Advisory Board on Toxic Substances and Worker Health

June 19, 2020

Mr. Eugene Scalia
Secretary, U.S. Department of Labor
Frances Perkins Building
200 Constitution Ave.
Washington, DC

Dear Mr. Scalia:

I am pleased to transmit two recommendations of the Department of Labor Advisory Board on Toxic Substances and Worker Health in relation to the Board's advisory capacity to the Energy Employees' Occupational Illness Compensation Program (EEOICP). These were adopted unanimously at our June 16, 2020 meeting. They include:

1) Revised Recommendation: Jobs Presumed to have pre-1995 Asbestos Exposure

2) Recommendation on Parkinson Disorders in the Energy Employees' Occupational Illness Compensation Program

The Board hopes that our input is useful to EEOICP. It remains an honor for the Board to be consulted on important issues that face the Program. I am available to answer any questions.

Sincerely,

Steven Markowitz MD, DrPH
Chair
Advisory Board on Toxic Substances
and Worker Health

Advisory Board on Toxic Substances and Worker Health

Revised Recommendation: Jobs Presumed to have pre-1995 Asbestos Exposure

Recommendation

We recommend that the Department of Labor evaluate the job categories and associated aliases for all DOE sites in the Site Exposure Matrices and revise its list of occupations with presumed pre-1995 asbestos exposure (Exhibit 15-4) to reflect current knowledge as summarized in the rationale provided below and associated data and references. Supervisors of the listed job categories should also be considered for inclusion. For people who have other job titles with claims in relation to asbestos exposure, a careful investigation of possible occupational sources of asbestos exposure should be undertaken. In the case of mesothelioma, with greater than 90% linkage to asbestos exposure, all cases should have additional inquiry into potential asbestos exposure, even if their job titles are not among those that have presumed asbestos exposure. A Committee of the Board should work with the Department to conduct this exercise and achieve a consensus on a revised list of occupations with presumed pre-1995 asbestos exposure.

Rationale

The Board previously recommended that the EEOICP expand the list of presumed asbestos-exposed job titles as provided in EEOICP Procedure Manual (PM) 4.2, Appendix 1, Exhibit 15-4 to include additional titles that can be reasonably presumed to have had asbestos exposure prior to 1995. The current list is shown in Table 1.

The Board agrees that all of the job titles currently listed in PM 4.2 can be presumed to be exposed to asbetsos. The list includes mostly construction and maintenance occupations. It encompasses most, but not all, of the occupations listed as such under construction trades in the Census 2000 occupational coding system (Census 2000). There are also several job titles on the list that correspond to job titles under two other job groups of the Census 2000 occupatuional codes: 1) Installation, Maintenance, and Repair Workers , and 2) Production occupations (Census 2000).

For the purposes of this recommendation, we refer to the names of job titles used by the Census 2000 occupational coding system , since they are standardized, are or were widely utilized, and most closely reflect the job titles used in the published medical literature and available databases. These job titles may differ somewhat from the categories used in the Department of Labor's Site Exposuire Matrices (SEM). We note that the job categories and their aliases that appear in the SEM appear to vary appreciably by DOE site. The DOE Former Worker Programs have encountered similar challenges: a large number of job titles, which vary across DOE sites and evolve over time. We note that the claims evaluation process requires that the claims examiners or others conform the job title(s) reported by the claimants to the classification system used in the SEM in order to access the information about potential exposures contained in the SEM.

The Board was asked by the Department to provide medical evidence for its proposal to add job titles to the current list in Table 1. We found that available published medical studies and database information use job classification systems that generally corresponds to the U.S. Census occupational coding system (or the related SOC) that is widely used, including by the Census Bureau and the Department of Labor. Studies from other countries use different standardized classification systems that bear substantial similarities to the U.S. Census occupational coding system. Cross-walking job titles over system versions that evolve over time or differ by geography can be challenging. We note that the SEM has undoubtedly spent considerable effort deciding which job titles are equivalent (cross-walking), since the SEM has matched job titles with aliases to facilitate use of the SEM in the claims evaluation process.

To identify job titles with presumed asbetsos exposure prior to 1995, we focused on available research and database information that link job titles with the cardinal asbetsos-related disease, malignant mesothelioma (MM). Since MM is very closely linked to a prior history of occupational asbestos exposure, and since it occurs with relatively modest level of asbestos exposure, MM is the best disease candidate for identifying at risk occupations for whom a presumption of sgnificant prior asbestos exposure can be made, per EEOICP PM 4.2. Any occupations that entail asbestos exposure and are associated with excess risk of asbestosis, lung cancer, ovarian cancer and laryngeal cancer would very likely also be identified in studies of occupation and MM, since the non-MM asbestos-related diseases generally require a higher dose of asbetsos exposure. In addition, the three other asbestos-related cancers have other causes, which can obfuscate the relationships between job titles, asbestos exposures, and these cancers.

<u>National Occupational Mortality System (NOMS)</u>

The National Occupational Mortality Surveillance System (NOMS) is a compilation of causes of death (underlying cause) in the United States by NIOSH according to ICD codes 9 and 10, together with usual occupation and industry of decedents as recorded on the death certificate, and coded according to the U.S. Census occupational coding systems (NIOSH 2019). NIOSH has maintained this system for nearly three decades, collecting mortality data from 26 states, according to a recent report (Robinson 2015) and the NOMS website (https://www.cdc.gov/niosh/topics/noms/about.html). A succinct description of NOMS and its recent application to occupation- and industry-based risk of leukemia and heart disease are available (Robinson 2015). NOMS data have been used in over 140 publications since its inception. NOMS calculates occupation- and industry-specific proportionate mortality ratios (PMR) as a measure of risk. PMR is the ratio of the proportion of deaths caused by the disease of interest in the specified occupation of interest compared to the proportion of deaths caused by the disease of interest in the total population of decedents in the data set. A PMR above 100 represents an increase in the proportion of the disease in the occupation of interest relative to the overall population.

In April 2020, Board member John Dement PhD queried the online NOMS data set to obtain proportionate mortality ratios for malignant mesothelioma (ICD code C45) by usual occupation of decedents for the years 1999, 2003-2004, and 2007-2014 in aggregate. Data included deaths for decedents aged 18-90 of all races and both sexes in 26 U.S. states, involving 550 occupational categories (NIOSH 2019). The total number of deaths due to malignant mesothelioma (C45) in the NOMS data set was approximately 6,800. Note that not all mesotheliomas are included in ICD code C45, because some cases are instead coded as malignant neoplasm of the pleura or peritoneum (C384 and C48). However, ICD code C45 in NOMS includes at least three-quarters of the deaths due to malignant mesothelioma in the NOMS dataset.

Table 2 shows the 62 occupations (2000 Census codes) that had statistically significant excess mortality (elevated PMR's) due to malignant mesothelioma in the combined years of 1999, 2003-2004, and 2007-2014 in the 26 states included in NOMS. All occupations on the list have increased proportions of deaths due to malignant mesothelioma (All PMR's with a lower 95% confidence interval ≥ 100 represent statistically significant excess PMR's.) Table 2 shows the occupations with elevated PMR's in the order in which the occupational titles appear in the 2000 Census coding system. Table 2 color codes the occupations with excess PMR's according to standardized hierarchy of job groupings used by the coding system. Major occupational groups (indicated in green) with excess PMR's include: 1) Architecture and Engineering Occupations, 2) Life, Physical, and Social Science Occupations, 3) Construction and Extraction Occupations, 4) Installation, Maintenance, and Repair Occupations, 5) Production Occupations, and 6) Transportation and Material Moving Occupations. It should be noted that census 2000 occupation classifications were based on the government-wide 2000 Standard Occupation Classification (SOC) system. In the SOC system supervisors of professional occupations are not coded separately and are assigned the same code as the occupation they supervise. Supervisors of professional occupations are classified with the occupations they supervise because they often need the same type of training, education, and experience as the workers they supervise.

Table 2 shows a significant number of occupations in engineering, maintenance and repair and production that are not included in PM 4.2, Appendix 1, Exhibit 15-4 (Table 1)

Table 3 shows the same NOMS occupations with elevated PMR's in descending order of the magnitude of the PMR. This listing provides the usual way that occupational risks are illustrated. The top occupations in terms of MM risk are those that customarily demonstrate the highest risk of MM in the scientific literature

Strengths of the NOMS data, especially for the purpose of updating the EEOICP procedure Manual and the SEM include: 1) use of a national dataset; 2) inclusion of deaths from a time period that is both broad (1999 to 2014) and recent (2007-2014); 3) use of a well-tested methodology; 4) employment of a standardized and broadly used set of codes for cause of death and occupation; 5) access to a large and geographically diverse data set. The latter feature is important, because it provides increased statistical power and increases the representativeness of the data, features that are important to a national compensation program such as EEOICP.

Other U.S. Studies of Malignant Mesothelioma

Attachment A includes excerpted Tables from published studies of occupational risk of MM. Copies of their source articles are also provided.

Mazurek and NIOSH colleagues combined a U.S. national mortality data set (CDC Wonder) with NOMS data to describe basic demographics of MM in the U.S. during 1999-2015 and to evaluate occupational risk of malignant mesothelioma death (n = 1,830) in 23 states during 1999-2007 (Mazurek 2016). Results from their 2016 publication are shown in the table on Attachment A (p. 10). 17 occupations showed a statistically significant elevation in PMR for malignant mesothelioma. These titles are also seen among the titles on our NOMS analysis of MM deaths. The number of MM deaths in the dataset analyzed by Mazurek et al was one-third of the deaths in our NOMS analysis and thus limited statistical power. Additional job titles with elevated PMR's may not have attained statistical significance.

