# **Field Study**



# Cancer risk assessment for occupational exposure to chromium and nickel in welding fumes from pipeline construction, pressure container manufacturing, and shipyard building in Taiwan

Show-Yi Yang<sup>1,2</sup>, Jia-Ming Lin<sup>1</sup>, Wan-Yu Lin<sup>3,4</sup> and Ching-Wen Chang<sup>1,4</sup>

<sup>1</sup>Institute of Environmental Health, College of Public Health, National Taiwan University, Taipei, Taiwan, <sup>2</sup>Institute of Labor, Occupational Safety and Health, Ministry of Labor in Taiwan, New Taipei City, Taiwan, <sup>3</sup>Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan and <sup>4</sup>Department of Public Health, College of Public Health, National Taiwan University, Taipei, Taiwan

Abstract: Objective: We assessed the cancer risks resulting from the exposure to chromium, hexavalent chromium (Cr (VI)), oxidic nickel (Ni), and soluble Ni in welding fumes during pipeline and shipyard construction and pressure container manufacturing in Taiwan. We also determined the roles of welding performance and demographic characteristics during the exposure to Cr and Ni. Methods: Personal air samples were collected for the analysis of Cr and Ni, and the concentrations of Cr (VI), oxidic Ni, and soluble Ni were quantified. We assessed cancer slope factors for Cr, Cr (VI), oxidic Ni, and soluble Ni, and we used the Incremental Lifetime Cancer Risk model proposed by the United States Environmental Protection Agency to calculate excess risk. Results: The risks of exposure to Cr and Cr (VI) in welding fumes exceeded the acceptable level of occupational exposure  $(10^{-3})$ . We ranked the excess cancer risk in three industries in decreasing order as follows: pipeline construction, shipyard construction, and pressure container manufacturing. The most sensitive parameters for the risk assessment were Cr and Ni concentrations. Statistically significant determinants of Cr (VI), oxidic Ni, and soluble Ni concentrations were the following: stainless steel as the base metal and the filler metals of shielded metal arc welding (SMAW) and of gas tungsten arc welding (GTAW). Conclusion: The study revealed that welders belong to a high cancer-risk group. Furthermore, we demonstrated the roles of filler metals and stainless steel

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Key words: Cancer risk assessment, Chromium VI, Oxidic nickel, Soluble nickel, Welding fumes

# Introduction

A 26% increase in the risk of lung cancer has been estimated in stainless steel welders<sup>1)</sup>, and animal studies have demonstrated that fumes from stainless steel welding are potentially mutagenic<sup>2)</sup>. Exposure to low-to-moderate welding fumes is associated with oxidative stress, telomere alterations, and deoxyribonucleic acid (DNA) methylation<sup>3)</sup>. Though there is limited evidence to weigh the carcinogenicity of welding fumes, stainless steel welding leads to exposure to chromium (VI) and nickel (Ni), which are recognized as carcinogens<sup>4)</sup>.

Chromium (Cr) significantly increases the risk of lung, nasal, and sinus cancers in epidemiological and animal studies<sup>5</sup>. A dose-response relationship between lung cancer mortality and cumulative hexavalent chromium [Cr (VI)] exposure was demonstrated in a chromate production facility<sup>6</sup>. Chromium damages cellular components (including DNA) because of the generation of free radicals during the reduction process of Cr (VI) to Cr (III)<sup>5</sup>.

The carcinogenic potency of Ni depends on its chemical form and route of entry in organisms. Soluble nickel

Correspondence to: S. Yang, Institute of Labor, Occupational Safety and Health, No. 99, Lane 407 Hengke Rd., Sijhih District, New Taipei City 22143, Taiwan (R.O.C.) (e-mail: year@mail.ilosh.gov.tw)

Supplementary materials (Appendices) are available in the online version of this article.

introduced through intraperitoneal or intramuscular administration results in tumorigenesis<sup>7)</sup>. A case-control study quantified the dose effect of water-soluble nickel on cancer incidence<sup>8)</sup>. Alveolar bronchiolar adenomas or carcinomas and pheochromocytoma were found in rats inhaling nickel oxide<sup>9)</sup>. Nickel oxide increases the incidence of lung tumors in female mice even when the dose is as low as 1.25 mg/m<sup>3 10)</sup>. However, metallic nickel is classified as 2B by International Agency for Research on Cancer<sup>11)</sup>. The carcinogenesis of Ni exposure is caused by the induction of oxidative stress, the disruption of DNA repair pathways, and modulation of the expression of several cancer-related genes<sup>12)</sup>.

Epidemiological studies are a useful tool for establishing causation between welding fumes and cancer risk, but the composition of welding fumes may vary with specific welding tasks and time. Therefore, it is difficult to apply previously established exposure profiles and determine the risk factors in welding. Recently developed risk assessment modeling techniques may provide useful approaches for quantifying the risk factors in welding. In this study, we have used exposure data and welding characteristics for welders in three scenarios to assess cancer risk. We aimed to do the following: (1) to quantify cancer risks in welders in relation to exposure to Cr, Cr (VI), oxidic Ni, and soluble Ni in pipeline construction, pressure container manufacturing, and shipyard building; (2) to analyze sensitive input parameters on cancer risk; and (3) to determine the roles of welding performance and demographic characteristics on exposure.

#### Subjects and methods

### Study subjects

The Institute of Labor, Occupational Safety and Health (ILOSH) of the Ministry of Labor in Taiwan conducted an exposure assessment of welders' exposure to welding fumes in 2006<sup>13</sup> and 2013<sup>14</sup>. Welders working in pipeline construction, pressure container manufacturing, and ship-yard building were recruited. The study was approved by the Institutional Review Board of the Tri-Service General Hospital in Taiwan. All participants were aware of the study aims and participated voluntarily.

