Mortality Among Hardmetal Production Workers

Occupational Exposures

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Objective: To generate quantitative exposure estimates for use in retrospective occupational cohort mortality studies of the hardmetal industry. **Methods:** Job-exposure matrices (JEMs) were constructed for cobalt, tungsten, and nickel over the time period 1952 to 2014. The JEMs consisted of job class categories, based on job titles and processes performed, and exposure estimates calculated from available company industrial hygiene measurements. **Results:** Exposure intervals of one-half order magnitude were established for all three agents. Eight job classes had significantly decreasing time trends for cobalt exposure; no significant time trends were detected for tungsten or nickel exposures. **Conclusions:** The levels of exposures determined for this study were similar to or lower than those previously reported for the hardmetal industry during the 1952 to 2014 study period.

Tungsten carbide (WC) with cobalt (Co), referred to as cemented carbide or hardmetal, is WC bound with a Co matrix. Hardmetal tools are used in machining and mining operations for their hardness and wear resistance. The Co content can vary from 3 to 30 weight percent depending on the end application, and other trace elements (eg, titanium, niobium, tantalum, nickel, chromium, molybdenum, and vanadium) may be added to the hardmetal mixture to impart specific properties.[1] Nickel (Ni) may also be used as a binding agent, alone or in conjunction with Co. The main processes in the production of hardmetal tools involve powder blending and pressing, forming, and shaping of tools, followed by tool sintering and finishing operations such as grinding, honing, sandblasting, and coating.

Prior occupational epidemiological studies of hardmetal manufacturing plants indicated a possible association between WC with Co (WCCo) exposure and lung cancer.[2–5] The findings from these studies, however, were limited by the small number of workers included, narrow industry representation (eg, one country or one company included in each study), few lung cancer deaths observed, and assessment of exposures using broad classes and limited data. The University of Illinois at Chicago (UIC) and the University of Pittsburgh (UPitt) were contacted by the International Tungsten Industry Association (ITIA) about the possibility of conducting a larger, more comprehensive mortality study to further examine the potential relationship between hardmetal industry exposures and lung cancer mortality.

Starting in 2008, UIC and UPitt conducted site visits at 14 United States (US) and nine European plants operated by three different companies to review available work history and industrial hygiene (IH) records and observe plant operations. Twelve US plants were initially deemed suitable for study inclusion; further work history record review restricted eligibility to eight US sites due to incomplete records from four plants. International sites in Austria ($n = 1$), Germany ($n = 3$), Sweden ($n = 3$), and the United Kingdom ($n = 2$) were also included in the study. Due to differing languages and country-specific regulations, principal investigators (PIs) were retained for each country and they shared their anonymized collected work history and IH data with the US. The occupational exposure reconstruction component of the study was led by UIC, and UPitt led the epidemiological and biostatistical component.

As is often encountered in occupational exposure reconstructions, there was limited IH data available for some operations and years. Therefore, due to the similarity of operations across countries, companies, and plants, all IH data from the initially included 12 US plants along with the IH data collected from the nine European plants were used in the reconstruction. The intent of this approach was not only to provide a greater number of IH measurements overall for generating the exposure estimates, but also the ability for the same estimates to be applied to a pooled cohort mortality analyses of all US and European workers combined.[6]

The details of the US-only cohort and case-control mortality analysis using the exposure estimates presented here are described elsewhere.[7] Briefly, the US cohort ($n = 7{,}304$) includes all individuals employed at any of eight US hardmetal sites for at least one day or more from 1952 (earliest US epidemiological observation year) through 2008 (last year of US work histories collected). The subjects contributed 166,941.2 person-years of observation during the 1952 to 2012 (last year of mortality follow-up) study observation period.

The process/job categories (ie, job classes) presented here were also used in a hardmetal mortality study conducted by the United Kingdom investigators and detailed elsewhere.[8] Investigators from Austria, Germany, and Sweden conducted independent exposure assessments for their cohort mortality studies using their country-specific IH data; these methods and results are described in separate reports.[9–12]

METHODS

Job-exposure matrices (JEMs) were formed for Co, tungsten (W), and Ni. The JEMs consisted of job dictionary classes and the exposure estimates generated from the available IH measurements. While there are concurrent exposures to, depending on the process step, carbon black, WC, and WCCo, there were no measurements specifically for these compounds, therefore they were not considered individually.

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Nickel is used as a binding agent or trace element in hardmetal formulations, but it is possible that Ni was present in certain materials aside from hardmetal (eg, in other alloys to which hardmetal inserts were attached). However, it was not possible to delineate hardmetal Ni exposures from potential non-hardmetal Ni exposures for each job class based solely on the IH measurements. Because Ni was known to be used as a binding agent or trace element, Ni was present at all plants (determined from known use or from available Ni measurements), Ni was not included in prior hardmetal epidemiological studies conducted,[2–5] and its inclusion has been previously recommended to evaluate cancer risk in the industry,[13] Ni exposures were assessed in this study using the available IH measurements.

Job Dictionary

Because UIC performed the exposure reconstruction component of the overall mortality study and not the epidemiological and biostatistical component, all work history information used by UIC was anonymized. Work history records were collected and abstracted by UPitt for the US sites; European PIs performed this task for their study sites. The work history records included all jobs held by each individual in the cohort over time. After collection of US work history records by UPitt, UIC received anonymized unique work history line combinations generated from the US records by UPitt. These data lines were based upon the following fields: job title, job code, grade, department title, department code, division, plant, location name, and location code. Prior to analyzing the IH data, US and European investigators formed job dictionary classes based upon familiarity with plant operations and worker tasks, consideration of potential exposures, and review of anonymized work history line combinations. Job dictionary classes were combined as warranted based upon the subsequent IH data analyses.