In 2006, Bang and NIOSH colleagues performed a similar analysis of MM that occurred in the U.S. during 1999-2001 (Bang 2006). Their overall data set was a smaller data set than the one used by Mazurek. They evaluated MM deaths (ICD-10 code C45) that occurred in 1999 in 19 states for which occupation and industry data were available. The number of MM deaths analyzed for occupation is not provided. Four occupations demonstrated statistically significant PMR elevations [see Attachment A (p. 11)]. To gain a sense of the size and statistical power of the Bang and Mazurek analyses versus our NOMS query, compare the number of deaths that occurred among "plumber, pipefitters and steamfitters": 18 deaths in the Bang study, 67 deaths in the Mazurek study, and 219 deaths in our NOMS analysis.

Tomasallo and colleagues recently published a case control study, profiling occupational and industrial risks of MM incidence and mortality in Wisconsin from 1997 to 2013 (Tomasallo 2018). They evaluated 1,083 deaths and 1,246 incident cases of MM. As indicated in the attached table [see Attachment A (p. 12)], constructions trades; installation, maintenance, repair workers; metal and plastics workers, and engineers showed significantly increased risk. The analysis was constrained by a relatively small number of cases of MM.

International Studies of Malignant Mesothelioma

We identified large case control and PMR studies from Great Britain, France, Canada, Spain, Germany, and Northern Ireland [see Attachment A (pp. 13-19)]. These will not be reveiwed individually in this summary. A perusal of the key publsihed tables from the relevant articles, as provided in Attachment A, pp. 10-20, indicates a relatively consistent increased MM risk for construction, maintenance, engineering, and selected production occupations.

<u>Comments</u>

Use of the NOMS results for the purpose of updating the list of job titles with presumptive asbestos exposure in EEOICP has several advantages. NOMS and DOE are both nationwide in scope and include many and varied facets of industry, so NOMS results may be more illustrative and relevant than more specific studies that reflect a single dominant geographic area or only one or a few industries. NOMS uses a standard classification system (Standard Occupational Classification, SOC) that is broadly used by agencies in the U.S. Government (U.S. Bureau of Labor Statistics, 2000). The SOC system includes detailed descriptions of each job title, which should facilitate cross-walking the NOMS job categories with SEM job categories and claimant-derived job titles. An additional Federal classification system, O*NET, which is based on the SOC, can also be used to classify job titles.

The NOMS –derived list of occupations at high risk of malignant mesothelioma differs from the current job list included in EEOICP, Exhibit 15-4 (Table 1) principally in adding titles in engineering, maintenance and repair, and selected production activities. The NOMS analysis represents an updated evaluation of the same type of national mortality data that was used in the data source for Exhibit 15-4, which is a 2014 report by ATSDR. The ATSDR report relied on NIOSH occupational mortality analyses; however, the ATSDR report had limited ability to address occupational mesothelioma risk as occupational data were only available for calendar year 1999. Advantages of the current NOMS analysis include 1) its inclusion of the most recent data available, i.e, the 1999-2014 period; and 2) the size of the NOMS data set, which includes many more mesothelioma deaths than previous analyses (and three times as many deaths as the most recent analysis published by Mazurek in 2016). The ability to examine large numbers of mesothelioma deaths adds statistical power, that is, the ability to understand the meaning of PMR estimates (i.e., detect an effect) in a much greater number of occupations.

Interestingly, the SEM currently recognizes that many of the additional job titles revealed by NOMS versus Exhibit 15-4 have potential exposure to asbestos. In the claims evaluation process, inclusion of a link between a job category and asbestos exposure in the SEM initiates consideration of the degree and extent of asbestos exposure by the claims examiner or industrial hygienist. Adding job titles to the list in Exhibit 15-4 based on results of NOMS and other studies recognizes that current scientific evidence justifies re-categorizing the asbestos exposure from "potential," as in the SEM to "presumed to be significant," as described in the EEOICP procedure manual.

Embedded in the list of job titles with elevated malignant mesothelioma risks in NOMS is the inclusion of numerous job titles that primarily have bystander exposure to asbestos, rather than direct asbestos exposure through manipulation of asbestos-containing materials. This is an important finding, because claimants may not report such exposure in completing the occupational health questionnaire as part of their claims submission. Industrial hygienists may also not factor in bystander exposure in their claims evaluations.

Conclusion

We recommend that the Department of Labor evaluate the job categories and associated aliases for all DOE sites in the Site Exposure Matrices and revise its list of occupations with presumed pre-1995 asbestos exposure (Exhibit 15-4) to reflect current knowledge as summarized in this rationale and associated data and references. Supervisors of the listed job categories should also be considered for inclusion. A Committee of the Board should work with the Department to conduct this exercise and achieve a consensus on a revised list of occupations with presumed pre-1995 asbestos exposure.

Table 1

EEOICP Procedure Manual (PM) 4.2, Appendix 1, Exhibit 15-4

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a. Asbestos exposure through December 31, 1995.

(1) CE is to consider the following labor categories to have had significant exposure to asbestos based on their job tasks.

- Automotive mechanic; Vehicle mechanic; Vehicle maintenance mechanic
- Boilermaker
- Carpenter; Drywaller; Plasterer
- Demolition technician; Laborer
- Electrical mechanic; Electrician; Floor covering worker
- Furnace & saw operator; Furnace builder; Furnace operator; Furnace puller;Furnace technician; Furnace tender; Furnace unloader
- Glazier; Glass installer; Glazer
- Grinder operator; Mason (concrete grinding); Tool grinder; Maintenance mechanic (general grinding); Welder (general grinding); Machinist (machine grinding)
- Insulation worker; Insulation trade worker; Insulator
- Ironworker; Ironworker-rigger
- Maintenance mechanic; Electrician; Insulator;
- Mason; Brick & tile mason; Concrete and terrazzo worker; Bricklayer, Tilesetter
- Millwright
- Heavy equipment operator; Operating Engineer
- Painter
- Pipefitter, Plumber steamfitter; Plumber/pipefitter; Plumbing & pipefittingmechanic; Plumbing technician, Steamfitter
- Roofer
- Sheet metal mechanic; Sheet metal fabricator/installer
- Welder; Welder burner; Welder mechanic
- Uranium Miner/Miller

Table 2 Occupations with Elevated PMR's for Malignant Mesothelioma according to Major and Specific Census Occupational Titles, (NOMS, 1999, 2003, 2004, 2007-2014)

2000 Census Major Occupational Groupings & NOMS Occupation Title	2000 Census Code	1990 Census Code	PMR	Number of deaths	95% CI Lower	95% CI Upper
Architects, Surveyors, and Cartographers (17-1000)						
Architects	130	43	337	19	203	526
Engineers (17-2000)						
Marine Engineers & Naval Architects	144	58	1031	9	471	1957
Chemical Engineers	135	48	449	30	303	642
Materials Engineers	145	45	266	7	107	549
Industrial, Health, & Safety Engineers	143	56	259	30	175	370
Mechanical Engineers	146	57	253	50	187	333
Electrical & Electronic Engineers	141	55	207	43	150	279
Civil Engineers	136	53	176	36	123	243
Engineers, NEC	153	59	174	28	115	251
Drafters, Engineering, and Mapping Technicians (17-3000)						
Engineering Technicians (except drafters)	155	214, 215, 216	228	38	161	312
Drafting Occupations	154	217	171	17	100	274
Life, Physical, and Social Science Technicians (19-4000)						
Chemical Technicians	192	224	369	15	206	608
Supervisors, Protective Service Workers (33-1000)						
Firefighters & Supervisors of Firefighters[1]	372, 374	413, 417	211	35	147	293
Law Enforcement Workers (33-3000)						
Detectives, criminal investigators, police & sheriff's patrol officers	382, 385	418	140	49	104	185
Supervisors, Construction and Extraction Workers (47-1000)						
First line Supervisors Const. & Ext Occupations	620	553-558, 613	215	97	174	262
Construction Trades Workers (47-2000)						
Insulation Workers	640	593	3539	52	2643	4641
Plumbers, pipefitters, & steamfitters	644	557, 585, 587	642	219	560	733
Sheetmetal Workers	652	596	418	34	289	584
Drywall Installers	633	573	412	18	244	651
Electricians[2]	635, 713	555, 575-577	405	197	351	466
Structural Iron & Steel Workers	653	597	299	21	185	457
Brickmasons & Stonemasons	622	553, 563, 564	242	42	174	327
Carpenters	623	554, 567, 569	185	137	156	219
Painters, Paperhangers, & Plasterers	642-643, 646	556, 579-584	158	44	115	213
Boilermakers & Oper. Engineers	621, 632	643, 844	153	54	115	199
Supervisors of Installation, Maintenance, and Repair Workers (49-1000)						
Supervisors of Mechanics & Repairers	700	503	275	47	202	366
Vehicle and Mobile Equipment Mechanics, Installers, and Repairers (49-3000)						
Heavy Vehicle & Mobile Equipment Mechanics	722	516, 517	190	21	118	290
Other Installation, Maintenance, and Repair Occupations (49-9000)						
Precision Instrument & Equipment Repairers	743	535	472	12	244	825
Heating, Air Conditioning, & Refrigeration Mechanics, Installers/Repairer	731	534	263	20	161	406
Maintenance and Repair: General and Helper	761-762, 734	865, 547, 549	199	54	149	260
Industrial & Refractory Machinery Mechanics[3]	733, 821	518	188	26	123	276