# Welders in pipeline construction

A total of 50 individuals were sampled between the 5<sup>th</sup> and the 10<sup>th</sup> of September 2013. The participants were recruited from full-time project welders working in the construction of transportation pipelines in an oil refinery factory in Mailiao Industry Park, Taiwan. They performed shielded metal arc welding (SMAW) and gas tungsten arc welding (GTAW) on butt-welding joints, flange neck, and fillet weld on pipes. The filler for GTAW was ER70S-G, and the filler for SMAW was E7016. In addition, 20% of the pipes were made of carbon steel, and 80% of the pipes

were made of stainless steel. The welders worked outdoors at temperatures of  $24.1^{\circ}$  C- $35.5^{\circ}$  C and in wind speeds averaging 24.8 km/h, with a maximum of 37.8 km/h.

### Welders in pressure container manufacturing

A total of 35 full-time welders were recruited and worked at pressure container manufacturing factories, including three factories located in Taoyuan County and one factory in Hsinchu City, Taiwan. The welding mainly applied GTAW with a non-consumable tungsten electrode, and only 10% of the welding employed SMAW. Welding was used to form a layer on the outside of hollow cylindrical containers. The base metal of the work pieces was 70% stainless steel and 30% carbon steel. The welders worked indoors at temperatures of 24.0°C-30.0° C, with fans operating in the workplace for ventilation.

## Welders in shipyard building

Twenty full-time welders employed in shipyard manufacturing were recruited as study subjects<sup>13)</sup>. The welders mainly used SMAW, but 20% of the welding was completed using gas metal arc welding (GMAW). Carbon steel was used as the base metal. The welders worked indoors at temperatures of 25.0°C-32.0°C, with fans for ventilation in the workplace.

# Personal air sampling and quantification of Cr and Ni in welding fumes

Air samplers with 37 mm mixed cellulose ester membranes (0.8  $\mu$ m pore size; SKC Corp., USA) were mounted on the shoulders of welders and operated at a flow rate of 2 *l*/min for 6 hours. A total of 105 air samples were taken. To analyze Cr and Ni in welding fumes, we followed the NIOSH analytical method 7301<sup>15</sup> and used inductively coupled plasma mass spectrometry (ICP-MS, Agilent 7500ce, WA, USA). For every 10 samples, recovery of sample analysis was checked by two consecutive spikes of a quality control standard, which found a range of 90%-110%. The limits of quantification (LOQs) of metals were 8.9 and 8.5 ng/sample for Cr and Ni, respectively.

# Estimation of Cr (VI), oxidic Ni, and soluble Ni concentrations

The Cr (VI), oxidic Ni, and soluble Ni concentrations were estimated using the following equation:

Equation 1:  $Cmi = \Sigma Ci \times Fi \times Wi$ ,

where Cm*i* is the concentration of Cr (VI), oxidic Ni, or soluble Ni ( $\mu$ g/m<sup>3</sup>); C*i* is the concentration of total Cr or total Ni ( $\mu$ g/m<sup>3</sup>); F*i* is the percentage of SMAW, GMAW, or GTAW used in 8-h work shifts (%); and W*i* is the percentage of Cr (VI), oxidic Ni, or soluble Ni in Cr or Ni corresponding to the welding methods presented in Table 1. For SMAW, which is performed primarily on stainless

Welding methods	Chemical species in Cr and Ni (%)			
	Cr (VI)	Oxidic Ni	Soluble Ni	
SMAW	$46.2 \pm 5.0^{(1)}$	33.0 ± 1.5 <sup>(2)</sup>	$44.0 \pm 2.0^{(2)}$	
GMAW	$6.0 \pm 5.4^{(3)}$	$79.0 \pm 0.5^{(2)}$	$15.0 \pm 0.5^{(2)}$	
GTAW	$13.2 \pm 2.5$ <sup>(4)</sup>	$88.0 \pm 2.0$ <sup>(5)</sup>	$2.5 \pm 0.5$ <sup>(6)</sup>	

 Table 1. Proportion of Cr (VI), oxidic Ni, or soluble Ni found in chromium (Cr) or nickel (Ni) according to welding methods

(1) Matczak et al., 1993<sup>16)</sup>

(2) Berlinger et al., 2009<sup>19)</sup>

(3) Cena et al., 2014<sup>17)</sup>

(4) Topham et al., 2009<sup>18)</sup>

(5) The percentage of oxidic nickel with the GTAW method was inferred to be 88%<sup>20)</sup>.
(6) The allotted percentage of soluble Ni with GTAW was 2.5%<sup>23)</sup>.

Abbreviations: SMAW: shielded metal arc welding; GTAW: gas tungsten arc welding; GMAW: gas metal arc welding.

steel, Cr (VI) occupies  $46.2 \pm 5.0\%$  of total Cr<sup>16</sup>). Cr (VI) accounted for  $6.0 \pm 5.4\%$  of total Cr when GMAW was used on stainless steel in a laboratory study<sup>17</sup>), and Cr (VI) accounted for  $13.2 \pm 2.5\%$  of total Cr when GTAW was used on stainless steel plates in a welding chamber<sup>18</sup>).

For the proportions of oxidic Ni and soluble Ni in total Ni, 79% oxidic nickel and 15% soluble nickel were found when GMAW was applied on corrosion-resistant steel, and 33% oxidic nickel and 44% soluble nickel were measured when SMAW was used<sup>19)</sup>. However, previously established percentages of oxidic and soluble Ni corresponding with GTAW were not available. We inferred the percentage of oxidic Ni in GTAW using the assumption that the percentage of oxidic Ni is proportional to the deposition efficiency (%) of the welding method. The percentages of oxidic Ni in welding fumes from SMAW and GMAW are 33% and 79%, respectively<sup>19</sup>; and the deposition efficiencies of SMAW, GMAW, and GTAW are 70%, 95%, and 100%, respectively<sup>20)</sup>. The percentage of oxidic Ni used in GTAW was therefore inferred to be 88%.

