnancy appointment, an increase in the risk in delivering a *small for gestation age* (SGA) baby was observed in women exposed to welding fumes/dusts compared to unexposed women. This relationship was stronger in women categorised as having had low exposures than it was in those considered highly exposed reducing the strength of the evidence and showing no dose response relationship between exposures and the risk of SGA. Further, when looking at birthweight, an increased risk of low birth weight was observed with the low exposure group showing a significant increase in risk of 52% and the high exposure group showing an increased risk of 22%. The risk of a preterm birth was highest in the high exposure group with an odds ratio of 1.22 and was also elevated in the low exposure group with an odds ratio of 1.16 (both significant). This is perhaps the best evidence of some risk to the unborn child in women exposed to welding who worked full time for most of the pregnancy but shows that the effects are not particularly strong and that they did not seem to markedly increase from the low exposure group to the high exposure group.

1.2.2 Urinalysis

Welders, being exposed to certain metals, generally show higher concentrations of metals in their urine and blood. Manganese, nickel, chromium and aluminum among others are commonly found at higher concentrations in the urine and blood/serum of welders. Manganese is an important metal exposure in welders as it is found in most consumables as well as in mild steel and stainless steel. The most common route of entry for manganese is by ingestion (Casarett et al., 2001) as manganese is commonly found in food. Its use in the metal industry as a ferroalloy has indeed increased in past years making it an important exposure to welders. There are very few reported cases of manganese toxicity in other settings than in an occupational one and more specifically the metal industry and welding. It generally concentrates in mitochondria and therefore primarily resides in the kidneys, liver, pancreas and can be reabsorbed long after it

has entered the body (Casarett et al., 2001). It can also cross the blood-brain barrier leading to neurological issues. Most manganese excretions are through feces but it is estimated that up to 1% of the absorbed manganese is excreted in urine (Lauwerys and Hoet, 2001).

Nickel is another metal that enters the body through various means but the most important occupational exposures occur through inhalation (Casarett et al., 2001) either in welders or refinery workers. Arc time in welding greatly increase nickel oxide exposures in welders and up to 35% of the inhaled nickel particles are absorbed into the blood. Nickel is also excreted through urine and has a urinary half-life of 30 to 53 hours in exposed workers and of about 11 hours in non-exposed workers (Casarett et al., 2001). It is often associated with cancers and dermatitis (Casarett et al., 2001; Lauwerys and Hoet, 2001; Cherry and Galarneau, 2020).

Another important and abundant metal found in welding fumes is that of chromium either as trivalent chromium or hexavalent chromium. Only the latter is of great biological importance in terms of toxicity and is associated with cancers and asthma (Casarett et al., 2001). Again, most chromium absorption in humans is through ingestion of either food or water but occupational exposures often occur in welders especially as it pertains to the hexavalent form of chromium (Meeker et al., 2010; Keane et al., 2012). Chromium exposures and overexposures are often observed through urinary analysis and the American Conference of Governmental Industrial Hygienists (ACGIH) has set the biological exposure index limit to 25µg/L in exposed workers (Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2020) and is considered the best biological monitoring medium through which to monitor hexavalent chromium exposures (Lauwerys and Hoet, 2001).

The last metal of interest in this study is that of aluminum, a metal most abundant in nature which has many industrial uses. The most common source of exposure is also through the ingestion of food and water but also through the use of certain pharmaceuticals (Casarett et al., 2001). Aluminum is not well absorbed through the lung or other membrane and can make its way to the brain directly through the olfactory system making those exposed to airborne aluminum especially at risk of toxic exposure. It concentrates mostly in the bone and aluminum does not remain in blood for a long time as the kidneys filter it excreting it through urine rather rapidly. Welders are very much exposed to airborne particles of aluminum with soluble portions of aluminum particulate rapidly absorbed while the non-soluble portion is deposited into the lung and absorbed at a slower rate (Lauwerys and Hoet, 2001). Urine is the main excretion medium of

aluminum with two phases of excretion: one that occurs rapidly with a urinary half-life of approximately 8 hours, followed by a slow release related to cumulative exposure. In welders, this half-life has ranged from 8 hours to as much as 6 months in those with prolonged, continued exposures (Lauwerys and Hoet, 2001). It has mainly been associated with diseases of the nervous system, vaguely with issues of the lung, dementia and potentially Alzheimer's although the latter is still subject to debate (Casarett et al., 2001).

These 4 metals are all, in part, excreted through urine and although they vary in the amount that can be absorbed into the blood and thus excreted in the urine, they have all been the subject of examination in welders in relation to airborne exposures.

The relationship between airborne exposures to metals and urinary excretions of these elements is not yet settled. This relationship is even more blurred when adding time between reported or measured exposures and urine sampling. One study aimed to assess the relationship between airborne exposures to manganese, nickel, chromium and urinary metal concentrations based on the fact that these metals are commonly found in both base metals and consumables with which welders work (Persoons et al., 2014). They gathered a week's worth of occupational exposure information ranging from workload to welding process and base metals used but no air sampling results. At the end of the workweek, urine samples were taken to be analysed against these exposure determinants. Chromium and nickel were clearly related to welding mild steel showing a negative relationship with this nickel and chromium sparse base metal while showing a positive relationship, in the case of nickel, to welding with GMAW. Manganese was not shown to relate to factors describing welding but rather was significantly shown to be related to welding in a confined space, as was the case with chromium. Both chromium and manganese related positively to longer hours welding but not nickel. Another study examined the relationship between airborne manganese, nickel, chromium and aluminum (among others) and urinary metal concentrations in welders that welded for at least 2 hours daily in their regular occupation from Monday to Thursday (Iarmarcovai et al., 2007). Urine samples were collected at the end of the workweek, in this case on Thursday evening. The study was designed such that welders were divided into two groups, one with no local exhaust ventilation present in the welding shop and another with local exhaust ventilation and only group comparisons were reported. The mean total dust concentrations gathered from personal samples taken in both groups were 3.26 mg/m³ for the ventilation group compared with 5.27 mg/m³ in the non-ventilation group. Urinary median

concentrations for manganese at the end of the week were not different between groups but both had increased over time. For chromium, beginning of week samples were lower in both groups than end of week samples and the non-ventilation group had higher concentrations, both beginning and end of week, than the ventilation group. Nickel did not relate well to temporality of urine samples or to exposure groups; in the non-ventilation group, concentrations in the urine remained unchanged while in the ventilation group, concentrations reduced from the beginning to the end of the week. Aluminum was not detected in the ventilation group at all but was indeed detected in the non-ventilation group showing marginal increases from the beginning of the week to the end. More direct evidence of a link between exposures and urinary aluminum comes from a study conducted in the 1980's showing that aluminum welders had elevated increases in urinary concentrations after welding aluminum which decreased over time after exposure with a small lag in this decline (Sjogren et al., 1985). In the same study, previously unexposed healthy individuals volunteered to expose themselves to aluminum welding fumes and saw their urinary excretions go up with exposures and down again after the exposures were removed. Another biological monitoring study on aluminum found that it was difficult to see changes in urinary aluminum concentrations from pre to post-shift samples (Rossbach et al., 2006). In this study, they studied aluminum welders in a manufacturing context and followed them up for 5 years. Personal air sampling was also performed on these welders and data on aluminum concentrations were correlated to urine samples taken during a yearly health examination. Welder urinary aluminum concentrations were also compared to concentrations from an unexposed control group. Their results show that welders had consistently higher median urinary aluminum concentrations than controls. They also found that urinary aluminum concentrations were positively related to cumulative total dust concentrations at least 2 out of the 5 years and also significantly overall.

Manganese was assessed in another study looking to investigate the relationship between a simulated lung environment (Hatch solution) and exposures captured therein and urinary/blood manganese concentrations (Ellingsen et al., 2013). The welders (n=137) welded one or two days before the urine and blood samples were taken and wore personal air sampling devices. Their results showed clear evidence of positive correlations and regressions between air manganese levels, both soluble and insoluble (in the Hatch solution), and urinary creatinine corrected manganese levels. Correlation coefficients as high as 0.46 were reported with no discernable

differences between air samples taken one day before the urine sample was collected and those taken 2 days before. In another study on manganese alloy (a metal with 11-25% Mn content) workers relating exposures taken from personal air monitoring to urinary manganese concentrations, it was found that there was no relation between air samples and urinary concentrations despite these being 24-hour samples (Barrington et al., 1998). Manganese, nickel and chromium were also measured in the urines of welders recruited from a shipyard and welding plant in Russia. The participating welders wore personal air sampling pumps and gave both blood and urine samples to the study staff. They found that air concentrations of manganese were nearly significantly correlated to urinary manganese concentrations ($r=0.16$) when post-shift urine samples were collected one day after the welding took place and a correlation of $r=0.19$ ($p<0.05$) was observed when urine was collected two days after welding (Ellingsen et al., 2006). They also found that urinary nickel and chromium correlated well with air concentrations for both 1-day-old samples and 2-day-old samples noting a slight increase in the effect size for chromium with the 2-day-old samples and the reverse for nickel.

More robust evidence of the presence of urinary nickel and chromium relating to airborne concentrations of these metals can be found in a study examining a cohort of stainless steel flux-cored arc welders (FCAW). Exposures to nickel and chromium were assessed for 1 week through the use of personal air samples and urine samples taken daily (Stridsklev et al., 2004). Significant correlations were observed between chromium VI and urinary post-shift chromium concentrations while nickel did not show significant relation to nickel exposures as measured by personal samples. These findings were similar to those found by Gube et al. (2013) where they recruited healthy non-smoking, non-welder participants to be exposed to various welding fume concentrations (0 mg/m^3 , 1 mg/m^3 , 2.5 mg/m^3). The participants gave biological samples before and after the exposure took place which lasted about 6 hours in duration. Welding fumes were generated from GMAW on stainless steel using an electrode that contained 19% chromium and 9% nickel. Ambient air monitoring was also performed during the 6-hour welding sessions and later analysed for nickel and chromium concentrations. Clear linear associations between exposures in the air and urinary chromium excretions were observed for chromium while nickel showed weaker but nevertheless significant associations between the two. Change from pre-shift to post-shift urinary concentrations for both chromium and nickel were also found to significantly relate to chromium and nickel air concentrations with nickel showing a less linear

dose response relationship. In a more recent study of welders from a primarily stainless steel welding shop using GMAW and argon gas (Stanislawska et al., 2020), a positive relationship between inhalable chromium and nickel were found with creatinine corrected urines. Welders were followed for 4-5 days and their exposures assessed throughout the entire day using personal air sampling pumps. They later gave biological samples of urine and blood and these were analysed for metal concentrations. A correlation of 0.59 was observed for the relation between urinary chromium and inhalable chromium VI and as high as 0.64 for the relation between urinary chromium and inhalable chromium III (both $p < 0.001$). Inhalable nickel was also found to correlate with urinary nickel concentrations but reported to be a weaker correlation. Data from the WELDOX study were also analysed with respect to chromium and nickel exposures and their relation to urinary concentrations (Weiss et al., 2013). In their study published in 2013, clear linear relationships were found in 241 post-shift urine samples taken from welders that also wore a personal sampling pump to get measurements of inhalable and respirable dust. They found correlations as high as 0.61 between respirable chromium and urinary chromium and 0.42 for nickel. In a linear regression adjusting for age, creatinine, respiratory equipment and increased physical workload, they found that respirable chromium and nickel both positively and significantly related to urinary chromium and nickel concentrations.

1.2.3 Primary emission factors in welding exposure matrices

Job exposure matrices can be very useful in determining and predicting exposures to metals and to dusts that are produced during arc time. To properly estimate a welder's exposures, one needs to incorporate all components of welding that lead to variations in exposures into one model that accounts for the effects of process and base metal in order to adequately predict exposures. The effects of a specific welding process relative to another must include adjustments made by base metal because the specific properties of a welding process will vary across base metals (Pires et al., 2006). Incorporating the effects of consumable in matrices that attempt to predict metal exposures adds to the precision of the estimates made by an exposure matrix composed of process and base metal as most of the welding emissions will be composed of materials that come from the consumable (Method for sampling airborne particulates generated by welding and allied processes, 2006). Published welding exposure matrices generally do not include both the base metal and the consumable in their models for two reasons: the first reason is that base metal is more likely to be known while consumable is often not known, and the

second reason is the statistical problems brought on by including two highly correlated variables in one single model (collinearity). For example, a consumable with 12% chromium will be far more likely to be used on stainless steel than it will on mild steel while a consumable with less than 1% chromium is more likely to be used on mild steel than on stainless steel producing issues of collinearity. Some have dealt with this problem by only including metal content found in consumables as a replacement for a base metal variable in their statistical modelling (Weiss et al., 2013) but this does not predict mismatching base metals and consumables and it assumes that the effects of the consumable contents will be the same across each welding process. Part of the collinearity problem can also be caused by empty cells in the matrix where in sampling of exposures, no instance (welding scenario) of a high in chromium consumable was used on mild steel and thus creates a modelling problem where one or multiple cells are empty. In the case of the What-me study, both base metal and consumable were known and it was thought that exposure estimates would be enhanced by considering the effects that both of these had on exposures while also considering the effects of process.

1.2.4 Other potential factors affecting exposures

Along with the known effects that welding process, base metals and consumables have on exposures come other factors that are known to influence exposure levels in welding. One of these well-known factors is the presence of ventilation and its efficiency. A rather extensive literature review was conducted in the mid 2000's by Flynn and Susi (2010) to identify potential exposure determinants to total dust, manganese and iron fumes. One of the factors extracted from the literature was the presence of local exhaust ventilation during welding activities. Their findings showed that in the case of total fumes, a reduction of 35% in total fume exposures could be observed in those welding with local exhaust ventilation when compared to those welding with no such ventilation. Further, manganese exposures were reduced by approximately 41% when welding with local exhaust ventilation. This finding was mirrored in the study by Pesch et al. (2012) who found significant increases in manganese exposures in welders welding without efficient ventilation. The importance of ventilation was also the subject of the study by Persoons et al. (2014) who looked at urinary chromium and nickel concentrations in welders. Welder urine samples of those working with mechanical ventilation were compared to those working without ventilation in a fully adjusted linear regression including other exposure determinants and they found that urinary chromium was markedly reduced in those working with mechanical

ventilation. The same authors also looked at welding in confined spaces and they found similar results in that urines of welders welding in a confined space were significantly higher in chromium than those not welding in confined spaces. Pesch et al. (2012) also found vast exposure increases in welders welding in confined spaces with large increases in both manganese exposures and iron exposures. In the review article by Flynn and Susi (2010), total fume exposures for those welding in confined spaces were more than twice those of welding not in confined space. These exposure determinants are well known and have been studied extensively but one exposure determinant that is cited less often is welding outdoors vs. welding indoors. In a study conducted by Susi et al. (2000) where welding exposure data were gathered in the mid 1990's, clear differences were found in total dust exposures in those welding outdoors compared to those welding indoors with a doubling of exposures to total dust for the those welding indoors. They do caution however, that although welding outdoors significantly reduced exposures, mean exposures were still above occupational limits and that local exhaust ventilation is much less effective outdoors than indoors. Nevertheless, the effect of welding outdoors is an important determinant of welding exposures but often not discussed.

The various exposure factors described above are indeed very important predictors of both airborne exposures and of internal dose. In this three-part series, they are not used in the construction of the welding exposure matrix and a rationale for their omission is given in chapter 2. Thus, it should be noted that their omission in the welding exposure matrix is no indication of their lack of importance.

1.2.5 Published welding exposure matrices

There were already some exposure matrices in the literature that included welding process and base metal but none included process, base metal and rod/filler metal in a comprehensive manner. Perhaps the most cited welding exposure matrix is the one developed by Gerin et al. (1993) used in the 1990's to estimate the risk of lung cancer in welders. The matrix was developed in order to estimate exposures to total dust, total chromium as well as Cr(VI) and nickel in more than 11 000 welders recruited in a large multicentre study conducted by the International Agency for Research on Cancer (IARC) spanning across 135 companies from 9 European countries. Detailed work histories were collected in the workplaces in question in order to compute cumulative exposures and a welding exposure matrix was developed through the review of literature, the inclusion of data, when available, collected in workplaces participating

in the study and with the expert opinions of two hygienists. They computed exposure estimates for 13 different scenarios, 8 of which were welding process by base metal combinations. The most total fume producing process/metal combination was GMAW on aluminum ($9000 \mu\text{g}/\text{m}^3$) followed by GMAW on mild steel ($6000 \mu\text{g}/\text{m}^3$) and MMAW on mild steel ($6000 \mu\text{g}/\text{m}^3$). For chromium, GMAW on stainless steel produced the highest total chromium concentrations ($300 \mu\text{g}/\text{m}^3$) followed but MMAW on stainless steel ($150 \mu\text{g}/\text{m}^3$). The same pattern was observed for nickel while for Cr(VI), MMAW on stainless steel produced the highest concentrations ($120 \mu\text{g}/\text{m}^3$). Their welding exposure matrix did not include other combinations of process/metal but it did include a multiplication factor of 2 if welding in a confined space as well as a multiplication factor of 0.5 if welding with a fume extractor or welding outdoors. No consumables were considered in the matrix, estimates showed little variability between the 8 welding scenarios and only chromium, nickel and total dust could be estimated from the matrix. The later matrix was expanded and modified in another study on the risk of lung cancer in welders (Pesch et al., 2019). In this study, the same scenarios were used to produce a welding exposure matrix to estimate exposures to total fumes, Cr(VI) and nickel but the personal sampling data used were from selected German workplaces replacing those used by Gerin et al. (1993). It was expanded to include, as a base metal, nickel alloys and thus produced estimates for 18 scenarios. FCAW on mild steel produced the highest total fumes ($4700 \mu\text{g}/\text{m}^3$) followed by GMAW on aluminum ($4100 \mu\text{g}/\text{m}^3$) and GMAW on mild steel ($3900 \mu\text{g}/\text{m}^3$). For chromium, the process/metal combination producing the highest Cr(VI) concentrations was for MMAW on nickel alloys ($12 \mu\text{g}/\text{m}^3$) followed by MMAW on stainless steel ($8 \mu\text{g}/\text{m}^3$) and FCAW on stainless steel ($5 \mu\text{g}/\text{m}^3$). For nickel, the highest producing combination was GMAW on nickel alloys ($48 \mu\text{g}/\text{m}^3$) followed by MMAW on nickel alloys ($37 \mu\text{g}/\text{m}^3$) and GMAW on stainless steel ($24 \mu\text{g}/\text{m}^3$). This matrix was more expansive and covered 18 scenarios, however, it only covered Cr(VI), nickel and total dust.

Another welding exposure matrix was developed to estimate chromium and nickel exposures, this one using personal samples taken from 2007 to 2009 in a cross-sectional study aiming to assess health effects of welders in relation to fume exposures within the framework of the WELDOX study (Weiss et al., 2013). This matrix was composed of processes, base metals but also of efficiency of ventilation and welding in a confined space. Base metals were defined as high in chromium vs. low in chromium, and high in nickel vs. low in nickel reducing base

metals to stainless steel, mild steel and other high alloyed steel not high in chromium. This produced 12 process/metal combinations for which the highest chromium producing combination was GMAW on stainless steel and the highest nickel particle production combination was in GMAW on high alloyed steel and/or stainless steel. Further, welding in a confined space produced a two-fold increase in exposures while efficient ventilation significantly reduced both chromium and nickel exposures by more than half. Manganese exposures were also assessed from the data collected between 2007 and 2009 described above and a welding exposure matrix was constructed using very much the same methods (Pesch et al., 2012). This exposure matrix was composed of process, a comparison of mild steel vs. stainless steel and a comparison of steel based on the manganese content. Accompanying the latter factors, confined space and efficiency of ventilation were also assessed. The highest producing process was FCAW with a factor of 4.47 times the emissions produced by GMAW while the lowest producing process was with GTAW with a factor 0.08 times the emissions produced by GMAW. Stainless steel compared to mild steel showed an emissions factor of 0.59 and metals with high manganese content produced 2.32 times more manganese emissions than those with low manganese content. Working in a confined space increased exposures by a factor of 1.67 (not significant) while efficient ventilation reduced manganese exposures by a factor of 0.38. In both the matrices produced from the same welders and described here, base metal is a reflection of the content in the base metal and consumable when one or both are known, it does not allow for a combination of base metal and consumable that do not match in metal content and limits the ability of the matrix to cover a large number of scenarios.

Another study published on the same group of welders from the WELDOX study described above set out to construct a welding exposure matrix for inhalable and respirable dust (Lehnert et al., 2012). Dual sampling was performed in the breathing zone of welders and the same matrix described above was constructed using the same methods. Again, FCAW produced the highest concentrations of respirable and inhalable dust when comparing to GMAW followed by MMAW and GTAW. Stainless steel also showed significant reductions in fume production while confined space showed significant increases in exposures with efficient ventilation showing significant reduction in exposures. These results largely agreed with the results from Kendzia et al. (2019) who constructed a welding exposure matrix from 15473 inhalable dust samples and 9161 respirable dust samples taken from the German Social Accident Insurance

database (MEGA). They reported that for both respirable and inhalable dust, the highest producing process was FCAW followed by MMAW and GTAW with the highest producing base metal being mild steel followed by aluminum alloys and stainless steel. Their exposure matrix was more varied in that it included different types of welding processes more rarely used and year of sampling but it did not include the effect of consumable.

None of the matrices included an independent effect for base metal and consumable. Although they may together cover a large amount of welding scenarios based on base metal and process, they do not cover a large number of scenarios that are based on process, base metal and the effect of consumable on exposures which was necessary for the What-me study. Also, taken separately, they leave many empty cells. One way to overcome this is to collect large amounts of data from multiple sources increasing the variability in base metal/consumable combinations thus reducing the number of empty cells. This was the approach taken here with the construction of a literature-based welding exposure matrix achieved through a systematic review of the literature. In addition to constructing matrices from multiple sources of data, an important component of developing exposure matrices is also to provide validation for them. Validation against external data points ensures that the matrix can be used and applied for predicting exposures for welders and welding scenarios outside of the samples used for constructing the matrices. In this particular case, validation of the matrix describes its ability to predict exposures for the most common welding combinations of process, base metal, consumable reported in the What-me study. The process outlining the construction of the matrix is found in the first part of this series (to be submitted as paper 1) followed by a validation of the matrix using external measurements representing the most common welding scenarios in the What-me study in the second part of this series (paper 2), and lastly, in the third part of this series (paper 3), an examination of the matrix's ability to predict internal dose is made.

Chapter 2: Paper 1 Construction of a welding exposure matrix to estimate exposures in Canadian welders

Abstract

Introduction:

This study aims to construct a welding exposure matrix that would provide estimates of personal airborne exposures to total dust, manganese, nickel, chromium and aluminum for women welders of the What-me cohort. Outlined here is a process that synthesizes data from multiple sources representing different summary statistics and brings them together to form exposure models, one for each outcome.

Methods:

A systematic literature search was first conducted to identify all relevant publications using a word search in select scientific databases. Title and abstracts from the articles identified through the word search was conducted and articles selected for data extraction. Data summarising airborne exposures to total dust, manganese, nickel, chromium and aluminum were extracted independently by two different researchers from the most relevant publications. Arithmetic means were estimated from other summary statistics when not available and finally entered into a mixed effects model.

Results:

Data from 92 articles were extracted with a total of 737 summary statistics of personal samples retained. This represented 4620 personal samples for total dust, 4762 for manganese, 4679 for nickel, 3972 for chromium and 676 for aluminum. Total dust showed highest exposures when welding using flux cored arc welding (FCAW) on mild steel. Manganese showed the same pattern as for total dust with the addition of an increase in exposures caused by manganese content in the consumable. For nickel, exposures were highest in the gas metal arc welding (GMAW) process on high alloyed steels with again an increase in nickel exposures being related to nickel content in the consumable. Chromium's highest producing process was manual metal arc welding (MMAW) on high alloyed steel with an increase in exposures caused by an increase in the chromium content of the consumable. Aluminum saw its highest exposures in FCAW with

a significant relation between the aluminum content of the consumable and aluminum air concentrations.

Conclusion:

This study proposes the first welding exposure matrix that includes welding process, base metal and consumable in one single model for each of the outcomes. It is the first of three papers with the second and third addressing validation and calibration of the models developed here.

2.1 Introduction

Understanding and describing welding exposures and how they may relate to specific health outcomes has been the subject of many studies in the past. Different exposures that are known to cause ill-health have been identified in the welding industry from radiation exposures to exposures to certain gases and most notably to airborne metal dusts and fumes (Antonini, 2003). Within these metal fumes/dusts, certain metals are specifically associated with ill-health and those most commonly found in welding fumes are manganese, chromium/hexavalent-chromium (Cr(VI)), nickel and aluminum (Antonini, 2003). Some of the more common health issues associated with these metals have been described as respiratory issues, metal fume fever, lung cancer, problems related to the nervous system (Antonini, 2003) and possibly, problems relating to pregnancy outcomes in women (Quansah and Jaakkola, 2009; Callan et al., 2013; Olgun et al., 2020). The latter is the primary focus of the *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* project: a cohort of welder women established in 2011 with the main aim to identify a possible relationship with reproductive ill-health among women welders. This cohort was later expanded to include men for the study of the relationship between welding exposures and other health outcomes. The What-me set out to collect detailed occupational task information and to identify specific exposure patterns related to welding that could potentially be harmful to the welders and in the case of women, to the unborn fetus (Cherry et al., 2018).