Table 1 shows the resulting job dictionary classes along with the number of individuals in each job class and the number of working-years contributed to each job class; all counts are through December 31, 2008. Plant-, company-, or country-specific processes were grouped into separate job class categories. The job class codes were assigned to the lines in each individual's work history by the country-specific investigators via programmatic or manual assignment, or a combination of both, to provide the necessary link to the exposure estimates in the JEMs. These assignments accommodated both the US mortality analyses[7] and pooled US and European mortality analyses.[6] There were 45 individuals in the US cohort for whom there was no identifying information in their work history to allow a precise job class assignment; these individuals were assigned job class 95 (unknown) and were not included in UPitt's exposure–response analysis.[7]

Industrial Hygiene Data

All electronic and hard copy IH records collected from the 21 US and European plants were abstracted into an Excel database by the country-specific investigators. A field for job class designation was also included so that the measurements could be more easily utilized in UIC's analyses. Because personal samples are better representative of worker exposure than are area samples,[14,15] only personal samples were used in the exposure reconstruction.

Particle Size Considerations

The countries in this study utilized different sampling devices to collect measurements, therefore the fractions collected, the properties of the aerosols collected, and the processes performed had to be considered. Generally, the US, Austria, and Sweden collected total aerosol, United Kingdom collected the inhalable fraction, and Germany collected both the inhalable fraction and total aerosol. The most common devices used were closed-faced cassettes (CFCs) and open-faced cassettes (OFCs) (Sweden only) for capturing total aerosol and the Institute for Occupational Medicine (IOM) sampler for capturing the inhalable fraction.

Across several industries inhalable mass has been found, somewhat counter-intuitively, to be greater than total mass.[16–19] Reported differences between the IOM sampler and 37 mm CFC are approximately 1.0 to 4.0 times depending on the substance measured and the process being performed.[17–20] In the 37 mm CFC, this observation has been attributed to sampler wall particle adhesion[21] and inefficient capture of larger particles (less than 50% efficiency for particles more than 20.0 μm).[22] The IOM sampler may collect particles more than 100.0 μm due to diameter (15 mm) and orientation of the sampler inlet and may also passively collect particles.[18,19,21,23] Additionally, IOM sampler collection efficiency increases for these larger particles as wind speeds increase[23] over velocities observed in workplaces (~0.1 to 1.0 m/s).[24] There are limited published data regarding the relationship between CFCs and OFCs, however, one paper reported a mean ratio difference of 1.3 between 37 mm OFCs and CFCs for total aerosol (ie, 30% greater mass collected by OFCs compared with CFCs).[25]

While there were no particle size-specific data found within any countries' IH data, there was a limited set of data that was obtained from one European study plant. The data included cascade impactor measurements taken during spray drying and particle counting measurements taken during pressing, coating, and laboratory operations. Mass and count median aerodynamic diameters for the measured operations were calculated using the procedure described by Hinds.[26] Cascade impactor data showed that the mass median aerodynamic diameters of the sampled particles were small (less than 3.5 μm) for total aerosol and for the Co and W components; count median aerodynamic diameters were even smaller (data not shown). Although production of special ultrafine and ultracourse hardmetal grades is possible, the common range of particle sizes for WC powder has been cited as 0.15 to 12.0 μm, and 1.0 to 5.0 μm for Co binders.[1] The mass and count mean aerodynamic diameters calculated here agree with these reported size ranges.

Total aerosol and inhalable fraction parallel sampling at Swedish study plants by the Swedish researchers reported an almost 1:1 relationship between inhalable and total Co stationary area measurements (Spearman correlation coefficient $\rho = 0.893$).[27] The highest correlation in their parallel sampling was between total Co aerosol and Co PM_{10} (particles with aerodynamic diameter less than or equal to 10.0 μm) (Spearman $\rho = 0.945$). Correlations were not reported for personal measurements, however, the area results indicate that mass-based differences between simultaneously measured total and inhalable Co is small.

Because of the different sampling instruments used to collect measurements (primarily inhalable samplers, CFCs, and OFCs), a check of the sensitivity of exposure estimates generated in this study to changes related to these instruments was performed. Four job classes were tested using adjustments to personal Co measurements under four conditions based upon differences between inhalable and total aerosol samplers and between OFC and CFC samplers reported in the literature[17–20,25]: (1) a correction factor of 1.5 applied to inhalable measurements (ie, a reduction of 33.0%); (2) a 3.0 correction factor applied to inhalable measurements; (3) a 3.0 correction factor applied to inhalable measurements in conjunction with a 30.0% reduction applied to OFC measurements; and (4) a 5.0 correction factor applied to inhalable measurements. The exposure intervals were not sensitive to the corrections up to a factor of 5.0 (condition 4), a fairly extreme correction factor, and only one job class tested was affected at that level (data not shown). These results indicated that the application of any adjustments for inhalable

TABLE 1. Job Dictionary Classes with Number of Individuals and Working-Years by Country*