Deposition efficiency indicates the percentage of weight of the electrode (fillers) deposited in work pieces during the welding process. High deposition efficiency implies low loss of welding materials and reduced fume formation. GTAW has ~ 100% deposition efficiency and primarily forms insoluble oxidic Ni owing to an oxidation reaction<sup>21,22)</sup>. Thus, the allotted percentage of soluble Ni with GTAW was 2.5%. The tungsten electrode of GTAW is difficult to melt and consume, so GTAW generates few welding fumes. The generation of welding fumes by GTAW is 0.18 fold of that produced by GMAW,<sup>23)</sup> which has a 15% proportion of soluble Ni. The allotted percentage of soluble Ni generated by GTAW was founded on the assumption that the low generation of fumes by GTAW also reduces the proportion of soluble Ni, due to the lower number of alkali elements and fluoride present

in the filler of the GTAW electrode<sup>24,25)</sup>.

### Dose-response assessment for Cr and Ni compounds

Cancer slope factors for Cr, Cr (VI), and soluble Ni have been proposed by Health Canada<sup>26)</sup> and the United States Environmental Protection Agency<sup>27)</sup>. The cancer slope factors for Cr and Cr (VI) by inhalation were found to be 47.6  $(mg/kg/day)^{-1}$  and 41  $(mg/kg/day)^{-1}$ , respectively<sup>26,27)</sup>. The cancer slope factor for soluble Ni by inhalation was 3.0  $(mg/kg/day)^{-1}$  <sup>26,28)</sup>. The cancer slope factor for oxidic Ni was assessed based on the dose-response dataset from a toxicology test on male rats9, in which F344/ N rats inhaled 0.5-2.0 mg Ni/m<sup>3</sup> of Ni oxide for 6 h/day, 5 d/wk for 104 weeks, leading to neoplastic effects including alveolar/bronchiolar adenoma in the lung and pheochromocytoma in the adrenal medulla. The benchmark dose method (BMD)<sup>29)</sup> was applied to determine a benchmark dose lower-confidence limit (BMDL) of 1.416 mg/ kg/day. Then, the human equivalent dose (HED) was calculated using the following equation:

Equation 2: HED (mg/kg/day) = animal BMDL (mg/kg/day)× Km,

where the factor Km was 0.162, given to a human with a body weight of 60 kg and a body surface area of 1.62 m<sup>2 30)</sup>. Thus, the HED was 0.229 mg/kg/day. Accordingly, the cancer slope factor of Ni oxide was estimated to be 4.4 (mg/kg/day)<sup>-1</sup>, which is between 3 (mg/kg/day)<sup>-1</sup> for soluble Ni and 5.5 (mg/kg/day)<sup>-1</sup> for refinery dust, which is mainly composed of insoluble Ni.

### Cancer risk assessment

We applied the US EPA Incremental Lifetime Cancer Risk (ILCR) model<sup>31)</sup> to determine the cancer risk for exposure to Cr, Cr (VI), oxidic Ni, or soluble Ni through inhalation of welding fumes. The ILCR was calculated using the following equation:

Parameters		Input estimates	Distribution type	Data source
Breathing rate	m³/h	$1.37 \pm 0.042$	Normal	US EPA, 2009 <sup>35)</sup>
Average work hours	h/day	8.87	Point estimate	DBAS, 2016 <sup>32)</sup>
Exposure frequency	d/yr	$246 \pm 1.5$	Normal	MOL, 2016 <sup>33)</sup>
Exposure duration	year	45	Point estimate	MOL, 2016 <sup>34)</sup>
Body weight	kg	$69.81 \pm 1.39$	Normal	MHW, 2016 <sup>52)</sup>
Time to cancer	year	$77.01 \pm 2.01$	Normal	MOI, 2016 <sup>53)</sup>
Cancer slope factor	(mg/kg/day) -1			
- Cr		47.6	Point estimate	Health Canada, 2007 <sup>26)</sup>
- Cr (VI)		41	Point estimate	US EPA, 2007 <sup>27)</sup>
- Oxidic nickel		4.4	Point estimate	NTP, 1996 <sup>9)</sup>
- Soluble nickel		3.0	Point estimate	Health Canada, 2007 <sup>26)</sup>
Concentration				
- Cr	10 <sup>-3</sup> mg/m <sup>3</sup>			
Pipeline construction		$1361.6 \pm 639.8$	Log-normal	Field sampling
Pressure container manufacturing		$33.8 \pm 59.8$	Log-normal	Field sampling
Shipyard building		$1.1 \pm 0.9$	Log-normal	Field sampling
- Cr (VI)	$10^{-3} \text{ mg/m}^3$			
Pipeline construction		$503.8 \pm 294.7$	Log-normal	Field sampling
Pressure container manufacturing		$4.4 \pm 8.0$	Log-normal	Field sampling
Shipyard building		$0.4 \pm 0.3$	Log-normal	Field sampling
- Oxidic Ni	$10^{-3} \text{ mg/m}^3$			
Pipeline construction		$145.2 \pm 119.4$	Log-normal	Field sampling
Pressure container manufacturing		$13.0 \pm 11.5$	Log-normal	Field sampling
Shipyard building		$0.1 \pm 0.1$	Log-normal	Field sampling
- Soluble Ni	$10^{-3} \text{ mg/m}^3$			
Pipeline construction		$101.8 \pm 85.8$	Log-normal	Field sampling
Pressure container manufacturing		$1.0 \pm 0.9$	Log-normal	Field sampling
Shipyard building		$0.1 \pm 0.1$	Log-normal	Field sampling

Table 2. Summary of input parameters in the ILCR model

Abbreviations: ILCR, Incremental Lifetime Cancer Risk

# Equation 3: ILCR= $\left(\frac{C \times BR \times DS \times EF \times ED}{BW \times AT \times 365}\right) \times SF$ ,

where C is the exposure concentration ( $mg/m^3$ ), BR is the breathing rate ( $m^3/h$ ), DS is the average work hours per day (h), EF is the exposure frequency in a year (day/yr), ED is the exposure duration during the work life (years), BW is the body weight (kg), AT is the time to cancer expressed in life expectancy (years), and SF is the cancer slope factor (mg/kg/day)<sup>-1</sup> (Table 2).