Supervisors, Production Workers (51-1000)						
Supervisors, production occupations	770	628	207	138	174	245
Assemblers and Fabricators (51-2000)						
Millwrights, Engine Installers[4]	773, 736	544	440	50	327	580
Aircraft & Structural Metal Fabricators	771, 774	636	186	15	104	308
Food Processing Workers (51-3000)						
Furnace, Kiln, & Oven Operators, exc. Food[5]	783, 804, 873	766	374	15	209	617
Metal Workers and Plastic Workers (51-4000)						
Lay-out Workers	816	646	752	5	244	1755
Molding & Casting Machine Operators	810	719	262	10	126	483
Welders & Cutters	814	783	250	98	203	304
Machinists	803	637, 639	196	110	161	237
Extruding/Drawing Machine Operators	792	755, 777	193	16	110	314
Tool & Die Makers	813	634, 635	151	27	100	220
Plant and System Operators (51-8000)						
Stationary Engineers[6]	861, 965	696	453	55	341	589
Other Production Occupations (51-9000)						
Separating, Filtering, & Clarifying Machine Operators	864	757	315	16	180	511
Mixing & Blending Machine Operators	865	756	291	11	146	522
Painting & Paint Spraying Machine Operators	881	759	202	14	110	338
Production Samplers & Weighers	874	798	148	38	105	203
Machine Operators, not specified	896	779	124	122	103	148
Water Transportation Workers (53-5000)						
Ship Captains & Mates, Engineers exc. Fishing Boats	930-931	828, 833	293	19	176	458
Material Moving Workers (53-7000)						
Crane & Tower Operators	951	849	183	15	103	302

1. Groups 372 in Supervisors, Protective Service Workers 33-1000 & 374 in Firefighting and Prevention Workers 33-2000

2. Groups 635 in Construction and Trades Workers 47-2000 & 713 in Electrical and Electronic Equipment Mechanics, Installers, and Repairers 49-2000

3. Groups 733 in Other Installation, Maintenance, and Repair Occupations 49-9000 & 821 in Metal Workers and Plastic Workers 51-4000

4. Groups 773 in Assemblers and Fabricators 51-2000 & 736 in Other Installation, Maintenance, and Repair Occupations 49-9000

5. Groups 783 in Food Processing Workers 51-3000, 804 in Metal Workers and Plastic Workers 51-4000, & 873 in Other Production Occupations 51-9000

6. Groups 861 in Plant & System Operators 51-8000 & 965 in Material Moving Workers 53-7000

Table 3 Occupations with Elevated PMR's for Malignant Mesothelioma in Descending Order of PMR, (NOMS, 1999, 2003, 2004, 2007-2014)

Census Occupational Code Job Titles As Used in NOMS	2000 Census Code	1990 Census Code	PMR	Number of deaths	95% CI Lower	95% CI Upper
Insulation Workers	640	593	**3539**	52	2643	4641
Marine Engineers & Naval Architects	144	58	**1031**	9	471	1957
Lay-out Workers	816	646	**752**	5	244	1755
Plumbers, pipefitters, & steamfitters	644	557, 585, 587	**642**	219	560	733
Precision Instrument & Equipment Repairers	743	535	**472**	12	244	825
Stationary Engineers	861, 965	696	**453**	55	341	589
Chemical Engineers	135	48	**449**	30	303	642
Millwrights, Engine Installers	773, 736	544	**440**	50	327	580
Sheetmetal Workers	652	596	**418**	34	289	584
Drywall Installers	633	573	**412**	18	244	651
Electricians	635, 713	555, 575-577	**405**	197	351	466
Furnace, Kiln, & Oven Operators, exc. Food	783, 804, 873	766	**374**	15	209	617
Chemical Technicians	192	224	**369**	15	206	608
Architects	130	43	**337**	19	203	526
Separating, Filtering, & Clarifying Machine Operators	864	757	**315**	16	180	511
Structural Iron & Steel Workers	653	597	**299**	21	185	457
Ship Captains & Mates, Engineers exc. Fishing Boats	930-931	828, 833	**293**	19	176	458
Mixing & Blending Machine Operators	865	756	**291**	11	146	522
Supervisors of Mechanics & Repairers	700	503	**275**	47	202	366
Materials Engineers	145	45	**266**	7	107	549
Heating, Air Conditioning, & Refrigeration Mechanics, Installers/Repairer	731	534	**263**	20	161	406
Molding & Casting Machine Operators	810	719	**262**	10	126	483
Industrial, Health, & Safety Engineers	143	56	**259**	30	175	370
Mechanical Engineers	146	57	**253**	50	187	333
Welders & Cutters	814	783	**250**	98	203	304
Brick masons & Stonemasons	622	553, 563, 564	**242**	42	174	327
Engineering Technicians (except drafters)	155	214, 215, 216	**228**	38	161	312
First line Supervisors Const. & Ext Occupations	620	553-558, 613	**215**	97	174	262
Firefighters & Supervisors of Firefighters	372, 374	413, 417	**211**	35	147	293
Electrical & Electronic Engineers	141	55	**207**	43	150	279
Supervisors, production occupations	770	628	**207**	138	174	245
Painting & Paint Spraying Machine Operators	881	759	**202**	14	110	338
Maintenance and Repair: General and Helper	761-762, 734	865, 547, 549	**199**	54	149	260
Machinists	803	637, 639	**196**	110	161	237
Extruding/Drawing Machine Operators	792	755, 777	**193**	16	110	314
Heavy Vehicle & Mobile Equipment Mechanics	722	516, 517	**190**	21	118	290
Industrial & Refractory Machinery Mechanics	733, 821	518	**188**	26	123	276
Aircraft & Structural Metal Fabricators	771, 774	636	**186**	15	104	308
Carpenters	623	554, 567, 569	**185**	137	156	219
Crane & Tower Operators	951	849	**183**	15	103	302
Civil Engineers	136	53	**176**	36	123	243
Engineers, NEC	153	59	**174**	28	115	251
Drafting Occupations	154	217	**171**	17	100	274
Painters, Paperhangers, & Plasterers	642-643, 646	556, 579-584	**158**	44	115	213
Boilermakers & Operating. Engineers	621, 632	643, 844	**153**	54	115	199
Tool & Die Makers	813	634, 635	**151**	27	100	220
Production Samplers & Weighers	874	798	**148**	38	105	203
Detectives, criminal investigators, police & sheriff's patrol officers	382, 385	418	**140**	49	104	185
Machine Operators, not specified	896	779	**124**	122	103	148

Attachment A

Case control and surveillance studies from various countries that identify occupations at high risk for malignant mesothelioma

1. US – Mazurek (2016), Bang (2016), Tomasallo (2018)
2. England- Peto (1995); McElvenny (2012)
3. France - Rolland (2010)
4. Canada – Teschke (1997)
5. Spain – Agudo (2000)
6. Germany - Rodelsperger (2001)
7. Northern Ireland - O'Reilly (1999)

Malignant Mesothelioma Mortality — United States, 1999–2015

Jacek M. Mazurek, MD, PhD[1]; Girija Syamlal, MBBS[1]; John M. Wood, MS[1]; Scott A. Hendricks, MS[2]; Ainsley Weston, PhD[1]

TABLE 2. Industries and occupations with significantly elevated proportionate mortality ratios, 1,830 malignant mesothelioma decedents aged ≥25 years — 23 states,* 1999, 2003, 2004, and 2007

Characteristic	No. of deaths	PMR† (95% CI)
Industry		
Ship and boat building	24	6.7 (4.3–9.9)
Petroleum refining	25	4.1 (2.6–6.0)
Industrial and miscellaneous chemicals	58	3.8 (2.9–5.0)
Labor unions	7	3.7 (1.5–7.6)
Miscellaneous nonmetallic mineral product manufacturing	5	3.6 (1.2–8.4)
Electric and gas and other combinations	7	3.1 (1.3–6.5)
Water transportation	12	2.3 (1.2–3.9)
Electric power generation transmission and distribution	24	2.2 (1.4–3.3)
U.S. Navy	11	2.0 (1.0–3.6)
Architectural, engineering, and related services	23	1.9 (1.2–2.8)
Construction	280	1.6 (1.4–1.8)
Unknown	42	—
All other industries	1,312	—
Occupation		
Insulation workers	19	26.9 (16.2–42.0)
Chemical technicians	8	4.9 (2.1–9.6)
Pipelayers, plumbers, pipefitters, and steamfitters	67	4.8 (3.7–6.1)
Chemical engineers	12	4.0 (2.1–7.1)
Sheet metal workers	17	3.5 (2.0–5.5)
Sailors and marine oilers	5	3.4 (1.1–8.0)
Structural iron and steel workers	10	3.3 (1.6–6.0)
Millwrights	14	3.1 (1.7–5.2)
Stationary engineers and boiler operators	15	2.9 (1.6–4.8)
Electricians	53	2.8 (2.1–3.7)
Welding, soldering, and brazing workers	30	2.1 (1.4–3.0)
Construction managers	37	2.0 (1.4–2.8)
Engineers, all other	12	2.0 (1.0–3.5)
Mechanical engineers	14	1.9 (1.0–3.2)
First-line supervisors or managers of mechanics, installers, and repairers	27	1.8 (1.2–2.6)
Machinists	39	1.6 (1.1–2.1)
First-line supervisors or managers of production and operating workers	40	1.4 (1.0–2.0)
Unknown	49	—
All other occupations	1,362	—

Abbreviations: CI = confidence interval; PMR = proportionate mortality ratio.