Job Class Number and Name‡		Number of Workers in Job Class†						Working-Years§ (All Workers)
		US	Austria	Germany	Sweden	United Kingdom	Total	
Background and support operations								
00	Background (office, administration, etc.)	1,187	245	623	1,912	248	4,215	31,062
01	Laboratory/Research and development	238	144	32	1,901	110	2,425	10,817
02	Supervisory (foreman, production supervisor, etc.)	487	319	0	297	4	1,107	8,280
03	Engineering	433	59	0	413	63	968	6,306
04	Maintenance (electrician, custodian, mechanic, etc.)	1,912	88	495	3,341	136	5,972	32,180
05	Material handling	497	30	2,218	508	34	3,287	20,447
06	Assembly	21	0	0	986	3	1,010	5,578
07	Marking and packing	582	50	200	1,414	19	2,265	8,912
08	Inspection	711	189	823	808	47	2,578	15,646
General production operations								
09	Powder weigh	21	0	8	8	0	37	171
10	Powder mix	1	0	248	0	0	249	2,092
11	Powder sieve	1	0	0	0	0	1	0
12	Pelletize	42	0	0	2	0	44	194
13	Powder package	0	0	2	10	0	12	85
14	Press set-up	107	39	0	83	80	309	2,195
15	Press	1,028	146	883	1,285	73	3,415	14,544
16	Shape	497	224	209	20	37	987	7,100
17	Extrude	39	174	73	5	24	315	1,493
18	Cold isostatic press (CIP)	13	3	37	3	36	92	393
19	Furnace set-up	96	0	9	0	3	108	453
20	Furnace	466	147	402	179	65	1,259	8,323
21	Computerized numerical control (CNC) operation	151	0	266	28	24	469	2,074
22	Hone	343	35	0	637	2	1,017	5,037
23	Grind	1,503	345	1,657	2,122	137	5,764	35,338
24	Slow operations (bore, drill, etc.)	48	175	0	581	25	829	2,939
25	Electro-discharge machining (EDM)	14	8	0	9	2	33	163
26	Blast	84	16	121	89	1	311	1,080
27	Coat	341	60	283	561	5	1,250	7,272
Powder production operations								
28	Ball mill	35	0	0	1	0	36	191
29	Fitz mill	0	0	0	0	0	0	0
30	Attritor	0	0	0	0	0	0	0
31	Spray dry	44	0	0	61	31	136	733
32	Mill and spray dry (combined tasks)	188	0	0	0	0	188	714
33	Ammonium paratungstate (APT) process	0	0	29	0	0	29	150
34	Thermit process	304	0	0	0	0	304	1,133
Additional operations								
35	Weld (parts)	72	0	0	0	0	72	342
36	Braze	539	3	0	120	1	663	2,795
39	Powder room operations (weigh, mill, and dry powder)	302	101	0	0	128	531	2,530
40	Ceramic grind	3	0	16	0	0	19	45
41	Ceramic weigh	0	0	62	1	0	63	404
42	Dry grind	6	0	593	0	0	599	2,401
43	Recycling (scrap material)	66	0	0	0	20	86	410
44	Mechanical production (steel production of toolholders)	892	0	252	0	0	1,144	5,410
45	Graphite (graphite tray cleaning and servicing)	7	6	4	0	0	17	51
46	Heavy metal powder (tungsten plus cobalt or other binder)	0	0	20	631	0	651	1,124
47	Medical engineering (medical implants and dental alloys)	0	0	98	0	0	98	758
50	Press/form/sinter (combined tasks)	0	0	0	34	0	34	101
51	Hone/coat (combined tasks)	0	0	0	0	0	0	0
52	Tungsten carbide powder production unspecified	9	0	0	176	33	218	845
53	Tungsten production	0	0	0	821	0	821	1,291
54	Carbon production	0	0	0	0	0	0	0
55	Tungsten carbide parts production unspecified	631	0	0	136	130	897	3,254
56	Rolls unspecified‖	0	0	0	78	0	78	215
57	Rolls press	0	0	0	10	0	10	139
58	Rolls shape	0	0	0	5	0	5	39
59	Rolls sinter	0	0	0	6	0	6	74
60	Rolls grind	0	0	0	10	0	10	143
61	Rolls inspect/pack	0	0	0	0	0	0	0
62	Hydrogen gas production	0	0	0	83	0	83	295
63	Ceramic other (ceramic tasks other than weigh and grind)	0	0	0	76	0	76	256
64	Tungsten carbide parts or powder production unspecified	95	0	0	1,411	281	1,787	13,846
65	Foundry operations	34	0	0	0	0	34	171
66	Tube milling (welding rods loaded with tungsten carbide)	6	0	0	0	0	6	16
75	Blue collar worker (tasks unspecified)	0	0	659	0	0	659	9,100
85	Leave of absence, out of plant	207	69	780	0	3	1,059	2,907
95	Unknown¶	45	0	0	0	218#	263	3,058
	Total	14,348	2,675	11,102	20,862	1,805	51,010	285,112

*All counts of individuals and working-years through 12/31/2008 only.
†Individuals may have more than one job over time and thus be counted in more than one job class.
‡Job class 37 was combined with class 65 and job classes 38, 48, and 49 were combined with class 85 due to class similarity/overlap.
§Working-years is the total time all individuals were employed in the job class.
‖Job classes 56–61 refer to special production operations for huge rolls rather than standard hardmetal parts.
¶Only one job per person and no identifying work information.
#Does not include 118 United Kingdom workers due to lack of valid work date information.

versus total aerosol or CFCs versus OFCs would not have a marked effect on the exposure intervals generated for the job classes.