The concentrations of total Cr and total Ni in welding fumes were determined by ICP-MS analysis. The concentrations of Cr (VI), oxidic Ni, and soluble Ni were estimated according to Equation 1 and Table 1. Average work hours per day (DS) were 8 h/day, with an extra work period of 0.87 h/day in this industry sector in Taiwan<sup>32)</sup>. The exposure frequency in a year (EF) was 246 ± 1.5 d/year, based on statistics in Taiwan<sup>33)</sup>. Exposure duration (ED) was set at 45 years, provided that an employee begins working at 20 years old and retires at 65 years old, which is the proposed age of retirement by the Ministry of Labor in Taiwan<sup>34)</sup>. The breathing rate (BR) of  $1.37 \pm 0.042 \text{ m}^3/\text{h}$  was given for an adult male with a body weight of 69.8 kg (the average body weight of male adult in Taiwan) and moderate activities with metabolic equivalents between 3.0 and  $6.0^{35}$ . Cancer slope factors for Cr, Cr (VI), nickel oxide and soluble nickel are given in the previously mentioned dose-response assessment.

# Statistical analysis

The distribution frequency of risk and sensitive parameters for ILCR were obtained using Monte Carlo simulations (n = 10,000) using Crystal Ball 11.1.1.100 (Oracle, Redwood Shores, CA, USA) in the Excel<sup>©</sup> environment. SPSS software (SPSS, Inc., Chicago, IL, version 16) was used for statistical analyses. A non-parametric one-way analysis of variance (the Kruskal-Wallis test) was performed to test the differences in workers' age, length of employment, and exposure to Cr and Ni between the exposure groups.

To assess the factors associated with Cr or Ni exposure

Characteristics	Pipeline construction Pressure containe manufacturing		Shipyard building	
Number of participants	50	35	20	
Sex	male	male	male	
Age (year) *	43.7±7.9	40.7±12.4	48.9±7.5	
Length of employment (year) *	22.2±13.9	15.3±12.7	25.0±10.0	
Percentage use of welding method	GTAW (25%), SMAW (75%)	GTAW (90%), SMAW (10%)	GMAW (20%), SMAW (80%)	
Welding type	manual	manual or automatic	manual or automatic	
Percentage use of base metal	stainless steel (80%), carbon steel (20%)	stainless steel (70%), carbon steel (30%)	carbon steel (100%)	
Filler materials	E7016, ER308, ER70S-2	ER70S-G, ER308	ER70S-G, E7016	

Table 3. Demographics of the participants in the three exposure groups

\*Kruskal-Wallis test, *p*-value < 0.05

Abbreviations: SMAW: shielded metal arc welding; GTAW: gas tungsten arc welding; GMAW: gas metal arc welding.

concentrations ( $\mu g/m^3$ ), we applied a multiple linear regression model:

Equation 3:  $Y_i = \beta_0 + \beta_1 \chi_{i1} + \beta_2 \chi_{i2} + \dots + \beta_p \chi_{ip} + \varepsilon_i$ , (4)

where the dependent variable ( $Y_i$ ) was the log-transformed exposure concentration of Cr or Ni, and the explanatory variables were the demographic characteristics (age and length of employment), welding methods (GTAW, SMAW, or GMAW), welding types (manual or automatic), base metals (stainless steel or carbon steel), and filler materials (ER70S-G, E7016, ER308, or ER70S-2). Information is shown in Table 3 and Supplementary Table 1. Base metals and fillers were expressed as the percentage of Cr or Ni in base metals or fillers. A *p*-value < 0.05 was considered statistically significant.

### Results

### Demographics of study subjects

All welders were male. The ages and lengths of employment were statistically different between the three work groups. Welders' ages were ranked by work group in decreasing order: shipyard building, pressure container manufacturing, and pipeline construction. Welders' lengths of employment were ranked in decreasing order: shipyard building, pipeline construction, and pressure container manufacturing. Welders in the three groups were subject to different welding methods, base metals, and filler electrodes (Table 3).

# Determination of Cr(VI), oxidic Ni, and soluble Ni concentrations of welders

The levels of exposure to Cr and Ni in the three groups significantly differed (*p*-value < 0.05). The average level of Cr was always higher than that of Ni in all groups. Ranges of estimated mean concentrations of Cr, Cr (VI), Ni, oxidic Ni, and soluble Ni were 1.1-1361.6  $\mu$ g/m<sup>3</sup>, 0.4-503.8  $\mu$ g/m<sup>3</sup>, 0.3-307.3  $\mu$ g/m<sup>3</sup>, 0.1-145.2  $\mu$ g/m<sup>3</sup>, and 0.1-

101.8 μg/m<sup>3</sup>, respectively (Table 2 and Supplementary Table 2). The percentages of Cr (VI) in Cr, oxidic Ni in Ni, and soluble Ni in Ni were estimated at 13.1%-38.2%, 8.4%-47.3%, and 4.9%-41.8% among groups, respectively (Supplementary Table 2).

# Lifetime cancer risk assessment for exposure to Cr, Cr (VI), oxidic Ni, and soluble Ni in welding fumes

The excess cancer risk due to exposure to Cr, Cr (VI), oxidic Ni, and soluble Ni for welders in pipeline construction ranged from  $6.2 \times 10^{-2}$ - $3.7 \times 10^{1}$ ,  $8.5 \times 10^{-2}$ - $1.0 \times 10^{1}$ ,  $1.5 \times 10^{-3}$ - $3.6 \times 10^{-1}$ , and  $4.9 \times 10^{-4}$ - $2.9 \times 10^{-1}$ , respectively (Table 4). The cancer risks of exposure to Cr and Cr (VI) in all three groups and Ni (oxidic and soluble Ni) in pipeline construction were over  $10^{-3}$ . The cancer risks due to exposure to Ni in pressure container manufacturing and shipyard building were below  $10^{-3}$ . The probability density of risk fitted a logistic distribution with kurtosis > 3. Sensitive parameters for modeling included exposure concentration and breathing rate, which contributed to approximately 99.5% of the total variance. Life expectancy and body weight had minor negative contributions (Fig. 1).