The welding information gathered for the What-me study included questions on welding in confined spaces, welding indoors vs. outdoors, the type of ventilation used (if any), protective clothing worn and the type of respiratory equipment used (if any). Other information on the welding itself was gathered which included welding process, base metals welded, consumables (filler metal/rod, shielding gas) and information on welding fluxes (Appendix A). It was envisioned that these data would be used to construct a welding exposure matrix with which specific exposure estimates could be made for each welder in the study. This matrix would include welding process, base metal and consumable making it the first welding exposure matrix to include all three factors in one exposure model. Previous exposure matrices had not included these three components of welding, Gerin et al. (1993) for example, had published three exposure matrices that included major welding processes and base metals only. This covered manual metal arc welding (MMAW), gas metal arc welding (GMAW) and gas tungsten arc

welding (GTAW) on the most commonly welded metals: mild steel, stainless steel and aluminum. It provided estimates for total dust/fumes, chromium exposures and nickel exposures. The categories or cells from this matrix were later reused by Pesch et al. (2019) in a matrix published in 2019 with the main difference being that they had substituted the concentrations published by Gerin et al. (1993) with their own measurements and included a category for high alloyed steel essentially expanding the matrix and its applicability. Another welding exposure matrix was published to estimate nickel and chromium exposures including additional factors that could potentially greatly affect exposures (Weiss et al., 2013). This exposure matrix included ventilation and welding in confined spaces and had introduced the effects of flux-cored arc welding (FCAW) which had not been previously included in matrices estimating chromium and nickel exposures. The latter matrix was used again to predict manganese including the same categories and factors (Pesch et al., 2012). A matrix was also constructed to estimate inhalable and respirable dust with welding process and base metal as primary exposure factors (Lehnert et al., 2012). It included mild steel and stainless steel as base metals and the main four welding processes (GMAW, MMAW, FCAW, GTAW). It also included additional factors of efficiency of local exhaust ventilation, welding in confined spaces and use of general ventilation. A more detailed matrix was constructed by Kendzia et al. (2019) that also included aluminum as a base metal and less commonly used welding process like submerged arc welding and plasma arc welding. Their matrix also included different welder activities like grinding and torch cutting and was constructed to estimate both respirable and inhalable dusts.

Although the matrices outlined above include many welding combinations primarily composed of process and base metal, none include the effects of consumable. Consumables are the greatest source of emissions (Antonini, 2003; Method for sampling airborne particulates generated by welding and allied processes, 2006) and constructing a welding exposure matrix that would include their effect given other factors in order to estimate exposures in an existing cohort was the primary motivation behind this study.

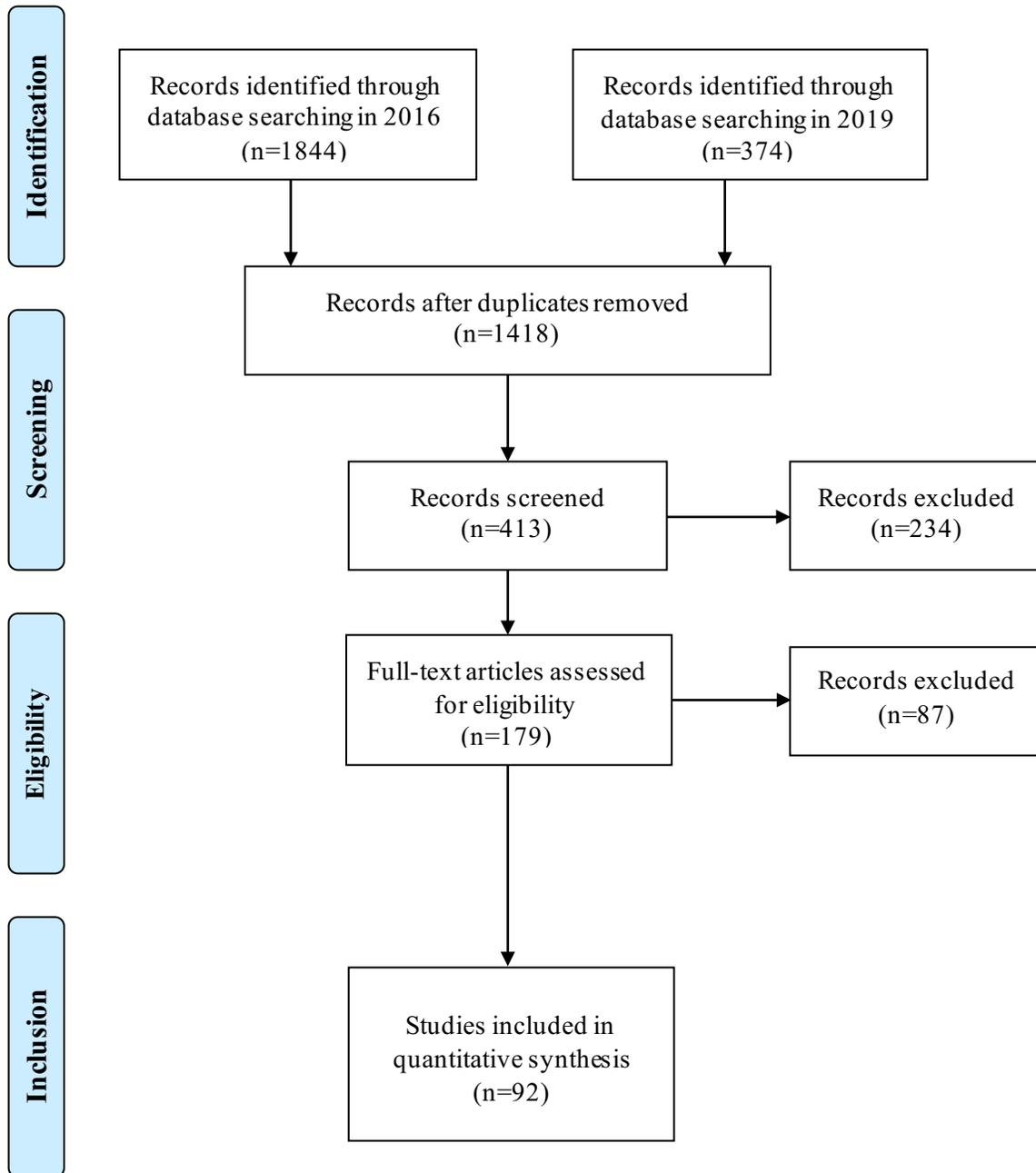
2.2 Methods

2.2.1 Literature search

Exposures to certain agents have been estimated, in the past, using data from systematic reviews (Lavoue et al., 2007; Van Rooij et al., 2008; Locke et al., 2017; Aidoo et al., 2018) and

useful models and exposure matrices have been developed from these. This accompanied with the fact that no exposure matrix had previously been published that contained process, base metal and consumable led the authors of the present study to conduct a systematic review on occupational welding exposures. This was conducted in 2016 and revisited in 2019 to gather more recently published articles. Search terms were selected to find the most relevant articles for this literature review. Only articles published in English or French in peer-reviewed journals were included. The terms used in the search were *exposure*, *welding*, *metal* and they were run in 3 databases, MEDLINE (PubMed), Web of Science and CINAHL. The terms were searched together and produced a total of 1844 articles in 2016 and 309 in 2019. Duplicates were removed and all titles and abstracts were downloaded for further scrutiny. A total of 413 articles were reviewed and considered for data extraction by two independent reviewers and identified as either containing useful information on welding exposures (air concentrations) or not. At that stage, any article that had not received a unanimous decision on whether or not to include it in the data extraction stage was included as not to pre-emptively remove potentially relevant articles. The next stage was to read the articles and extract the data where applicable or to make the decision to discard the article. Any discrepancies in the decision to keep the article or not were reviewed by a third researcher and a final decision was made. Finally, data were extracted from 92 articles (Figure 2.1). Articles were not excluded on the basis of a quality index and all results were included unless data reported in the articles were not observed values but rather estimated or if the data reported were of a particularly unusually rare metal or welding process not seen in the What-me study.

Figure 2.1: Flow chart of the systematic review process



2.2.2 Data extraction and preparation

The data extracted were particulate concentrations either as total dust, inhalable dust, respirable dust, or presented as specific metal concentrations (sometimes separated for particle size as well). Data on the sampling procedures were gathered such as the number of hours sampled, personal sampling vs. area sampling, whole shift sampling vs. grab sampling, number of sites visited, year and country of sampling along with industry where the sampling took place. All summary statistics given in each article were gathered. These were any of the following: means with standard deviations, geometric means and geometric standard deviations, medians, interquartile or numeric ranges. These data were then cross-checked between the two reviewers and any discrepancy in the data was then verified in the original articles. Along with information on the sampling itself and on occupation, data were gathered on welding processes, base metals, rods or filler metals, confined spaces and the use of ventilation, coatings and shielding gases (see extraction sheet in Appendix B). Only full shift samples or samples 2.5 hours or more in length, and samples that were personal samples (in the breathing zone of the welder) were kept for final analysis.

2.2.3 Statistical analysis

Most environmental or occupational hygiene sampling will yield positively skewed results and it is generally better to analyse data that are geometric means along with their geometric standard deviations (Lavoue et al., 2007; Perkins, 2008) than other summary statistics. However, in this case, the majority (68%) of summary statistics were given in arithmetic means and it was decided that it was better to estimate fewer values through various methods than to estimate the majority of them by approximating geometric means. The formulae used to estimate the means for other summary statistics reported can be seen in Appendix C. Arithmetic means were then log transformed for modelling.

For each outcome, before modelling, means were summarised, where the means are shown stratified by each predictor with a distribution of the number of articles, number of means extracted from the literature and number of samples represented by the extracted means displayed in one single table. Following that, modelling was done in Stata 15.1 using a mixed linear regression adjusting for the effects of heterogeneity or variability between articles by including a random effect to represent the article from which the data were extracted as seen in (Lavoue et al., 2007; Van Rooij et al., 2008) while also adjusting for the correlation between

observations (i.e., extracted means) within each source article. This analysis used frequency weights due to the large amount of missing variances also seen in (Van Rooij et al., 2008).

To maximize the number of measurements that could be included in the models, total or inhalable fractions were modelled together with respirable fraction denoted by a binary variable indicating total or inhalable vs. respirable. Chromium and Cr(VI) were also modelled together with a binary variable separating Cr(VI) from total chromium. For process and base metals, some articles reported results that were a combination of 2 or more processes or base metals with no distinction between the two. These would have been coded as, for example, *MMAW + GTAW* representing a single result from an article that stated welders were using MMAW and GTAW. The same is applied to a study reporting on the welding of mild steel and stainless steel and would be coded as *mild steel + stainless steel*.

Variable selection for the development of this exposure matrix was done by first testing each variable in a univariate model then adding all the variables together to obtain a multivariate model. The multivariate model was not restricted to only the significant variables from the univariate model. Each variable in the multivariate model was then tested using a Wald test to ensure that they significantly added to the model before regrouping. The decision on how to regroup processes or base metals was pragmatic rather than statistical. First, a single process or base metal like MMAW or GTAW was not regrouped with another single process at any time; only combinations of processes or base metals, for example GMAW + GTAW, were regrouped. This was done when the combination category did not add to the model and showed very close effects to those of its parent category in a multivariate model: for example, GMAW + GTAW could be regrouped with the parent category of GMAW but not with MMAW. Process and base metal were entered as categorical variables into the model with the same reference for all 5 outcomes. Final models' assumptions and fit were assessed with an examination of the variance inflation factor (VIF) and with an examination of predicted vs. residuals plots. Further, changes in variability between and within articles were assessed and shown in each modelling table of the results section and the proportion of reduction in residual variances from the null model to the final model were computed using the method proposed by Bryk (1992).

Data that lacked information on both process and base metal were not kept for the final analysis. Given that most of the welding fumes come from the consumable (Antonini, 2003) and because of the inevitable collinearity between rods/filler metals, process and base metals, it was

decided that the contents for each of the elemental outcomes (Mn, Ni, Cr, Al) would be recorded for each consumable and entered as a continuous variable in the model. Further, the effect of consumable on total dust would also be difficult to quantify without the presence of collinearity and because the metal concentrations in the fumes/dusts are not the primary focus in an analysis of total dust, it was decided to model total dust with just process and base metal. When specific metal contents were not available in an article but the name of the consumable or classification was given, the metal contents were extracted from a comprehensive welding catalogue that included consumables with many different specifications (LincolnElectric). If no information was given on consumable, it was estimated from those with consumable data computing weighted means stratified by base metal (Appendix D).

2.3 Results

The article and data extraction process yielded data from 92 articles producing a total of 737 summary statistics used in the modelling of the various outcomes (Appendix E). Altogether, 75 means were estimated from the minimum and maximum values, 217 were estimated from the geometric mean or median and either the geometric standard deviation or one estimated from minimum/maximums values, 146 means were estimated from the interquartile range and medians given, 26 were estimated from medians or geometric means only and 6 were estimated from medians and standard deviations. Information about the rods or filler metals were known in 57% of cases (details given in Appendix D), information about base metals was known in 85% of cases and process was known in 98.5% of cases. Forty percent of the studies published were on exposures measured in European countries (excluding Russia) and 36% of studies were on exposures measured in North America well representing the welders of the What-me study.

2.3.1 Total dust

A total of 219 means representing 4620 samples from 54 articles with samples taken between 1965 and 2016 were included in the final analysis of total dust. Table 2.1 shows the weighted mean total dust concentration by process, base metal and type of sampling (total or inhalable vs. respirable) along with the number of articles, means and samples contributing to each category.

Table 2.2 shows the univariate and multivariate analysis side-by-side for total dust. The final multivariate model reduced the within source variability by 74% compared to the null

model. GMAW was the reference category with mild steel for base metal and total dust; these were the most commonly seen across all outcomes and therefore remained as the reference categories throughout. Only the category GMAW + MMAW was not significant ($p=0.149$) while other process categories were significantly different from the category GMAW in a univariate model. For base metals, all of the base metal categories were significantly different from the mild steel category in a univariate model. The mean difference between total and respirable dust was not significant ($p=0.669$). In a multivariate model, the categories GMAW + GTAW and GMAW + MMAW were regrouped with GMAW. The category MMAW + GMAW + GTAW + FCAW was regrouped with MMAW. The category Mild steel + stainless steel was regrouped with stainless steel. In the final multivariate model, all the process categories were significantly different from GMAW. FCAW was the highest fume producing process and was significantly ($p<0.001$) higher than GMAW along with the unknown category ($p=0.007$). MMAW was significantly ($p=0.001$) less than GMAW along with the MMAW + GTAW category ($p<0.001$) and the GTAW category ($p<0.001$). For base metals, mangalloy and aluminum both showed a significant reduction in fumes produced ($p<0.001$, $p=0.026$) with stainless steel, high alloyed steel and the unknown category all showing reductions in fumes that were not significantly different from mild steel ($p=0.342$, $p=0.217$, $p=0.422$). Respirable dust showed a significant ($p<0.001$) reduction in fumes when compared to total/inhalable dust. Base metal was not collapsed further and a Wald test showed that the variable as a whole added significantly to the model ($p<0.001$) while collapsing the metal categories further showed a decrease in model performance based on Akaike's and the Bayesian information criteria.

Table 2.1: Summary of extracted data - total dust

Process	Mean*	SD*	Mean	Min	Max	n_p	n_l	n_t
GMAW	7.769	0.648	2365.737	199.999	13600.000	27	70	1348
MMAW	8.042	0.954	3109.586	900.005	2152.929	21	62	875
GTAW	6.428	0.580	618.833	64.032	3012.769	15	25	838
FCAW	8.890	0.435	7260.288	547.282	12126.698	7	12	322
MMAW + GTAW	7.413	0.798	1657.382	387.089	5000.008	3	3	89
GMAW + MMAW	7.553	1.357	1906.158	74.200	13000.001	8	33	413
GMAW + GTAW	9.393	-	12000.034	12000.034	12000.034	1	1	51
MMAW + GMAW + GTAW + FCAW	6.871	2.269	963.666	63.200	6121.269	1	2	47
Unknown	7.543	0.680	1886.832	499.998	27000.070	5	11	637
Metal								
Mild steel	7.665	1.021	2131.785	74.000	27000.070	23	45	797
Stainless steel	7.097	1.053	1208.342	63.200	18380.484	15	37	676
Aluminum	7.665	0.932	2131.401	199.999	13600.000	8	38	632
High alloyed steel	7.973	0.937	2902.259	131.000	13000.001	4	38	60
Mild steel + stainless steel	7.315	0.830	1501.537	639.998	5400.003	4	6	276
Mangalloy	5.837	0.943	342.611	90.000	1070.001	1	7	7
Unknown	7.761	1.069	2346.300	280.001	21519.929	15	49	2172
Sample type								
Respirable fraction	7.169	1.049	1298.097	63.200	8615.901	29	51	1815
Total particulates	7.891	0.957	2672.246	64.032	27000.070	32	168	2805

*Natural log conc($\mu\text{g}/\text{m}^3$)

n_p=number of articles, n_l=number of summary statistics, n_t=total samples

Table 2.2: Univariate and multivariate models - total dust

Process	Univariate					Multivariate				
	β	se	95% CI		p-value	β	se	95% CI		p-value
			lower	upper				lower	upper	
MMAW	-0.435	0.139	-0.707	-0.162	0.002	-0.448	0.131	-0.704	-0.192	0.001
GTAW	-1.650	0.118	-1.882	-1.418	0.000	-1.591	0.154	-1.893	-1.289	0.000
FCAW	0.938	0.069	0.803	1.073	0.000	0.938	0.082	0.777	1.099	0.000
MMAW + GTAW	-1.335	0.091	-1.514	-1.156	0.000	-1.290	0.144	-1.572	-1.008	0.000
GMAW + MMAW ^b	-0.203	0.141	-0.480	0.073	0.149					
GMAW + GTAW ^b	-0.452	0.091	-0.631	-0.273	0.000					
MMAW + GMAW + GTAW + FCAW ^a	-0.200	0.003	-0.205	-0.194	0.000					
Unknown	1.061	0.291	0.491	1.631	0.000	0.928	0.344	0.254	1.602	0.007
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal										
Stainless steel	-1.759	0.480	-2.700	-0.817	0.000	-0.545	0.573	-1.668	0.579	0.342
Aluminum	-0.822	0.418	-1.641	-0.003	0.049	-0.953	0.429	-1.794	-0.113	0.026
High alloyed steel	-1.169	0.200	-1.560	-0.778	0.000	-0.447	0.362	-1.157	0.262	0.217
Mild steel + stainless steel ^c	-1.109	0.520	-2.129	-0.090	0.033					
Mangalloy	-2.547	0.376	-3.284	-1.810	0.000	-1.978	0.353	-2.669	-1.286	0.000
Unknown	-1.443	0.734	-2.881	-0.004	0.049	-0.430	0.535	-1.479	0.619	0.422
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Sample type										
Respirable fraction	-0.094	0.219	-0.522	0.335	0.669	-0.328	0.135	-0.591	-0.064	0.015
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Constant^d	7.463	0.150	7.169	7.757	0.000	8.262	0.368	7.451	8.984	0.000
N	4620					4620				

^aregrouped with MMAW, ^bregrouped with GMAW, ^cregrouped with stainless steel, rc=reference category

^dunconditional model: within paper variance 0.509 and between paper variance 1.168; adjusted model: within paper variance 0.131 and between paper variance 1.310.

2.3.2 Manganese

Manganese concentrations were analysed from 164 means extracted from 48 articles representing 4762 samples. The final manganese model derived from these data showed a 50% reduction in within source variability. Table 2.3 contains summary statistics of the mean manganese concentrations by process, base metal and type of sampling along with the corresponding totals. The mean manganese content in the consumable is represented by a continuous variable measured in the percentage of the total weight of the consumable weld containing manganese (LincolnElectric). In a univariate model, GTAW, GMAW + MMAW, MMAW + GMAW + GTAW were significantly lower than GMAW. The categories for MMAW, FCAW, GMAW + GTAW, FCAW + MMAW and unknown process were not significantly different from GMAW (see Table 2.4 for β -coefficients, confidence intervals and p-values). Aluminum, mild steel + stainless steel + galvanized steel and the unknown metal categories were all significantly lower than mild steel while the stainless steel and the mild steel + stainless steel categories were not significantly different from mild steel. The manganese content in the consumable was not significantly different from 0 and respirable dust was not significantly different from total dust. In a multivariate model, the category of GMAW + GTAW was regrouped with the unknown category while FCAW + MMAW was regrouped with FCAW. GTAW, GMAW + MMAW and MMAW + GMAW + GTAW were significantly lower than GMAW ($p < 0.001$, $p < 0.001$, $p = 0.011$). The categories of MMAW and unknown process were both lower than GMAW but neither was significantly so. For base metals, the category Mild steel + stainless steel was highly correlated, following a VIF test (VIF score of 15.79), with the variable representing manganese content and so was regrouped with the unknown category. Stainless steel, aluminum, mild steel + stainless steel + galvanized steel and the unknown category were all significantly lower than the mild steel category ($p = 0.001$, $p < 0.001$, $p = 0.002$, $p = 0.003$). The manganese content in the consumable significantly ($p = 0.010$) predicted manganese exposure in that an increase in the Mn content of the consumable was linked to an increase in the mean manganese concentration. The difference between total/inhalable and respirable dust was not significant in a multivariate model but was kept in the model as a necessary adjustment.

Table 2.3: Summary of extracted data - manganese

Process	Mean*	SD*	Mean	Min	Max	n_p	n_i	n_t
GMAW	5.519	1.143	249.319	14.000	2595.993	26	68	1735
MMAW	3.712	1.455	40.946	5.200	872.999	19	49	1317
GTAW	2.400	0.486	11.019	4.000	22.642	9	10	378
FCAW	4.978	1.283	145.157	2.750	903.960	9	17	648
GMAW + MMAW	3.764	0.969	43.119	18.710	1229.994	6	10	245
GMAW + GTAW	5.213	-	183.595	183.595	183.595	1	1	54
FCAW + MMAW	5.347	-	209.999	209.999	209.999	1	1	40
MMAW + GMAW + GTAW	4.382	-	80.000	80.000	80.000	1	1	6
Unknown	5.302	0.733	200.777	29.400	1740.008	3	5	339
Metal								
Mild steel	5.431	1.008	228.475	13.030	2595.994	22	77	1698
Stainless steel	4.437	1.360	84.499	4.000	1241.201	8	11	217
Aluminum	2.639	-	14.000	14.000	14.000	1	1	34
Mild steel + stainless steel	4.447	1.153	85.341	18.710	334.600	8	14	476
Mild steel + stainless steel + galvanized steel	4.605	-	100.007	100.007	100.007	1	1	4
Unknown	4.041	1.684	56.890	2.750	1099.999	19	58	2333
Manganese in consumable (%)¹		0.567	1.295	0.383	3.000	48	162	4762
Sample type								
Respirable fraction	4.351	1.288	77.542	2.750	2595.994	18	48	1165
Total particulates	4.662	1.617	105.850	4.000	1740.008	35	114	3597

*Natural log conc($\mu\text{g}/\text{m}^3$)

n_p=number of articles, n_i=number of summary statistics, n_t=total samples

¹representing overall mean manganese content in consumables (%)

Table 2.4: Univariate and multivariate models - manganese

Process	Univariate 95% CI					Multivariate 95% CI				
	β	se	lower	upper	p-value	β	se	lower	upper	p-value
MMAW	-0.529	0.461	-1.432	0.373	0.251	-0.543	0.455	-1.435	0.348	0.232
GTAW	-2.530	0.270	-3.059	-2.000	0.000	-2.372	0.290	-2.940	-1.803	0.000
FCAW	0.302	0.435	-0.550	1.154	0.487	0.254	0.436	-0.601	1.109	0.561
GMAW + MMAW	-1.573	0.427	-2.410	-0.736	0.000	-1.931	0.402	-2.719	-1.144	0.000
GMAW + GTAW^a	0.015	0.230	-0.436	0.466	0.948					
FCAW + MMAW^b	0.239	0.314	-0.376	0.855	0.446					
MMAW + GMAW + GTAW	-0.353	0.001	-0.354	-0.351	0.000	-0.317	0.124	-0.561	-0.073	0.011
Unknown	-0.181	0.780	-1.710	1.349	0.817	-0.619	0.667	-1.926	0.688	0.353
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal										
Stainless steel	-0.668	0.353	-1.359	0.023	0.058	-0.841	0.265	-1.360	-0.323	0.001
Aluminum	-3.698	0.317	-4.319	-3.078	0.000	-2.768	0.272	-3.301	-2.236	0.000
Mild steel + stainless steel^c	-0.212	0.235	-0.673	0.250	0.369					
Mild steel + stainless steel + galvanized	-0.232	0.101	-0.430	-0.034	0.022	-1.325	0.421	-2.151	-0.499	0.002
Unknown	-3.773	0.183	-4.131	-3.415	0.000	-1.248	0.414	-2.059	-0.437	0.003
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Manganese in consumable (%)	0.004	0.117	-0.226	0.234	0.912	0.674	0.260	0.164	1.183	0.010
Sample type										
Respirable fraction	-0.077	0.087	-0.247	0.094	0.379	-0.066	0.086	-0.235	0.103	0.442
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Constant^d	4.712	0.193	4.334	5.091	0.000	5.149	0.294	11.480	12.633	0.000
N	4762					4762				

^aregrouped with unknown process, ^bregrouped with FCAW, ^cregrouped with unknown metal, rc=reference category.

^dunconditional model: within paper variance 0.652 and between paper variance 1.722; adjusted model: within paper variance 0.325 and between paper variance 1.451

2.3.3 Nickel

A model was derived for nickel using 88 means from 28 articles representing 4679 samples. The final model for nickel reduced the within source variability by 73% when compared to the null model. Table 2.5 shows the mean concentrations by process, base metal and type of sampling. It also contains the number of articles and samples each category includes and a continuous variable representing the nickel content of the consumables found in the weld as seen in manganese. In a univariate model, for processes, all but the unknown category were significantly lower than GMAW and all base metals were significantly higher than mild steel with respirable dust showing a significantly lower mean nickel concentration than total dust. Nickel content in the consumable was also positively and significantly related to nickel concentration in a univariate model. For the multivariate model, the category for MMAW + GTAW was regrouped with GTAW; the category for mild steel + stainless steel was regrouped with mild steel. As seen in Table 2.6, MMAW, GTAW, FCAW were all significantly lower than GMAW ($p < 0.001$, $p < 0.001$, $p < 0.001$). The unknown process category was also significantly lower than GMAW ($p = 0.002$). For metals, both stainless steel and high alloyed steel were positively and significantly ($p = 0.003$, $p < 0.001$) higher than mild steel. The unknown category was also significantly higher than mild steel ($p = 0.017$). Nickel content in the consumable was significantly ($p < 0.001$) related to nickel concentrations in the air with a positive coefficient with respirable dust also significantly ($p < 0.001$) different from total/inhalable dust with a negative coefficient.