* Multiple cause-of-death mortality files. https://webappa.cdc.gov/ords/norms-io14.html.

† PMR is defined as the observed number of deaths with malignant mesothelioma in a specified industry/occupation, divided by the expected number of deaths with malignant mesothelioma. The expected number of deaths is the total number of deaths in industry or occupation of interest multiplied by a proportion defined as the number of malignant mesothelioma deaths in all industries and/or occupations, divided by the total number of deaths in all industries/occupations. The malignant mesothelioma PMRs were internally adjusted by five-year age groups, gender, and race. CIs were calculated assuming Poisson distribution of the data.

Malignant Mesothelioma Mortality in the United States, 1999–2001

KI MOON BANG, PHD, MPH, GERMANIA A. PINHEIRO, MD, MSC, PHD, JOHN M.WOOD, MS, GIRIJA SYAMLAL, MBBS, MPH

Malignant mesothelioma is strongly associated with asbestos exposure. This paper describes demographic, geographic, and occupational distributions of mesothelioma mortality in the United States, 1999–2001. The data (n = 7,524) were obtained from the National Center for Health Statistics multiple-cause-of-death records. Mortality rates (per million per year) were age-adjusted to the 2000 U.S. standard population, and proportionate mortality ratios (PMRs) were calculated by occupation and industry, and adjusted for age, sex, and race. The overall age-adjusted mortality rate was 11.52, with males (22.34) showing a sixfold higher rate than females (3.94). Geographic distribution of mesothelioma mortality is predominantly coastal. Occupations with significantly elevated PMRs included plumbers/pipefitters and mechanical engineers. Industries with significantly elevated PMRs included ship and boat building and repairing, and industrial and miscellaneous chemicals. These surveillance findings can be useful in generating hypotheses and developing strategies to prevent mesothelioma. *Key words:* mesothelioma; mortality; occupations; industries.

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Some cases of mesothelioma have been associated with exposure to chrysotile.[7]

In the past, asbestos was used for many applications, including building materials (e.g., insulation materials), manufacturing products (e.g., asbestos cement pipe), and automobile industry (e.g., vehicle brake shoes and clutch pads). Asbestos use declined substantially in the 1980s in the United States and is still currently decreasing.[8] However, legacy exposures still occur during remediation and handling of existing asbestos applications. For example, approximately 1.3 million workers were exposed to asbestos in the United States in 2002,[4] including shipbuilders, miners, construction workers (e.g., insulation workers, plumbers, and pipe fitters), electricians, sheet metal workers, and makers of asbestos products. Although asbestos was eliminated in the manufacturing of some products such as electric hair dryers, gas fireplaces, and wallboard patching compounds, the product is still used in the United States.

In 1999, the 10th revision of the International Classification of Diseases (ICD-10) was adopted by the

TABLE 3 Malignant Mesothelioma Proportionate Mortality Ratios (PMRs) by Usual Industry and Occupation, 1999 (19 States)*

Census Industry Code (CIC)	Industry	Number of Deaths	PMR	95% CI
360	Ship and boat building and repairing	7	5.95	2.39–12.27
192	Industrial and miscellaneous chemicals	19	4.81	2.90–7.51
200	Petroleum refining	5	3.80	1.23–8.87
460	Electric light and power	10	3.08	1.48–5.66
60	Construction	77	1.55	1.23–1.94
Census Occupation Code (COC)	**Occupation**	**Number of Deaths**	**PMR**	**95% CI**
585	Plumber, pipefitters, and steamfitters	18	4.76	2.81–7.51
57	Mechanical engineers	6	3.04	1.11–6.62
575	Electricians	12	2.42	1.25–4.22
156	Teachers, elementary school	13	2.13	1.13–3.64

*Colorado, Georgia, Hawaii, Idaho, Indiana, Kansas, Kentucky, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Rhode Island, South Carolina, Utah, Vermont, West Virginia, and Wisconsin.

ORIGINAL ARTICLE

An Occupational Legacy

Malignant Mesothelioma Incidence and Mortality in Wisconsin

Carrie D. Tomasallo, PhD, MPH, Krista Y. Christensen, PhD, MPH, Michelle Raymond, MS, Paul D. Creswell, PhD, Henry A. Anderson, MD, and Jon G. Meiman, MD

Objectives: The aim of the study was to describe mesothelioma occurrence in Wisconsin from 1997 to 2013 by usual industry and occupation (I&O), including occupations generally considered low risk. **Methods:** Population-

mesothelioma per year in the United States.[1] However, previous surveillance indicates that mesothelioma incidence rate per million residents over 15 years in Wisconsin is elevated compared with the

TABLE 5. Detailed Industry and Occupation Groups* With Significantly Elevated Adjusted Odds Ratios† (ORs) and 95% Confidence Intervals (CIs) for Mesothelioma Death

Industry or Occupation Group	Total (n)	Cases (n)	OR (95% CI)
Industry Group – Reference is Public Administration			
Chemical manufacturing	20	15	3.92 (1.36–13.07)
Construction	240	160	2.93 (1.79–4.84)
Utilities	50	33	2.66 (1.30–5.58)
Fabricated metal product manufacturing	34	23	2.65 (1.17–6.30)
Paper manufacturing	59	37	2.38 (1.22–4.73)
Occupation Group – Reference is Other Management Occupations			
Construction trades workers	215	157	4.20 (2.78–6.42)
Operations specialties managers	35	21	2.37 (1.13–5.12)
Primary, secondary, and special education school teachers	49	28	2.10 (1.05–4.26)
Engineers	51	28	2.02 (1.07–3.86)
Other installation, maintenance, and repair occupations	52	29	1.92 (1.03–3.62)
Metal workers and plastic workers	115	62	1.77 (1.11–2.85)

*Limited to those industries and occupation groups with at least five mesothelioma cases and five controls.
†Model adjusted for frequency matched characteristics of age, race and sex, in addition to ethnicity, year of death, industry or occupation group, and educational attainment.

Continuing increase in mesothelioma mortality in Britain

Julian Peto, John T Hodgson, Fiona E Matthews, Jacqueline R Jones

Summary

Mesothelioma is closely related to exposure to asbestos, and mesothelioma mortalitv can be taken as an index of

Introduction

Mesothelioma is almost always fatal; most patients affected die within a year of diagnosis. The majority of

LANCET 1995

Table 3: **Proportional mortality ratios (PMR) of men aged 16–74 from mesothelioma in England and Wales 1979–80, 1982–90**

Job	PMR (all men=100)	Number	Percent	Cumulative percent
Metal plate workers	700·4*	110	2·5	2·5
Vehicle body builders	618 7*	35	0·8	3 2
Plumbers and gas fitters	442 8*	201	4·5	7·7
Carpenters	365·7*	258	5·7	13·5
Electricians	290·5*	161	3·6	17·0
Upholsterers	283·3†	19	0·4	17·5
Construction workers nec	255·6*	187	4·2	21·6
Boiler operators	253·9*	39	0·9	22·5
Electrical plant operators	253·5*	18	0·4	22·9
Chemical engineers & scientists	248·4*	18	0·4	23·3
Sheet metal workers	233 2*	48	1·1	24·4
Scaffolders	225·6‡	11	0·2	24·6
Production fitters	216·3*	304	6·8	31·4
Professional engineers nec	210·6*	105	2·3	33·7
Plasterers	202 8*	27	0·6	34 3
Welders	202·6*	70	1·6	35·9
Managers in construction	196·8*	40	0·9	36·8
Dockers and goods porters	195·1*	69	1·5	38·3
Electrical engineers	187·0*	39	0·9	39·2
Technicians nec	171·9‡	24	0·5	39·7
Buildings and handymen	164·4*	98	2·2	41·9
Laboratory technicians	164·2‡	27	0·6	42·5
Draughtsmen	160·6‡	28	0·6	43·1
Machine tool operators	133·0*	179	4·0	47·1
Painters and decorators	131·0‡	100	2·2	49·4

*p<0·001, †p<0·01, ‡p<0·05. Highest 25 occupational PMRs based on 10 or more deaths

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doi:10.1093/occmed/kqi034

Mesothelioma mortality in Great Britain from 1968 to 2001

Damien M. McElvenny, Andrew J. Darnton, Malcolm J. Price and John T. Hodgson

Background The British mesothelioma register contains all deaths from 1968 to 2001 where mesothelioma was mentioned on the death certificate.

Aims To present summary statistics of the British mesothelioma epidemic including summaries by occupation and geographical area.