# Determinants associated with Cr (VI), oxidic Ni, and soluble Ni concentrations

Cr (VI) and oxidic Ni concentrations were significantly associated with the percentages of Cr or Ni in the filler of stainless steel (SS) with SMAW (SMAW-SS,  $\chi_1$ ) and the percentages of Cr or Ni in the filler of stainless steel (SS) with GTAW (GTAW-SS,  $\chi_2$ ). Soluble Ni concentration was significantly associated with the percentages of Ni in the filler of SMAW-SS ( $\chi_1$ ) and the percentages of Ni in the base metal stainless steel (SS,  $\chi_3$ ) (Table 5).

Work facilities	Metals	Incremental lifetime cancer risk				
		Mean	SD	Minimum	Maximum	
Pipeline construction	Cr	4.2	2.8	6.2×10 <sup>-2</sup>	3.7×10 <sup>1</sup>	
	Cr (VI)	1.4	9.6×10 <sup>-1</sup>	$8.5 \times 10^{-2}$	$1.0 \times 10^{1}$	
	Oxidic Ni	3.6×10 <sup>-2</sup>	$1.6 \times 10^{-2}$	$1.5 \times 10^{-3}$	$3.6 \times 10^{-1}$	
	Soluble Ni	2.1×10 <sup>-2</sup>	$1.8 \times 10^{-2}$	$4.9 \times 10^{-4}$	$2.9 \times 10^{-1}$	
Pressure container manufacturing	Cr	$1.1 \times 10^{-1}$	9.9×10 <sup>-2</sup>	$1.2 \times 10^{-3}$	1.3	
	Cr (VI)	$1.3 \times 10^{-2}$	$1.2 \times 10^{-2}$	$1.8 \times 10^{-4}$	$2.8 \times 10^{-1}$	
	Oxidic Ni	3.3×10 <sup>-4</sup>	$2.8 \times 10^{-4}$	$4.8 \times 10^{-6}$	$3.0 \times 10^{-3}$	
	Soluble Ni	$1.2 \times 10^{-4}$	7.1×10 <sup>-5</sup>	$3.2 \times 10^{-5}$	$7.5 \times 10^{-4}$	
Shipyard building	Cr	3.4×10 <sup>-3</sup>	$3.1 \times 10^{-3}$	7.4×10 <sup>-5</sup>	$6.6 \times 10^{-2}$	
	Cr (VI)	$1.1 \times 10^{-3}$	$8.7 \times 10^{-4}$	9.8×10 <sup>-6</sup>	$1.1 \times 10^{-2}$	
	Oxidic Ni	$3.1 \times 10^{-5}$	$2.8 \times 10^{-5}$	9.2×10 <sup>-7</sup>	$6.5 \times 10^{-4}$	
	Soluble Ni	9.8×10 <sup>-5</sup>	$3.5 \times 10^{-6}$	$2.0 \times 10^{-7}$	$2.8 \times 10^{-4}$	

 Table 4.
 Estimated incremental lifetime cancer risk from exposure to Cr, Cr (VI), oxidic Ni, and soluble Ni in welding by groups

Abbreviations: Cr: chromium; Ni: nickel



Fig. 1. Input parameters contributing to total variance in chromium (Cr), hexavalent chromium (Cr (VI)), oxidic nickel (Ni), and soluble Ni in three welding exposure groups. Exposure concentration and breathing rate were the dominant contributors to total variance. A: Cr; B: Cr (VI); C: oxidic Ni; D: soluble Ni. Abbreviations: C: exposure concentration; BR: breathing rate; AT: life expectancy; BW: body weight; MI: miscellaneous.

Dependent variable	Independent variables	β	SE	<i>p</i> -value	$\mathbb{R}^2$
Cr VI concentration (1)	Intercept	-0.508	0.086	< 0.05	0.96; 0.93 (adjusted)
	$\chi_1$ (filler of SMAW-SS) <sup>(4)</sup>	0.239	0.007	< 0.05	
	$\chi_2$ (filler of GTAW-SS) <sup>(5)</sup>	0.101	0.013	< 0.05	
Oxidic Ni concentration <sup>(2)</sup>	Intercept	-1.247	0.095	< 0.05	0.95; 0.90 (adjusted)
	$\chi_1$ (filler of SMAW-SS)	0.293	0.011	< 0.05	
	$\chi_2$ (filler of GTAW-SS)	0.542	0.030	< 0.05	
Soluble Ni concentration (3)	Intercept	-1.047	0.095	< 0.05	0.95; 0.90 (adjusted)
	$\chi_1$ (filler of SMAW-SS) <sup>(6)</sup>	0.103	0.017	< 0.05	
	$\chi_3$ (base metal of SS)	0.285	0.013	< 0.05	

 Table 5.
 Multiple regression analysis of Cr (VI), oxidic Ni, and soluble Ni concentrations corresponding to significant independent variables

(1) Log (Cr (VI) concentration,  $\mu g/m^3$ ) = -0.508 + 0.239  $\chi_1$  + 0.101  $\chi_2$ 

(2) Log (oxidic Ni concentration,  $\mu g/m^3$ ) =  $-1.247 + 0.293 \chi_1 + 0.542 \chi_2$ 

(3) Log (soluble Ni concentration,  $\mu g/m^3$ ) =  $-1.047 + 0.103 \chi_1 + 0.285 \chi_3$ 

(4) The percentage of Cr or Ni content in the filler welding on stainless steel (SS) with the SMAW method.

(5) The percentage of Cr or Ni content in the filler welding on stainless steel (SS) with the GTAW method.