Table 2.5: Summary of extracted data - nickel

Process	Mean*	SD*	Mean	Min	Max	n_p	n_s	n_t
GMAW	3.032	1.179	20.745	0.760	204.334	17	33	1944
MMAW	3.220	0.600	25.034	1.105	232.601	15	27	1076
GTAW	1.913	0.673	6.768	0.757	330.001	8	13	1255
FCAW	2.202	0.880	9.045	1.175	111.001	6	12	301
MMAW + GTAW	3.404	1.321	30.082	11.700	186.721	2	2	88
Unknown	2.944	-	18.996	18.996	18.996	1	1	15
Metal								
Mild steel	1.228	1.211	3.415	0.760	204.334	8	20	496
Stainless steel	2.962	1.354	19.335	0.757	186.721	17	35	741
High alloyed steel	4.451	0.508	85.734	37.132	330.001	2	5	55
Mild steel + stainless steel	3.142	0.572	23.162	8.147	50.000	2	6	297
Unknown	2.843	0.771	17.167	1.175	232.601	8	22	3090
Nickel in consumable (%)¹		3.763	6.036	0.000	52.500	28	88	4679
Sample type								
Respirable fraction	2.114	1.394	8.284	0.757	204.334	8	22	603
Total particulates	2.819	0.992	16.767	7.598	330.001	66	66	4076

*Natural log conc($\mu\text{g}/\text{m}^3$)

n_p=number of articles, n_s=number of summary statistics, n_t=total samples,

¹representing overall mean nickel content in consumables (%)

Table 2.6: Univariate and multivariate models - nickel

Process	Univariate					Multivariate				
	β	se	95% CI		p-value	β	se	95% CI		p-value
			lower	upper				lower	upper	
MMAW	-0.384	0.069	-0.518	-0.249	0.000	-0.391	0.086	-0.559	-0.223	0.000
GTAW	-1.580	0.171	-1.915	-1.245	0.000	-1.631	0.195	-2.013	-1.249	0.000
FCAW	-1.213	0.315	-1.829	-0.596	0.000	-1.127	0.243	-1.604	-0.650	0.000
MMAW + GTAW ^a	-1.466	0.136	-1.732	-1.199	0.000					
Unknown	-0.557	0.301	-1.147	0.033	0.064	-0.963	0.318	-1.586	-0.341	0.002
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal										
Stainless steel	1.246	0.433	0.398	2.095	0.004	0.405	0.138	0.135	0.675	0.003
High alloyed steel	2.311	0.429	1.469	3.153	0.000	1.260	0.133	1.000	1.521	0.000
Mild steel + stainless steel ^b	0.536	0.148	0.246	0.826	0.000					
Unknown	1.132	0.405	0.339	1.925	0.005	0.839	0.353	0.148	1.531	0.017
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Nickel in consumable (%)	0.044	0.024	-0.003	0.092	0.015	0.111	0.025	0.063	0.159	0.000
Sample type										
Respirable fraction	-0.753	0.054	-0.860	-0.647	0.000	-0.768	0.056	-0.878	-0.658	0.000
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Constant ^c	2.959	0.273	2.423	3.495	0.000	2.219	0.439	1.358	3.079	0.000
N	4679					4679				

^aregrouped with GTAW, ^bregrouped with mild steel, rc=reference category

^cunconditional model: within paper variance 0.607 and between paper variance 1.974; adjusted model: within paper variance 0.166 and between paper variance 2.217

2.3.4 Chromium

For chromium, a model was derived from 224 means from 39 articles representing 3028 samples with the final model reducing the within source variability by 61%. Table 2.7 shows the mean chromium concentration by process, base metal and type of sampling (includes type of chromium particle). It also includes a mean chromium content for the consumable. The univariate models seen in Table 2.8 show that GTAW, FCAW, MMAW + GTAW, GMAW + MMAW, MMAW + GMAW + GTAW, and the unknown process category were all significantly lower than GMAW. MMAW was significantly higher than GMAW. For metals, stainless steel showed significant increases in chromium exposures compared to mild steel along with high alloyed steel, mild steel + stainless steel and the unknown category. Aluminum was not significantly different from mild steel. The chromium content in the consumables was significantly related (and positively so) to chromium exposures. Hexavalent chromium and respirable dust were significantly less than total chromium/dust. The multivariate model saw a regrouping of MMAW + GTAW with GTAW, a regrouping of GMAW + MMAW with GMAW and finally of mild steel + stainless steel with stainless steel. The model showed that MMAW was still significantly ($p=0.023$) higher than GMAW while GTAW, FCAW, MMAW + GMAW + GTAW were all significantly ($p<0.001$, $p<0.001$, $p<0.001$) lower than GMAW with the unknown process category significantly higher ($p=0.006$). Stainless steel and high alloyed steel were both significantly higher than mild steel ($p<0.001$ & $p=0.008$) while aluminum showed a reduction in chromium fumes but was not significant ($p=0.485$). The unknown metal category was also significantly higher than mild steel ($p=0.006$). Chromium content in the consumable was significantly ($p<0.001$) positively related to chromium exposure while Cr(VI) and respirable dust were both significantly ($p<0.001$ & $p<0.001$) lower than total chromium/dust.

Table 2.7: Summary of extracted data - chromium

Process	Mean*	SD*	Mean	Min	Max	n_p	n_i	n_t
GMAW	2.500	1.488	12.188	0.254	646.999	24	69	1434
MMAW	3.557	1.416	35.063	0.100	602.842	17	52	1200
GTAW	1.754	1.272	5.773	0.100	52.000	13	25	660
FCAW	1.604	1.596	4.974	0.943	281.999	5	12	213
MMAW + GTAW	3.835	2.550	46.310	0.820	1867.990	3	4	103
GMAW + MMAW	2.626	2.171	13.819	0.190	579.998	4	55	275
MMAW + GMAW + GTAW	-0.986	-	0.373	0.373	0.373	1	1	15
Unknown	4.570	0.579	96.564	4.000	124.000	3	6	72
Metal								
Mild steel	1.877	1.249	6.531	0.254	646.999	12	47	1005
Stainless steel	3.326	1.837	27.834	100.000	1867.199	25	78	1544
Aluminum	1.099	-	2.999	2.999	2.999	1	1	34
High alloyed steel	2.785	1.969	16.204	0.100	579.998	4	62	123
Mild steel + stainless steel	3.230	1.700	25.286	0.190	229.999	3	10	448
Unknown	2.367	1.315	10.665	0.373	239.999	10	26	818
Chromium in consumable (%)¹		8.111	11.032	0.000	23.300	39	224	3972
Form of chromium particle								
Total Cr	3.005	1.512	20.185	0.100	510.977	35	132	3028
Cr(VI)	1.786	1.940	5.965	0.190	1867.199	20	92	944
Sample type								
Respirable fraction	2.235	1.951	9.342	0.190	646.999	10	31	796
Total particulates	2.836	1.616	17.042	0.100	1867.199	31	193	3176

*Natural log conc($\mu\text{g}/\text{m}^3$)

n_p=number of articles, n_i=number of summary statistics, n_t=total samples

¹representing overall mean chromium content in consumables (%)

Table 2.8: Univariate and multivariate models - chromium

Process	Univariate					Multivariate				
	β	se	95% CI		p-value	β	se	95% CI		p-value
MMAW	0.961	0.423	0.132	1.790	0.023	0.816	0.360	0.110	1.522	0.023
GTAW	-1.115	0.368	-1.836	-0.393	0.002	-1.753	0.198	-2.142	-1.365	0.000
FCAW	-1.676	0.418	-2.496	-0.856	0.000	-1.647	0.210	-2.057	-1.236	0.000
MMAW + GTAW^a	-1.000	0.330	-1.647	-0.353	0.002					
GMAW + MMAW^b	-2.450	0.411	-3.255	-1.644	0.000					
MMAW + GMAW + GTAW	-1.848	0.060	-1.965	-1.730	0.000	-0.979	0.118	-1.209	-0.748	0.000
Unknown	-3.414	0.818	-5.016	-1.811	0.000	1.419	0.514	0.411	2.426	0.006
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal										
Stainless steel	2.200	0.443	1.333	3.068	0.000	0.598	0.084	0.434	0.762	0.000
Aluminum	-0.183	0.405	-0.978	0.611	0.651	-0.308	0.442	-1.175	0.558	0.485
High alloyed steel	1.461	0.297	0.878	2.044	0.000	1.011	0.383	0.261	1.760	0.008
Mild steel + stainless steel^c	0.813	0.150	0.519	1.107	0.000					
Unknown	1.393	0.417	0.576	2.210	0.001	0.536	0.183	0.177	0.896	0.003
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Chromium in consumable (%)	0.139	0.035	0.071	0.208	0.000	0.066	0.016	0.034	0.098	0.000
Type of chromium particle										
Cr(VI)	-1.486	0.194	-1.867	-1.106	0.000	-1.535	0.186	-1.899	-1.171	0.000
total cr	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Sample type										
Respirable fraction	-0.724	0.074	-0.869	-0.578	0.000	-0.714	0.101	-0.912	-0.515	0.000
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Constant^d	2.722	0.305	2.124	3.320	0.000	1.391	0.443	0.523	2.259	0.000
N	3972					3972				

^aregrouped with GTAW, ^bregrouped with GMAW, ^cregrouped with stainless steel, rc=reference category

^dunconditional model: within paper variance 1.615 and between paper variance 3.458; adjusted model: within paper variance 0.629 and between paper variance 2.841

2.3.5 Aluminum

There were fewer articles reporting on aluminum, most only describing aluminum welding, but there were still some articles that reported aluminum air concentrations emitted from welding on mild steel and stainless steel. This was somewhat exemplified in the rather small reduction (12%) in within source variability that the final model brought on when compared to the null model. Table 2.9 shows the mean aluminum concentrations with the corresponding descriptive information regarding number of papers, means and samples used in the final analysis stratified by process, metal and respirable vs. total dust. A total of 44 means were kept for the final analysis extracted from 10 articles representing 676 samples. The univariate models (Table 2.10) show that all processes were significantly different from the GMAW category where we saw a significant decrease in aluminum exposure for MMAW, GTAW, and GMAW + MMAW while FCAW showed a significant increase in exposure. Stainless steel showed a significant reduction in exposures while, not surprisingly, aluminum showed a significant increase in exposures when compared to mild steel. The unknown base metal category and the mild steel + stainless steel category were not significantly different from mild steel but both showed reductions in exposure to aluminum. The mean aluminum content of the consumable was significantly related to aluminum exposures in a univariate model with respirable dust also showing a significant reduction in aluminum exposures when compared to total dust. In a multivariate model, multicollinearity did not allow the model to converge with both base metal and aluminum content in the model at the same time and respirable dust showed significantly higher concentrations than total dust. A comparison was made between a model with process and base metal vs. a model with process and aluminum content in the consumable showing that the model that did the best, based on Akaike's and the Bayesian information criteria, was the model with consumable contents. In a multivariate model, the direction and significance of the process categories did not change with MMAW, GTAW and GMAW + MMAW still significantly ($p < 0.001$, $p < 0.001$, $p < 0.001$ reducing aluminum exposures while FCAW remained significantly ($p < 0.001$) higher than GMAW. The coefficient for the aluminum content in the consumable remained largely unchanged and significant ($p < 0.001$) while a reversal of polarity was seen in the total vs. respirable dust variable where respirable dust significantly ($p = 0.024$) increased exposure.

Table 2.9: Summary of extracted data - aluminum

Process	Mean*	SD*	Mean	Min	Max	n_p	n_i	n_t
GMAW	5.101	2.095	164.124	8.000	6100.004	9	37	499
MMAW	3.947	0.473	51.795	9.600	59.049	2	2	97
GTAW	4.704	1.799	110.415	0.599	290.001	2	3	20
FCAW	5.151	-	172.560	172.560	172.560	1	1	29
GMAW + MMAW	1.623	-	5.070	5.070	5.070	1	1	31
Metal								
Mild steel	3.789	1.683	44.214	9.600	708.999	3	8	253
Stainless steel	-0.512	-	0.599	0.599	0.599	1	1	2
Aluminum	7.050	1.084	1152.403	8.000	6100.004	4	28	201
Mild steel + stainless steel	3.895	1.017	49.138	5.070	172.560	2	4	208
Unknown	3.102	0.182	22.240	18.000	28.000	1	3	12
Aluminum, in consumable (%)¹		27.905	42.797	0.000	93.657	10	44	676
Sample type								
Respirable fraction	5.386	2.438	218.421	5.070	1179.994	4	4	108
Total particulates	4.648	1.884	104.392	0.599	6100.000	7	40	568

*Natural log conc($\mu\text{g}/\text{m}^3$)

n_p=number of articles, n_i=number of summary statistics, n_t=total samples

¹representing overall mean aluminum content in consumables (%)

Table 2.10: Univariate and multivariate models - aluminum

Process	Univariate 95% CI					Multivariate 95% CI				
	β	se	lower	upper	p-value	β	se	lower	upper	p-value
MMAW	-0.131	0.012	-0.154	-0.108	0.000	-0.122	0.026	-0.173	-0.072	0.000
GTAW	-2.427	0.109	-2.640	-2.214	0.000	-2.570	0.133	-2.831	-2.310	0.000
FCAW	0.944	0.008	0.929	0.959	0.000	0.962	0.013	0.936	0.987	0.000
GMAW + MMAW	-3.578	0.663	-4.877	-2.279	0.000	-2.557	0.392	-3.325	-1.789	0.000
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal										
Stainless steel	-2.979	0.059	-3.094	-2.863	0.000					
Aluminum	3.497	0.691	2.141	4.852	0.000					
Mild steel + stainless steel	-0.641	1.164	-2.923	1.641	0.582					
Unknown	-0.248	0.565	-1.356	0.859	0.387					
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Aluminum in consumable (%)	0.038	0.007	0.025	0.052	0.000	0.036	0.006	0.024	0.048	0.000
Sample type										
Respirable fraction	-1.148	0.248	-1.635	-0.662	0.000	0.624	0.276	0.083	1.165	0.024
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Constant ^a	4.725	0.680	3.392	6.058	0.000	3.550	0.342	2.879	4.220	0.000
N	670					670				

rc=reference category

^aunconditional model: within paper variance 1.320 and between paper variance 4.085; adjusted model: within paper variance 1.159 and between paper variance 0.515

2.4 Discussion

This study attempted to generate a welding exposure matrix composed of process and base metal in the case of total dust and of process, base metal and consumable in the case of the metals of interest for the purposes of estimation of exposures in a pre-existing welding cohort. The results of the matrix for total dust tied in well with previous exposure matrices (Lehnert et al., 2012; Kendzia et al., 2019; Pesch et al., 2019) showing the highest exposures emitted from FCAW followed by GMAW and with the lowest from GTAW. Mild steel producing higher exposures than stainless steel also tied in well with the later studies. For manganese, the model developed here showed similar results to the manganese model produced by Pesch et al. (2012) showing that FCAW produced the highest manganese exposures with welding mild steel also producing higher manganese exposures than welding stainless steel. The model for nickel showed similar results to those found by Weiss et al. (2013) indicating that the largest nickel exposures were in GMAW welders welding on high alloyed steels. This result differed slightly from Pesch et al. (2019) who reported that the highest nickel exposures were in those welding stainless steel using FCAW. The same authors reported that the highest chromium exposures in the models developed here were for MMAW, high alloyed steel welders, a finding that is reported here also.

In this systematic review, the data were not modelled under the assumption that each factor was independent and brought difficulties in modelling the data with respect to collinearity. The purpose was to develop a welding exposure matrix that would satisfy the needs of the Whatme study and not necessarily to obtain the most parsimonious and statistically significant model. Despite that, a substantial effort at removing redundancy in different β -coefficients was undertaken and attempts at indeed obtaining parsimonious models were made while being careful not to reduce the effects of single processes or of base metals. Regrouping certain categories was not ideal but allowed for collinearity to be reduced substantially despite having potentially negative effects on the models' ability to make out of sample predictions. Notwithstanding these challenges, all models were tested for collinearity using the *vif* command in Stata as a post-estimation command following a cluster adjusted linear regression and none of the models showed mean VIF scores of more than 2 for the entire models and with no single score of more than 5.33. An examination of the residuals was also performed (not shown here)

and all plots of residuals against predicted values showed a good dispersion with no visible slope indicating that all or enough of the assumptions of linear regressions were met. Further, the proportions of variances reduced by the final models when compared to the null models were all but in one case exceeding 50% with total dust and nickel exceeding 70%. It could be argued that the models could have been collapsed further to remove non-significant categories but that would have defeated the purpose of obtaining estimates of the effects of each welding process and base metal in the What-me study. Another potential limitation was the fact that models did not include other important exposure modifiers like ventilation, the use of local exhaust ventilation, welding outdoors or in a confined space. These data were missing for the vast majority of articles included in the final analysis and attempting to include them was simply not possible. Additionally, there was a rather large degree of missing or estimated data when it came to the percentage of metal contents in the consumables; however, the method of estimation adopted here would have more likely reduced the effect size of the variable representing consumables rather than enhance it adding to the credibility of the final models that showed significant effects caused by the presence of a variable for consumable.

In a study that aims to develop a welding exposure matrix by quantifying differences in relative exposure using summarised data from the literature, it seemed appropriate to include both respirable and total dust in the same model with an indicator variable showing the mean difference between the two. Although there are possibly noticeable differences in the emission of respirable dust between different processes or different metals (Kendzia et al., 2019), modelling respirable and total dust separately in order to obtain two different sets of agreeing β -coefficient ranks from multivariate models was considered redundant and likely to introduce more error than it would have attempted to remove. The same could be said of Cr(VI) and total chromium; a predictable mean total chromium could be computed from Cr(VI) rendering the separation of the two only useful in situations where Cr(VI) itself was the outcome of interest. A study reporting only respirable dust would report means that are smaller for the same welding process base metal combination as another study reporting only on total or inhalable dust. This was the basis for the approach taken in this study to include the mean difference between respirable and total dust, or chromium and Cr(VI), shown in a binary variable which accounts at least in part for the possibility of such confounding introduced by including both these particle sizes or forms in the same model. It was also found that for manganese, the variable denoting the different particle

sizes of each data point was not significant which is parallel to the findings by Harris et al. (2005) where some process base metal combinations showed equal amounts of respirable and total dust while others showed very small reductions in respirable dust. In the case of aluminum, the fact that there was a reversal in the polarity of the respirable dust variable when it was added to a multivariate model and that it was significant in its positive form showed that there was likely some dependence on the fact that only 4 means were respirable dust means, 3 of which from the highest producing process (FCAW).

There are other limitations in this study that could sometimes be mitigated against but not always knowingly so. One of these is the fact that there are no obvious quality indices one could use in deciding on the removal or inclusion of articles reporting on exposures. The approach taken here was to remove any that had insufficient information for the research team to be able to ascertain important aspects of the sampling, for example sampling duration, total or respirable sampling and units given in air concentrations, units of measurement and at least one known process or known base metal for each summary statistic given. Additionally, only articles reporting on sampling in occupational settings including vocational schools were kept and studies welding inside chambers in order to characterise the fumes were not kept as they did not represent welding exposures that could be applied to a cohort of welders in the context of estimating occupational exposures. A concerted effort was made to exclude different articles reporting on the same data but this was not always clear and it is possible that some articles included in this analysis shared data with other articles also included in the analysis. It was assumed that each article equally contributed to the validity of the model and was treated as such but this is likely not to be a correct assumption – studies that were conducted in a more rigorous manner are not treated with more weight than other studies. A temporal trend analysis was not made here and could have potentially affected the results. The reason for this omission was that questionnaire data from the What-me cohort was not for a time period outside of 2012 to 2018 and although temporal trends could potentially affect the exposure estimates here, these trends would have yielded β -coefficients that would have remained constant for the What-me cohort.

2.4.1 Conclusion

Although a number of authors have looked at welding exposures, none have developed an exposure matrix that goes beyond looking at a small number of process/base metal combinations and none have done so including consumables. This study achieves this and provides the What-

me study with a usable welding exposure matrix, one that could be used by any other researcher. Despite the large numbers of articles used in the construction of this welding exposure matrix, validation should still be undertaken to verify and perhaps calibrate these models.

Chapter 3: Paper 2 External validation of a welding exposure matrix to estimate exposures in Canadian welders

Abstract

Introduction:

Following the construction of a welding exposure matrix based on data from the literature that estimate personal airborne exposures to total dust, manganese, nickel, chromium and aluminum, this study aimed to validate the models using exposure data gathered under controlled conditions in a welding laboratory.

Methods:

The most common welding scenarios were identified in the *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* study: a scenario was defined as a combination of process, base metal and consumable. The different welding combinations reported in the study were replicated under controlled conditions in a welding laboratory with the welder equipped with a personal air sampling pump. The samples were analysed gravimetrically to determine total dust and ICP-MS was used to determine metal concentrations for each sample. Using the welding exposure matrix models produced previously, out of sample predictions were made for the scenarios replicated under controlled conditions and these were rank correlated against the means observed from the welding scenario replication.

Results:

In total, 21 scenarios representing more than 90% of welding scenarios in the What-me study were identified. A total of 61 welding sessions took place representing a minimum of 2 samples per scenario and up to 4 per scenario. Total dust was highest in flux cored arc welding (FCAW) on mild steel with the most commonly used consumable within that welding process. The highest manganese producing scenario was using gas metal arc welding (GMAW) on mild steel using the most common filler metal reported. For nickel, GMAW on stainless steel using a consumable with 10% nickel content and 20% chromium content was the highest producing scenario which was also observed for chromium. Aluminum saw its highest exposures with FCAW on mild steel. The predictions made for these scenarios using the models derived

previously showed Spearman rank correlations of $\rho=0.93$ ($p<0.001$) for total dust, $\rho=0.87$ ($p<0.001$) for manganese, $\rho=0.54$ ($p<0.024$) for nickel, $\rho=0.43$ ($p=0.055$) for chromium and a rho of 0.29 ($p=0.210$) for aluminum.

Conclusion:

This second of three papers has demonstrated good concordance between the predicted exposures for each scenario and the observed exposures from the welding laboratory. The third paper investigates the relationship between these estimates and internal dose using biological samples.

3.1 Introduction

The potential adverse effects that welding exposures have on the health of welders has been well documented and variations in welding have been associated with different effects on the health of welders. Stainless steel welding, for example, has been associated with increased risk of developing lung cancer or asthma while other reports show increased risks of metal fume fever in galvanized steel welders (Antonini, 2003).

The most used welding exposure matrices do not currently cover many welding combinations where a combination would be welding process and base metal and none cover a variety of consumables (Gerin et al., 1993; Lehnert et al., 2012; Pesch et al., 2012; Weiss et al., 2013; Kendzia et al., 2019; Pesch et al., 2019). Nevertheless, important differences have been measured in fume/dust emissions from different welding processes, base metals and combinations of these; Kendzia et al. (2019) found that the highest dust production (inhalable and respirable) came from flux-cored arc welding (FCAW) followed by gas metal arc welding (GMAW), manual metal arc welding (MMAW) and gas tungsten arc welding (GTAW). They also reported that mild steel produced more fumes than stainless steel in GMAW and that mild steel and aluminum produced more fumes in MMAW and GTAW than stainless steel welding. Lehnert et al. (2012) also found the highest fume producing process was FCAW while GTAW was found to be the lowest. The same findings were made of mild steel and stainless steel. These findings pertained to particulates, but similar studies were also conducted to identify different emission patterns for specific metals. Manganese was found in higher concentrations in GMAW mild steel welding when compared to FCAW mild steel with lower concentrations in MMAW and GTAW (Ellingsen et al., 2006). Additional to these findings, they also found that there were no significant differences in airborne manganese between MMAW mild steel and MMAW stainless steel welding but that large differences in airborne chromium could be observed with the same metals using the same method. Both GMAW and FCAW mild steel welding produced higher manganese emissions than welding stainless steel using the same processes. This was similar to what was found by Stanislawska et al. (2017) with the addition that they found nearly twice the amount of manganese emissions when welding on mild steel compared to stainless steel. Nickel, another metal found in welding fumes, was found to be highest among FCAW welders when compared to GMAW followed by MMAW, GMAW and GTAW. They also found that welding on high chromium content metals like stainless steel, which also has high nickel

content, a significant increase in nickel exposures could be observed. A finding similar to the one made by Karlsen et al. (1992) who found that GMAW combined with stainless steel produced more fumes than MMAW with stainless steel but that it had produced fewer fumes than MMAW on Inconel metal, a high in nickel content metal. The variations in fume production that can be seen in different welding processes and base metals when compared to the variations in metal concentrations found in the fumes is more reason to construct a welding exposure matrix but even more so that a validation and calibration of the matrix be made.

3.2 Methods

The validation was developed to provide estimates for an existing welding cohort part of the What-me study (Cherry et al., 2018) of 1001 welders, 447 women and 554 men that were followed up for 3 years in the case of men and 5 years in the case of women. The length of follow up produced more than 2200 welding questionnaires requiring exposure estimates. The welding questionnaire was asked to all participants that were in a welding trade at the time of their routine 6-monthly follow-up and that had been welding in the past 6 months. The welding questionnaire had questions on tasks performed such as pipe welding, repairing or manufacturing etc., process used for welding, base metal and consumables including fluxes and shielding gases. Other questions relating to occupational hygiene were also asked but are not discussed in this study (see Appendix A for a complete list of questions asked on the welding questionnaire). The most common combinations of process, base metal and consumable (referred to as welding scenarios) were identified. Some respondents could not recall what consumable they had used on their last day of welding and so these unknown consumables were replaced by the most common consumables found in those doing the same task, using the same process and matching the base metal. This was done by a welding professional that looked at the entire welding history of the participant while also looking at the most commonly used consumables in Canada for the specific tasks reported by the participant. A total of 21 welding scenarios were identified as being the most important welding scenarios in the What-me study, those are listed in Table 3.1. The most common welding scenarios were then replicated in a laboratory by an experienced welder and personal air samples taken during each welding session. To do this, an air sampling protocol was developed and is described below.