Table 3. Highest and lowest risk occupations for males

Southampton occupation code*	Occupation description	Deaths	Expected deaths	PMR	95% CI	
					Lower	Upper
Top 20 ranked occupations with PMRs greater than 100						
146	Metal plate workers	265	53	502	444	565
153	Vehicle body builders	83	16	526	419	652
144	Plumbers and gas fitters	619	150	413	381	446
104	Carpenters	887	229	388	362	413
137	Electricians	496	178	279	255	304
145	Sheet metal workers	144	61	235	198	275
138	Electrical plant operators	54	21	263	197	343
132	Production fitters	850	406	209	196	224
174	Construction workers nec	486	228	213	195	232
143	Electrical engineers (so described)	140	65	216	181	253
194	Boiler operators	83	38	219	175	272
136	Electrical and electronic production fitters	27	10	260	171	378
39	Managers in construction	123	61	200	166	237
27	Chemical engineers and scientists	52	24	221	165	290
149	Welders	204	108	188	163	215
169	Builders etc.	338	195	174	156	193
30	Professional engineers nec	276	160	173	153	194
160	Painters and decorators nec	361	224	161	145	178
111(O)	Managers nec	212	138	154	134	175
148	Scaffolders	36	19	188	132	260

AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 53:1207–1219 (2010)

Occupations and Industries in France at High Risk for Pleural Mesothelioma: A Population-Based Case–Control Study (1998–2002)

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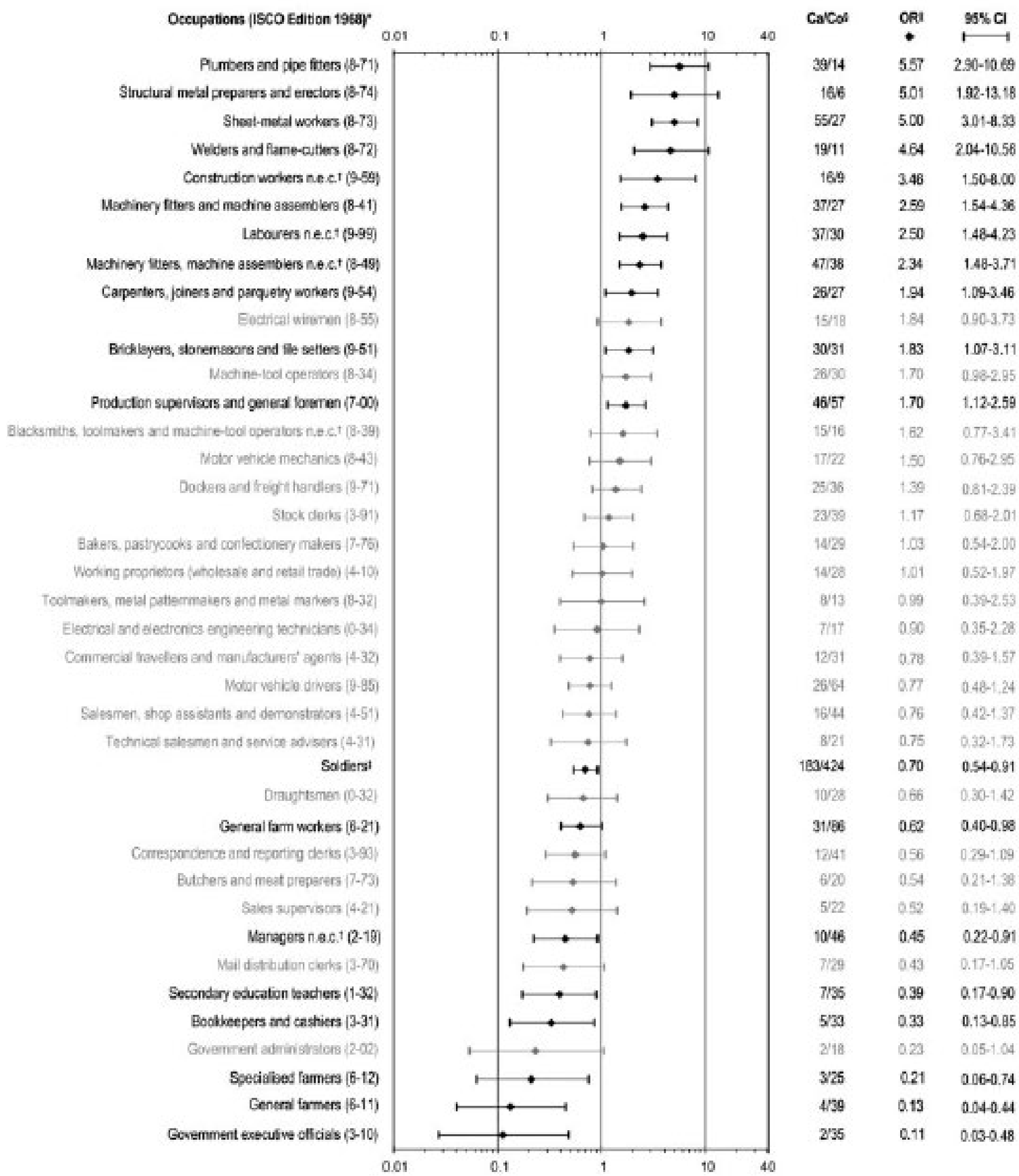

* ISCO codes with at least 20 subjects (cases and controls); † n.e.c.: not elsewhere classified; ‡ NAF code 75.2C

§Ca/Co: numbers of cases and controls who held a job in the occupation (job coded with a minimum of 6 months duration)

‖Matched for age and district; reference category defined by cases and controls who never held a job in that occupation

FIGURE 2. Pleural mesothelioma among men: odds ratios in occupations (ISCO Edition 1968), 1,103 subjects (371 cases; 732 controls). French case–control study 1998–2002.

A B S T R A C T

To determine whether there were previously unrecognized sources of asbestos exposure in British Columbia, incident mesothelioma cases (n=51) and population-based controls (n=154) were interviewed about their occupational histories and asbestos exposures. The following occupations were at elevated risk: sheet metal workers (OR=9.6, 95% CI: 1.5-

Mesothelioma Surveillance to Locate Sources of Exposure to Asbestos

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TABLE II
Odds Ratios* Showing Associations Between Occupational Groups and Pleural Mesothelioma, All Cases (n = 51) and Controls (n = 154) Included

	Ever Employed			Most Recent 20 Years Removed		
	Number of Cases/ Controls	Odds Ratio Ever Employed	95% Confidence Interval	Number of Cases/ Controls	Odds Ratio Ever Employed	Confidence Interval
Occupational Groups with OR ≥ 3.0						
Sheet metal workers[M]	6/2	9.6	1.5-106	6/2	9.6	1.5-106
Plumbers and pipefitters[M]	7/2	8.3	1.5-86.3	6/2	7.1	1.2-75.1
Shipbuilding workers, nec[M]	7/5	5.0	1.2-22.7	7/4	6.9	1.5-37.1
Painters	6/4	4.5	1.0-23.7	5/3	5.4	0.9-39.3
Welders[M]	5/4	3.9	0.8-21.8	5/3	4.9	0.9-34.5
Gardeners[M]	5/4	3.9	0.8-21.9	3/4	2.5	0.3-16.8
Bricklayers, plasterers, & cement workers[M]	7/6	3.5	0.9-14.0	7/5	4.5	1.1-19.8
Miners, drillers, & blasters[M]	7/7	3.4	0.9-13.1	7/7	3.4	0.9-13.1
Machinists[M]	8/8	3.2	1.0-11.1	8/7	3.9	1.1-14.2
Construction foremen[M]	8/7	3.1	0.9-11.0	7/5	3.7	0.9-16.0
Electricians & electrical equipment installers[M]	6/8	3.0	0.8-11.6	6/7	3.7	0.9-15.6
***A Priori* Suspect Occupational Groups**						
Industrial mechanics[M]	7/9	2.4	0.7-8.2	6/9	2.1	0.6-7.3
Stationary engineers, boilermakers[M]	6/11	1.8	0.5-5.9	6/11	1.8	0.5-5.9
Construction labourers	11/22	1.5	0.6-3.8	10/19	1.5	0.6-3.9
Transport engineers & firemen[M]	2/6	1.3	0.1-8.3	2/6	1.3	0.1-8.3
Vehicle mechanics[M]	6/20	0.8	0.2-2.3	6/20	0.8	0.2-2.3

Occupation and Risk of Malignant Pleural Mesothelioma: A Case–Control Study in Spain

TABLE IV. Risk of Pleural Malignant Mesothelioma for Occupations with Risk of Exposure to Asbestos, According to the Expert's Evaluation[a]

ISCO code	Job title	Cases/controls	OR	CI-95%
560	Launderers, dry-cleaners, and pressers	6/1	17.91	(2.08–155)
841	Machinery fitters	6/6	3.59	(1.08–12.0)
849	Machinery fitters and assemblers n.e.c.	9/8	4.07	(1.44–11.5)
851	Electrical fitters	5/2	9.10	(1.68–49.4)
855	Electricians	7/9	2.87	(0.97–8.45)
871	Plumbers	4/2	7.49	(1.30–43.3)
872	Welders	6/8	2.45	(0.78–7.63)
873	Sheet metal workers	5/7	2.53	(0.74–8.64)
943	Manufacture of non-metallic products	12/2	21.17	(4.45–101)
951	Bricklayers	20/36	1.99	(1.01–3.95)
974	Driver of material-handling and related equipment	3/1	10.76	(1.08–107)
	Any occupation with high risk of exposure to asbestos[a]	81/109	2.59	(1.60–4.22)

[a]See text for definition of occupations with risk of asbestos exposure. Only occupations with at least 5 cases or a significant OR are presented in the table. In addition to those in the table, other occupations with risk of asbestos exposure are listed below with the corresponding ISCO code and job title (in parentheses, cases/controls):

039 Draughtsman (1/2), 043 Ships officers (1/-); 079 Nurses, medical assistants (-/3), 322 Card-and type-punching machine operators (-/1), 399 Other clerical and related workers n.e.c. (-/1), 410 Working proprietors (wholesale and retail trade) (1/2), 500 Managers, catering and lodging services (1/-), 589 Protective services workers n.e.c. (2/6), 722 Metal processors, rolling mill (-/1), 723 Metal processors, smelters (3/7), 724 Metal processors, casting (3/-), 726 Metal processors, treating and coating (1/-), 741 Chemical processors, crushing and mixing (2/3), 744 Chemical processors, still operator (1/-), 771 Food processors, miller (1/-), 833 Machine-tool fitters (1/-), 834 Machine-tool operators (3/4), 839 Blacksmiths, machine-tool operators n.e.c. (4/10), 843 Mechanics, motor vehicles (3/14), 874 Structural metal workers (2/-), 891 Glass formers (3/5), 893 Glass workers, furnace operator (2/2), 932 Painters, vehicles (-/1), 959 Construction workers n.e.c. (3/-), 969 Stationary engine and related equipment operators (3/4), 973 Driver of material-handling and elevator equipment (2/4), 981 Sailor, dockhand and foreman (1/1).