Based upon the available data specific to this study and the reported literature, the determination was made to use both total aerosol and inhalable fraction measurements without correction because total and inhalable sampler collection differences become pronounced at much larger particle sizes (ie, at approximately 20.0 μm)[22] than observed here and because the exposure intervals were insensitive to rather large correction factors.

Exposure estimates relating to the respirable size fraction were not pursued due to limited respirable data overall and the limited number of processes/tasks measured ($n = 126$ for all Co, W, and Ni respirable measurements combined; $n = 67$ for all personal Co, W, and Ni measurements combined taken across nine job classes). While this is an important fraction with regard to lung disease, the insufficiency of the data did not allow the direct use of respirable measurements. Modeled respirable data could not be pursued because process-specific operational data were not available to estimate generation rates. Lacking process/engineering data and having minimal respirable measurements, any exposure estimates related to the respirable fraction would have been pure conjecture. The error introduced from the conjecture would be more drastic than from not considering this fraction.[28]

Sampling Time

One issue with IH data is varying sampling times, which arises from the combination of short task-based measurements (a few minutes to a few hours) and full-shift measurements (from a few to 8 hours or more) in the dataset. Task-based measurements are generally collected for purposes other than determining exposures across an entire shift, for example, to assess high exposure tasks, to evaluate the function of an installed or repaired ventilation system, or to assess exposures from a new or modified process. Tasks that are routinely performed and result in ''peak'' exposures would be monitored in workers' full-shift measurements. Because the goal of the study was not to quantify peak exposures specifically, but rather to generate exposure estimates reflective of full-shift conditions encompassing all tasks performed, task-based measurements were excluded from the IH data analyses.

In order to assess whether or not personal non-task based measurements of varying duration could be combined in the exposure analyses, the relationships of sampling time to year of measurement and to reported concentration were examined. These relationships were assessed by Pearson correlation coefficient ($|\rho|$) in Minitab 17[29] to determine if measurements taken in earlier study years were of significantly shorter duration than in later study years, and if shorter duration measurements had significantly higher concentrations than longer duration samples. There were measurements in the Austrian dataset with sampling times listed as 480 minutes for full-shift samples instead of the precise sampling times. Due to the uncertainty surrounding these sampling times, the Austrian measurements were excluded from the sampling time evaluations, as were any measurements without a sampling time indicated.

Due to its right-skewed characteristics most environmental data are best represented by a lognormal distribution,[30] and this was assumed for evaluating sampling time relationships. (Measurement concentrations given as less than the limit of detection (LOD) were included as LOD/2 for Pearson correlation tests.) Of the agent and job class combinations examined, the highest correlation coefficient for sampling time versus year of measurement was for personal Co measurements taken during powder milling and spray drying operations (job class 32; $|\rho| = 0.567$). All other values were lower and ranged from 0.090 to 0.195. The highest correlation detected for measured concentration versus sampling time was for personal W measurements taken during pressing (job class 15; $|\rho| = 0.427$). All other correlation coefficients were lower, ranging from 0.026 to 0.253.

After confirming no measurements required exclusion due to sampling time, the IH data to be used for generation of the exposure estimates were tested for lognormality using the Ryan-Joiner correlation test. (Measurements given as less than the LOD were included as LOD/2.) Measurements for all agents, individually and cumulatively, were statistically lognormal (all correlations more than 0.9 at $\alpha = 0.05$; all $P < 0.01$). The IH measurements were, therefore, log-transformed for all exposure estimate analyses.

Hierarchical Exposure Estimation Approach

The important parameter in epidemiological studies is to obtain a valid measure of exposure ranks rather than physically defined absolute exposure levels. With that parameter in mind, the objective of the IH data analysis was to generate median yearly exposures over time for each job class that could then be used to determine ranked exposure intervals for each class over time.

In order to generate the median yearly exposures, the presence or absence of significant time trends had to first be determined. The measurements were sorted by agent, job class, and year. At least 10 data points, of which at least five were not censored (below the LOD), were required for each ''year'' category so that the overall censoring level for each year category was less than or equal to 50.0%. To help lessen the likelihood that trends would be detected by chance, time trend analysis required 5 valid year categories.

Potential biases may arise when estimates for highly censored datasets are generated using substitution (eg, replacement of censored values with zero, LOD/2, LOD/$\sqrt{2}$, or the LOD) or regression-based methods.[31,32] Therefore, each year category was analyzed by censored data analysis (CDA), using a maximum likelihood estimation (MLE) of censored data as described by Cohen,[33] in Excel to determine the year category's median exposure value. Regression was then performed in Minitab 17[29] on concentration (median) over time (years) to determine the presence of any time trends. If no significant time trend was detected, or there was insufficient data to meet the specified requirements for time trend analysis, then all available data for a job class was analyzed using CDA to generate an overall job class median applicable to all study years 1952 to 2014, where 1952 is the earliest US epidemiological observation year and 2014 is the latest year of European work history records collected. There were limited measurements available for some job class and agent combinations. In these cases, job classes were combined for the exposure analyses. For example, measurements for job classes 11 (powder sieve) and 12 (pelletize) were combined for all agent exposure analyses, whereas measurements for job classes 19 (furnace set-up) and 20 (furnace) were combined for W and Ni exposure analyses only.