Table 3.1: Most common scenarios in the What-me study counting occurrence in the What-me study and number of replications

Process	Metal	Consumable	n	n _e
MMAW	MS	E6010	272	4
MMAW	MS	E7018	1081	5
MMAW	GS	E6010	16	2
MMAW	GS	E7018	74	2
MMAW	SS	E308	27	3
MMAW	SS	E316	22	3
GMAW	MS	ER70S6	700	3
GMAW	MS	ER70S2	30	2
GMAW	GS	ER70S6	49	2
GMAW	SS	ER308L	21	4
GMAW	SS	ER316L	7	2
GMAW	AL	ER5356	49	3
GMAW	AL	ER4043	17	4
FCAW	MS	E71T1	147	4
MCAW	MS	E70MC6	51	4
GTAW	MS	ER70S2	62	2
GTAW	MS	ER70S6	34	2
GTAW	SS	ER316L	48	3
GTAW	SS	ER308L	46	2
GTAW	AL	ER5356	21	3
GTAW	AL	ER4043	21	2

MS=mild steel, GS=galvanized steel, SS=stainless steel, AL=aluminum, n=number occurrences of scenario, n_e=number of scenario replications

3.2.1 Air sampling

In the summer of 2019, air samples were collected on 37 different days. The welding sessions took place in the Canadian Centre for Welding and Joining at the University of Alberta using the same GMAW, GTAW or MMAW machine for the majority of samples. The aluminum GMAW sessions were performed using a machine provided to the research team by the Northern Alberta Institute of Technology (NAIT) because it had a spool gun attachment that was needed to complete the aluminum welding scenarios. On some days only 1 welding session was completed while on other days 2 were completed and on one occasion 3. On days with more than one welding session, each session was separated by a 1-hour period of high flow ventilation to

ensure that the second sample would not be contaminated by the particles from the first. A test was conducted to see if the 1-hour ventilation returned the room to its initial background levels using a P-track real time particle counter. Particle counts before welding started were compared to particle counts after the 1-hour of ventilation period which was done immediately after the welding session. It was determined that the 1 hour of high flow ventilation was sufficient to return the room to background particle concentration levels. Additionally, in order to ensure that first sessions were not systematically different from second sessions, scenarios were partially quasi-randomized such that each scenario would not only be completed as a first session or as a second session etc. The same welder was used for all welding sessions with the cassette attached to the right side of the lapel inside the breathing zone (Personal Sampling for Air Contaminants, 2014). The welder was equipped with protective clothing, gloves, a welding helmet and wore a P100 mask for every session and was also accompanied by a welding buddy who was there to ensure the welder's safety and proper functioning of the sampling equipment.

In order to maximize our chances of representing a full shift sample and to minimize non-detects, following the guidance of an occupational hygienist, it was decided that 3 hours would provide sufficient sampling material to obtain a full metals analysis along with a total dust estimate for each scenario. The base metals used were of the same classification within each scenario such that all mild steel scenarios used the same classification of steel and the same was true of the other base metals. Consumables were from the same manufacturer within each scenario. All mild steel scenarios (including galvanized steel) were performed with A36 mild steel, the stainless steel scenarios were performed on 304 stainless steel and the aluminum was classified as 5052. All metals were purchased at the same location from a single provider ensuring that they were indeed the correct classification and variations such as structural steel vs. steel plates were avoided to ensure a homogeneity of base metals within scenarios. Consumables were purchased mainly from one source but some were donated from NAIT and one spool was donated from Lincoln Electric. The mild steel GMAW and MCAW welding scenarios were accompanied with a mix of carbon dioxide and argon gas (75/25%) while the GTAW sessions were all performed with 100% argon. The GMAW stainless steel and aluminum sessions were both performed with 100% argon gas. FCAW was performed gasless as self-shielded. For MMAW, rods of the same size (1/8") were used across scenarios in an attempt to reduce

confounding by the amount of consumable used. For the GMAW, FCAW and MCAW sessions, 0.035” filler wire size was used for all of the metals and for GTAW welding 3/32” was used.

Before each welding session, 5 µm PVC filters (37 mm diameter) were carefully treated for static control then weighed on a microbalance (Mettler Toledo[®], Mississauga, Canada) and their weight was recorded. The filters were mounted in a total dust cassette that was pre-cleaned in a solution containing 5% nitric acid and both sides of the cassettes were sealed until the welding session began (Organization). Using a flow rater, the sampling pumps were calibrated before and after each welding session to obtain the average flow rate for each welding session. Cassettes were connected to a Gilian Plus personal air sampling pump (Sensidyne[®], St. Petersburg, Florida, USA). After each sampling session, the cassettes were again sealed, brought back to the laboratory and stored in a desiccator for at least 2 days before the filters were removed from the cassettes and weighed. The weighing procedure again included a static control procedure followed by weighing on the microbalance according to NIOSH method 0500 (Burton, 2001). The mean of the blank analysis and its standard deviation was used as the limit of detection for all 5 outcomes (Armbruster and Pry, 2008). Values below the limit of detection were replaced by using the beta substitution method described by Ganser and Hewett (2010).

For the metals analysis, filter digestion was performed at the Soil, Water, Air, Manure, and Plants (SWAMP) laboratory at the University of Alberta. All preparation procedures were carried out in a Class 100 cleanroom. Filter samples were digested in a high-pressure microwave (Ultraclave, Milestone[®], Leutkirch, Germany) using a mixture of 3 mL nitric acid and 0.1 mL of tetrafluoroboric acid (HBF₄) following NIOSH method 7304 (Ashley, 2015). All acids were sub-boiled and plasticware was acid cleaned prior to use to avoid any metal contamination during sample preparation and analysis. Samples were completed to 10 mL and diluted 10-fold for field blanks and ambient air samples and 100-fold for welding fume samples. Analysis was performed using iCAP-Q Inductively Coupled Plasma Mass Spectrometry (ICP/MS), (Thermo-Finnigan[®], Bremen, Germany).

3.2.2 Statistical analysis

Sample concentration means with standard deviations and 95% confidence intervals stratified by scenario were calculated. The results were also stratified by process, base metal and consumable. Predictions that included means and confidence intervals were made for the 21 scenarios using the models produced and shown in the first paper of this series. Differences

between the observed and predicted values were examined along with their direction and relative bias was computed for the 5 parameters being estimated ($\text{predicted-observed/observed} \times 100$) (Perkins, 2008). Additionally, a Spearman rank correlation was computed between the predicted and observed values and an examination was made of how many confidence intervals of the observed values overlapped with their corresponding predicted confidence intervals. Lastly, the data were combined to form one single model with the scenario replications serving as a calibration to the existing model constructed in the first part of this series with a side-by-side comparison of the changes in β -coefficients. A binary variable was included to differentiate the data from the laboratory with those from the systematic review and its effect in the multivariate model confirmed with a Wilcoxon matched-pair rank test. A final examination of the fit of the model was made and final models were kept for all 5 parameters being estimated.

3.3 Results

3.3.1 Scenario replication

The welding/sampling time was on average 178 minutes (median 180) and the results of the welding scenario replications stratified by scenario can be seen in Table 3.2 while the results stratified by process, base metal and consumable can be seen in Table 3.3. The replications showed that the highest total dust concentration was produced by FCAW, followed by MCAW, GMAW, MMAW and GTAW. These findings correspond well with the findings from the systematic review and can be found in Table 3.4 where a multivariate model of total dust containing samples from the scenario replications can be seen side by side with the multivariate model from the literature. Mild steel and galvanized steel were the most particle producing base metals followed by stainless steel and aluminum (Table 3.3) and remained so in the multivariate model, also comparable to the initial multivariate model from the literature.

Table 3.2: Mean concentrations for total dust and metal air concentrations stratified by welding scenario

			Total dust ¹				Manganese				Nickel				Chromium				Aluminum			
			95% CI				95% CI				95% CI				95% CI				95% CI			
			Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper
MMAW	MS	E6010	9.10	0.47	8.64	9.56	5.41	0.50	4.92	5.90	1.14	0.30	0.85	1.44	1.46	0.49	0.97	1.94	-1.35	2.51	-3.80	1.11
MMAW	MS	E7018	8.59	0.61	8.05	9.12	5.55	0.69	4.94	6.15	-0.11	0.53	-0.58	0.36	1.77	0.63	1.22	2.32	2.69	0.41	2.33	3.04
MMAW	GS	E6010	9.44	0.48	8.78	10.10	5.61	0.61	4.76	6.45	0.66	0.24	0.33	0.99	1.10	0.26	0.75	1.46	-1.34	4.38	-7.40	4.73
MMAW	GS	E7018	9.47	0.05	9.40	9.54	5.86	0.16	5.64	6.08	-0.10	0.39	-0.64	0.44	1.49	0.27	1.12	1.86	3.12	0.01	3.11	3.14
MMAW	SS	E308	7.43	0.18	7.22	7.64	4.01	1.55	2.26	5.76	1.98	0.11	1.86	2.10	3.94	0.21	3.70	4.17	2.28	0.25	1.99	2.56
MMAW	SS	E316	8.40	0.61	7.71	9.09	5.11	0.83	4.17	6.05	3.32	0.08	3.23	3.41	5.04	0.49	4.48	5.60	3.24	0.36	2.83	3.65
GMAW	MS	ER70S6	9.94	0.27	9.63	10.25	7.53	0.10	7.41	7.65	0.70	0.20	0.48	0.93	2.63	0.25	2.35	2.91	-0.04	3.81	-4.35	4.28
GMAW	MS	ER70S2	9.46	0.28	9.08	9.84	6.46	0.17	6.23	6.69	0.89	0.88	-0.33	2.10	2.01	0.45	1.38	2.63	-0.58	5.11	-7.66	6.50
GMAW	GS	ER70S6	9.75	0.45	9.12	10.37	6.03	0.36	5.53	6.54	0.74	0.15	0.53	0.95	2.13	0.10	2.00	2.27	2.72	0.06	2.64	2.80
GMAW	SS	ER308L	8.79	0.39	8.40	9.17	6.16	0.18	5.99	6.34	5.52	0.44	5.09	5.94	6.52	0.25	6.27	6.76	-0.48	4.50	-4.88	3.93
GMAW	SS	ER316L	7.06	0.11	6.91	7.21	4.82	0.16	4.61	5.04	3.87	0.25	3.51	4.22	4.51	0.04	4.46	4.56	1.80	1.01	0.40	3.19
GMAW	AL	ER5356	7.56	0.67	6.81	8.32	2.37	1.22	0.99	3.75	-0.96	0.81	-1.88	-0.05	1.19	0.73	0.37	2.01	6.14	0.15	5.98	6.31
GMAW	AL	ER4043	8.23	0.15	8.06	8.40	2.05	0.67	1.39	2.70	-0.74	0.36	-1.09	-0.39	1.11	0.13	0.98	1.24	5.97	0.09	5.88	6.06
FCAW	MS	E71T1	10.96	0.39	10.58	11.34	6.24	0.37	5.88	6.61	0.69	0.66	0.04	1.33	2.54	0.30	2.25	2.83	7.28	0.65	6.65	7.92
MCAW	MS	E70MC6	9.37	0.51	8.87	9.87	6.03	1.23	4.82	7.24	-0.49	1.66	-2.11	1.14	1.19	1.50	-0.28	2.66	-2.81	3.09	-5.83	0.22
GTAW	MS	ER70S2	7.10	0.32	6.66	7.55	3.66	0.00	3.66	3.66	0.42	0.29	0.03	0.82	1.30	0.20	1.03	1.57	2.41	0.06	2.33	2.50
GTAW	MS	ER70S6	7.15	0.04	7.09	7.21	3.09	0.03	3.04	3.13	0.70	0.47	0.05	1.35	1.60	0.14	1.40	1.80	2.96	0.55	2.20	3.73
GTAW	SS	ER316L	5.87	0.02	5.84	5.89	2.49	0.49	1.81	3.16	1.09	0.22	0.78	1.39	2.41	0.38	1.88	2.94	2.78	0.02	2.75	2.81
GTAW	SS	ER308L	6.96	0.28	6.65	7.28	1.96	1.37	0.40	3.51	-0.03	1.52	-1.75	1.69	2.11	1.35	0.58	3.64	3.92	0.87	2.95	4.90
GTAW	AL	ER5356	6.93	0.25	6.64	7.21	1.94	1.10	0.70	3.18	0.29	2.11	-2.11	2.68	2.17	1.40	0.58	3.75	3.81	0.50	3.24	4.38
GTAW	AL	ER4043	6.20	0.39	5.65	6.74	2.18	0.52	1.45	2.90	0.47	1.28	-1.30	2.25	2.16	1.27	0.40	3.92	3.52	0.43	2.93	4.11

¹Natural log conc($\mu\text{g}/\text{m}^3$); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum
²a sample was excluded

Table 3.3: Descriptive statistics of total dust and metal air concentrations resulting from the welding scenario replications ($\mu\text{g}/\text{m}^3$) stratified by process, base metal and consumable

Process	N	Total dust*				Manganese				Nickel				Chromium				Aluminum			
		Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
MMAW	19	7508.5	5054.2	1384.3	17589.0	255.4	165.1	21.1	568.9	6.8	9.6	0.5	30.3	38.0	63.9	2.2	214.7	12.9	10.3	0.3	32.2
GMAW	20*	9143.6	8031.5	966.3	26338.7	500.6	638.5	3.1	2089.2	58.9	114.0	0.2	352.0	152.4	284.5	1.9	827.2	157.2	205.2	0.3	551.5
FCAW	4	60837.6	23597.2	36215.6	92965.9	539.8	182.8	317.6	731.5	2.3	1.5	1.0	4.4	13.1	4.1	9.3	19.0	1694.9	1061.3	676.2	3145.7
MCAW	4	12961.0	7041.4	6640.0	23045.0	655.2	625.8	80.4	1536.8	1.1	0.8	0.1	1.8	5.3	3.5	0.4	7.8	1.6	3.1	0.3	6.2
GTAW	14	939.3	400.6	348.6	1524.7	17.1	13.3	2.9	38.9	2.9	3.8	0.3	14.9	11.6	13.4	2.9	42.3	35.7	26.4	10.7	91.3
Metal																					
Mild steel	26	17702.8	21571.7	971.5	92965.9	551.1	586.6	21.4	2089.2	2.0	1.2	0.1	4.7	7.8	4.7	0.4	19.0	268.3	721.2	0.3	3145.7
Stainless	17	3170.9	2941.9	348.6	9230.6	191.3	205.3	2.9	556.5	75.1	118.0	0.3	352.0	216.0	286.2	3.3	827.2	25.0	27.5	0.3	91.3
Aluminum	12*	2009.6	1458.3	371.5	4444.3	11.5	10.2	3.1	35.6	2.0	4.2	0.2	14.9	8.3	11.9	1.9	42.3	265.9	202.2	25.0	551.5
Galvanized	6	14741.8	5108.4	8961.0	23514.7	360.4	121.6	176.6	539.0	1.7	0.6	0.7	2.3	5.4	2.6	2.5	9.1	13.6	9.2	0.3	22.9
Consumable																					
E6010	6	10943.1	5179.5	6353.7	17589.0	263.1	124.9	140.5	419.1	2.8	1.0	1.6	4.7	4.1	1.8	2.2	6.8	2.1	2.2	0.3	5.8
E7018	7	8137.1	4440.6	2573.5	13437.4	322.9	177.3	138.2	568.9	1.0	0.5	0.5	1.6	6.2	3.7	3.1	13.0	17.7	6.1	8.7	24.4
E308L	3	1706.5	304.1	1384.3	1988.6	124.5	176.5	21.1	328.3	7.3	0.8	6.7	8.2	51.9	10.1	40.4	59.3	10.0	2.4	7.6	12.5
E316L	3	4974.6	2585.5	2253.7	7399.1	213.1	191.1	100.9	433.7	27.8	2.2	26.1	30.3	166.0	68.5	87.7	214.7	26.6	8.5	16.8	32.2
ER70S6	7	14607.5	10288.7	971.5	26338.7	934.9	896.9	38.9	2089.2	1.9	0.4	1.2	2.5	9.6	5.2	3.2	17.7	10.8	6.6	0.3	18.7
ER70S2	4	7164.5	7103.0	1235.1	15563.7	332.3	363.6	21.4	718.1	2.5	1.5	1.3	4.5	6.4	2.6	4.5	10.2	15.7	12.0	0.3	28.6
E71T1	4	60837.6	23597.2	36215.6	92965.9	539.8	182.8	317.6	731.5	2.3	1.5	1.0	4.4	13.1	4.1	9.3	19.0	1694.9	1061.3	676.2	3145.7
E70C6M	4	12961.0	7041.3	6640.0	23045.0	655.2	625.8	80.4	1536.8	1.1	0.7	0.1	1.8	5.3	3.5	0.4	7.8	1.8	3.0	0.3	6.2
ER308L	6	4710.4	3827.9	348.6	9230.6	324.7	250.3	8.5	556.5	178.0	155.7	2.5	352.0	464.8	371.2	8.5	827.2	19.1	25.7	0.3	69.5
ER5356T	6	1627.7	1081.1	811.7	3644.8	13.6	13.5	3.1	35.6	2.9	5.9	0.2	14.9	10.4	15.7	1.9	42.3	258.8	234.7	25.3	551.5
ER316L	5	1119.7	227.1	806.0	1403.4	58.3	63.2	2.9	139.1	20.7	26.2	0.3	57.1	45.8	43.8	3.3	93.3	40.2	40.3	3.0	91.3
ER4043	6*	2467.9	1837.0	371.5	4444.3	9.4	6.2	4.5	20.5	1.1	1.4	0.3	4.0	6.2	7.4	2.5	21.3	273.1	186.4	25.0	426.9

*1 sample excluded.

Table 3.4: Side by side comparison of multivariate models - total dust

Process	Literature model 95% CI					Scenario replication model 95% CI					Combined model 95% CI				
	β	se	lower	upper	p-value	β	se	lower	upper	p-value	β	se	lower	upper	p-value
MMAW	-0.448	0.131	-0.704	-0.192	0.001	-0.441	0.182	-0.806	-0.075	0.019	-0.448	0.126	-0.695	-0.202	0.000
GTAW	-1.591	0.154	-1.893	-1.289	0.000	-1.795	0.200	-2.196	-1.394	0.000	-1.588	0.146	-1.875	-1.302	0.000
FCAW	0.938	0.082	0.777	1.099	0.000	1.642	0.169	1.303	1.982	0.000	0.949	0.084	0.784	1.114	0.000
MMAW + GTAW	-1.290	0.144	-1.572	-1.008	0.000						-1.297	0.138	-1.567	-1.027	0.000
GMAW + MMAW ^a															
GMAW + GTAW ^b															
MMAW + GMAW + GTAW + FCAW ^a															
MCAW						0.050	0.169	-0.289	0.389	0.768	0.228	0.262	-0.285	0.741	0.383
Unknown	0.928	0.344	0.254	1.602	0.007						0.899	0.317	0.278	1.521	0.005
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal															
Stainless steel	-0.545	0.573	-1.668	0.579	0.342	-1.023	0.190	-1.404	-0.643	0.000	-0.598	0.526	-1.628	0.432	0.255
Aluminum	-0.953	0.429	-1.794	-0.113	0.026	-1.179	0.195	-1.570	-0.789	0.000	-1.028	0.368	-1.749	-0.306	0.005
High alloyed steel	-0.447	0.362	-1.157	0.262	0.217						-0.484	0.326	-1.124	0.156	0.138
Mild steel + stainless steel ^c															
Mangalloy	-1.978	0.353	-2.669	-1.286	0.000						-2.015	0.324	-2.65	-1.379	0.000
Galvanized steel						0.528	0.101	0.325	0.730	0.000	0.711	0.238	0.245	1.177	0.003
Unknown	-0.430	0.535	-1.479	0.619	0.422						-0.477	0.492	-1.44	0.486	0.332
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Sample type															
Respirable fraction	-0.328	0.135	-0.591	-0.064	0.015	-	-	-	-	-	-0.327	0.134	-0.589	-0.065	0.015
Total particulates	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Data Source															
Scenario replications											0.84	0.173	0.501	1.180	0.000
Literature search											rc	rc	rc	rc	rc
Constant^d	8.262	0.368	7.451	8.984	0.000	9.318	0.169	8.978	9.657	0.000	8.300	0.341	7.631	8.968	0.000
N	4620					60					4680				

^aregrouped with MMAW, ^bregrouped with GMAW, ^cregrouped with stainless steel, rc=reference category

^dinitial model within paper variance 0.131 and between paper variance 1.310, calibrated model within paper variance 0.133 and between paper variance 1.306

Manganese saw its highest concentrations with MCAW followed immediately by FCAW, GMAW, MMAW and GTAW. The model from the scenario replications (Table 3.5) showed that the highest manganese producing process was FCAW followed by MCAW, GMAW, MMAW and GTAW. These findings were parallel to those from the literature model. The highest manganese producing base metal was mild steel followed by galvanized steel, stainless steel and aluminum also reiterated by the multivariate model again agreeing well with the model from the literature. For consumables, the filler metal producing the highest manganese concentration was ER70S6 (Table 3.2) and in the multivariate model manganese content did not add to the model significantly while negatively predicting manganese exposure. The consumables producing the least manganese fumes were the aluminum consumables.

The highest nickel concentrations were produced by GMAW followed by MMAW, GTAW, FCAW and MCAW. The multivariate model was severely affected by collinearity between base metal and nickel content in the consumable therefore nickel content was omitted from the multivariate model shown in Table 3.6. The model showed GMAW to be the highest producing category followed by FCAW, MMAW, GTAW and MCAW. This was relatively similar to the results from the literature where GMAW produced the highest nickel fumes followed by MMAW, FCAW and GTAW. The base metal producing the highest nickel concentrations was stainless steel followed by mild steel and aluminum with almost equal concentrations ($1.96 \mu\text{g}/\text{m}^3$ vs. $1.98 \mu\text{g}/\text{m}^3$) and lastly by galvanized steel. The same remained in the multivariate model and corresponded to the model from the systematic review. ER308 produced the highest nickel concentrations followed by E316, ER316 and E308. The nickel content in ER308 is less than what is found in ER316 (LincolnElectric) but E316 is indeed higher in nickel content than E308 indicating that at least in the case of MMAW, the results from the welding replications align with the model from the literature.

GMAW produced the highest levels of airborne chromium followed by MMAW, FCAW, GTAW and MCAW. Again, multicollinearity did not allow to keep both base metal and chromium content in the same model thus the latter was omitted from Table 3.7. The multivariate model ranked FCAW and GMAW as the highest chromium producing processes followed by MMAW, GTAW and MCAW. Stainless steel produced the highest chromium fumes in our replications followed by aluminum, mild steel and galvanized steel. The model showed that stainless steel was the highest chromium producing base metal but that mild steel produced

more chromium fumes than aluminum although this difference was not significant. Galvanized steel was the base metal found to produce the lowest amounts of airborne chromium particles. ER308 produced the largest quantity of airborne chromium followed by E316, E308 and ER316. It follows the model in that ER308 does indeed have higher chromium concentrations by about 1-2% on average but that relationship did not hold in MMAW with E316 producing more chromium fumes than E308 despite being the one with slightly lower chromium content. The lowest chromium producing consumables were mild steel consumables.

For aluminum, 10 samples were below the limit of detection and values replaced by 0.248 µg/filter before air concentrations were calculated. FCAW produced the highest aluminum fumes followed by GMAW, GTAW, MMAW and MCAW. The model showed that FCAW produced the highest aluminium concentrations (Table 3.8) followed by GTAW, MMAW, GMAW and MCAW. This was similar to the results from the literature model both agreeing that FCAW produced the highest aluminum concentrations. The metal producing the highest aluminum concentration was mild steel closely followed by aluminum, stainless steel and galvanized steel, a finding driven solely by FCAW and E71T1 contents. The consumable that produced the highest aluminum concentration was E71T1, a mild steel consumable made up of less than 2% aluminum. The next two consumables producing the highest aluminum fumes were ER4043 and ER5356 which on average have very much the same aluminum content.