The reference category is always formed by the 51 cases and 148 controls who had never worked in any of the listed occupations.

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Asbestos and Man-Made Vitreous Fibers as Risk Factors for Diffuse Malignant Mesothelioma: Results From a German Hospital-Based Case–Control Study

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Background *This study examines the role of occupational factors in the development of diffuse malignant mesothelioma with special emphasis on the dose–response relationship*

TABLE V. Number of Cases and Controls and Odds Ratio from an Ever/Never Evaluation of 22 of 32 Occupations Where At Least Five Cases or Five Controls were Exposed. Within Each of the Occupations the Job Periods are Characterized by the Percentage of Jobs with an Asbestos Exposure and by the Arithmetic Mean of the Fiber Concentration

Key[a]	Occupation[a]	Cases No.	Controls No.	OR[b]	Jobs periods of cases and controls: All periods: n periods	All periods: % of all	Only periods with an asbestos exposure: Fiber concentration GM × 5 f/ml
11,41–43	Farmer	17	25	0.60	92	0	0.00
21–32, 44,52	Forestry worker, fisherman, Animal husbandry worker	4	6	0.67	15	13.3	0.10
12,51	Gardener, vineyard worker	2	5	0.40	16	0	0.00
71–91	Miner	6	8	0.75	21	0	0.00
141–150	Chemical processor and related worker	13	11	1.18	48	60.4	1.39
181–184, 501–504	Joiner, wood processing worker	9	8	1.12	79	21.5	0.34
191–252	Metal production and processing worker	26	14	2.09*	81	45.7	0.80
261–306	Mechanician, fitter, plumber	62	21	2.82*	359	72.1	0.79
311–315	Electrician	15	5	3.00*	88	37.5	0.41
391–433	Food production and processing worker	3	5	0.60	47	0	0.00
441–453	Carpenter, bricklayer, roofer	8	10	0.78	96	34.4	0.69
461–472	Road construction worker, pipe layer, well digger, Unskilled construction worker	17	17	1.00	96	15.6	0.73
481–492	Tile setter, plasterer, paviour, upholsterer	11	3	3.67*	30	63.3	2.94
531	Unskilled worker not elsewhere classified	5	8	0.57	19	31.6	0.14
541–549	Stationary engine and heavy equipment operator	19	7	3.40*	41	65.9	0.70
601–635	Technician engineer	19	9	2.25	89	46.1	0.28
681–706	Sales assurance agent	11	26	0.38*	80	3.8	0.06
711–744	Transportation & store worker	48	39	1.32	227	22.9	0.20
751–784	Administrative & organization clerk	34	49	0.57*	201	4.0	0.07
791–805	Protective service worker	59	71	0.56	240	7.5	0.09
861–893	Teacher, scientist, social worker	4	7	0.57	41	14.6	0.10
901–937	Housekeeper, cleaner, hairdresser, bartender	5	7	0.71	28	14.3	0.62

[a] Apriori defined occupational groups, see [Jöckel et al., 1994, 1998], code according to standard classification of industries [Statistisches Bundesamt, 1975, 1979].
[b] Odds ratio matched for age and region of residence.
[c] Cases, population controls and control patients.

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Asbestos related mortality in Northern Ireland: 1985–1994

D. O'Reilly, J. Reid, R. Middleton and A. T. Gavin

Abstract

Background The association between Belfast and research into the hazardous effects of asbestos exposure goes back many years. This paper aims to update previous papers and review the burden of asbestos related disease in Northern Ireland today.

Methods A study was carried out of all deaths in Northern Ireland between 1985 and 1994 inclusive, in which an asbestos related disease was mentioned anywhere on the death certificate.

of asbestos exposure goes back many years.[5] A cluster of three cases of pleural tumour had been reported as early as 1935,[6] and in 1950 a pathological description of 15 pleural tumours was collected and subsequently reported.[7] However, the link between mesothelioma and asbestos exposure was made by Wagner *et al.* in a study of crocidolite miners in South Africa in 1960.[8] Elmes in 1965[9] established the association between occupational exposure to asbestos and pleural cancer in Belfast shipyard workers. He also showed that about 20 per cent of

Table 3 Proportional mortality ratios for pleural cancer and asbestosis by occupation: Northern Ireland 1985–1994 (inclusive)

	Pleural cancer					Asbestosis				
Occupation	No.	%	PMR	LL	UL	No.	%	PMR	LL	UL
Builder	<4					6	5.55	998*	366	2172
Builder's mate	<4					4	3.6	1863*	508	4772
Building labourer	<4					7	6.4	554*	223	1143
Carpenter or joiner	21	6.8	397*	245	607	12	10.9	626*	329	1095
Docker	5	1.6	108	12	253	<4				
Electrical fitter	18	5.8	555*	329	877	<4				
Fitter	37	11.9	403*	284	556	6	5.5	201	74	437
Fitter's mate	9	2.9	717*	373	1378	<4				
General labourer	21	6.8	69	43	105	12	10.9	109	57	110
Painter or decorator	7	2.3	170	68	350	<4				
Plate metal worker	15	4.8	675*	378	1100	14	12.7	1648*	901	2765
Plumber	10	3.2	480*	230	882	6	5.5	825*	302	1796
Sheet metal worker	4	1.3	385*	105	986	<4				
Storeman	5	1.6	238	77	555	<4				
Welder	4	1.3	241	66	618	7	6.4	1231*	495	2538
All other	154	49.6				36	32.7			
Total cases	310					110				

*All confidence levels are at 5 per cent level.

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Advisory Board for Toxic Substances and Worker Health

Parkinsonian Disorders in the Energy Employees Occupational lllness Compensation Program

In 2018, the Department of Labor requested that the Board assist in evaluating aspects of the recognition and causation of Parkinsonian disorders in the Energy Employees Occupational Illness Compensation Program. We list below the questions and our responses and recommendations.

A. Diagnosis and Terminology in Parkinson's-related Disorders

1. What are the appropriate aliases of Parkinson's disease?
2. Should Parkinsonism and/or Manganism be treated the same as Parkinson's disease? What are the criteria for a finding that the diagnosis is appropriate? (For example, many claimants are symptomatic for "the shakes," but what medical evidence allows for the diagnosis of Parkinsonism or other related diagnoses?) Inclusion of ICD-10 codes would be ideal for ascertaining coverage under such policy.

Recommendation:

The Board recommends that the clinical diagnosis of Parkinsonism, as established primarily but not exclusively by a neurologist, is treated the same as the diagnosis of Parkinson disease throughout the EEOICP claim adjudication process, with respective entries of both terms and aliases recommended in the DOL's Site Exposure Matrix (SEM). The Board has identified the following aliases that are in use for both terms with corresponding ICD 9 and ICD 10 codes

ICD 9 332	-	Parkinson's Disease
ICD 9 332.0	-	Paralysis agitans, Parkinsonism or Parkinson's Disease NOS – not otherwise specified, idiopathic, primary
ICD 9 332.1	-	Secondary parkinsonism
ICD 10 G20	-	Parkinson's Disease, Hemiparkinsonism, Idiopathic Parkinsonism, Paralysis Agitans, Primary Parkinsonism
ICD 10 G21	-	Secondary parkinsonism

Rationale:

Parkinsonism is a general term that refers to a group of related neurodegenerative movement disorders or syndromes affecting the extrapyramidal system. Impairment of motor function is a common clinical characteristic in these disorders which include several neurological entities with broad spectrum of clinical symptomatology, risk factors, pathological features, and rates of progression. As there are no biomarkers or clinically valid diagnostic tests to clearly differentiate between these disorders, the Board recommends combining these under a common diagnosis of Parkinsonism.

The earliest and typically the most prominent symptom of motor function impairment in Parkinsonism is bradykinesia, a slowness in initiation and carrying out of movements. Often progressive, it may be accompanied by other motor symptoms, including muscle rigidity with involvement of individual or entire muscle groups, frequently asymmetric; resting “pill rolling” tremor, and postural instability, all presenting in any combination, and with varying degree of intensity over time (Postuma et al., 2015; Rizek et al., 2016).

Parkinsonian syndromes are classified based on clinical presentation with response/or lack thereof to known therapeutic agents (dopamine replacement therapy) as well potential risk factors. Medications (neuroleptics, antipsychotic, metoclopramide), drugs (synthetic meperidine, MPTP); infections (syphilis, post-encephalitis); metabolic (parathyroid, post-anoxic) and vascular abnormalities (strokes, i.e., lower body parkinsonism); as well as pathologic growth of, and/or injury to brain structures, have been known to result in parkinsonian symptoms (Rizek et al., 2016) and are classified as secondary parkinsonisms.