(6) The percentage of Cr or Ni content in stainless steel (SS) base metal.

Abbreviations: Cr: chromium; Ni: nickel; SE: standard error; R<sup>2</sup>: R-squared value.

### Discussion

The risks of exposure to Cr and Cr (VI) in the welding fumes generated by pipeline construction, pressure container manufacturing, and shipyard building were over the acceptable level of risks in occupational exposure  $(10^{-3})$ , which is equivalent to 1.3 excess cases per 100,000 person-years. The risk of exposure to oxidic Ni and soluble Ni in welding fumes in pipeline construction also exceeded  $10^{-3}$ . A similar risk was found in a gas and oil factory in Iran, where the risks for Cr (VI) and Ni exceeded  $10^{-2}$  for project welders and exceeded  $10^{-3}$  for maintenance welders<sup>36</sup>.

Welding is a common working task in industrialized countries. Studies have estimated that approximately 1% of workers engage in welding<sup>37)</sup>. In 2016, the workforce in Taiwan was around 11.7 million<sup>38)</sup>, and the number of welders was estimated to be 117,000. Using the ILCR assessment, the excess cases of cancer for pipeline construction, pressure container manufacturing and shipyard building would be 1892.0, 17.5, and 1.6 per 100,000 person-years, respectively. The incidence rate of cancer in Taiwan is 520.12 per 100,000 person-years for males<sup>39)</sup>.

Concentrations of Cr and Ni are sensitive parameters in risk modeling. Concentrations of Cr and Ni in welding fumes vary with welding methods, base metals, and filler materials. In this study, about 75% of the welding in pipeline construction employed SMAW on stainless steel, and 70% of the welding in pressure container manufacturing employed GTAW on stainless steel. Approximately 80% of welding in shipyard building employed SMAW on carbon steel.

The three welding tasks resulted in different profiles of exposure to Cr (VI) and Ni. The concentrations of Cr (VI) and Ni in the different groups in decreasing order are pipeline construction, pressure container manufacturing, and shipyard building. A recent study showed that 90%-95% of fumes are generated from the filler metal and flux coating/core of consumable electrodes<sup>22,40</sup>. Only small amounts of fumes are formed from the base metal, because the base metal weld pool is much cooler than the electrode tip<sup>22)</sup>. Our study shows that the concentrations of Cr (VI), oxidic Ni, and soluble Ni correspond to the Cr and Ni contents of the fillers used in different welding methods ( $\chi_1$  with SMAW and  $\chi_2$  with GTAW), and the Cr and Ni contents in the base metal of stainless steel  $(\chi_3)$ . Thus, the statistically significant determinants are the filler materials ( $\chi_1$  and  $\chi_2$ ) and the base metal of stainless steel ( $\chi_3$ ). Stainless steel is the only base metal that is a significant determinant, possibly because stainless steel is composed of 16%-18% Cr and 10%-14% Ni. Carbon steel is composed of only 0.04% Cr and 0.04% Ni (Supplementary Table 1). Ranking welding methods by the amount of fumes formed in decreasing order resulted in the following sequence: flux cored arc welding (FCAW), SMAW, GMAW, and GTAW<sup>22)</sup>. Alkali metals, such as sodium and potassium present in the SMAW electrode, stabilize the formation of Cr (VI).

To reduce the exposure to Cr and Ni in welding fumes, source control is a fundamental solution. Designed according to a systematic plan for the work process, work pieces are first sorted and then welded by a robot in an enclosed space<sup>37,41</sup>. To minimize fume emission, selection of welding processes should consider fume generation rates. For example, the GTAW method has the lowest

fume generation rate<sup>37,41)</sup>. For the SMAW method, parameters such as welding voltage, current, and speed should be optimized to reduce fume emission<sup>37)</sup>. The use of stable welding fillers to reduce Cr (VI) generation has been previously reported<sup>42)</sup>. The use of local exhaust equipment with extended and movable tubes to efficiently capture fumes in accordance with the welding operation, in addition to the use of on-gun extraction, which is compatible with weld fume exhaust systems and welding machines, has also been reported<sup>43)</sup>.

Employers are responsible for conducting working environment measurement regularly or on important occasions such as when the working process, materials, or equipment are changed, which might increase the risks of exposure to hazardous substances<sup>44</sup>. Further, exposure levels of hazardous substances should be below the permissible exposure limits (PELs)<sup>45</sup>. Appropriate sampling strategies are required to execute working environment measurements. Several studies have reported sampling strategies appropriate for measurement of the work environment<sup>46-48</sup>.

If engineering controls cannot adequately reduce exposure levels, employers must provide respiratory protection equipment (respirators), which should be worn by employees when necessary to protect their health<sup>49</sup>. Employers must also establish and implement a respiratory protection program comprising worksite-specific procedures, respirator selection, employee training, fit testing, etc.<sup>49,50</sup>. Employee training should include instructions regarding respirator use, maintenance, cleaning, and storage<sup>49,51</sup>. Welding fumes contain particulates that can only be trapped using particulate filters. Determining the maximum concentration of a hazardous substance at which a respirator can be used is necessary. In Taiwan, the PEL for Cr (VI) is 50  $\mu$ g/m<sup>3 45)</sup>, and pipeline construction welders may be exposed to Cr (VI) levels as high as  $800 \ \mu g/m^3$ during welding. Therefore, the respiratory protection equipment selected should be such that it has an assigned protection factor (AFP) of >16; for example, a full facepiece air-purifying respirator with an AFP of  $50^{49,51}$ .

# Conclusions

The risks of exposure to Cr and Ni in welding fumes were high for the three exposure groups. Our results imply that cancer risks from exposure to Cr and Ni in welding fumes are comparable in different exposure groups because welding performance affected the formation of fumes. The most sensitive parameters in risk modeling were the concentrations of Cr and Ni. Multiple regression analysis showed that the determinants of Cr and Ni concentrations were the filler materials in SMAW and GTAW and base metal materials, particularly stainless steel. Thus, the management of risk through engineering controls and/or respiratory protection should account for the characteristics of welding methods, fillers, and base metals.