Table 3.5: Side by side comparison of multivariate models - manganese

Process	Literature model					Scenario replication model					Combined model				
	β	se	95% CI		p-value	β	se	95% CI		p-value	β	se	95% CI		p-value
			lower	upper				lower	upper				lower	upper	
MMAW	-0.543	0.455	-1.435	0.348	0.232	-1.064	0.312	-1.690	-0.437	0.001	-0.536	0.442	-1.402	0.331	0.225
GTAW	-2.372	0.290	-2.940	-1.803	0.000	-2.250	0.345	-2.941	-1.558	0.000	-2.397	0.257	-2.901	-1.894	0.000
FCAW	0.254	0.436	-0.601	1.109	0.561	-0.140	0.290	-0.723	0.443	0.632	0.262	0.428	-0.576	1.100	0.540
GMAW + MMAW	-1.931	0.402	-2.719	-1.144	0.000						-1.843	0.378	-2.584	-1.102	0.000
GMAW + GTAW ^a															
FCAW + MMAW ^b															
MMAW + GMAW + GTAW	-0.317	0.124	-0.561	-0.073	0.011						-0.277	0.141	-0.553	0.000	0.050
MCAW						-0.380	0.295	-0.971	0.211	0.203	-0.026	0.182	-0.382	0.330	0.886
Unknown	-0.619	0.667	-1.926	0.688	0.353						-0.503	0.625	-1.728	0.723	0.421
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Metal															
Stainless steel	-0.841	0.265	-1.360	-0.323	0.001	-0.921	0.262	-1.448	-0.395	0.001	-0.823	0.187	-1.190	-0.456	0.000
Aluminum	-2.768	0.272	-3.301	-2.236	0.000	-3.807	0.516	-4.842	-2.771	0.000	-2.327	0.327	-2.968	-1.686	0.000
Mild steel + stainless steel ^c															
Mild steel + stainless steel + galvanized steel	-1.325	0.421	-2.151	-0.499	0.002						-1.110	0.362	-1.819	-0.400	0.002
Galvanized steel						0.025	0.204	-0.384	0.433	0.904	0.277	0.152	-0.020	0.575	0.068
Unknown	-1.248	0.414	-2.059	-0.437	0.003						-1.070	0.336	-1.728	-0.411	0.001
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Manganese in consumable (%)	0.674	0.260	0.164	1.183	0.010	-0.393	0.205	-0.804	0.019	0.061	0.530	0.237	0.065	0.995	0.026
Sample type															
Respirable fraction	-0.066	0.086	-0.235	0.103	0.442						-0.065	0.087	-0.236	0.105	0.452
Total particulates	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Data Source															
Scenario replications											0.105	0.255	-0.395	0.605	0.681
Literature search											rc	rc	rc	rc	rc
Constant^d	5.149	0.294	11.480	12.633	0.000	6.952	0.469	6.011	7.894	0.000	5.220	0.309	4.615	5.825	0.000
N	4762					61					4823				

^aregrouped with unknown, ^bregrouped with FCAW, ^cregrouped with unknown, rc=reference category

^dinitial model within paper variance 0.325 and between paper variance 1.451, calibrated model within paper variance 0.330 and between paper variance 1.329

Table 3.6: Side by side comparison of multivariate models - nickel

Process	Literature model					Scenario replication model					Combined model				
	β	se	95% CI		p-value	β	se	95% CI		p-value	β	se	95% CI		p-value
			lower	upper				lower	upper				lower	upper	
MMAW	-0.391	0.086	-0.559	-0.223	0.000	-0.726	0.334	-1.397	-0.055	0.034	-0.400	0.086	-0.567	-0.232	0.000
GTAW	-1.631	0.195	-2.013	-1.249	0.000	-1.175	0.501	-2.180	-0.170	0.023	-1.627	0.191	-2.002	-1.252	0.000
FCAW	-1.127	0.243	-1.604	-0.650	0.000	-0.501	0.268	-1.039	0.038	0.068	-1.120	0.239	-1.588	-0.651	0.000
MMAW + GTAW ^a															
MCAW						-1.676	0.268	-2.214	-1.138	0.000	-1.939	0.143	-2.219	-1.660	0.000
Unknown	-0.963	0.318	-1.586	-0.341	0.002						-0.975	0.316	-1.595	-0.355	0.002
GMAW	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Metal															
Stainless steel	0.405	0.138	0.135	0.675	0.003	2.225	0.391	1.441	3.008	0.000	0.450	0.171	0.116	0.784	0.008
Aluminum						-1.036	0.412	-1.862	-0.210	0.015	-1.111	0.165	-1.435	-0.788	0.000
High alloyed steel	1.260	0.133	1.000	1.521	0.000						1.307	0.170	0.974	1.641	0.000
Mild steel + stainless steel ^b															
Galvanized steel						-0.270	0.226	-0.725	0.184	0.238	-0.784	0.174	-1.125	-0.444	0.000
Unknown	0.839	0.353	0.148	1.531	0.017						0.878	0.341	0.210	1.546	0.010
Mild steel	rc	rc	rc	rc	rc	rc	rc	rc	rc	Rc	rc	rc	rc	rc	rc
Nickel in consumable (%)	0.111	0.025	0.063	0.159	0.000						0.111	0.020	0.071	0.150	0.000
Sample type															
Respirable fraction	-0.768	0.056	-0.878	-0.658	0.000						-0.768	0.056	-0.878	-0.658	0.000
Total particulates	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Data Source															
Scenario replications											-0.736	0.331	-1.385	-0.088	0.026
Literature search											rc	rc	rc	rc	rc
Constant^c	2.219	0.439	1.358	3.079	0.000	1.188	0.268	0.650	1.727	0.000	2.188	0.413	1.378	2.998	0.000
N	4679					61					4740				

^aregrouped with GTAW, ^bregrouped with mild still, rc=reference category

^cinitial model within paper variance 0.166 and between paper variance 2.217, calibrated model within paper variance 0.180 and between paper variance 2.131

Table 3.7: Side by side comparison of multivariate models - chromium

Process	Literature model					Scenario replication model					Combined model				
	β	se	95% CI		p-value	β	se	95% CI		p-value	β	se	95% CI		p-value
MMAW	0.816	0.360	0.110	1.522	0.023	-0.607	0.261	-1.130	-0.085	0.024	0.774	0.359	0.071	1.477	0.031
GTAW	-1.753	0.198	-2.142	-1.365	0.000	-1.159	0.410	-1.981	-0.337	0.007	-1.725	0.198	-2.113	-1.338	0.000
FCAW	-1.647	0.210	-2.057	-1.236	0.000	0.179	0.209	-0.240	0.599	0.395	-1.596	0.218	-2.023	-1.169	0.000
MMAW + GTAW															
GMAW + MMAW ^a															
MMAW + GMAW + GTAW	-0.979	0.118	-1.209	-0.748	0.000						-0.981	0.118	-1.211	-0.750	0.000
MCAW						-1.173	0.209	-1.592	-0.753	0.000	-0.806	0.252	-1.299	-0.312	0.001
Unknown	1.419	0.514	0.411	2.426	0.006						1.373	0.507	0.380	2.366	0.007
GMAW	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Metal															
Stainless steel	0.598	0.084	0.434	0.762	0.000	2.499	0.298	1.901	3.098	0.000	0.584	0.080	0.428	0.740	0.000
Aluminum	-0.308	0.442	-1.175	0.558	0.485	-0.307	0.358	-1.025	0.412	0.396	0.277	0.211	-0.137	0.691	0.190
High alloyed steel	1.011	0.383	0.261	1.760	0.008						0.982	0.378	0.241	1.724	0.009
Mild steel + stainless steel															
Galvanized steel						-0.380	0.128	-0.637	-0.122	0.005	-0.934	0.111	-1.151	-0.717	0.000
Unknown	0.536	0.183	0.177	0.896	0.003						0.518	0.181	0.165	0.872	0.004
Mild steel	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Chromium in consumable (%)	0.066	0.016	0.034	0.098	0.000						0.118	0.011	0.096	0.139	0.000
Type of chromium particle															
Cr(VI)	-1.535	0.186	-1.899	-1.171	0.000						-1.534	0.186	-1.898	-1.170	0.000
Total Cr	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Sample type															
Respirable fraction	-0.714	0.101	-0.912	-0.515	0.000						-0.713	0.102	-0.913	-0.513	0.000
Total particulates	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Data Source															
Scenario replications											0.586	0.303	-0.009	1.180	0.053
Literature search											rc	rc	rc	rc	rc
Constant ^b	1.391	0.443	0.523	2.259	0.000	2.360	0.209	1.941	2.779	0.000	1.407	0.433	0.559	2.255	0.000
N	3972					61					4033				

^aregrouped with GMAW, rc=reference category

^binitial model within paper variance 0.629 and between paper variance 2.841, calibrated model within paper variance 0.642 and between paper variance 2.740

Table 3.8: Side by side comparison of multivariate models - aluminum

Process	Literature model 95% CI					Scenario replication model 95% CI					Combined model 95% CI				
	β	se	lower	upper		β	se	lower	upper		β	se	lower	upper	p-value
MMAW	-0.122	0.026	-0.173	-0.072	0.000	0.306	0.614	-0.924	1.536	0.620	-0.158	0.083	-0.321	0.004	0.057
GTAW	-2.570	0.133	-2.831	-2.310	0.000	0.893	0.534	-0.178	1.964	0.100	-1.266	0.979	-3.185	0.653	0.196
FCAW	0.962	0.013	0.936	0.987	0.000	6.106	0.395	5.314	6.899	0.000	1.527	0.764	0.030	3.025	0.046
GMAW + MMAW	-2.557	0.392	-3.325	-1.789	0.000						-2.062	0.428	-2.901	-1.224	0.000
MCAW						-3.984	0.395	-4.777	-3.192	0.000	-5.020	0.275	-5.560	-4.480	0.000
GMAW	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc	rc
Aluminum in consumable (%)	0.036	0.006	0.024	0.048	0.000	0.038	0.006	0.025	0.050	0.000	0.036	0.003	0.030	0.042	0.000
Sample type															
Respirable fraction	0.624	0.276	0.083	1.165	0.024						0.123	0.418	-0.696	0.942	0.769
Total particulates	rc	rc	rc	rc	rc						rc	rc	rc	rc	rc
Data Source															
Scenario replications											-1.343	0.415	-2.157	-0.530	0.001
Literature search											rc	rc	rc	rc	rc
Constant ^a	3.550	0.342	2.879	4.220	0.000	1.178	0.395	0.385	1.970	0.000	3.556	0.320	2.928	4.184	0.000
N	676					61					737				

^ainitial model within paper variance 1.159 and between paper variance 0.515, calibrated model within paper variance 1.433 and between paper variance 0.424, rc=reference category

There was, overall some degree of concordance between the replications and the multivariate models when both comparing the ranks of means from Table 3.2 to the literature model ranks of β -coefficients from Tables 3.4 through Tables 3.8 but also when comparing the ranks of β -coefficients from the literature to those from the model of scenario replications. Nevertheless, a more robust analysis of concordance is necessary.

3.3.2 Validation

When using the total dust multivariate model developed from the systematic review data to make out of sample predictions of the observed values, 4/21 (19%) predicted confidence intervals contained the observed value (i.e., measurements from scenario replications). The predictions were consistently smaller than the observed values except in 2 cases and the results of these comparisons can be seen in Table 3.9. When using the replications' own confidence intervals to examine the degree of overlap between the observed confidence intervals and the predicted confidence intervals, we saw a much higher concordance with 14/21 (67%) overlapping. A rank correlation (Spearman) was also computed to see if, irrespective of the calculated relative bias of 50%, the relative position of each prediction corresponded with the observed values. This yielded a rho of 0.93 ($p < 0.001$) and showed a very high degree of concordance.

Table 3.9: Total dust measurements: observed and predicted with degree of deviation and overlapping CI's

	Observed 95% CI			Predicted 95% CI			Deviation	Overlapping CI's
	Mean	Lower	Upper	Mean	Lower	Upper		
MMAW MS E6010	9777.22	4697.52	14856.92	2476.17	1240.12	4944.21	-7301.05	Yes
MMAW MS E7018	6197.95	3034.40	9361.49	2476.17	1240.12	4944.21	-3721.77	Yes
MMAW GS E6010	13275.01	4819.61	21730.40	2476.17	1240.12	4944.21	-10798.83	Yes
MMAW GS E7018	12984.85	12097.75	13871.94	2476.17	1240.12	4944.21	-10508.68	No
MMAW SS E308	1706.50	1362.37	2050.64	1436.03	763.72	2700.16	-270.48	Yes
MMAW SS E316	4974.61	2048.87	7900.35	1436.03	763.72	2700.16	-3538.58	Yes
GMAW MS ER70S6	21275.05	15049.60	27500.50	3875.36	1883.09	7975.43	-17399.69	No
GMAW MS ER70S2	13054.30	8135.94	17972.66	3875.36	1883.09	7975.43	-9178.93	No
GMAW GS ER70S6	17965.57	7089.18	28841.95	3875.36	1883.09	7975.43	-14090.20	Yes
GMAW SS ER308L	6889.13	4604.62	9173.65	2247.48	1204.25	4194.42	-4641.66	No
GMAW SS ER316L	1172.00	994.99	1349.01	2247.48	1204.25	4194.42	1075.48	Yes
GMAW AL ER5356	2214.01	687.92	3740.10	1493.53	1025.04	2176.15	-720.47	Yes
GMAW AL ER4043	3773.42	3114.90	4431.94	1493.53	1025.04	2176.15	-2279.89	No
FCAW MS E71T1	60837.63	37712.35	83962.91	9903.11	4925.39	19911.42	-50934.52	No
MCAW MS E70MC6	12961.00	6060.48	19861.53	3875.36	1883.09	7975.43	-9085.64	Yes
GTAW MS ER70S2	1248.10	705.88	1790.31	789.62	340.44	1831.44	-458.48	Yes
GTAW MS ER70S6	1274.71	1196.98	1352.43	789.62	340.44	1831.44	-485.09	Yes
GTAW SS ER316L	352.99	344.42	361.55	457.93	281.41	745.17	104.94	Yes
GTAW SS ER308L	1084.90	744.66	1425.15	457.93	281.41	745.17	-626.97	Yes
GTAW AL ER5356	1041.44	738.34	1344.54	304.31	197.20	469.60	-737.13	No
GTAW AL ER4043	509.73	238.82	780.64	304.31	197.20	469.60	-205.42	Yes

*conc($\mu\text{g}/\text{m}^3$); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum

The same analysis was repeated for the metals and for manganese, 13 of the 21 (62%) observed values were within their predicted confidence intervals while 17 (81%) of the predicted confidence intervals overlapped with the observed confidence intervals (Table 3.10). A total of 8 observed values were lower than their predicted values with 2 of these being in the 5 non-overlapping scenarios. The rank correlation showed a rho of 0.87 ($p < 0.001$) again, showing a very high degree of concordance between the observed and predicted values. The relative bias was 11%.

For nickel, the observed values taken from the base metal aluminum were excluded from this part of the analysis because no metals were included in the systematic review model that resemble aluminum resulting in predictions on aluminum that would be made only based on process and consumable content which is not the entire exposure matrix. Therefore, 17 observations remained and 6/17 (35%) had observed values that fit in their predicted confidence intervals with 8/17 (47%) of the observed confidence intervals overlapping with their predicted confidence intervals (Table 3.11). Of the 17, 15 scenarios were lower than their predicted values which indicated that our welding scenario replications generally produced less nickel than what was observed in the systematic review. A rho of 0.54 ($p = 0.024$) was observed indicating good concordance between the observed and predicted values with a relative bias of 237%, a higher degree of relative bias than seen in total dust or manganese.

Chromium observed 10/21 (48%) values that fell within their predicted confidence interval and 14/21 (67%) that had overlapping confidence intervals (Table 3.12). The rho was 0.43 ($p = 0.055$) although only nearly significant at a 95% confidence level, still a moderate effect size. Fifteen of the observed values were higher than the predicted values and 6 of those were for scenarios without an overlapping confidence interval. The relative bias was -8%.

The final outcome was aluminum and was difficult to model because of the very small number of articles that included the minimum necessary information for the analysis, and the small number of cells within the matrix covered by articles reporting on this metal. Only 8 of the 21 (38%) observed means fell within their predicted confidence interval and 11/21 (52%) had overlapping confidence intervals (Table 3.13). The performance of the model did not do as well in the case of aluminum with a rho of only 0.29 ($p = 0.21$) and a relative bias of 290%, markedly higher than the other outcomes. The data from the systematic review and from the scenario replications were then combined for the next phase of the analysis.

Table 3.10: Manganese measurements: observed and predicted with degree of deviation and overlapping CI's

	Observed 95% CI			Predicted 95% CI			Deviation	Overlapping CI's
	Mean	Lower	Upper	Mean	Lower	Upper		
MMAW MS E6010	245.70	125.65	365.76	145.38	73.88	286.09	-100.32	Yes
MMAW MS E7018	311.04	123.63	498.45	228.56	117.64	444.06	-82.48	Yes
MMAW GS E6010	297.86	60.22	535.51	145.38	73.88	286.09	-152.48	Yes
MMAW GS E7018	352.55	274.39	430.72	228.56	117.64	444.06	-124.00	Yes
MMAW SS E308	124.54	-75.16	324.24	79.74	31.64	201.00	-44.79	Yes
MMAW SS E316	213.13	-3.07	429.34	77.94	30.71	197.84	-135.19	Yes
GMAW MS ER70S6	1868.22	1647.07	2089.38	487.51	224.33	1059.45	-1380.71	No
GMAW MS ER70S2	642.65	494.69	790.62	386.57	199.92	747.48	-256.08	Yes
GMAW GS ER70S6	430.74	218.54	642.95	487.51	224.33	1059.45	56.77	Yes
GMAW SS ER308L	480.66	398.20	563.13	253.05	131.25	487.87	-227.62	Yes
GMAW SS ER316L	125.25	98.12	152.38	579.42	187.99	1785.85	454.17	No
GMAW AL ER5356	16.55	-2.60	35.70	14.00	14.00	14.00	-2.55	Yes
GMAW AL ER4043	9.37	2.06	16.67	11.18	9.44	13.26	1.82	No
FCAW MS E71T1	539.80	360.71	718.89	589.58	273.50	1270.95	49.78	Yes
MCAW MS E70MC6	655.20	41.95	1268.45	436.40	212.96	894.26	-218.80	Yes
GTAW MS ER70S2	38.91	38.85	38.98	45.50	12.92	160.26	6.58	Yes
GTAW MS ER70S6	21.92	20.94	22.91	36.08	11.62	111.97	14.15	Yes
GTAW SS ER316L	12.74	4.48	20.99	23.62	8.37	66.61	10.88	Yes
GTAW SS ER308L	13.63	-6.76	34.02	54.08	11.51	254.06	40.45	Yes
GTAW AL ER5356	10.66	-2.81	24.13	1.31	0.74	2.31	-9.35	Yes
GTAW AL ER4043	9.44	2.87	16.01	1.04	0.65	1.67	-8.40	No

*conc(µg/m³); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum

Table 3.11: Nickel measurements: observed and predicted with degree of deviation and overlapping CI's

	Observed 95% CI			Predicted 95% CI			Deviation	Overlapping CI's
	Mean	Lower	Upper	Mean	Lower	Upper		
MMAW MS E6010	3.25	2.26	4.24	6.22	2.42	15.99	2.97	Yes
MMAW MS E7018	1.00	0.53	1.48	6.87	2.76	17.11	5.87	No
MMAW GS E6010	1.96	1.32	2.60	6.22	2.42	15.99	4.26	Yes
MMAW GS E7018	0.94	0.45	1.43	6.87	2.76	17.11	5.93	No
MMAW SS E308	7.28	6.39	8.17	27.15	15.09	48.83	19.87	No
MMAW SS E316	27.80	25.30	30.29	33.58	18.52	60.91	5.79	Yes
GMAW MS ER70S6	2.05	1.57	2.53	9.19	3.89	21.74	7.14	No
GMAW MS ER70S2	2.91	-0.24	6.06	9.19	3.89	21.74	6.28	Yes
GMAW GS ER70S6	2.11	1.67	2.55	9.19	3.89	21.74	7.08	No
GMAW SS ER308L	265.48	168.58	362.37	40.98	22.49	74.68	-224.50	No
GMAW SS ER316L	48.48	31.66	65.29	58.47	30.55	111.91	10.00	Yes
GMAW AL ER5356								
GMAW AL ER4043								
FCAW MS E71T1	2.33	0.85	3.82	3.20	1.24	8.28	0.87	Yes
MCAW MS E70MC6	1.09	0.38	1.81	9.19	3.89	21.74	8.10	No
GTAW MS ER70S2	1.56	0.95	2.17	1.80	0.68	4.74	0.24	Yes
GTAW MS ER70S6	2.13	0.79	3.46	1.80	0.68	4.74	-0.33	Yes
GTAW SS ER316L	3.00	2.10	3.89	8.02	4.31	14.94	5.02	No
GTAW SS ER308L	2.13	-1.24	5.50	11.44	6.02	21.74	9.31	No
GTAW AL ER5356								
GTAW AL ER4043								

*conc(µg/m³); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum

Table 3.12: Chromium measurements: observed and predicted with degree of deviation and overlapping CI's

			Observed 95% CI			Predicted 95% CI			Deviation	Overlapping CI's
			Mean	Lower	Upper	Mean	Lower	Upper		
MMAW	MS	E6010	4.66	2.70	6.62	9.09	4.27	19.35	4.43	Yes
MMAW	MS	E7018	6.85	3.15	10.54	9.09	4.27	19.35	2.24	Yes
MMAW	GS	E6010	3.06	1.99	4.14	9.09	4.27	19.35	6.02	No
MMAW	GS	E7018	4.51	2.87	6.16	9.09	4.27	19.35	4.58	Yes
MMAW	SS	E308	51.89	40.50	63.29	162.55	78.41	336.96	110.66	No
MMAW	SS	E316	166.05	88.48	243.62	143.74	69.80	296.00	-22.31	Yes
GMAW	MS	ER70S6	14.20	10.32	18.08	4.02	1.69	9.58	-10.18	No
GMAW	MS	ER70S2	7.81	3.09	12.53	4.02	1.69	9.58	-3.79	Yes
GMAW	GS	ER70S6	8.46	7.30	9.63	4.02	1.69	9.58	-4.44	Yes
GMAW	SS	ER308L	691.49	539.22	843.76	78.58	40.95	150.79	-612.91	No
GMAW	SS	ER316L	91.06	86.63	95.50	68.76	35.84	131.89	-22.31	Yes
GMAW	AL	ER5356	3.97	0.48	7.47	3.00	3.00	3.00	-0.97	Yes
GMAW	AL	ER4043	3.06	2.68	3.43	2.95	2.94	2.96	-0.10	Yes
FCAW	MS	E71T1	13.11	9.07	17.15	0.77	0.32	1.85	-12.34	No
MCAW	MS	E70MC6	5.34	1.93	8.74	4.02	1.69	9.58	-1.32	Yes
GTAW	MS	ER70S2	3.71	2.70	4.71	0.70	0.31	1.57	-3.01	No
GTAW	MS	ER70S6	4.98	4.00	5.96	0.70	0.31	1.57	-4.28	No
GTAW	SS	ER316L	11.51	5.55	17.46	13.61	7.35	25.21	2.10	Yes
GTAW	SS	ER308L	15.63	-7.48	38.74	11.91	6.44	22.03	-3.72	Yes
GTAW	AL	ER5356	16.86	-8.08	41.79	0.52	0.35	0.77	-16.34	Yes
GTAW	AL	ER4043	12.41	-4.97	29.80	0.51	0.35	0.75	-11.90	Yes

*conc(µg/m3); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum

Table 3.13: Aluminum measurements: observed and predicted with degree of deviation and overlapping CI's

			Observed 95% CI			Predicted 95% CI			Deviation	Overlapping CI's
			Mean	Lower	Upper	Mean	Lower	Upper		
MMAW	MS	E6010	1.62	0.11	3.13	30.79	15.26	62.13	29.17	No
MMAW	MS	E7018	15.69	10.25	21.13	30.79	15.26	62.13	15.11	Yes
MMAW	GS	E6010	3.03	-2.40	8.46	30.79	15.26	62.13	27.76	No
MMAW	GS	E7018	22.75	22.47	23.03	30.79	15.26	62.13	8.04	Yes
MMAW	SS	E308	9.95	7.18	12.72	30.79	15.26	62.13	20.84	No
MMAW	SS	E316	26.61	16.96	36.25	30.79	15.26	62.13	4.19	Yes
GMAW	MS	ER70S6	7.56	-3.56	18.68	34.80	17.80	68.04	27.24	Yes
GMAW	MS	ER70S2	10.54	-9.47	30.54	34.80	17.80	68.04	24.26	Yes
GMAW	GS	ER70S6	15.17	13.98	16.36	34.80	17.80	68.04	19.63	No
GMAW	SS	ER308L	20.55	-11.89	52.99	34.80	17.80	68.04	14.25	Yes
GMAW	SS	ER316L	7.62	-1.51	16.76	34.80	17.80	68.04	27.17	No
GMAW	AL	ER5356	468.68	387.55	549.80	994.15	376.01	2628.46	525.47	Yes
GMAW	AL	ER4043	391.98	355.92	428.03	985.99	373.78	2600.97	594.02	Yes
FCAW	MS	E71T1	1694.91	654.84	2734.98	91.04	46.17	179.53	-1603.87	No
MCAW	MS	E70MC6	1.76	-1.14	4.66	34.80	17.80	68.04	33.04	No
GTAW	MS	ER70S2	11.17	10.21	12.13	2.66	1.16	6.09	-8.50	No
GTAW	MS	ER70S6	20.83	5.66	36.00	2.66	1.16	6.09	-18.17	Yes
GTAW	SS	ER316L	16.13	15.60	16.65	2.66	1.16	6.09	-13.46	No
GTAW	SS	ER308L	61.972	18.73	105.20	2.66	1.165	6.09	-59.30	No
GTAW	AL	ER5356	48.84	25.78	71.91	76.05	25.52	226.65	27.21	Yes
GTAW	AL	ER4043	35.42	15.09	55.75	75.43	25.36	224.33	40.01	Yes

*conc(µg/m3); MS, mild steel; GS, galvanized steel; SS, stainless steel; AL, aluminum

3.3.3 Calibration

The data from the welding scenario replications were added to the data from the systematic review to form 1 calibrated model. The same variables and regroupings were re-entered into a multivariate model alongside an additional binary variable denoting the provenance of the data (systematic review vs. replications). Because the scenario replications also included MCAW welding and galvanized steel, these were kept as new categories given that obtaining estimates for these was part of the objectives. Table 3.4 shows the results from the multivariate model derived from the systematic review side by side with that of the combined model that includes results from the scenario replications. Overall, confidence intervals remain largely unchanged along with β -coefficients in the case of total dust. Additionally, categories that were significant before the data were combined remained significant at a very similar level. MCAW showed an increase in total dust exposures but that increase was not significant ($p=0.383$) while galvanized steel showed a significant ($p=0.003$) increase in total dust when compared to mild steel. The effect of type of particle (respirable vs. total dust) was unchanged and retained its significance. The variable denoting the source of the data shows that the means from the scenario replications were significantly ($p<0.001$) higher for total dust than they were in the systematic review, a finding also confirmed by a Wilcoxon test ($z=3.667$, $p<0.001$).

Manganese saw a very similar result as total dust where the β -coefficients and their confidence intervals remained largely unchanged after combining the data (Table 3.5). MCAW was lower than GMAW but not significantly so ($p=0.886$) and galvanized steel was nearly significantly ($p=0.068$) higher than mild steel in manganese fume production. The remainder of the process categories and of the base metal categories remained significant with β -coefficients relatively intact. The effect of the manganese content in the consumable was also relatively intact and remained significant along with the comparison of total vs. respirable dust. The provenance of the data showed that the scenario replications had higher mean manganese concentrations than the systematic review but this difference was not significant ($p=0.681$). A Wilcoxon test also showed that the predictions from the model were not significantly ($z=0.608$, $p=0.543$) different from the observed data but that they indeed were on average higher.