Figure 1 summarizes the hierarchical approach employed for the analysis of the available IH measurements in order to generate median yearly exposure estimates for each job class. Exposure intervals were defined in an iterative process. After CDA was performed for several job classes, the resulting estimates were used to define intervals at convenient bandwidths that helped minimize potential exposure misclassification.[34] Job classes were then assigned to the corresponding interval either annually (for significant time trends) or over all study years (for non-significant time trends).

Despite the large number of personal measurements available in the pooled dataset from the five countries and 21 sites (Co = 6,175; W = 1,023; Ni = 1,138), there were still some job class and agent combinations that had extremely limited (fewer than three measurements or all available measurements censored) or no measurements. These classes were, therefore, assigned to an exposure interval using professional judgment based on knowledge of the operations and worker exposure potential.

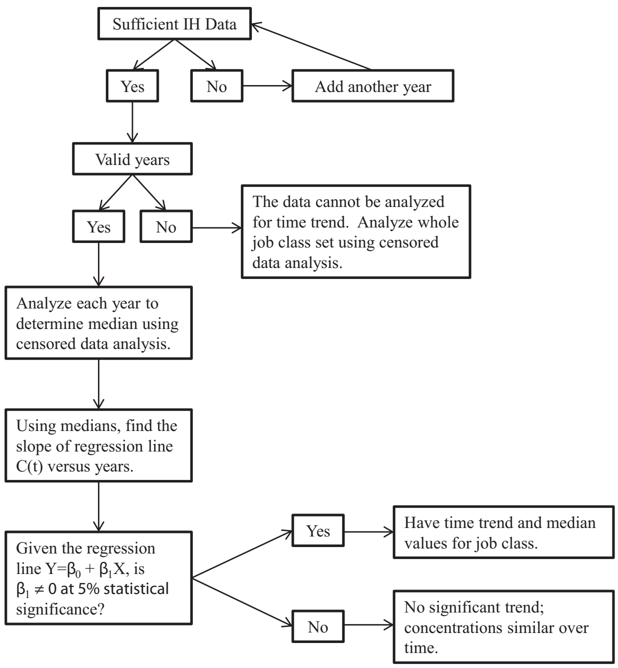

FIGURE 1. Hierarchical approach used for the analysis of industrial hygiene measurements.

RESULTS

The exposure intervals established for Co, W, and Ni are given in Table 2. The interval midpoints are the values applied to the JEMs for use in UPitt's exposure-related analyses.[6,7] Job classes with sufficient data according to the hierarchical approach presented in Fig. 1 were tested for the presence of time trends. Those classes without sufficient data were analyzed as a set.

The resulting Co, W, and Ni exposure intervals for all job classes with and without sufficient data for time trend testing are shown in Table 3; job classes assigned by professional judgment are indicated. Where time trends were tested, the corresponding *P* values for non-significant trends are shown. Among the three agents, there were 19 job classes tested for a time trend for Co, six classes for W, and one for Ni. Eight Co classes had significant time trends.

Table 4 shows the exposure intervals for job classes with significant Co time trends and lists the range of years at each interval. For example, job class 23 (grind) experienced a Co exposure interval of 0.01 to less than 0.05 mg/m^3 during the years 1952 to 1983, an exposure interval of 0.005 to less than 0.01 mg/m^3 during the years 1984 to 2001, and an exposure interval of 0.001 to less than 0.005 during the years 2002 to 2014.

DISCUSSION

Particle sizes larger than 18.0 μm for some hardmetal operations such as scrap reclamation and pressing have been reported.[35,36] Other studies found generally small particles sizes (well below 20.0 μm) for the operations characterized,[37–42] and these studies agree with the particle sizes given by Lassner and Schubert[1] as common to the hardmetal industry and with the particle sizes determined from the data available for this study. Because differences between inhalable samplers and 37 mm CFCs are most pronounced for particle sizes greater than 20.0 μm,[22] the particle sizes encountered in hardmetal operations are relatively small, and the exposure interval analyses performed here are insensitive to correction factors applied to individual IH measurements, the determination not to apply corrections for total aerosol/inhalable fraction measurements or CFC/OFC measurements in this study is supported.

The exposure intervals generated for this study are based on IH measurements from the hardmetal study plants and are quantitative in relation to one another; each interval is one-half order of magnitude different from the intervals above and below. Because the intervals are quantitative, they may be compared generally with other published exposure values and limits. With the exception of the lower geometric means of five Co and two W job classes reported in 2016 for measurements recently performed,[27] the Co, W, and Ni exposure intervals assigned to cohort members here are similar to or lower than other published values from the hardmetal industry.

Breathing zone total aerosol Co samples were taken by the Occupational Safety and Health Administration (OSHA) in 1981 at a hardmetal plant.[43] The measurements ranged from 0.01 to 0.1 mg/m^3 for lathe room machinists; an inspector in the furnace room had an exposure of 0.014 mg/m^3. Personal total aerosol Co measurements in a 1983 study found geometric mean concentrations ranging from 0.018 mg/m^3 during sintering to 1.29 mg/m^3 during dry grinding.[44] Mean Co concentrations for personal total aerosol samples reported in a 1985 study ranged from 0.028 mg/m^3 for sintering to 0.367 mg/m^3 for rubber press operations.[45] Short-term (45 to 60 minute) personal total aerosol Co concentrations were collected for a 1985 study; two of the 26 measurements exceeded the 1985 TLV of 0.1 mg/m^3 and 10 exceeded the 1985 recommended TLV change standard of 0.05 mg/m^3.[46] All of the 12 measurements over the two TLV values were taken during forming and hand pressing operations. A 1986 study reported mean total aerosol Co concentrations ranging from 0.003 mg/m^3 for blasting operations to 1.29 mg/m^3 for dry grinding, though it was noted that one of the two grinder operators sampled had an extremely high measurement which decreased after local exhaust ventilation was installed.[40]