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## Conflicts of interest: None declared.

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#### References

- Ambroise D, Wild P, Moulin JJ. Update of a meta-analysis on lung cancer and welding. Scand J Work Environ Health 2006; 32(1): 22-31.
- Hedenstedt A, Jenssen D, Lidesten B-M, et al. Mutagenicity of fume particles from stainless steel welding. Scand J Work Environ Health 1977; 3(4): 203-211.
- 3) Li H, Hedmer M, Wojdacz T, et al. Oxidative stress, telomere shortening, and DNA methylation in relation to low-tomoderate occupational exposure to welding fumes. Environ Mol Mutagen 2015; 56(8): 684-693.
- 4) International Agency for Research on Cancer. Chromium, Nickel and Welding, IARC monographs on the evaluation of carcinogenic risks to humans. [Online]. 1990 Available from: URL: http://monographs.iarc.fr/ENG/Monographs/vol49/inde x.php
- Agency for Toxic Substances and Disease Registry. Toxicological profile for chromium. [Online]. 2012 Available from: URL: https://www.atsdr.cdc.gov/toxprofiles/tp7.pdf
- 6) Luippold RS, Mundt KA, Austin RP, et al. Lung cancer mortality among chromate production workers. Occup Environ Med 2003; 60(6): 451-457.
- 7) Sunderman FW Jr. Carcinogenicity of nickel compounds in animals. In: Sunderman FW Jr, et al, editor. Nickel in the Human Environment. Lyon (France): IARC; 1984. p. 127-142.
- Grimsrud TK, Berge SR, Martinsen JI, Andersen A. Lung cancer incidence among Norwegian nickel-refinery workers 1953-2000. J Environ Monit 2003; 5(2): 190-197.
- 9) National Toxicology Program. Toxicology and carcinogenesis studies of nickel oxide (CAS No. 1313-99-1) in F344/N rats and B6C3F1 mice (Inhalation studies). USA: NIH; 1996. p. 5-317.
- 10) Dunnick JK, Elwell MR, Radovsky AE, et al. Comparative carcinogenic effects of nickel subsulfide, nickel oxide, or nickel sulfate hexahydrate chronic exposures in the lung. Cancer Res 1995; 55(22): 5251-5256.
- International Agency for Research on Cancer. Nickel and nickel compounds. [Online]. 1990 Available from: URL: htt p://monographs.iarc.fr/ENG/Monographs/vol49/mono49-7.pdf
- 12) Hartwig A, Asmuss M, Ehleben I, et al. Interference by toxic

metal ions with DNA repair processes and cell cycle control: molecular mechanisms. Environ Health Perspect 2002; 110 supplement5: 797-799.

- 13) Institute of Labor, Occupational Safety and Health, Ministry of Labor in Taiwan (ILOSH). Heavy metal exposure assessment of steel welding workers. [Online]. 2006 Available from: URL: https://laws.ilosh.gov.tw/ioshcustom/Web/YearlyResera chReports/Detail?id=1093 [in Chinese]
- 14) Institute of Labor, Occupational Safety and Health, Ministry of Labor in Taiwan (ILOSH). Assessment of metallic fume exposure from welding processes of pressure vessel manufacturing industry. [Online]. 2013 Available from: URL: https://law s.ilosh.gov.tw/ioshcustom/Web/YearlyReserachReports/Detai l?id=2733 [in Chinese]
- 15) National Institute for Occupational Safety and Health (NI-OSH). Manual of Analytical Methods (NMAM). In: Elements by ICP (Aqua Regia Ashing). Fourth Edition. Cincinnati(OH): NIOSH; 2003. p. 1-5.
- 16) Matczak W, Chmielnicka J. Relation between various chromium compounds and some other elements in fumes from manual metal arc stainless steel welding. Br J Ind Med 1993; 50(3): 244-251.
- 17) Cena LG, Chisholm WP, Keane MJ, et al. Size distribution and estimated respiratory deposition of total chromium, hexavalent chromium, manganese, and nickel in gas metal arc welding fume aerosols. Aerosol Sci Technol 2014; 48(12): 1254-1263.
- 18) Topham N, Kalivoda M, Hsu YM, et al. Reducing Cr<sup>6+</sup> emissions from gas tungsten arc welding using a silica precursor. J Aerosol Sci 2010; 41(3): 326-330.
- Berlinger B, Náray M, Sajó I, et al. Critical evaluation of sequential leaching procedures for the determination of Ni and Mn species in welding fumes. Ann Occup Hyg 2009; 53(4): 333-340.
- 20) Navy BMR. Welding Costs. [Online]. 2013 Available from: URL: http://navybmr.com/study%20material/14251a/14251A \_ch5.pdf
- 21) Graczyk H, Lewinski N, Zhao J, et al. Characterization of tungsten inert gas (TIG). Ann Occup Hyg 2016; 60: 205-219.
- 22) Spear JE. Fume and gas exposure. [Online]. 2011 Available from: URL: http://jespear.com/Publications/welding.pdf
- 23) Lehnert M, Pesch B, Lotz A, Weldox Study Group, et al. Exposure to inhalable, respirable, and ultrafine particles in welding fume. Ann Occup Hyg 2012; 56(5): 557-567.
- 24) Yoon CS, Paik NW, Kim JH, et al. Total and soluble metal contents in flux-cored arc welding fumes. Aerosol Sci Technol 2009; 43(6): 511-521.
- 25) Taube F. Manganese in occupational arc welding fume-aspect on physiochemical properties, with focus on solubility. Ann Occup Hyg 2013; 57(1): 6-25.
- 26) Health Canada. Slope factors for carcinogens from Health Canada. [Online]. 2007 Available from: URL: http://www.pop stoolkit.com/tools/HHRA/SF\_HealthCanada.aspx
- 27) United States Environmental Protection Agency. Slope factors for carcinogens from US EPA. [Online]. 2007 Available from:

URL: http://www.popstoolkit.com/tools/HHRA/SF\_USEPA.a spx

- 28) The Risk Assessment Information System. Toxicity profiles: formal toxicity summary for nickel and nickel compounds. [Online]. 1998 Available from: URL: https://rais.ornl.gov/tox/ profiles/nickel\_and\_nickel\_compounds\_f\_V1.html
- 29) United States Environmental Protection Agency. Benchmark dose technical guidance. [Online]. 2015 Available from: URL: https://www.epa.gov/risk/benchmark-dose-technical-guidance
- Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm 2016; 7(2): 27-31.
- 31) United States Environmental Protection Agency. Guidelines for Carcinogen Risk Assessment. [Online]. 2005 Available from: URL: https://www.epa.gov/sites/production/files/2013-0 9/documents/cancer\_guidelines\_final\_3-25-05.pdf
- 32) Directorate-General Budget, Accounting and Statistics, Taiwan. Statistics of average employee working hour per month of industry sector of Taiwan. [Online]. 2016 Available from: URL: https://www.dgbas.gov.tw/ct.asp?xItem=39398&ctNode =3103 [in Chinese]
- 33) Ministry of Labor. The annual working hours of workers have been declining in Taiwan. [Online]. 2016 Available from: URL: https://www.mol.gov.tw/announcement/2099/29849/
- 34) Ministry of Labor. Chapter VI Retirement, Article 54, In: Labor Standards Law. [Online]. 2016 Available from: URL: htt p://law.moj.gov.tw/Eng/LawClass/LawAll\_print.aspx?PCode= N0030001
- 35) United States Environmental Protection Agency. Metabolically derived human ventilation rates: a revised approach based upon oxygen consumption rates. [Online]. 2009 Available from: URL: https://cfpub.epa.gov/ncea/risk/recordisplay.c fm?deid=202543
- 36) Barkhordari A, Zare Sakhvidi MJ, Zare Sakhvidi F, et al. Cancer risk assessment in welder's under different exposure scenarios. Iran J Public Health 2014; 43(5): 666-673.
- 37) Hewitt PJ. Strategies for risk assessment and control in welding: challenges for developing countries. Ann Occup Hyg 2001; 45(4): 295-298.
- 38) Ministry of Labor. Workforce in Taiwan. [Online]. 2018 Available from: URL: http://statdb.mol.gov.tw/html/nat/10500 1%e8%a1%a83.pdf [in Chinese]
- 39) Taiwan cancer registry. Cancer incidence and mortality rates in Taiwan. [Online]. 2018 Available from: URL: http://tcr.cph. ntu.edu.tw/main.php?Page=N2
- 40) Antonini JM, Lewis AB, Roberts JR, et al. Pulmonary effects of welding fumes: review of worker and experimental animal studies. Am J Ind Med 2003; 43(4): 350-360.
- 41) The Welding Institute. Control of welding fume. [Online]. 2018 Available from: URL: https://www.twi-global.com/techn ical-knowledge/job-knowledge/health-safety-and-accident-pre vention-control-of-welding-fume-032/
- 42) Keane M, Siert A, Stone S, Chen BT. Profiling stainless steel welding processes to reduce fume emissions, hexavalent chromium emissions and operating costs in the workplace. J Occup

Environ Hyg 2016; 13(1): 1-8.

- 43) Saunders CJ, Pocock D, Carter G. Controlling gas shielded arc welding fumes using an on-gun extraction system. Int J Vent 2016; 29(1): 77-82.
- 44) Ministry of Labor. Working Environment Monitoring Implementation Act. [Online]. 2018 Available from: URL: https://la ws.mol.gov.tw/FLAW/FLAWDAT0201.aspx?lsid=FL015045 [in Chinese]
- 45) Ministry of Labor. Standards of Permissible Exposure Limits of Airborne Hazardous Substances in Workplace, 2010. [Online]. 2018 Available from: URL: https://law.moj.gov.tw/Eng/ LawClass/LawContent.aspx?PCODE=N0060004
- 46) Sakurazawa H, Iwasaki A, Higashi T, Nakayama T, Kusaka Y. Assessment of exposure to magnetic fields in occupational settings. J Occup Health 2003; 45(2): 104-110.
- 47) Bullock WH, Ignacio JS. A strategy for assessing and managing occupational exposures. In: establishing the exposure assessment strategy. (3rd ed.). Fairfax, Virginia: American Industrial Hygiene Association; 2006. p. 15-20.
- 48) Leidel NA, Busch KA, Lynch JR. Occupational exposure sampling strategy manual. In: exposure measurement sampling strategy. Cincinnati, Ohio. U.S. Department of Health and Hu-

man Services, NIOSH 77-179; (1977). p. 33-45.

- 49) Ministry of Labor. Occupational Safety and Health Act. [Online]. 2018 Available from: URL: https://laws.mol.gov.tw/En g/FLAWDAT01.aspx?lsid=FL015013
- 50) United States Department of Labor. Occupational Safety and Health Administration. Respiratory protection. [Online]. 2018 Available from: URL: https://www.osha.gov/Publications/osh a3079.pdf
- 51) Chinese National Standard (CNS). Guidance for selection, use and maintenance of Method for respirator selection, use and maintenance of respiratory protective devices (CNS 14258 Z 3035). 1998. Bureau of Standards, Metrology and Inspection of the Ministry of Economic Affairs. R.O.C. [in Chinese]
- 52) Ministry of Health and Welfare. Statistic data: body weight of adult (19-64 years old) of Taiwan area from 2005-2008 nutrition and health surveys. [Online]. 2016 Available from: URL: https://dep.mohw.gov.tw/DOS/cp-1720-7366-113.html [in Chinese]
- 53) Ministry of the Interior. Statistic data: rank of life expectancy at birth by country. [Online]. 2016 Available from: URL: http s://goo.gl/ry3p8D [in Chinese]