The combined nickel model had a similar pattern (Table 3.6) as that of the previous models showing slight changes in β -coefficients. Additional notable findings were observed, however, one of which was the effect of aluminium on nickel concentrations. Aluminium, a

category not found in the previous model but added with the replication data, produced significantly ($p < 0.001$) lower nickel concentrations than mild steel while the same was observed with MCAW and galvanized steel ($p < 0.001$, $p < 0.001$). Both the effect of the nickel content in the consumable and the comparison of total vs. respirable dust remained unchanged and significant. The variable denoting the source of the data was also significant showing that the scenario replication yielded significantly ($p = 0.026$) lower nickel emissions than those found in the systematic review and was confirmed by a Wilcoxon test ($z = -3.458$, $p < 0.001$).

The model for chromium saw more adjustments than the models for total dust, manganese and nickel (Table 3.7). The β -coefficients and confidence intervals remained similar for the welding processes when comparing the systematic review model to the combined model with the addition of MCAW showing a significant ($p = 0.001$) reduction in chromium concentrations when compared to GMAW. The categories for MMAW, GTAW, MMAW + GMAW + GTAW and unknown were only slightly affected by the inclusion of the replication data and all retained their levels of significance. Stainless steel, high alloyed steel, and the unknown categories all remained largely unchanged but aluminum saw an important change with the direction of the β -coefficient where aluminum now showed a non-significant increase in chromium concentrations when compared to mild steel ($p = 0.190$). Galvanized steel was significantly lower in chromium fume production than mild steel ($p < 0.001$). A noticeable change in the effect size of the variable denoting chromium content in the consumable was seen and its relationship to airborne metal concentrations strengthened. The binary variable indicating the difference between hexavalent chromium from total chromium remained unchanged with the variable denoting the difference between respirable and total dust also remaining unchanged. The variable indicating the source of the data showed that the scenario replications were higher in chromium concentrations than the data from the systematic review with this difference nearly statistically significant ($p = 0.053$) in the combined multivariate model but less so following a Wilcoxon test ($z = 1.477$, $p = 0.140$).

Not unlike the model for chromium, aluminum saw many adjustments with the only unaffected category for welding process as MMAW which showed a β -coefficient that was relatively close in both models and in the same direction but was now not significantly different from the reference category ($p = 0.057$). GTAW saw a large correction in its β -coefficient and was no longer significant in the combined model ($p = 0.196$). FCAW remained significantly ($p = 0.046$)

different from GMAW with its effect growing from a β -coefficient of 0.962 in the systematic review model to 1.527 in the combined model. MCAW was significantly lower in aluminum concentrations than GMAW ($p < 0.001$). The aluminum content in the consumable remained very similar in both models while the variable representing the difference between respirable and total dust changed more importantly from a β -coefficient of 0.626 to 0.124 becoming non-significant ($p = 0.769$). The source variable showed that the data from the scenario replications were significantly lower in aluminum concentrations than the systematic review data ($p = 0.001$). This finding, however, somewhat contradicted the results from the Wilcoxon test which showed that the mean concentrations from the replications were indeed lower than the predicted concentrations but this difference was only nearly significant ($z = -1.790$, $p = 0.074$).

3.4 Discussion

The purpose of this study was to obtain welding exposure data under controlled conditions replicating certain scenarios that represented the most important welding scenarios in the What-me study and to perform air sampling of the fumes/dusts produced by these scenarios. These scenarios were not chosen at random and were primarily to provide estimates for the What-me study but also to serve as calibrations of the models developed from the systematic review. Clear differences were observed between each welding scenario with ranks that largely agreed with the systematic review model for total dust, manganese, nickel, chromium and less for aluminum. It is notable that the later had far fewer datapoints to model from but what is also notable is that aluminum is more sparsely distributed across the base metals observed and only aluminum and aluminum alloys contain aluminum so researchers reporting on aluminum are more likely to be looking for aluminum and sampling aluminum welding. This makes the modelling of aluminum exposures using process, base metal and aluminum content in the consumable more difficult and as seen in the model from the first article in this series, it was not possible to include both base metal and aluminum content of consumables in one model. This point is well reflected by the large significant reduction in aluminum concentrations noted by the source variable in the data showing that the welding scenario replications, which were not primarily focused on aluminum, had much lower aluminum concentrations than the data from the systematic review. The same logic applies to nickel in that some authors specifically intended to describe nickel concentrations in welding dusts and fumes concentrating their efforts in settings

where welders worked on high nickel alloyed steels while the welding replications did not include any high nickel alloyed steels. Chromium, mainly found in stainless steel, was well represented in the welding replications with stainless steel welding in 3 different types of welding processes and did not see a significant difference between the replication data and the systematic review data in the combined model. A rather large difference between the mean total dust concentration was observed between the welding replication data and the systematic review data which could be explained by the fact that in the welding replications, ventilation was turned off in order to ensure that 3 hours of sampling would be sufficient in avoiding non-detects for the metals analysis. Additionally, a significant amount of time was spent grinding to remove slag in the scenario replication which likely far exceeds what is generally the case in work settings.

A noteworthy observation made in this study was that FCAW was particularly high in aluminum concentrations when compared to GMAW or other processes and this was true in both the review data and the scenario replication data despite the latter being focused only on mild steel welding in the case of FCAW. This was mainly caused by the very high deposition rate of FCAW and the presence of a small amount of aluminum (<2%) in the consumable used in the replications reiterating the need for the inclusion of consumables along with base metals in welding exposure matrices. A large proportion of fumes and dusts come from the consumable (Method for sampling airborne particulates generated by welding and allied processes, 2006) and it is important to note that emissions from a process or scenario using a large amount of a specific consumable will be affected by the contents of that consumable. FCAW was not the highest producer of nickel or chromium despite it being the largest producer of total dust and manganese which are findings both in the review and in the replications; this was predominantly explained by the fact that it is used with stainless steel less often than GMAW. This introduces some degree of confounding in the systematic review models but that fact represents reality in that the scenarios from the What-me did not have very many instances of welding of metals that were not mild steel using FCAW.

Ideally, researchers would do air sampling directly in the settings reported by their study participants but this was not possible for the What-me study which was a study conducted across Canada including welders in places not easily accessible by the research team. An estimate of personal exposures derived from an exposure matrix was therefore a good alternative and the first immediate source of data was journal publications. Among other limitations of systematic

reviews, the first limitation encountered was that the systematic review process did not yield results that covered enough of the most important scenarios in the What-me study covering all 5 outcomes. This would have led to poor estimates that would likely not represent the exposures experienced by the participants of the study and added weight to the importance of sampling replicated scenarios that specifically aimed to reproduce exposures likely experienced by the study cohort.

Another limitation this study faced was the number of samples from the welding scenario replications where a more ideal number of samples would have been favoured over the minimum of 2 seen in some scenarios. Despite the low number of scenario replications, a clear relative rank could still be observed between scenarios which was well represented by the data from the systematic review. It is also unfortunate that a specific consumable could not be tested in all of the welding processes and equally so for base metals but it was not necessary to do so.

3.4.1 Conclusion

Validation of the welding exposure matrix constructed previously was not without some difficulties but overall showed good concordance between measurements taken from the laboratory and those reported in the literature. The calibration adds to the welding exposure matrix and the combined model exceeds the 90% of welding scenarios identified in the What-me study and will be available for any researcher that aims to estimate exposures in welding. The final paper in this set examines whether or not these exposure models related to internal dose, as reflected in urinary metal concentrations.

Chapter 4: Paper 3 Biological validation of a welding exposure matrix to estimate exposures in Canadian welders

Abstract

Introduction:

As part of a Canada-wide cohort study of welders and workers in the electrical trades (the *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* study), spot urine samples were taken from both welders and electricians to investigate the relationship between trade and metal exposures. Following that, exposure estimates were made for all welders in the cohort using a welding exposure matrix previously constructed and validated in papers 1 and 2 of this series. The aim of the analysis described here in the final paper was to investigate the relationship between metal urinary concentrations and estimated exposures.

Methods:

Urine samples were collected from 2011 to 2016 from participants in the What-me study. Exposure estimates were made from the welding exposure matrix for over 2000 welding questionnaires. These were correlated against urine sample metals analysis results, for those that had both, and linear regression models, adjusting for confounders, constructed using estimated exposures as an independent variable.

Results:

This process produced a total of 1087 valid urine samples of which 429 were welders with a corresponding exposure estimate. Of these, 204 were women and 225 men, with 58% reporting doing some manual metal arc welding, 88% reporting gas metal arc welding, 11% reporting flux-cored arc welding and 9% reporting gas tungsten arc welding. Spearman rank correlations of urine sample results with estimated exposures were 0.08 ($p=0.108$) for manganese, 0.081 ($p=0.093$) for nickel, 0.14 ($p<0.005$) for chromium and 0.13 ($p<0.01$) for aluminum. Results from the linear regressions showed that manganese had a slight positive log linear relation to urinary manganese while nickel did not show the same results. Chromium and aluminum both showed strong positive log linear relations between urinary concentrations and exposure estimates.

Conclusion:

Data obtained from questionnaires detailing the participant's last day welding taken as representing welding on the day the urine sample was given related well to the results from the urinalysis. A more robust analysis would include one that replicates the scenarios found in the questionnaires with personal monitoring of exposures paired with end of shift samples.

4.1 Introduction

This is the third of a series of papers designed to construct a welding exposure matrix to be used in an existing cohort to estimate total dust and exposures to certain metals. It is not uncommon for welders to be exposed to hazardous materials while working in their trade. Among others, metal fumes and dusts containing manganese, nickel, chromium and aluminum have been identified as contaminants that can lead to ill-health in welders that are overexposed (Antonini, 2003). Monitoring exposure to these contaminants can successfully be done through different methods ranging from air sampling to biomonitoring through blood samples (Pesch et al., 2012), nail clippings (Ward et al., 2017), hair clippings (Reiss et al., 2016) and urine samples (Arrandale et al., 2015). This study focuses on the latter in order to validate a welding exposure matrix which estimates exposures to airborne metal fumes and dusts through the use of self-reported questionnaires completed in the context of the What-me study. The *Workers' Health in Apprenticeship Trades: metal and electrical (What-me)* study established a cohort of welders starting in 2011 with the intent to study the effects of welding exposures on pregnancy outcomes and other health outcomes (Cherry et al., 2018). As part of assessing and estimating exposures to metals including manganese, chromium, nickel, aluminum among others, urine samples were taken from consenting participants in a campaign that began in late 2011 and continued until early 2016. Along with these, detailed welding questionnaires were completed and paired with the results of the urine samples. This study investigates the relationship between urinary metal concentrations gathered for the What-me study and exposure estimates derived from the welding exposure matrix described in the first 2 papers of this series.

Biomonitoring through the collection of urine or other biological samples can only be used as an additional tool of exposure assessment and should in no way replace air monitoring (Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2020) as a means of exposure estimation and mitigation. Most studies that find a good association between airborne exposures and urinary concentrations of a particular agent do so by either taking pre-shift urine samples and comparing them with post-shift samples, or they do so by correlating exposures with urine samples taken at the end of an exposure period. Other routes of entry of a specific agent may also affect what is measured in urinary excretions along with the physiological makeup of the workers and other occupational factors such as ventilation or work intensity (Threshold Limit Values for Chemical Substances and Physical Agents & Biological

Exposure Indices, 2020) which should be considered when attempting to study the relationship between airborne exposures and urinary concentrations. The most favourable conditions to measure the relationship between airborne metal exposures and urinary metal concentrations would ideally be to expose those not previously exposed to such metals with varying degrees of air concentrations taking urine samples after the exposure. This practice has indeed been tried in welding contexts proving successful where other methods, without chelation, had been unable to show relationships between certain metal exposures and urinary concentrations (Sjogren et al., 1985; Rossbach et al., 2006). Assessing airborne exposures to manganese, nickel, chromium and aluminum through biomonitoring is therefore not trivial. Some have found associations between airborne metal exposures and urinary metal excretions while others have not. In the case of aluminum, one study failed to detect a link between aluminum airborne exposures and changes in pre to post shift urines (Sjogren et al., 1985) with another more recent observing the same relationship between exposures and pre to post urinary changes (Rossbach et al., 2006) while still noting a difference in urinary aluminum concentrations in welders exposed to aluminium dusts and fumes when compared to unexposed controls. Manganese was assessed in another study that also failed to detect a clear association between manganese airborne exposures and urinary manganese excretions (Barrington et al., 1998) in manganese alloy welders. The later was somewhat parallel to the findings by Ellingsen et al. (2006) who reported nearly significant correlations between manganese exposures and post-shift urinary manganese with a significant correlation, albeit weak, between the same air samples and urine samples taken 2 days after exposure. Urinary chromium, on the other hand, has been found to relate well to airborne chromium exposures in a group of stainless steel welders when comparing exposures to post-shift urines (Stridsklev et al., 2004). The same authors could not find associations between nickel exposures and urinary nickel, both findings that correspond to the study by Gube et al. (2013) who also reported clear associations between airborne chromium exposures and urinary chromium while reporting weaker associations between urinary nickel and airborne nickel exposures. In contrast, Weiss et al. (2013) found much stronger associations between nickel exposures and urinary nickel with even stronger associations between chromium exposures and urinary chromium a finding also reported by Stanislawski et al. (2020). While being fully conscious of the reservations pertaining to the varying evidence that airborne metal exposures

can be reflected in urinary excretions, this study undertook an investigation of the relation between estimated airborne exposures and urinary metal concentrations and is presented below.

4.2 Methods

4.2.1 Urine sample collection

As part of the What-me cohort study, urine samples were collected in two campaigns, one beginning in 2011 and ending in 2012 (Arrandale et al., 2015) followed by another beginning in 2014 and ending in 2016. To do this, urine sample collection kits were mailed out to participants with return packaging. This was initially done at the completion of their first follow-up questionnaire and only for women but a second campaign was later launched and included men as well as women. In addition urines were collected as close as possible to the date of conception in pregnant welders and included in this analysis. Upon receipt of the samples by study staff, samples were shaken, separated into 3 aliquots and immediately frozen in a -80 C freezer until the day of urine analysis. On the day of urine analysis, they were transported on dry ice to the University of Alberta Hospital Laboratory. Metal concentrations were determined by ICP-MS while creatinine was analyzed using the Beckman Jaffe method. Samples were not corrected for creatinine by adjusting for dilution but rather, a covariate was included in the linear regression analysis that adjusted for creatinine as proposed by Barr et al. (2005) and seen in Weiss et al. (2013) which allowed for the inclusion of all urine samples. Metals resulting in a value below the limit of quantification (LOQ) noted on the reports from the laboratory were replaced, using the beta substitution method developed by Ganser and Hewett (2010). This replacement was done using urine results from 1087 trades women and men with replacement values as follows: manganese=0.3329 µg/L, nickel=0.1676 µg/L, chromium=0.0822 µg/L and aluminum=0.9061 µg/L.

4.2.2 Time between welding and urine sample

Each follow-up questionnaire contained a section on work history since the last questionnaire with questions pertaining to whether or not they were employed in their trade. For those that were in their trade for any amount of time between the previous questionnaire and the current questionnaire, a question about the date of the last day welding was asked with which it was possible to compute the number of days between the date on which the urine sample was

collected and the last day welding. Further, a complete job history was constructed for each welder such that their last day welding could represent a typical day welding and so the urine sample collection date, provided it occurred within a job interval, would have been considered to have occurred on the same day as the exposure. The date of sample collection was not always known because some participants did not record that information so an estimated date was derived from those that had recorded the date of collection by taking the mean number of days between sample collection and the date the sample was received by the study staff at the University of Alberta. Finally, only twelve percent of the cohort had repeated samples and these were only women.

4.2.3 Exposure estimates from welding questionnaires

A welding exposure matrix was developed which contained three elements: welding process, base metal and consumable. Using this exposure matrix, estimates were computed for welders in the What-me study based on the answers they gave to the welding questionnaire that accompanied each follow-up during the study period (Appendix A). Questions pertaining to welding process, base metal and consumables were asked along with questions on amount of time spent welding in that specific welding scenario. A welding scenario is defined as a combination of process, base metal and consumable; multiple scenarios can be derived from one welding questionnaire. The welding questionnaires were divided into welding processes with questions on base metals, consumables etc. answered in the context of that specific welding process. A person reporting using 2 different welding rods, for example E6010 and E7018, in the context of manual metal arc welding (MMAW) on mild steel would therefore have two welding scenarios within that welding questionnaire. If the same participant reported welding using MMAW for a duration of 5 hours, they would then get an exposure estimate computed for the combination $\left(\frac{MMAW + mild\ steel + E7018}{2} + \frac{MMAW + mild\ steel + E6010}{2}\right) * 5\ hours$. The estimates produced from adding up the scenarios within each welding questionnaire were summed representing an estimated dose or concentration*hours and are used in the analysis of the relationship between urinary metal concentrations. Although the welding exposure matrix also included a distinction between total/inhalable dust vs. respirable dust as well as the provenance of the data (scenario replications vs. literature), these were both estimated as the reference category and kept constant.

4.2.4 Statistical analysis

To reduce skew, both urinary metal concentrations and exposure estimates were log transformed prior to the statistical analysis. The distribution for creatinine was closer to normal in its original form when compared to log transformed and so was kept as such. The analysis was performed in Stata 15.1. The first analysis was a non-parametric rank correlation of the urinary concentrations against the estimated concentration*hours using Spearman's rho. This was followed by a univariate linear regression with the urinary analyte as the dependent variable, exposure estimates for that analyte and potential confounders such as age, sex, bmi, smoking and creatinine all potentially important confounders (Barr et al., 2005; Weiss et al., 2013).

The multivariate models were derived by including creatinine and the exposure estimate, whether significant or not, while introducing other confounders. This was done by entering all variables that had a p-value of less than 0.2 in a univariate analysis into one initial model. From the initial model, all variables with p-values higher than 0.05 were removed to obtain a model that included creatinine, the metal exposure, and whatever significant confounder that remained. Each removed variable was reintroduced to see if it affected any coefficient by 15% or more and if it did it was kept in the model. This produced a final main effects model from which statistical interaction terms were tested and retained if significant ($p < 0.05$). Final models were assessed for multicollinearity with the variance inflation factor (VIF), followed by visual analyses of residual plotted against predicted values. The last step was a visual examination of the slope and linearity between estimated exposures and predicted urinary concentrations derived from the final linear regression models.

4.3 Results

In total, 429 urine samples could be paired with exposure estimates produced from the welding exposure matrix, 225 samples coming from male welders and 204 from female welders. The median time elapsed between the reported welding was said to have taken place and sample collection was 12 days with 70 participants reporting sample collection on the same day the welding took place. The mean age of the 429 participants was 33 years with a mean body mass index of 26 (Table 4.1). There was a total of 120 smokers and 309 non-smokers at the time the urine samples were taken. The cohort had a mean creatinine concentration of 1.18 $\mu\text{g/L}$ with a

significant difference between men and women (men showing a mean concentration of 1.30 µg/L and women 0.95 µg/L, (p<0.001)).

Table 4.1: Description of confounders in cohort

	Mean	SD	Min	Max
Age	32.988	8.912	17.000	64.000
BMI	26.313	4.678	17.218	50.906
Creatinine (µg/L)	1.132	0.664	0.009	3.563
Smoking	Yes	No	Percent (%)	
	120	309	28	
Sex	Male	Female	Percent (%)	
	225	204	52	
N=429				

Table 4.2 shows the means, standard deviations, medians and interquartile ranges of the urinary metal concentrations along with the LOQ's and the number of samples below the LOQ. The number of samples below the LOQ for manganese was 31 (7%), for nickel 56 (13%), for chromium 131 (31%) and for aluminum 32 (7%). The highest metal urinary concentration was for aluminum with a mean concentration of 6.81 µg/L, followed by nickel (1.92 µg/L), manganese (1.51 µg/L) and chromium (0.45 µg/L).

Table 4.2: Urinary concentrations of metals (µg/L)

	Mean	SD	Log Mean*	Log SD*	Min	Max	LOQ	n<LOQ
Manganese	1.505	1.463	0.202	0.625	0.332	25.001	1.505	31
Nickel	1.921	1.582	0.268	1.000	0.168	12.593	1.921	56
Chromium	0.446	1.025	-1.414	0.959	0.082	17.181	0.152	131
Aluminum	6.808	6.387	1.598	0.813	0.906	58.547	6.808	32
N=429								

*Natural log

On their last day of welding, 58% (n=247) of welders in this population had welded using MMAW at least once (Table 4.3), 88% (n=378) with GMAW, 11% (n=47) with FCAW, 9% (n=39) with GTAW and 3% (n=13) with MCAW. Mild steel was the most commonly welded metal with 92% (n=395) of welders reporting welding mild steel while 8% (n=34) reported welding with galvanized steel, 10% (n=43) reporting welding with stainless steel, 3% (n=11) reporting welding with high alloy steel and 6% (n=24) reporting welding with aluminum. Twenty three percent (n=100) welded outdoors most of the time while 7% (n=30) of the cohort welded in a confined space most of the time. Thirty five percent (n=148) of the cohort welded

with respiratory equipment at least half of the time and 48% (n=208) of welders welded with general mechanical ventilation at least half of the time with 18% (n=76) of welders using local exhaust ventilation (LEV) for 50% of their welding time.

Table 4.3: Description of work activities on last day welding

	N	%
Mild steel	230	53.61
Stainless steel	43	10.02
High alloyed steel	11	2.56
Aluminum	25	5.83
Galvanized steel	34	7.93
GMAW	378	88.11
MMAW	247	57.58
FCAW	47	10.96
GTAW	39	9.09
MCAW	13	3.03
Outdoor		
<=50% of time	329	76.69
>50% of time	100	23.31
Confined		
<=50% of time	399	93.01
>50% of time	30	6.99
Respirator		
<=50% of time	281	65.5
>50% of time	148	34.5
Ventilation		
<=50% of time	221	51.52
>50% of time	208	48.48
Local exhaust ventilation		
<=50% of time	353	82.28
>50% of time	76	17.72

Table 4.4 shows the mean exposure metal concentration*hours estimated from the welding exposure matrix along with medians and interquartile ranges. We see that the highest estimated exposures were for manganese with a mean concentration*hours estimate of 1059 $\mu\text{g}/\text{m}^3$ followed by aluminum (236 $\mu\text{g}/\text{m}^3$), nickel (61 $\mu\text{g}/\text{m}^3$) and chromium (47 $\mu\text{g}/\text{m}^3$).

Manganese exposures and urinary concentrations had a rank correlation of 0.078 ($p=0.108$) while for nickel, exposures and urinary concentrations correlated slightly better with a rho of 0.081 ($p=0.093$). Urinary chromium and aluminum correlated better with exposures with a rho of 0.14 for chromium ($p<0.005$) and a rho of 0.13 for aluminum ($p<0.01$).

Table 4.4: Mean metal concentration*hours estimated from the welding exposure matrix

	Mean	SD	Log Mean*	Log SD*	Min	Max
Manganese ¹	1058.628	1039.993	6.336	1.343	4.021	5356.981
Nickel ¹	61.395	641.077	2.837	1.237	0.220	13267.490
Chromium ¹	47.209	161.891	2.746	1.425	0.149	2379.985
Aluminum ¹	236.170	528.662	4.490	1.461	0.463	5153.079
N=429						

*Natural log, ¹concentration($\mu\text{g}/\text{m}^3$)*hours

Univariate linear regressions were performed on log transformed urine concentrations and estimated exposures and are shown in Table 4.5. For all four metals, creatinine was positively and significantly related to the urinary concentration as would be expected. Each showed the same relationship where an increase in creatinine predicted an increase in urinary metal concentrations reflecting dilution of urine samples. For manganese, estimated airborne manganese concentration*hours were positively related to urinary manganese but this relationship was not significant (at a 95% confidence level). Time spent working outdoors, in a confined space, wearing a respirator, working with mechanical ventilation or time working with LEV did not show any significant effect on urinary manganese concentrations. Sex showed a positive relationship with manganese in that women had significantly higher urinary manganese concentrations than men ($p<0.05$). Age and smoking negatively related to urinary manganese but neither significantly so while BMI was positively related to manganese but not significantly. An increase in airborne nickel concentration*hours was related to an increase in urinary nickel in a univariate model but this relationship was not significant. Again, no effect was observable for time working outdoors, in confined spaces, wearing a respirator, with ventilation or with LEV. Age and BMI both positively related to urinary nickel and were nearly significant ($p<0.058$, $p<0.050$) while sex (being a woman) and smoking were negatively related to urinary nickel and both significantly so ($p<0.001$, $p<0.05$). For chromium, an increase in airborne chromium was indeed positively significantly related to urinary chromium concentrations ($p<0.001$) with age and BMI both positively relating to urinary chromium but neither significantly so. Working outdoors more than 50% of the time significantly reduced urinary chromium while wearing a

respirator 50% or more of the time also significantly reduced urinary chromium. Working with ventilation, in a confined space or with an LEV did not show any significant effect on urinary chromium. Smoking and sex both showed negative relationships with urinary chromium but neither was significant. The results for aluminum were very similar to those for chromium in that airborne aluminum concentration*hours related well ($p < 0.005$) to urinary aluminum with a positive β -coefficient. Working outdoors did not show a significant reduction in urinary aluminum nor did working with LEV, however, both ventilation and wearing respiratory equipment more than 50% of the time significantly reduced urinary aluminum at a 90% confidence level with ventilation significant at a 95% confidence level. Working in confined spaces more than 50% of the time did not significantly increase urinary aluminum. Age negatively predicted urinary exposures and was nearly significant ($p = 0.054$) with BMI also showing a negative relationship to urinary aluminum but not significantly so. Sex was positively related to urinary aluminum showing women with higher urinary aluminum but this relationship was not significant. Smoking was negatively related to aluminum but again, not significantly so.