Single personal total aerosol Co measurements taken during four operations at one hardmetal plant were 0.023 mg/m^3 for powder mixing and 0.029 mg/m^3 for cutting; measurements for pressing and grinding/boring were less than the detection limit.[39] A 1989 study of three hardmetal factories reported personal total aerosol Co arithmetic mean concentration ranges of 0.045 to 0.272 mg/m^3 for powder operations, 0.03 to 0.22 mg/m^3 for pressing, 0.06 to 0.16 mg/m^3 for forming, and 0.03 to 0.21 mg/m^3 for finishing operations.[47] Hardmetal grinders monitored in 1992 had total aerosol geometric mean concentrations of 0.013 and 0.001 mg/m^3 for Co and Ni, respectively.[38]

Scansetti et al[48] collected short-term personal total aerosol measurements in 1987. Mean Co concentrations ranged from less than or equal to 0.05 mg/m^3 for warehouse, grinding, and furnace

TABLE 2. Exposure Intervals for Cobalt, Tungsten, and Nickel

Interval	Interval Width (mg/m^3)	Interval Midpoint* (mg/m^3)
0	0 (outside plant)	
1	<0.0001	
2	0.0001 to <0.0005	0.0003
3	0.0005 to <0.001	0.00075
4	0.001 to <0.005	0.003
5	0.005 to <0.01	0.0075
6	0.01 to <0.05	0.03
7	0.05 to <0.1	0.075
8	0.1 to <0.5	0.3
9	≥0.5	

*Interval midpoint is the numerical value used in the job exposure matrices and epidemiological exposure-related calculations.

TABLE 3. Time Trend Testing and Exposure Intervals by Job Class

Job Class Number and Name*		Cobalt Exposure Interval	Tungsten Exposure Interval	Nickel Exposure Interval
Background and support operations				
00	Background (office, administration, etc.)	3	4†	3†
01	Laboratory/Research and development	NS ($P = 0.393$); 4‡	7	4
02–03	Supervisory, engineering	4	5	4†
04	Maintenance (electrician, custodian, mechanic, etc.)	NS ($P = 0.680$); 5	8	5
05	Material handling	4	4	4
06	Assembly	4†	4	4
07	Marking and packing	4	4	4
08	Inspection	4	4	4
General production operations				
09	Powder weigh	NS ($P = 0.378$); 6	NS ($P = 0.171$); 8	NS ($P = 0.951$); 5
10	Powder mix	6	8	5
11–12	Powder sieve, pelletize	NS ($P = 0.383$); 6	8	5
13	Powder package	NS ($P = 0.186$); 6	6	5
14	Press set-up	NS ($P = 0.354$); 5	6	5
15	Press	Significant TT§	NS ($P = 0.891$); 6	5
16	Shape	Significant TT	NS ($P = 0.302$); 7	5
17	Extrude	6	7	5†
18	Cold isostatic press (CIP)	NS ($P = 0.053$); 6	7	5
19	Furnace set-up	6	8	4
20	Furnace	Significant TT	8	4
21	Computerized numerical control (CNC) operation	Significant TT	6	4
22	Hone	4	6	4
23	Grind	Significant TT	NS ($P = 0.593$); 6	4
24	Slow operations (bore, drill, etc.)	4	7	4
25	Electro-discharge machining (EDM)	4	7†	4†
26	Blast	4	7†	4†
27	Coat	3	4	3†
Powder production operations				
28–30	Powder milling processes (ball mill, Fitz mill, attritor)	Significant TT	8	5
31	Spray dry	NS ($P = 0.065$); 6	NS ($P = 0.157$); 8	5
32	Mill and spray dry (combined tasks)	NS ($P = 0.084$); 7	8	5
33	Ammonium paratungstate (APT) process	3†	8†	3†
34	Thermit process	4	8	6
Additional operations				
35	Weld (parts)	4	4†	4
36	Braze	4	4†	3
39	Powder room operations (weigh, mill, and dry powder)	Significant TT	8	6
40–41, 63	Ceramic processes (weigh, grind, other)	3†	4†	3†
42	Dry grind	5	6	4
43	Recycling (scrap material)	NS ($P = 0.252$); 7	8	5
44	Mechanical production (steel production of toolholders)	4	4†	4
45	Graphite (graphite tray cleaning and servicing)	6	8†	4†
46	Heavy metal powder (tungsten plus cobalt or other binder)	Significant TT	NS ($P = 0.690$); 7	5
47	Medical engineering (cobalt and nickel based steel alloys)	4†	4†	4†
50	Press/form/sinter (combined tasks)	5	6	6
52	Tungsten carbide powder production unspecified	6†	7†	5†
53	Tungsten production	3†	8†	3†
55	Tungsten carbide parts production unspecified	5	6	4
56–61	Rolls processes (press, shape, sinter, grind, inspect)	6	7	6
62	Hydrogen gas production	3†	4†	3†
64	Tungsten carbide parts or powder production unspecified	5	6†	5†
65	Foundry operations	4	4	5
66	Tube milling (welding rods loaded with tungsten carbide)	4	7	4†
75	Blue collar worker (tasks unspecified)	5†	6†	5†
85	Leave of absence, out of plant	0	0	0
	Number of classes with time trend possible	19	6	1
	Number of classes with significant time trend	8	0	0

*Job classes combined for all three agent exposure analyses are in same row.
†Exposure interval assigned by professional judgment due to lack of available industrial hygiene measurements and/or high censoring.
‡Results given as NS (not significant) at $\alpha = 0.05$ with corresponding P value and resulting exposure interval assignment.
§Significant TT, significant time trend; $P < 0.05$.