Inhalational exposures to toxic agents, including manganese (Mn) and carbon monoxide (CO), have also been known to present with motor abnormalities consistent with Parkinsonian symptomatology, and are classified under toxic effects of each exposure respectively, i.e., carbon monoxide poisoning (ICD-10 T58.94 vs ICD-9 332.1); manganese, manganism (ICD-10 T57.2X1 vs ICD-9 332.1). These disorders may occur at any age, with motor function impairment typically within days to weeks following the exposures (Choi and Cheon, 1999; Choi, 2002). A longer latency, up to a decade or more, associated with low, chronic exposures is not uncommon in their pathogenesis (Huang et al. 1993; Huang et al., 1998).

No biomarkers have been found to date to confirm the individual diagnoses of parkinsonism. Functional testing, including brain imaging techniques such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) have been increasingly used to assess neurochemical changes in the brain and differentiate among different types of parkinsonian disorders. Their clinical validity, however, is still under study (Loane and Politis, 2011; Politis, 2014; Rizek et al., 2016). The diagnostic gold standard is the post-mortem pathology.

Parkinson disease (PD) is the most common of all Parkinsonisms with estimates of up to 80% of all cases, (Schwartz and Henchcliffe, 2009). Frequently referred to in earlier literature as Parkinson’s disease, paralysis agitans, primary parkinsonism, idiopathic parkinsonism, or hemiparkinsonism, Parkinson disease affects individuals primarily over the age of 50 with risk increasing with age and males predominantly over females with a 2:1 ratio. Early onset of this disease (<50 years) is rare, estimated at less than 5% of cases (Van Den Eeden et al., 2003; Ferguson et al., 2016). Genetic mutations have been identified in the etiology of Parkinson but are estimated to account for less than 15% of all PD cases, mostly early onset (Tanner et al., 1999; Martin et al., 2011), A combination of genetic, environmental and occupational factors are thought to play a role in the etiology of the remainder 85% of cases of this disease (Caudle et al. 2012; Caudle, 2015).

The clinical onset of motor function impairment in Parkinson Disease is typically over the age of 50. Studies have shown that motor deficits may be preceded, up-to 20 years or more, by a prodromal stage of non-specific impairment in a sense of smell, chronic constipation, depression, and sleep disorders (Kalia and Lang, 2015). Research is underway to identify and evaluate clinical tests and biomarkers in this prodromal stage of the disease (Politis, 2014; Berg et al., 2015; Heinzel et al.,2019).

The diagnostic gold standard in Parkinson disease is post-mortem pathology with degeneration of dopaminergic nerve cells in the basal ganglia, substantia nigra part of the mid-brain and abnormal protein, α-synuclein depositions leading to impairment in the production of dopamine neurotransmitter (Dickson, 2012).

Sets of diagnostic criteria have been developed including UK's Parkinson Disease Society Brain Bank Clinical Diagnostic Criteria (Hughes et al. 1992) and, more recently, the International Parkinson and Movement Disorder Society (MDS) Clinical/Research Diagnostic Criteria (Table 1), to assist in the clinical and research diagnosis and differentiation of Parkinsonisms (Postuma et al., 2015). The primary diagnosis of bradykinesia accompanied by at least one of three other motor symptoms and an unequivocal response to dopaminergic therapy is supportive of the diagnosis of Parkinson disease.

Parkinson-Plus syndromes are disorders that present with classical motor impairment symptoms of Parkinsonian syndromes but lack a response to dopamine substitute therapies. These disorders are sporadic, have additional (''plus'') clinical features and diverse pathology with neurodegeneration typically more extensive and progressive than that seen in classical PD. Genetic mutations as well as other factors including brain injury have been shown to play a role in their pathogenesis (Wenning et al., 2011; Olfati et al., 2019; Armstrong and McFarland, 2019). Parkinson-Plus syndromes are also known as Atypical Parkinsonisms and are classified as Multiple Systems Atrophy (MSA) (ICD-10 G13.8 vs ICD 9 333.0), Progressive Supranuclear Palsy (PSP) (ICD-10 G23.9 vs ICD 9 333.0), Corticobasal Degeneration (CBD) (ICD -10 G31.85 vs ICD-9 331.6) and Lewy Body Dementia (LBD) (ICD -10 G31.83 vs ICD-9 331.82).

B. <u>Causation and Presumptions</u>

1) What toxins are associated with each of the diagnosis? (Any input would require supporting medical health science literature from peer reviewed human studies to support any proffered associations)

2) Are there any presumptions that the Board could offer regarding worker exposure to these toxins? For example, if the committee finds the exposure to manganese as a causal connection to Parkinson's disease, are there certain labor categories or work processes that are associated with this exposure?

3) Are there any causation presumptions that can be made? For example, when an employee has a diagnosis of X, exposure to Y, for a period of Q years, and a latency period of Z, DEEOIC should accept the claim.

Recommendation:

The Board recommends that in addition to carbon monoxide and steel/manganese products already included in the EEOICPA Procedure Manual and DOL Site Exposure Matrix, exposures to carbon disulfide (CS_2) and trichloroethylene (TCE) be presumed to cause, contribute, or aggravate Parkinsonism claims. These exposures were present in the DOE weapons complex and have been shown to be associated with increased risk of Parkinsonism in human studies. The Board also recommends, based on epidemiologic studies, a minimum exposure duration of eight (8) years for Part E causation in adjudicating Parkinsonism claims with exposures to carbon disulfide and trichloroethylene.

At present, the Board issues no recommendations for methanol, toluene, n-hexane, and polychlorinated biphenyls (PCBs), or other work–related exposures common throughout the DOE weapons complex. The Board also issues no recommendation for pesticides or specific pesticide products that may have been used on DOE installations. Current evidence is not sufficient to support a presumption of these additional agents with regard to Parkinsonism. As new research is emerging, the Board recommends a periodic review of human studies literature on risk factors for Parkinsonism for DOL to provide updates in this field.

Presumption of causation implies the judgment that the literature at the current time is sufficient to support the statement that the exposure can contribute to causation of the disease or aggravate the course of the disease in exposed populations, and the judgment that the degree of exposure in the individual is sufficient to have produced this contribution to causation in that individual. This use of presumptions is intended to identify the subset of people with the straightforward presentations to streamline the compensation process by eliminating the need for detailed causal evaluation by the physician and industrial hygienist. It must be emphasized that if an individual DOEs not meet the criteria for the presumption of causation, this DOEs not imply that there is not sufficient evidence of causation. It simply means that individuals who do not meet these presumptive criteria and would need to be evaluated through a fact-based process entailing industrial hygiene and medical review to make the judgment whether the exposure contributed to causation of the disease.

Rationale:

Inhalational exposures to carbon monoxide and manganese resulting in Parkinsonian type deficits have been well-documented in the literature and are included, along with related work processes, in the DOL's EEOICP Procedure Manual and Site Exposure Matrix (SEM). Recent studies and case reports provide description of parkinsonian symptomatology following inhalational and dermal occupational exposures to carbon disulfide ($CS_{2,}$) and trichloroethylene (TCE) solvents. There is also a growing body of epidemiological research showing exposures to trichloroethylene (TCE) to increase the risk of Parkinson Disease (PD) in occupationally exposed populations. These exposures and studies are briefly reviewed herein.

Solvents have been used commonly throughout industry, as degreasing agents and varnishes, in cleaning parts and machining equipment, in dry cleaning, in construction and as substrates in paints and paint thinners (Sainio, 2015). Unpublished former DOE worker medical screenings' program data shows extensive use of organic (hydrocarbon) solvents in DOE weapons operations throughout the decades, primarily in degreasing and machining operations, with the highest exposed jobs including painters, equipment mechanics and production workers (BAECP FWP, 2011). A 2011 Bahr et al. study of DOE workers from Paducah Gaseous Diffusion Plant identified workers who worked in laboratory, in maintenance/electricians, in maintenance/lubrication, in waste or chemical operations as those with highest exposures to TCE. Solvents use has also been common in uranium and plutonium recovery processes in nuclear weapons programs (Todd, 2011). The DOE's Office of Health and Environmental Research Subsurface Science Program study identified TCE and toluene in most of soil, sediments and ground water samples collected from or near the disposal sites at eighteen (18) DOE facilities within the weapons complex around the country (Riley et al. 1992).

Main routes of exposure to solvents are through inhalation, skin and/or ingestion uptake. Liver, kidney damage, depression of bone marrow and cancers (In some) have been reported following exposure to many organic solvents solvents, with other effects including respiratory impairment, reproductive system abnormalities and dermatitis following low-level exposures (Dick, 2006). Organic solvents are also predominantly neurotoxic with acute, high concentration exposures leading to central nervous system suppression of respiration and long-term exposures associated with chronic solvent encephalopathy (Bale et al., 2011; van Valen et al.,2012; Sainio, 2015) and Parkinsonian type deficits following chronic solvents abuse (Uitti et al., 1994; Pezzolli et al., 1996). A possible dose-response relationship with duration of exposure to solvents and increased risk of death from PD has been reported in a mortality study of 20,256 Rolls-Royce plants workers from the UK (McDonnell et al., 2003). A recent meta-analysis of peer-reviewed epidemiological studies found an overall increase in risk for PD associated with exposure to solvents (OR=1.35 95%CI 1.09-1.67) (Pezzoli and Cereda, 2013).