Table 4.5: Univariate analysis of the relation between estimated airborne metal exposures and urinary metal concentrations

		β	SE	95% CI		P-value
				Lower	Upper	
Urinary manganese	Mn exposure¹	0.036	0.022	-0.008	0.081	0.105
	Outdoor	0.000	0.001	-0.001	0.002	0.882
	Confined	-0.000	0.001	-0.003	0.002	0.725
	Respirator	0.000	0.001	-0.001	0.001	0.900
	Ventilation	-0.000	0.001	-0.002	0.001	0.608
	LEV²	-0.002	0.001	-0.002	0.001	0.806
	Creatinine $\mu\text{g/L}$	0.325	0.043	0.241	0.409	0.000
	Age	-0.003	0.003	-0.010	0.003	0.347
	BMI	0.005	0.006	-0.008	0.017	0.468
	Sex (women)	0.152	0.060	0.034	0.270	0.012
	Smoking	-0.067	0.067	-0.199	0.065	0.319
Urinary nickel	Ni exposure¹	0.051	0.039	-0.025	0.128	0.190
	Outdoor	0.000	0.001	-0.002	0.002	0.870
	Confined	-0.001	0.002	-0.005	0.002	0.495
	Respirator	-0.001	0.001	-0.003	0.001	0.524
	Ventilation	0.000	0.001	-0.003	0.001	0.524
	LEV²	-0.000	0.001	-0.003	0.002	0.888
	Creatinine $\mu\text{g/L}$	0.401	0.070	0.263	0.539	0.000
	Age	0.010	0.005	0.000	0.021	0.058
	BMI	0.020	0.010	0.000	0.041	0.050
	Sex (women)	-0.368	0.095	-0.555	-0.181	0.000
	Smoking	-0.241	0.107	-0.451	-0.030	0.025
Urinary chromium	Cr exposure¹	0.117	0.032	0.054	0.180	0.000
	Outdoor	-0.003	0.001	-0.006	-0.001	0.002
	Confined	-0.001	0.002	-0.004	0.003	0.746
	Respirator	-0.002	0.001	-0.005	-0.000	0.017
	Ventilation	0.001	0.001	-0.001	0.003	0.233
	LEV²	-0.001	0.001	-0.003	0.002	0.574
	Creatinine $\mu\text{g/L}$	0.683	0.062	0.562	0.804	0.000
	Age	0.002	0.005	-0.009	0.012	0.762
	BMI	0.008	0.010	-0.011	0.028	0.407
	Sex (women)	-0.093	0.093	-0.275	0.090	0.319
	Smoking	-0.038	0.103	-0.240	0.165	0.716
Urinary aluminum	Al exposure¹	0.084	0.027	0.031	0.136	0.002
	Outdoor	-0.000	0.001	-0.002	0.002	0.871
	Confined	0.001	0.002	-0.002	0.004	0.702
	Respirator	-0.002	0.001	-0.003	0.002	0.082
	Ventilation	-0.001	0.001	0.382	-0.002	0.001
	LEV²	-0.000	0.001	-0.002	0.002	0.749
	Creatinine $\mu\text{g/L}$	0.557	0.053	0.454	0.661	0.000
	Age	-0.008	0.004	-0.017	0.000	0.054
	BMI	-0.003	0.008	-0.020	0.013	0.706
	Sex (women)	0.055	0.079	-0.100	0.209	0.485
	Smoking	-0.124	0.087	-0.296	0.047	0.156

N=429

*natural log of urine concentrations and metal exposures, ¹concentration($\mu\text{g}/\text{m}^3$)*hours, ²local exhaust ventilation

The final multivariate models after variable selection are shown in Table 4.6. Manganese showed a positive β -coefficient for manganese concentration*hours ($\beta=0.033$, $p=0.111$) but was not significantly related to urinary manganese when adjusting for creatinine and sex. Creatinine was positively and significantly related to urinary manganese ($\beta=0.379$, $p<0.001$) with sex also being positively related to urinary manganese ($\beta=0.293$, $p<0.001$). A somewhat different model was derived for nickel where the airborne exposures did not significantly relate to urinary concentrations ($\beta=0.019$, $p=0.648$) when controlling for creatinine, sex, and smoking. Creatinine was positively related to urinary nickel concentrations ($\beta=0.341$, $p<0.001$), while contrary to manganese, sex was negatively related to urinary nickel ($\beta=-0.239$, $p<0.05$) and smoking also negatively relating to urinary nickel. Smoking was kept in the model because it acted as a confounding variable affecting the β -coefficient for nickel exposures by more than 20% and so was kept in the final model despite not being significant at a 95% confidence level; it showed a negative relation to urinary nickel and was nearly significant ($\beta=-0.196$, $p=0.059$). Chromium concentration*hours, when adjusting for creatinine and sex, was positively and significantly related to urinary concentrations with a β -coefficient of 0.111 ($p<0.001$). Further, the effect of wearing respiratory protection more than 50% of the time showed a significant reduction in urinary chromium ($\beta=-0.308$, $p<0.001$) accompanied with an almost identical effect for time spent working outdoors ($\beta=-0.345$, $p<0.001$). Creatinine was also positively related to urinary chromium and significantly so ($\beta=0.701$, $p<0.001$). The effect of sex was parallel to the effect of sex in the model for manganese where a significant increase in urinary chromium could be observed for women ($\beta=0.212$, $p<0.05$). Concentration*hours in the case of aluminum also showed a significant relation to urinary aluminum when controlling for sex and creatine ($\beta=0.064$, $p<0.005$). As in the models for the other metals, creatinine was significantly and positively related to urinary aluminum ($\beta=0.600$, $p<0.001$) with sex showing a positive relationship to urinary aluminum with a β -coefficient of 0.270 ($p<0.001$). Wearing a respirator showed a reduction ($\beta=-0.112$, $p=0.080$) of urinary aluminum but was not significant at a 95% confidence level and so was dropped from the final model. None of the models showed violations of regression assumptions and all showed relatively low adjusted R^2 values with the lowest of these for nickel (8%, followed by manganese with 17%, aluminum with 24% and chromium with 28%).

Table 4.6: Multivariate analysis of the relation between estimated concentration*hours and urinary metal concentrations

		β	SE	95% CI		P-value
				Lower	Upper	
Urinary manganese	Mn exposure¹	0.033	0.021	-0.008	0.073	0.111
	Outdoor					
	Confined					
	Respirator					
	Ventilation					
	LEV²					
	Creatinine µg/L	0.379	0.043	0.295	0.464	0.000
Age						
BMI						
Sex (women)	0.293	0.057	0.180	0.406	0.000	
Smoking						
Constant	-0.576	0.147	-0.864	-0.288	0.000	
Urinary nickel	Ni exposure¹	0.017	0.038	-0.057	0.092	0.648
	Outdoor					
	Confined					
	Respirator					
	Ventilation					
	LEV²					
	Creatinine µg/L	0.341	0.072	0.199	0.484	0.000
Age						
BMI						
Sex (women)	-0.239	0.096	-0.428	-0.049	0.014	
Smoking	-0.196	0.103	-0.399	0.007	0.059	
Constant	0.001	0.161	-0.315	0.317	0.994	
Urinary chromium	Cr exposure¹	0.111	0.028	0.056	0.166	0.000
	Outdoor	-0.345	0.095	-0.531	-0.159	0.000
	Confined					
	Respirator	-0.308	0.084	-0.473	-0.142	0.000
	Ventilation					
	LEV²					
	Creatinine µg/L	0.701	0.061	0.581	0.822	0.000
Age						
BMI						
Sex (women)	0.212	0.082	0.051	0.373	0.010	
Smoking						
Constant	-2.426	0.129	-2.680	-2.173	0.000	
Urinary aluminum	Al exposure¹	0.064	0.023	0.018	0.110	0.007
	Outdoor					
	Confined					
	Respirator					
	Ventilation					
	LEV²					
	Creatinine µg/L	0.600	0.054	0.495	0.706	0.000
Age						
BMI						
Sex (women)	0.270	0.071	0.131	0.410	0.000	
Smoking						
Constnat	0.504	0.131	0.246	0.761	0.000	

N=429

*natural log of urine concentrations and metal exposures, ¹concentration(µg/m³)*hours, ²local exhaust ventilation

Predictions of fully adjusted urinary metal concentrations were produced from the final models in Table 4.6. These were scattered against exposures and a linear fitting line was superimposed to observe the linearity and slope between urinary concentrations and airborne concentration*hours – they can be seen in Figures 4.1 through 4.4. Figure 4.1 shows the relation between predicted urinary manganese and estimated manganese exposures. The fitted line shows a slope that is not steep but moving up with manganese concentration*hours nonetheless. Figure 4.2 shows the relation between predicted urinary nickel and nickel exposures with, again, a slope that is not steep but still rising. Three data points were omitted in the case of nickel because they distorted the slope making it look far more pronounced than the multivariate model would have predicted. Figure 4.3 shows the relation between urinary chromium and chromium exposures with a steeper slope than the previous two metals and intersection points that are well clustered around the fitted line. Figure 4.4 shows the relation between urinary aluminum and aluminum exposures with a steep slope and again, a good clustering of the intersection points around the fitted line.

Figure 4.1: Urinary manganese in relation to manganese exposure

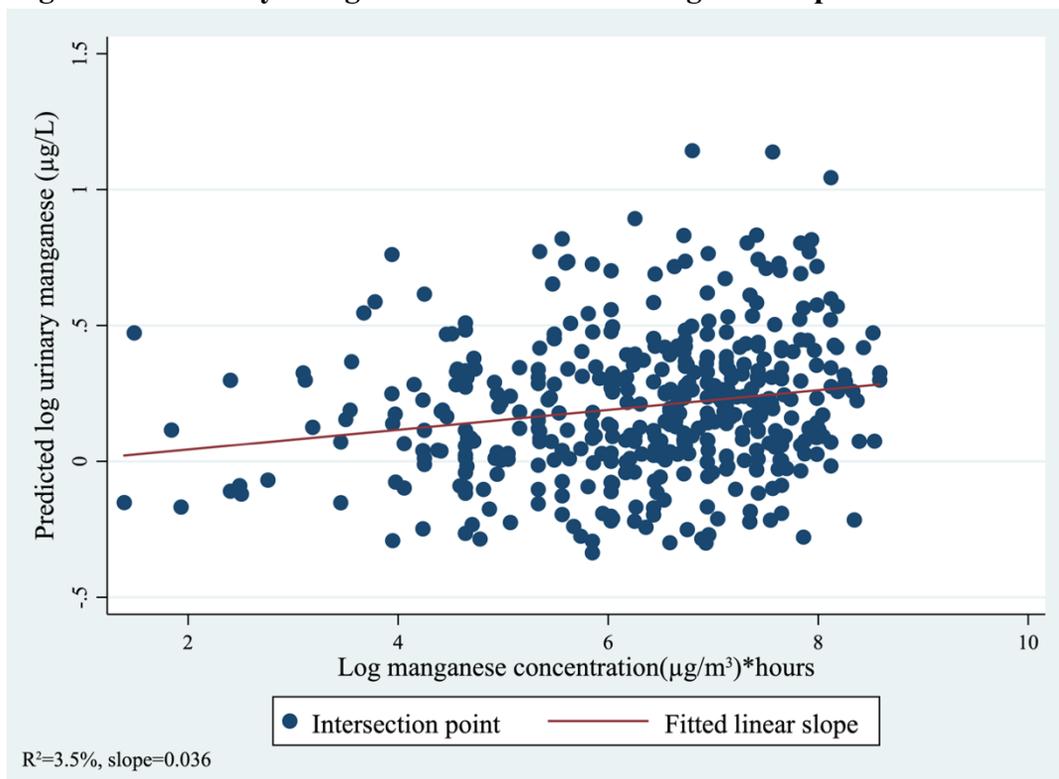


Figure 4.2: Urinary nickel in relation to nickel exposure

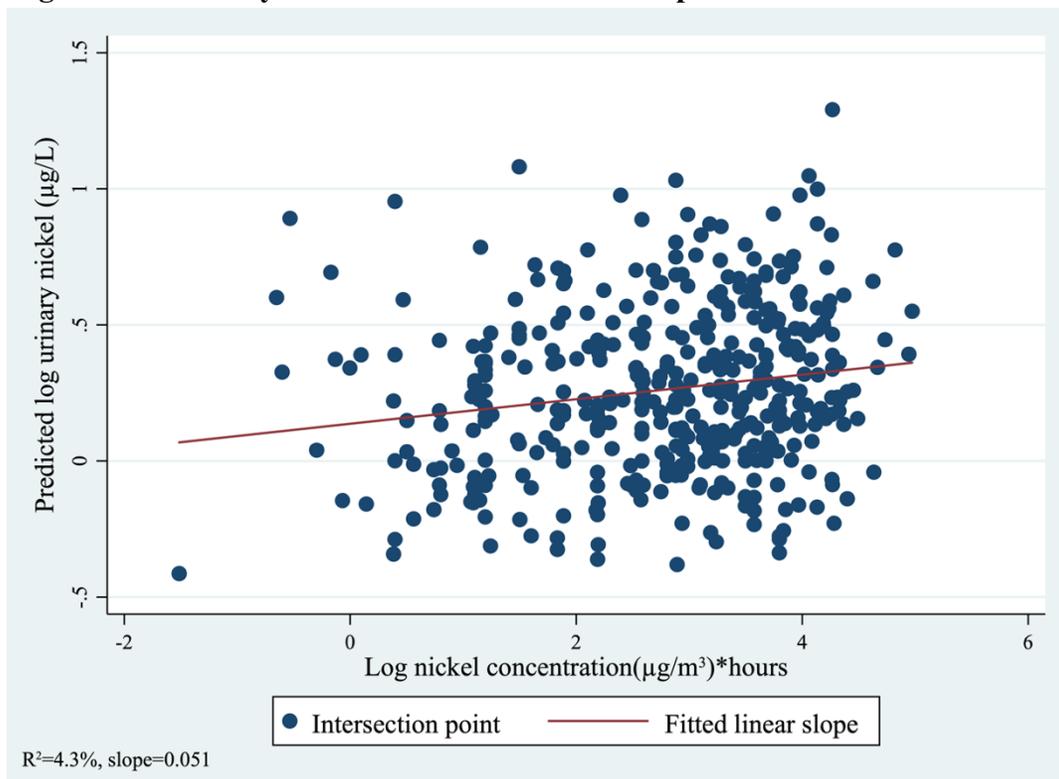
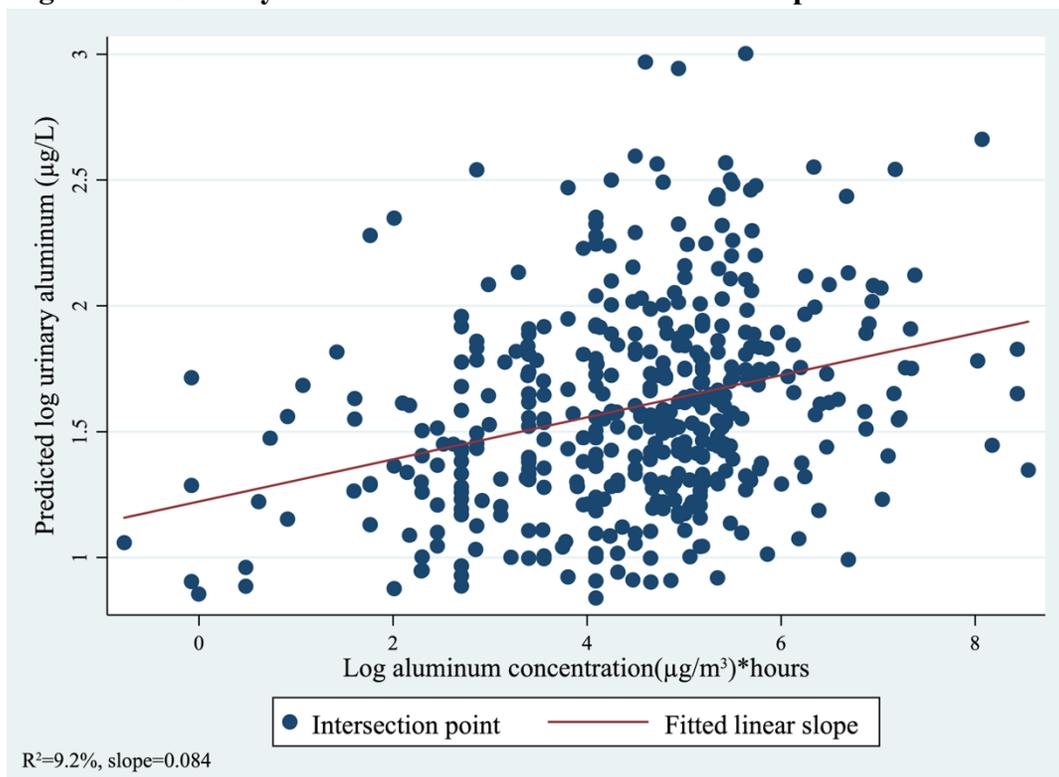


Figure 4.3: Urinary chromium in relation to chromium exposure



Figure 4.4: Urinary aluminum in relation to aluminum exposure



4.4 Discussion

In this study, urinary manganese related to airborne manganese exposure estimates but not well which seemed to reiterate the findings made by others (Barrington et al., 1998; Ellingsen et al., 2006) in recent years. Further, mean urinary manganese concentrations in this cohort resembled those reported by Ellingsen et al. (2006). The ACGIH does not have a reliable biological exposure index (BEI) for manganese in the context of monitoring through urinalysis. It is estimated that only about 1% of manganese absorbed by the body will be excreted in the urine (Lauwerys and Hoet, 2001) and it is generally understood that biomonitoring of manganese exposures is better achieved through blood samples (Pesch et al., 2012) although even blood samples are not excellent predictors of manganese exposures. Women tend to absorb more manganese than men (Lauwerys and Hoet, 2001) and possibly metabolize it differently, this related well with the results from the study showing that women tended to show higher urinary manganese than men (Table 4.6) in the fully adjusted model and in the unadjusted univariate analysis (Table 4.5). It is therefore unlikely that all of the effect of sex is caused by higher creatinine in men and the subsequent adjustment for creatinine. A very weak correlation ($\rho=0.11$, $p=0.13$) can be observed between women's manganese exposures and urinary manganese with this correlation higher in women than in men ($\rho=0.07$, $p=0.31$). A range (5th-95th percentiles) of 0.11 $\mu\text{g/L}$ to 1.32 $\mu\text{g/L}$ was proposed by Gouille et al. (2005) as the typical range for the general population. In this study, 209 urine samples exceeded the 95th percentile reported above and had a mean estimated manganese concentration*hours about 10% higher than those below the 95th percentile reported by Gouille et al. (2005) (1112 $\mu\text{g/m}^3$, 1008 $\mu\text{g/m}^3$, $p=0.30$). Paschal et al. (1998) proposed a 95th percentile of 3.33 $\mu\text{g/L}$ in their study of trace metals in the normal US population. In this study, 17 welders had urinary manganese exceeding 3.33 $\mu\text{g/L}$ and had a mean manganese exposure estimate of 1391 $\mu\text{g/m}^3$ compared to 1045 $\mu\text{g/m}^3$ ($p=0.30$, unequal variances assumed) for those that were below the estimated 95th percentile. Although in both cases these mean differences are not statistically significant, the groups exceeding the boundaries proposed are both higher, even if marginally, than the group below the proposed top percentiles and the mean difference increasing as you increase the estimated 95th percentile. Despite the caveats of using urinary manganese for biological monitoring, it showed promise of at least some relation to estimated exposures with a positive, near significant, β -coefficient (Table 4.5: $\beta=0.033$, $p=0.111$) in a fully adjusted model, a small but present linear

relation to estimated exposures for predicted urinary concentrations and a small but somewhat consistent increase in urinary manganese in those most exposed.

Nickel concentrations in the urine proved to be the most elusive of the four metals. It was difficult to show any relation, despite Figure 2 showing some linear increase in predicted urinary nickel with increases in nickel exposures. Moreover, our findings showed lower urinary nickel concentrations than those reported by Weiss et al. (2013) perhaps in part explaining the lack of an association between nickel exposures and urinary concentrations in our cohort. This finding, however, concurred with another study (Iarmarcovai et al., 2007) who reported that urinary nickel concentrations at the beginning of the week resembled those taken at the end of the work week while somewhat contradicting the findings reported by Gube et al. (2013) that indicated a dose response relationship between airborne nickel exposures and urinary nickel concentrations. Weiss et al. (2013) also reported associations between respirable nickel and urinary nickel concentrations which also differs from the findings reported in this study. Their linear relationship, however, was not strong and that does resemble the findings reported in this study. The lack of positive associations reported here could be related to the fact that soluble nickel compounds like those produced from stainless steel welding fumes are not absorbed well by the lung (Lauwerys and Hoet, 2001). Additionally, nickel compounds can be absorbed through other means like the skin possibly influencing urinary excretions despite not necessarily having had high airborne nickel exposures (Lauwerys and Hoet, 2001). Further, a high exposure to such scarcely soluble nickel compounds produced in welding may not lead to an immediate increase in urinary excretions and can be reflected in the urine years after the exposures have ended (Lauwerys and Hoet, 2001). Nevertheless, nickel was shown to relate well to exposures in welders at least on 5 different occasions (Stridsklev et al., 2004; Ellingsen et al., 2006; Gube et al., 2013; Weiss et al., 2013; Stanislawska et al., 2020). What was a common theme in the studies showing positive relationships between urinary nickel and airborne nickel exposures was that their focus was often on those welding stainless steel, a high in nickel content steel, which in this study only occurs in 43 of the 429 cases. There were 6 additional instances of high alloyed steel welding which is higher in nickel content as well totalling 49 welding high nickel content metals. The welders that indicated working with these metals had a mean nickel urinary concentration of 2.35 $\mu\text{g/L}$ compared to 1.87 $\mu\text{g/L}$ in those that reported not welding with stainless steel. This difference was nearly significant ($p=0.075$, one-tailed t-test unequal

variances assumed). The log transformed exposure*hours of those welding stainless steel were also significantly higher than those not welding with stainless steel with a mean of 3.75 $\mu\text{g}/\text{m}^3$ compared to 2.73 $\mu\text{g}/\text{m}^3$ ($p < 0.001$, t-test unequal variances assumed) providing some evidence that our exposure estimates are somewhat reflected in urines. Also, important to note is the fact that the effect of sex in univariate analyses was significant for manganese and nickel only and it became significant (and positive), in the case of chromium and aluminum, only after being reintroduced in a model that included exposure and creatinine. This is likely caused by the significant differences in creatinine between men and women shown earlier and must be interpreted with caution. That being said, it was notable that nickel was the only metal showing a decrease in the urinary analyte related to sex (being a woman) and significant reduction related to smoking. In a stratified analysis, the relationship, although not significant, between nickel exposures and urinary concentrations in a creatinine adjusted linear regression increased in strength when including only men in the model ($\beta = 0.054$, $p = 0.202$). For women, this relationship was inverse ($\beta = -0.017$, $p = 0.802$) albeit not approaching significance. Women are indeed more likely to experience nickel sensitisation (Ahlstrom et al., 2019) and women welders show higher rates of nickel allergies (Cherry and Galarneau, 2020) possibly leading them to avoid high nickel exposures earlier than men welders or taking more precautions when welding metals high in nickel. Following that women showed lower urinary nickel concentrations, we also see that they were exposed to less nickel fumes and dusts than men (mean log transformed exposure*hours men = 2.98 $\mu\text{g}/\text{m}^3$, women = 2.68 $\mu\text{g}/\text{m}^3$, $p < 0.05$). The ACGIH currently does not have a BEI value for nickel but intends to add one and announced it would do so in their 2020 publication on TLV's and BEI's (Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2020). The proposed BEI would be 5 $\mu\text{g}/\text{L}$. This study found that only 17 welders had exceeded that value and they were not more exposed than those below that value.

Urinary chromium is the only metal that has a reliable BEI (Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2020) in those studied here and it is therefore unsurprising to see how well the urinary chromium from this cohort related to the estimated exposures that were derived from the welding exposure matrix. Both a rank correlation that makes no assumptions about the data and a linear regression show the same results which provide additional validity to the welding exposure matrix and indicate that the

latter predicts internal doses well reiterating previous findings made by (Stridsklev et al., 2004; Gube et al., 2013; Weiss et al., 2013; Stanislawska et al., 2020). In this study, no urinary chromium concentrations exceeded the BEI of 25 µg/L with the maximum observed urinary chromium as 17.18 µg/L. The mean urinary chromium concentration in our cohort was indeed lower than the one reported in Weiss et al. (2013) but nevertheless allowed for a strong association between estimated concentration*hours and urinary concentrations. The ACGIH also proposes that occupational chromium exposures are considered those that exceed 0.7 µg/L; in this study, 53 samples exceeded 0.7 µg/L and when a Spearman rank correlation was performed on those urine samples alone, a rho of 0.43 could be observed ($p < 0.005$) providing even more evidence that the welding exposures derived from the matrix relate well with urinary chromium concentrations. Chromium's urinary half-life is estimated between 15 hours and 41 hours (Lauwerys and Hoet, 2001) which is perhaps well exemplified in Ellingsen et al. (2006) that show an increase in the correlation between urinary chromium and exposures two days after the exposure as opposed to just one. If we limit the analysis to samples taken with two days or less between the reported exposure and the urine sampling date, we still observe a strong relationship between estimated urinary chromium and estimated exposures ($\rho = 0.34$, $p < 0.001$, $n = 137$) which is a great improvement from the initial rho of 0.15 that included all 429 samples with a median of 12 days between the date for which we have a description of their last day welding and urine sample collection. One noteworthy limitation with the results from the chromium urinary concentrations was that 31% of the urinary concentrations were below the limit of quantification. However, repeating the regression analysis excluding these values did not alter the results of the final multivariate model.

This study found that there was both a significant, albeit small, rank correlation between urinary aluminum and aluminum concentration*hours and, in a fully adjusted model, a positive linear association between the two. The ACGIH does not currently have a BEI for aluminum (Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2020), nevertheless, urinary aluminum is preferred over blood monitoring (Lauwerys and Hoet, 2001). Others have found a positive relationship between exposures and urinary excretions (Roszbach et al., 2006; Iarmarcovai et al., 2007). In the What-me study, mean urinary aluminum resembled what had been previously observed by Iarmarcovai et al. (2007) adding confidence to the associations found between concentration*hours and urinary aluminum. An

important aspect of urinary aluminum concentrations is that a small fraction of exposures are immediately absorbed through the lungs while an undetermined amount is left for resorption long after the exposure providing an estimated half-life of 6 months (Riihimaki et al., 2000). This long biological half-life was also reported in a study by Rossbach et al. (2006) where they indicate that they observed similar findings whereby welders continue to excrete aluminum in their urine some time after exposures suggesting a long urinary half-life ranging from days to possibly years. In unexposed individuals, the aluminum half-life was estimated at about 8 hours (Sjogren et al., 1985). The long half-life in welders perhaps explains the results of this study and it would be difficult to test such a hypothesis using this study design. In those that indicated welding aluminum (n=25), the mean urinary aluminum concentration was higher, 11.85 µg/L compared with 6.50 µg/L (p<0.05, unequal variances assumed) than those that did not weld aluminum. The 95th percentile for urinary aluminum in the general population was estimated at 11.2 µg/L by Gouille et al. (2005) and in the current cohort, 55 samples showed higher urinary aluminum concentrations than the percentile shown above. These individuals were exposed to a log mean concentration*hours of 5.24 µg/m³ compared to 4.38 µg/m³ in those not exceeding the published 95th percentile (p<0.001). There is very little doubt that the estimates produced by the welding exposure matrix relate to urinary aluminum and it is further evidence that there is a high degree of validity in the ability for the welding exposure matrix to predict internal doses.