TABLE 4. Job Classes with Significant Cobalt Exposure Time Trends

Exposure Interval	Interval Width (mg/m³)	Press (JC* 15)	Shape (JC 16)	Furnace (JC 20)	CNC (JC 21)	Grind (JC 23)	Powder Milling (JC 28–30)	Powder Room (JC 39)	Heavy Metal Powder (JC 46)
0	0								
1	<0.0001								
2	0.0001 to <0.0005								
3	0.0005 to <0.001								
4	0.001 to <0.005	2010–2014		2008–2014	2005–2014	2002–2014			
5	0.005 to <0.01	2003–2009	2007–2014	1999–2007	1992–2004	1984–2001			2008–2014
6	0.01 to <0.05	1952–2002	1952–2006	1952–1998	1952–1991	1952–1983	1989–2014	2006–2014	1983–2007
7	0.05 to <0.1						1952–1988	2000–2005	1952–1982
8	0.1 to <0.5							1952–1999	
9	≥0.5								

*Job class.

operations to 0.23 mg/m^3 for pressing. Cobalt exposures were monitored at four hardmetal plants with recent LEV improvements.[49] The geometric means of personal total Co aerosol measurements were 0.751 mg/m^3 for powder weighing, 0.303 mg/m^3 for filling and pressing, 0.248 mg/m^3 for sintering, 0.039 mg/m^3 for sharpening and grinding, and 0.205 mg/m^3 for polishing. Kumagai et al[50] updated a previously monitored[38,40] hardmetal plant in Japan using additional measurements and determining exposures for nine job groups. The personal total aerosol Co geometric means ranged from 0.002 mg/m^3 for blasting and electron discharge machining to 0.233 mg/m^3 for rubber press operations.

Some hardmetal studies stated exposures but did not specify specific tasks performed. Lison et al[51] reported personal total aerosol Co geometric mean concentrations of 0.009 and 0.019 mg/m^3, Scansetti et al[37] reported personal total aerosol concentrations ranging from 0.005 to 0.092 mg/m^3 for Co and 0.004 to 0.247 mg/m^3 for Ni, and Torra et al[52] reported personal total aerosol Co concentrations ranging from 0.079 to 0.13 mg/m^3 with a mean of 0.1 mg/m^3.

In 2007, 11 area samples taken at approximately breathing height across six process areas using a 10-stage impactor yielded Co concentrations ranging from 0.001 mg/m^3 for dry grinding to 0.192 mg/m^3 for scrap loading during scrap reclamation.[36] Personal total aerosol measurements made for a 2009 study found Co geometric means ranging from 0.001 mg/m^3 for powder laboratory operations to 0.126 mg/m^3 for powder mixing, and W geometric means ranging from 0.011 mg/m^3 for sandblasting to 0.432 mg/m^3 for powder screening.[35] Geometric means of personal Co inhalable measurements reported in 2016 ranged from 0.00006 mg/m^3 during inspection to 0.004 mg/m^3 during powder production; the highest and lowest geometric means for W were also during inspection (0.0005 mg/m^3) and powder production (0.05 mg/m^3).[27]

The reported Co exposures experienced by hardmetal workers described above indicate a decline over time, and, though differing among process-specific exposures, were generally higher for pre-sintering operations as opposed to sintering and post-sintering operations, as was observed here. There were too few hardmetal studies that characterized W or Ni to determine whether these exposures decreased over time, however, observation of the general decline of exposures over time has been made in other industries.[53–55]

In this study there were only eight significant decreasing time trends detected, all for Co. An assumption could have been made that hardmetal exposures overall have declined since 1952 due to various implemented risk management measures (eg, ventilation improvements, process enclosures, automation, etc.). However, such measures had various implementation times and depended upon the specific plant, process, and even machine; control information was seldom contained with the IH measurements (less than 20% had ventilation information). Aside from personal protective equipment use, exposure reductions due to ventilation improvements and machine upgrades would have been generally reflected in the values of the personal IH measurements collected over the years. Therefore, no formal corrections were made for risk management measures. Lack of time trend detection does not imply that these measures had no effect on exposures, especially for individual workers. With the available data, however, statistically significant decreases over time for most job classes were not observed. The limited number of IH measurements available for some agent and job class combinations may have contributed to the number of significant trends detected.

The exposure interval estimates generated for Co were above the current American Conference of Governmental Industrial Hygienists (ACGIH) time-weighted average (TWA) threshold limit value (TLV) of 0.02 mg/m^3 (total aerosol, elemental and inorganic compounds)[56] for 13 job classes without time trends (Table 3). Two classes, scrap recycling and milling and drying, had interval 7 exposures (0.05 to less than 0.1 mg/m^3). The other 11 classes, mainly powder production and pre-sintering operations, had interval 6 exposures (0.01 to less than 0.05 mg/m^3). The remaining job classes in Table 3 had Co exposures less than 0.01 mg/m^3 (interval 5 or lower). For the eight job classes with significant time trends, all classes at some point experienced exposure intervals above the current Co TLV during the 1952 to 2014 study period (Table 4). No job classes in Table 3 were above the current 5.0 mg/m^3 TWA TLV for metal and insoluble W compounds (total aerosol)[56]; the highest W exposures were less than 0.5 mg/m^3. The current 1.5 mg/m^3 TWA TLV for elemental Ni is based on the inhalable fraction only.[56] Even assuming all Ni particles in the exposure interval concentrations were inhalable, there are no job classes above the TLV (Table 3). The highest Ni exposures were from 0.01 to less than 0.05 mg/m^3 (interval 6).

In 2016 ACGIH adopted a TLV of 0.005 mg/m^3 (thoracic fraction; as Co) for tungsten carbide and hardmetals containing Co.[56] The available Co data for this study were total aerosol and inhalable fraction measurements, however, minimal differences in collection efficiency among inhalable and thoracic fractions and total aerosol would be expected due to the small particle sizes observed in the hardmetal industry. All job classes with significant Co time trends experienced exposure interval 5 (0.005 to less than 0.01 mg/m^3) or higher at some point during the study period (Table 4), and 19 job classes without significant Co time trends experienced interval 5 or higher exposures (Table 3).

Country-specific investigators assigned job class to the work history lines of their countries' workers. There was the potential for misclassification of workers by assigning the job title/worker to the wrong class given the information present, and it is also possible that investigators from different countries could have assigned the same work history line differently. Because of language and privacy issues it was not possible for all work history lines to be assigned by a common group or person, therefore an attempt was made to reduce job misclassification by having all investigators use common, well-defined job classes during the process.

As is common in many retrospective exposure reconstructions, the study was limited by the extant data, which did not cover all time periods for all operations. In order to improve the coverage, IH measurements from all 12 US and nine European plants were pooled to generate exposure estimates that applied to all facilities. Country-specific investigators assigned job class to the IH measurements, which could have led to potential misclassification in cases where there may not have been enough relevant information to properly classify the measurement. Investigators used all information available and followed up with plant personnel when necessary in order to make the most informed assignment possible. Additionally, while the potential for plant-level exposure variations existed due to factors such as local exhaust ventilation and respirator use, this type of information was absent from the majority (over 80%) of the personal IH measurements thus precluding its consideration.

Due to the scarcity of IH measurements for certain operations and years, exposure intervals were assigned by professional judgment for some job classes as indicated in Table 3. In these cases, knowledge of the process and information from plant personnel were used to help make the most reasonable assignment. To mitigate bias during the entire exposure reconstruction process, UIC had no knowledge of the specific jobs held by any individual US or European worker or, if deceased, their cause of death. Despite the hierarchical approach used to avoid highly censored datasets for generating the exposure estimates, some job classes with limited measurements remained more than 50.0% censored. While it has been recommended not to use MLE CDA for greater than 50.0% censored datasets as a general rule of thumb,[57] simulations have shown satisfactory results using this approach on data similar to the type found in the majority of this study's job classes (ie, lognormally distributed data, sample sizes more than or equal to 5, censoring levels 0% to 80.0%).[31]

It was not possible to determine Co, W, and Ni exposures by particle size fraction, which can differ by operation,[35–37] given the available IH measurements. Because of the varying nature of the work performed in the hardmetal industry (eg, different powder formulations and production schedules), ideally repeated size distribution measurements or side-by-side sampling with different devices made at all study sites and processes under consideration would be obtained in order to determine any necessary process-specific correction factors. Applying a universal correction factor to change from one fraction to another, such as that suggested for conversion of total metalworking fluid aerosol to the thoracic fraction,[35,58,59] to the individual measurements in this study would not have had a substantial effect on their resulting rank order as demonstrated by the sensitivity analysis conducted using multiple conversion factors. Because the exposure interval estimates are insensitive to rather large known possible adjustments, other smaller known (eg, different analytical methods used, such as atomic absorption or inductively coupled plasma) or even unknown differences are unlikely to have had a pronounced effect on the estimates.

It was not possible to generate independent exposure estimates for carbon black, WC, or WCCo because there are no analytical methods specific to these combined agents (ie, usually reported as total aerosol) and therefore no IH measurements available. Because of the collinearity of the agents considered for the JEMs (ie, they are all present at some level for all job classes), it might not be possible to separate out the effects of Co, W, or Ni exposure alone should an association with a health effect be detected in the epidemiological analyses, although this is an issue common to hardmetal industry mortality studies. The exposure reconstruction did, however, generate job classes and exposure groups that provide the necessary level of differentiation for epidemiological analyses of mortality outcomes.

CONCLUSIONS

This study provided, to the authors' knowledge, one of the largest IH datasets used in exposure reconstruction for the hardmetal industry. The amount and time range of data collected from 21 plants, five countries, and three companies allowed a quantitative assessment of three agents to be conducted, two of which (W and Ni) were not considered separately in prior hardmetal cohort mortality studies,[2–5] and afforded the opportunity to use the exposure estimates in US-specific and pooled US and European mortality analyses.[6,7] The levels of exposures presented here were similar to or lower than those reported during the 1952 to 2014 study period.[35–40, 43–52]

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