4.4.1 Conclusion

All of the studies reviewed above were studies that looked directly at personal exposures prior to looking at urinary metal concentrations. It is therefore expected that they find more closely relating exposures to urinary metal concentrations. In the context of the What-me study it was not possible to directly assess exposures to metal fumes and dusts, a limitation that may have reduced our ability to relate estimated exposures to urinary metal concentrations. Yet despite this apparent weakness, it is reassuring that exposures could be estimated and relationships between concentration*hours and urinary metal concentrations found.

This study aimed to further validate a previously developed exposure matrix (paper 1) that used personal exposure estimates of total dust, manganese, nickel, chromium and aluminum from previously published articles along with measurements made by the authors of this current study (paper 2). An external validation was made previously (paper 2) of manganese, nickel, chromium and aluminum by correlating estimates from models derived solely from the literature

(paper 1) with results from a replication and sampling of the most common scenarios in the What-me study. The effect sizes observed (paper 2) for manganese, nickel, chromium and aluminum were $\rho=0.87$, $\rho=0.54$, $\rho=0.43$, $\rho=0.29$ respectively, with manganese and nickel having large effect sizes while chromium showed a medium effect size and aluminum a small effect size. Compounded with the strong association found between observed and estimated personal air samples seen above, the evidence that the exposure matrix predicts absorption/body burden as shown in urinary metal concentrations is well supported by the findings in this study adding confidence in the validity and ability of the welding exposure matrix to predict external exposure and internal dose.

Chapter 5

5.1 Conclusion

The overall objective of this three-part series was to construct and validate a welding exposure matrix; this goal was largely met. First the construction of a welding exposure matrix from the literature saw its difficulties; the data certainly were not independent and modelling data that could be highly correlated introduced challenges. Nevertheless, an effort to reduce collinearity and to have models that do not violate linear regression assumptions was made. Further, a significant effort was also made as to not over collapse categories in order to have what would seem to be the most impressive statistical model as opposed to the most pragmatic one. Deliberately avoiding such a practice was important because the models were not just for the sake of deriving the best statistical models but rather, they were to be used in the estimation of exposures in an existing cohort. It was therefore important to preserve the effect of processes and base metals even if those were not necessarily significantly different from the reference categories in the models. Modelling respirable and total dusts together is perhaps not generally advised and no study reviewed in the process of conducting this study had done this but it aided in solving the issue of empty cells and allowed for the inclusion of more data points. There are certainly differences in the type of particles being produced across processes and base metals which could have been denoted by a statistical interaction term but it would have been difficult to interpret such an interaction term that would have largely depended on other unmeasurable attributes and on the weights used in the analysis. The modelling of hexavalent chromium along with total chromium was also different from past studies and provided the authors with the ability to cover far more scenarios than if particle types had been modelled separately. To that effect, it must be said that the effect of particle type both in the context of total vs. respirable dust and hexavalent chromium vs. total chromium was indeed diluted only to reflect a mean difference between the two. This was seen as an acceptable cost of modelling two different types of particles together hopefully still preserving the data's relative rank across particle types. It is important to remember that the aim of this study was not to obtain models that would best serve statistical modelling needs but rather to obtain models that would serve as aids in the development of estimation models for an existing cohort. Further, the systematic review models obtained may not be the *best* statistical models from the point of view of pure mathematical

modelling, but they are most useful in the prediction of exposures for the What-me cohort and broadly cover the most common welding scenarios in that cohort.

The high degree of concordance between the scenario replications and the predictions made from the systematic literature models was further evidence to the success of this three-part study in developing a validated welding exposure matrix. In 3 of the 5 outcomes, significant Spearman rank correlations were observed ranging from 0.93 to 0.54 and chromium was nearly significant with a p-value of 0.055 and a rho of medium effect size ($\rho=0.45$). What is striking about the ability for the models to predict out-of-sample values was that as the number of samples and articles included in the modelling stage went down, so too did the Spearman rank correlations between observed and predicted values.

The degree to which coefficients from the regression only including data from the scenario replications concurred with the coefficients from the model produced from the literature is further testament to the validity and ability of the final models to predict exposures in a real cohort of welders. Including a variable that showed the mean difference, for all 5 outcomes, between the results from the literature and the replications was important in that it quantified the differences between the two methods. This variable was significant in the case of aluminum which is likely directly related to the fact that most articles reporting on aluminum were primarily studying aluminum welding and so would show higher aluminum exposures. In parallel, nickel too was significantly lower in the scenario replications than in the literature and was likely caused by the fact that no high alloyed steels were used in the replications but were often reported on in the literature. This was not the case for manganese because manganese is primarily found in mild steel, a ubiquitous metal in welding. The degree to which the means from the scenario replications were higher than the literature means in the case of total dust is most likely caused by the fact that no ventilation was used during scenario replications as to maximise the potential for a positive result in the metals analysis and likely compounded by the large amounts of time spent grinding in the replication phase of this study.

Correlations between urine samples and estimated exposures saw some difficulties despite finding that two of the outcomes were significantly positively correlated. Chromium was the only metal that had a BEI and so it was in that context that the relationship between urinary metal concentrations and airborne exposures was investigated. After fitting the best linear regression model with the confounders available, all 4 outcomes showed linear relationships

between log exposures and log urinary analytes and all urinary metal concentrations increased as exposures increased. Two of the 4 outcomes were not significant however, but it is still unlikely that chance alone was responsible for their visible log linear relationships. When investigating each outcome further by taking only subsets of data and testing different relations between urinary metals and exposures, in almost all cases, even if not always significant, arguments for the positive relationship between the two were strengthened. Part of the weak relationship between calculated concentration*hours and urinary concentrations is likely due to the fact that spot urine sampling, without chelation, is not the best medium by which exposures should be assessed (Lauwerys and Hoet, 2001).

Overall, the welding exposure matrix was supported by the validation techniques employed here. The very slight calibration that pooling the data provided was well received since some of the scenarios of interest in the What-me study were not represented with just data from the literature. Given that most welding exposure matrices only include process and base metal, it would be interesting in a future analysis to test the differences between the matrix produced here and a matrix that does not include the effect of consumable in how these predict out of sample values. Further, a more detailed description of the quantitative differences across welding scenarios produced from the replications with each as the unit of analysis would also be of interest to readers in the field of occupational hygiene. The full value of these exposure estimates will become apparent during the analysis of the health and reproductive outcomes in the What-me cohort. If, for example, estimated exposure to nickel were found to be related to new onset asthma or to smaller babies, this would be a strong justification for the work reported in these three papers.

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Appendix A

Sub-routine 1

- 1 At what time did you start this type of welding?
- 2 At what time did you stop this type of welding?

am/pm
am/pm
Duration
Hrs/mins
/

- 3 How long were you actually doing this type of welding for?
- 4 What were you welding? Please describe in your own words the things/pieces you were joining

- 5 What materials did you handle (i.e. what types of base metal were you welding)? (tick as many as appropriate)

- 5.1 Mild steel/carbon steel/low alloy
- 5.2 High chrome/stainless steel
- 5.3 Other high alloy steel (please specify _____)
- 5.4 Cast iron
- 5.5 Galvanized steel
- 5.6 Other plated steel (please specify _____)
- 5.7 Aluminium
- 5.8 Copper
- 5.9 Bronze
- 5.10 Lead
- 5.11 Other (please specify _____)

Yes	No

- 6 Which, if any, of the following filler rods or wires did you use? (tick as many as appropriate)
- 6.1 Mild steel/carbon steel/low alloy
- 6.1.2 If yes, please specify main rods or wires used

Yes	No

- 6.2 High chrome/stainless/alloy
- 6.2.1 If yes, please specify main rods or wires used

- 6.3 Other
- 6.3.1 If yes, please specify main rods or wires used

- 7 Did you use fluxes while doing this type of welding on this day? Yes 1 No 2
- 7.1 If yes, what type

- 7.1.1 incorporated in to rod/wire
- 7.1.2 not incorporated into rod/wire

Check one

- 8 Did you use a shielding gas while doing this type of welding on this day? Yes 1 No 2

- 8.1 If yes, which gas
- 8.1.1 Argon
- 8.1.2 Other inert gas
- 8.1.3 CO2
- 8.1.4 Argon/CO2 mixture
- 8.1.5 Other (please specify _____)

Yes	No

- 9 Were any of the metals you worked on while doing this type of welding coated? Yes 1 No 2
- 9.1 If yes, what were they coated with

- 9.1.1 Paints or primers
- If coated with paints or primers, what kind were they?
- 9.1.1.1 Lead oxide (red lead)
- 9.1.1.2 Lead chromate
- 9.1.1.3 Zinc chromate
- 9.1.1.4 Iron oxide
- 9.1.1.5 Epoxy
- 9.1.1.6 Other (please specify _____)
- 9.1.2 Other substances (please specify _____)

Yes	No

- 10 What proportion of your time when doing this type of welding on this day did you work indoors or outdoors?

Indoors %	Outdoors %
Yes	No

- 10.1 If you worked indoors, was it in a confined or enclosed space? (please circle)

- 10.2 If you worked in a confined or enclosed space, for what proportion of your time? _____%

Appendix B

Citation		Weiding and Sampling Scenarios						Usable Data Y or N	Extracted by	JM	Sheet #	1 of 1
Raw data	Smpl Yea	Process	Rod/electrode	Shielding gas/flux	Base metal	Coating	Ventilation	Comments				
# welders:	1											
# sites	2											
location	3											
Industry	4											
	5											
	6											
Comments		tot./inhal./resp/nano	Sample time	Personal (P)	Task (T) or shift (S)							
	A											
	B											
	C											
	D											
	E											
Air Sample Results - Fumes												
Welding Scenario	Sampling Scenario	Metal										Total Particulates
		Units										mg/m ³
		n										
		Mean										
		SD										
		Median										
		GM										
		GSD										
		Range										
		n										
		Mean										
		SD										
		Median										
		GM										
		GSD										
		Range										
		n										
		Mean										
		SD										
		Median										
		GM										
		GSD										
		Range										

Appendix C

1)

Estimation of geometric standard deviation from (min=a, max=b) and from the median (W_{median}) with which to estimate the arithmetic mean when geometric means are present but not GSD:

$$GSD = e^{\left(\frac{\ln(b)-\ln(a)}{W_{\text{median}}}\right)}$$

Estimation the geometric mean from (min=a, max=b):

$$GM = e^{\left(\frac{\ln(a)+\ln(b)}{2}\right)}$$

Both of the above formulae can be found in Lavoue et al. (2007). Further, R code was provided by the same authors for the GSD estimation.

2)

With the interquartile range (q3-q1) and median (m), formula can be found in (Wan et al., 2014):

$$\bar{X} = q1 + m + q3/3$$

3)

For those with no additional information (n=32) other than a median and/or geometric mean, the median value of 2.4297 was assigned to the gsd based on all data that had both geometric means and geometric standard deviations before formula 4 was applied.

4)

With the geometric mean and geometric standard deviation either known or estimated from the equations above, the following formula was used to estimate the arithmetic mean and can be found in Perkins (2008) chapter 16.

$$MVU = [\exp(\widehat{x}_L)] * \Psi_n$$

Where $\Psi_n = a$ multiplication factor obtained from $t(0.5 * s_y^2)$ & n

Appendix D

Replacement values for unknown consumables by base metal

	Weighted means			
	Mn %	Ni %	Cr %	Al %
Mild steel	1.234	1.517	0.420	0.217
Stainless steel	1.810	11.599	19.593	0.015
Aluminum	0.370	0.000	0.107	93.657
High alloyed steel	1.136	11.998	15.850	0.000
Galvanized steel	1.205	0.800	0.033	0.000
Mild steel + Stainless steel	2.919	3.457	4.109	0.178
Unknown	1.050	5.524	12.267	0.000
Number of values replaced	104	68	121	12

Appendix E

	References	Total dust	Mn	Ni	Cr	Al
[1]	J. Angerer, W. Amin, R. Heinrich-Ramm, D. Szadkowski, and G. Lehnert, "Occupational chronic exposure to metals. I. Chromium exposure of stainless steel welders--biological monitoring," <i>Int Arch Occup Environ Health</i> , vol. 59, no. 5, pp. 503-12, 1987, doi: 10.1007/BF00377845.				X	
[2]	J. Angerer and G. Lehnert, "Occupational chronic exposure to metals. II. Nickel exposure of stainless steel welders--biological monitoring," <i>Int Arch Occup Environ Health</i> , vol. 62, no. 1, pp. 7-10, 1990, doi: 10.1007/BF00397842.			X		
[3]	M. G. Baker et al., "Variance components of short-term biomarkers of manganese exposure in an inception cohort of welding trainees," <i>Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)</i> , vol. 29, pp. 123-9, Jan 2015, doi: 10.1016/j.jtemb.2014.05.004.		X			
[4]	M. G. Baker, B. Stover, C. D. Simpson, L. Sheppard, and N. S. Seixas, "Using exposure windows to explore an elusive biomarker: blood manganese," (in English), <i>International archives of occupational and environmental health</i> , vol. 89, no. 4, pp. 679-87, 2016. [Online]. Available: <Go to ISI>://MEDLINE:26589320.		X			
[5]	W. W. Barrington, C. R. Angle, N. K. Willcockson, M. A. Padula, and T. Korn, "Autonomic function in manganese alloy workers," <i>Environ Res</i> , vol. 78, no. 1, pp. 50-8, Jul 1998, doi: 10.1006/enrs.1997.3826.	X				
[6]	R. Bast-Pettersen, V. Skaug, D. Ellingsen, and Y. Thomassen, "Neurobehavioral performance in aluminum welders," <i>Am J Ind Med</i> , vol. 37, no. 2, pp. 184-92, Feb 2000, doi: 10.1002/(sici)1097-0274(200002)37:2<184::aid-ajim4>3.0.co;2-o.					X
[7]	L. M. Blade et al., "Hexavalent chromium exposures and exposure-control technologies in American enterprise: results of a NIOSH field research study," <i>J Occup Environ Hyg</i> , vol. 4, no. 8, pp. 596-618, Aug 2007, doi: 10.1080/15459620701463183.				X	
[8]	F. W. Boelter, C. E. Simmons, L. Berman, and P. Scheff, "Two-zone model application to breathing zone and area welding fume concentration data," <i>J Occup Environ Hyg</i> , vol. 6, no. 5, pp. 298-306, May 2009, doi: 10.1080/15459620902809895.	X	X			
[9]	J. P. Bonde, "Semen quality and sex hormones among mild steel and stainless steel welders: a cross sectional study," <i>Br J Ind Med</i> , vol. 47, no. 8, pp. 508-14, Aug 1990, doi: 10.1136/oem.47.8.508.	X			X	
[10]	J. P. Bonde and J. M. Christensen, "Chromium in biological samples from low-level exposed stainless steel and mild steel welders," <i>Arch Environ Health</i> , vol. 46, no. 4, pp. 225-9, Jul-Aug 1991, doi: 10.1080/00039896.1991.9937453.	X	X		X	
[11]	R. M. Bowler et al., "Dose-effect relationships between manganese exposure and neurological, neuropsychological and pulmonary function in confined space bridge welders," (in eng), <i>Occup Environ Med</i> , vol. 64, no. 3, pp. 167-77, Mar 2007, doi: 10.1136/oem.2006.028761.		X			
[12]	M. Buchta et al., "Longitudinal study examining the neurotoxicity of occupational exposure to aluminium-containing welding fumes," <i>Int Arch Occup Environ Health</i> , vol. 76, no. 7, pp. 539-48, Sep 2003, doi: 10.1007/s00420-003-0450-9.	X				

[13]	S. Casjens et al., "Influence of welding fume on systemic iron status," <i>Ann Occup Hyg</i> , vol. 58, no. 9, pp. 1143-54, Nov 2014, doi: 10.1093/annhyg/meu068.	X	X			
[14]	H. R. Castner and C. L. Null, "Chromium, nickel and manganese in shipyard welding fumes," 1998 1998, 1998.	X			X	
[15]	J. M. Cavallari et al., "PM2.5 metal exposures and nocturnal heart rate variability: a panel study of boilermaker construction workers," <i>Environ Health</i> , vol. 7, p. 36, Jul 9 2008, doi: 10.1186/1476-069X-7-36.	X			X	X
[16]	S. V. Chandra, G. S. Shukla, R. S. Srivastava, H. Singh, and V. P. Gupta, "An exploratory study of manganese exposure to welders," <i>Clin Toxicol</i> , vol. 18, no. 4, pp. 407-16, Apr 1981, doi: 10.3109/15563658108990264.		X			
[17]	C. Chang, P. Demokritou, M. Shafer, and D. Christiani, "Physicochemical and toxicological characteristics of welding fume derived particles generated from real time welding processes," <i>Environ Sci Process Impacts</i> , vol. 15, no. 1, pp. 214-24, Jan 2013, doi: 10.1039/c2em30505d.	X				
[18]	Y. Chang et al., "Pallidal index measured with three-dimensional T1-weighted gradient echo sequence is a good predictor of manganese exposure in welders," <i>J Magn Reson Imaging</i> , vol. 31, no. 4, pp. 1020-6, Apr 2010, doi: 10.1002/jmri.22104.		X			
[19]	H. C. Chuang et al., "Pulmonary exposure to metal fume particulate matter cause sleep disturbances in shipyard welders," <i>Environmental pollution (Barking, Essex : 1987)</i> , vol. 232, pp. 523-532, Jan 2018, doi: 10.1016/j.envpol.2017.09.082.	X				
[20]	J. L. Edmé et al., "Assessment of biological chromium among stainless steel and mild steel welders in relation to welding processes," <i>International Archives of Occupational and Environmental Health</i> , vol. 70, no. 4, pp. 237-242, 1997/09/01 1997, doi: 10.1007/s004200050213.				X	
[21]	D. G. Ellingsen, M. Chashchin, B. Berlinger, V. Fedorov, V. Chashchin, and Y. Thomassen, "Biological monitoring of welders' exposure to chromium, molybdenum, tungsten and vanadium," <i>Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)</i> , vol. 41, pp. 99-106, May 2017, doi: 10.1016/j.jtemb.2017.03.002.	X			X	
[22]	D. G. Ellingsen et al., "Air exposure assessment and biological monitoring of manganese and other major welding fume components in welders," <i>J Environ Monit</i> , vol. 8, no. 10, pp. 1078-86, Oct 2006, doi: 10.1039/b605549d.		X	X	X	X
[23]	M. R. Flynn and P. Susi, "Manganese, iron, and total particulate exposures to welders," <i>J Occup Environ Hyg</i> , vol. 7, no. 2, pp. 115-26, Feb 2010, doi: 10.1080/15459620903454600.	X	X			
[24]	F. Golbabaee et al., "Assessment of welders exposure to carcinogen metals from manual metal arc welding in gas transmission pipelines, iran," <i>Iran J Public Health</i> , vol. 41, no. 8, pp. 61-70, 2012. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/23113226 .	X		X	X	
[25]	M. Gube et al., "Experimental exposure of healthy subjects with emissions from a gas metal arc welding process--part II: biomonitoring of chromium and nickel," <i>Int Arch Occup Environ Health</i> , vol. 86, no. 1, pp. 31-7, Jan 2013, doi: 10.1007/s00420-012-0738-8.	X		X	X	
[26]	T. Halatek, H. Sinczuk-Walczak, and K. Rydzynski, "Early neurotoxic effects of inhalation exposure to aluminum and/or		X			

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[28]	K. W. Hanley, R. Andrews, S. Bertke, and K. Ashley, "Manganese Fractionation Using a Sequential Extraction Method to Evaluate Welders' Shielded Metal Arc Welding Exposures During Construction Projects in Oil Refineries," (in eng), Journal of occupational and environmental hygiene, vol. 12, no. 11, pp. 774-784, 2015, doi: 10.1080/15459624.2015.1047022.		X			
[29]	K. W. Hanley, R. Andrews, S. Bertke, and K. Ashley, "Exploring Manganese Fractionation Using a Sequential Extraction Method to Evaluate Welders' Gas Metal Arc Welding Exposures during Heavy Equipment Manufacturing," Ann Work Expo Health, vol. 61, no. 1, pp. 123-134, Jan 1 2017, doi: 10.1093/annweh/wxx005.		X			
[30]	A. Hariri, N. Mohamad Noor, N. A. Paiman, A. M. Ahmad Zaidi, and S. F. Zainal Bakri, "Heavy metals found in the breathing zone, toenails and lung function of welders working in an air-conditioned welding workplace," (in eng), International journal of occupational safety and ergonomics : JOSE, vol. 24, no. 4, pp. 646-651, 2018/12// 2018, doi: 10.1080/10803548.2017.1368950.	X	X	X	X	X
[31]	A. Hariri, N. A. Paiman, A. M. Leman, and M. Z. Md Yusof, "Development of Welding Fumes Health Index (WFHI) for Welding Workplace's Safety and Health Assessment," Iran J Public Health, vol. 43, no. 8, pp. 1045-59, Aug 2014. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/25927034 .		X		X	X
[32]	H. Hassani et al., "Occupational exposure to manganese-containing welding fumes and pulmonary function indices among natural gas transmission pipeline welders," Journal of occupational health, vol. 54, no. 4, pp. 316-22, 2012, doi: 10.1539/joh.11-0269-fs.	X	X			
[33]	H. Hassani, F. Golbabaie, H. Shirkanloo, and M. Tehrani-Doust, "Relations of biomarkers of manganese exposure and neuropsychological effects among welders and ferroalloy smelters," Ind Health, vol. 54, no. 1, pp. 79-86, 2016, doi: 10.2486/indhealth.2014-0250.		X			
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[38]	A. J. Jafari and M. J. Assari, "Respiratory effects from work-related exposure to welding fumes in Hamadan, Iran," <i>Arch Environ Health</i> , vol. 59, no. 3, pp. 116-20, Mar 2004, doi: 10.3200/AEOH.59.3.116-120.		X	X	X
[39]	J. Jarvisalo et al., "Urinary and blood manganese in occupationally nonexposed populations and in manual metal arc welders of mild steel," <i>Int Arch Occup Environ Health</i> , vol. 63, no. 7, pp. 495-501, 1992, doi: 10.1007/BF00572116.	X	X		
[40]	Ø. Jelmert, I.-L. Hansteen, and S. Langård, "Chromosome damage in lymphocytes of stainless steel welders related to past and current exposure to manual metal arc welding fumes," <i>Mutation Research/Genetic Toxicology</i> , vol. 320, no. 3, pp. 223-233, 1994/02/01/ 1994, doi: https://doi.org/10.1016/0165-1218(94)90049-3 .			X	X
[41]	Ø. Jelmert, I.-L. Hansteen, and S. Langård, "Cytogenetic studies of stainless steel welders using the tungsten inert gas and metal inert gas methods for welding," <i>Mutation Research/Genetic Toxicology</i> , vol. 342, no. 1, pp. 77-85, 1995/03/01/ 1995, doi: https://doi.org/10.1016/0165-1218(95)90092-6 .			X	X
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[44]	B. Kendzia et al., "Modelling of occupational exposure to inhalable nickel compounds," <i>J Expo Sci Environ Epidemiol</i> , vol. 27, no. 4, pp. 427-433, Jul 2017, doi: 10.1038/jes.2016.80.			X	
[45]	E. Kiesswetter et al., "Longitudinal study on potential neurotoxic effects of aluminium: II. Assessment of exposure and neurobehavioral performance of Al welders in the automobile industry over 4 years," <i>Int Arch Occup Environ Health</i> , vol. 82, no. 10, pp. 1191-210, Nov 2009, doi: 10.1007/s00420-009-0414-9.	X			
[46]	E. Kiesswetter et al., "Longitudinal study on potential neurotoxic effects of aluminium: I. Assessment of exposure and neurobehavioural performance of Al welders in the train and truck construction industry over 4 years," <i>Int Arch Occup Environ Health</i> , vol. 81, no. 1, pp. 41-67, Oct 2007, doi: 10.1007/s00420-007-0191-2.	X			
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[51]	J. Kucera, V. Bencko, A. Papayova, D. Saligova, J. Tejral, and L. Borska, "Monitoring of occupational exposure in manufacturing of stainless steel constructions. Part I: Chromium, iron, manganese, molybdenum, nickel and vanadium in the workplace air of stainless steel welders," <i>Cent Eur J Public Health</i> , vol. 9, no. 4, pp. 171-5, Nov 2001. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/11787242 .		X	X	X	
[52]	W. Laohaudomchok et al., "Assessment of occupational exposure to manganese and other metals in welding fumes by portable X-ray fluorescence spectrometer," <i>J Occup Environ Hyg</i> , vol. 7, no. 8, pp. 456-65, Aug 2010, doi: 10.1080/15459624.2010.485262.	X	X			
[53]	W. Laohaudomchok et al., "Neuropsychological effects of low-level manganese exposure in welders," <i>Neurotoxicology</i> , vol. 32, no. 2, pp. 171-9, Mar 2011, doi: 10.1016/j.neuro.2010.12.014.		X			
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[55]	M. Lehnert et al., "Exposure to inhalable, respirable, and ultrafine particles in welding fume," <i>Ann Occup Hyg</i> , vol. 56, no. 5, pp. 557-67, Jul 2012, doi: 10.1093/annhyg/mes025.	X				
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