Carbon disulfide (CS_2) has been used as a solvent for phosphorus, asphalt, resins, and rubber and as a building block for other substances in organic chemistry. Primarily used in textile, rubber and cellophane manufacture, this chemical has also been found in soils/sediments and ground water samples from DOE's nuclear weapons facilities across the country (Riley et al., 1992). According to Site Exposure Matrix, CS_2 has been used at DOE sites for activities associated with chemistry laboratories, isotope separation, laser research and development, and medical equipment sterilization. It is also used in paints, enamels, varnishes, paint removers, explosives, rocket fuel, putty preservatives, and rubber cement as well as a solvent for waxes, lacquers, camphor, resins, and vulcanized rubber. CS2 is also used as an insecticide for soil treatment and grain storage to control insects and nematodes and as an overall process solvent (DEEOIC SEM, 2020).

Cardiovascular, developmental and neurotoxic effects have been described following exposures to CS_2 with neurotoxicity involving both central and peripheral nervous system (ATSDR, 1996).

Case reports document four (4) cases of chronically exposed viscose rayon plants' workers with Parkinsonian symptoms following presumably inhalational exposures to CS_2. Each of those workers had 20 plus years of exposure with three of them working in jobs involving fiber cutting and cellulose production and one as a painter (Hageman et al 1999; Huang et al., 2004).

TCE has been widely used as a degreasing and cleaning agent, in metal fabrications, as an anesthetic and a building block for number of household chemicals (ATSDR, 2019). Its peak use occurred before 1970's and DOE's Subsurface Science Program reported TCE as the most commonly found solvent in ground water and soil samples collected from or near the disposal sites in the nuclear weapons facilities (Riley et al., 1992). SEM documents TCE's use at DOE sites for activities associated with boiler and pressure vessel erection, repair, and testing; chemistry laboratories; drum/box/container stenciling; dry cleaning; electrical maintenance; HVAC maintenance; machining; mechanical maintenance; metal degreasing; painting; plumbing/pipefitting; and sheet metal fabrication. Per SEM, Trichloroethylene has also been used as an extraction solvent for greases, oils, fats, waxes, and tars; by the textile processing industry to scour cotton, wool, and other fabrics; in dry cleaning operations; and as a component of adhesives, lubricants, paints, varnishes, paint strippers, pesticides, and cold metal cleaners (DEEOIC SEM, 2020)

A link between TCE exposure and Parkinson disease has been reported in case studies and epidemiologic observations (Guehl et al., 1999; Kochen et al., 2003). Gash et al. (2008) reported most recently on a cluster of thirty (30) chronically TCE-exposed workers, all from a small measuring instruments manufacturing plant, with Parkinsonian type deficits, three of whom were eventually diagnosed with PD. This group of workers ranged in age from 46 to 67 years, with exposure duration between 8 and 33 years and each of the three workers diagnosed with PD held jobs in degreasing metal parts involving daily work in TCE exposure for over 25 years.

The association between TCE exposure and increase in risk of PD has also been shown by Goldman et al. in their 2012 nested case - control study of twin pairs from the National Academy of Sciences/National Research Council World War II Veteran Twins Registry Cohort. Ninety-nine (99) twin pair participants in this study who were discordant for diagnosis of PD, and whose lifetime exposure to solvents was assessed based on self-reports and industrial hygiene guided interviews had greater than six-fold increase in risk for PD when exposed to TCE up to 2% of work time or one hour per week, compared to those never exposed to TCE (OR=6.1, 95% CI 1.2-33). The risk was also elevated for those exposed to either TCE or perchloroethylene (OR=8.9, 95% CI 1.7-47), as well as those with longer duration of TCE exposure (OR=3.2, 95% CI 1.1-10 for TCE and OR=4.1 95% CI 1.4-11.8 for either TCE or PERC) and highest cumulative exposure dose (OR=5.2, 95% CI 1.03-26). Electricians, dry cleaners, industrial machinery repairmen and health workers were identified as at risk for most frequent TCE exposure.

In addition, in their assessment of evidence for TCE and tetrachloroethylene (PCE) exposures as drinking water contaminants at Camp Lejeune, the ATSDR (2017) concluded, based on animal, mechanistic studies and epidemiological evidence from Goldman's 2012 twins study and Bove et al. (2014) study of mortality among Camp Lejeune workers, that the evidence for TCE is "equipoise and above for causation for TCE and Parkinson Disease".

Although not yet a presumption, a brief review of up-to-date literature on pesticides is presented below to serve as a basis for further review and future recommendations in this area.

Pesticides are a group of chemical compounds used widely in farming, agricultural and household applications to control crop health and eliminate rodents (rodenticides), fungus (fungicides), plants/weeds (herbicides) and insects (insecticides). Exposure to pesticides has been associated with various health outcomes, description of which is beyond the scope of this review. However, over the last two decades, a growing number of epidemiological studies have been conducted showing these compounds to be a potential risk factor for Parkinson Disease, with analyses of pooled data repeatedly showing increase in risk and incidence rates of this disease (Priyadarshi et al., 2000; Pezzoli and Cereda, 2013; Breckenridge et al.,2016; Ahmed et al., 2017; Gunnarson and Bodin, 2018), specifically with occupational exposures (van der Mark et al., 2012; Van Maele-Fabry et al., 2012). The systematic reviews also point to a potential dose-response relationship with duration of exposure (Yan et al, 2017). While these studies provide a wealth of information and identify jobs with highest exposure potential (farmers, pesticide applicators, workers in pesticide manufacturing, horticulturists, green house workers, and gardeners) the results demonstrate a high degree of variability in studies designs, exposure assessment methods, and/or case definitions. Additionally, most studied populations were exposed to numerous combinations of pesticides, making attribution of specific compounds problematic.

DOE Subsurface Science Research Program reported pesticides among the least commonly found compounds, shown in concentrations ranging from trace to parts per thousand in soil/sediment samples from two to five facilities and water samples from only one site under study (Riley et al. 1992). The use of pesticides throughout the DOE's weapons complex has been documented in DOL's SEM which provides listing of several products and chemical compounds. Some of these compounds, specifically in the insecticides and herbicides groups (paraquat, chlorpyriphos, rotenone, maneb, dieldrin, heptachlor and atrazine) have been shown previously in animal models to induce dopaminergic cell degeneration and α-synuclein deposition, consistent with Parkinsonian pathology (Betarbet et al., 2000; Caudle et al., 2005; Cichetti et al. 2005; Filipov et al. 2007; Hatcher et al. 2007; Cannon et al. 2009). These compounds have been further studied in human studies over the years and while the results indicate increase in risk of Parkinson Disease associated with exposures to chlorpyriphos OR= 2.0, 95% CI 1.02–3.8 (Dhilon et al. 2008); 2,4-dichlorophenoxyacetic acid OR=2.59, 95% CI 1.03-6.48 (Tanner et al. 2009); rotenone (OR= 2.5, 95% CI 1.3–4.7) and paraquat OR= 2.5, 95% CI 1.4–4.7 (Tanner et al. 2011), and the combination of paraquat and maneb OR=1.75, 95% CI 1.13-2.73 (Costello et al. 2009) the potential for co-exposures to additional pesticide compounds is present in most studies, making a conclusive link between any specific pesticide difficult to establish.

Table 1 MDS Clinical Diagnostic Criteria for PD—Executive Summary/Completion Form

The first essential criterion is parkinsonism, which is defined as bradykinesia, in combination with at least one of rest tremor or rigidity. Examination of all cardinal manifestations should be carried out as described in the MDS-Unified Parkinson Disease Rating Scale (Goetz, Tilley, Shaftman, et al., 2008). Once parkinsonism has been diagnosed:

Diagnosis of Clinically Established PD requires:

(1) absence of absolute exclusion criteria,
(2) at least two supportive criteria, and
(3) no red flags

Diagnosis of Clinically Probable PD requires:

(1) absence of absolute exclusion criteria
(2) presence of red flags counterbalanced by supportive criteria
- If one red flag is present there must also be at least one supportive criterion.
- If two red flags, at least two supportive criteria are needed.
- No more than two red flags are allowed for this category.

Supportive criteria (Check box if criteria met)

☐ 1. Clear and dramatic beneficial response to dopaminergic therapy. During initial treatment, patient returned to normal or near-normal level of function. In the absence of clear documentation of initial response a dramatic response can be classified as:
(a) Marked improvement with dose increases or marked worsening with dose decreases. Mild changes do not qualify. Document this either objectively (>30% in UPDRS III with change in treatment) or subjectively (clearly documented history of marked changes from a reliable patient or caregiver).
(b) Unequivocal and marked on/off fluctuations, which must have at some point included predictable end-of-dose wearing off.

☐ 2. Presence of levodopa-induced dyskinesia.

☐ 3. Rest tremor of a limb, documented on clinical examination (in past, or on current exam)

☐ 4. The presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Absolute exclusion criteria: The presence of any of these features rules out PD:

☐ 1. Unequivocal cerebellar abnormalities, such as cerebellar gait, limb ataxia, or cerebellar oculomotor abnormalities (e.g., sustained gaze-evoked nystagmus, macro square wave jerks, hypermetric saccades).

☐ 2. Downward vertical supranuclear gaze palsy or selective slowing of downward vertical saccades.

Table 1 MDS Clinical Diagnostic Criteria for PD—Executive Summary/Completion Form—cont'd

☐	3. Diagnosis of probable behavioral variant frontotemporal dementia or primary progressive aphasia, defined according to consensus criteria (Rascovsky et al., 2011) within the first 5 years of disease.
☐	4. Parkinsonian features restricted to the lower limbs for more than 3 years.
☐	5. Treatment with a dopamine receptor blocker or a dopamine-depleting agent in a dose and time-course consistent with drug-induced parkinsonism.
☐	6. Absence of observable response to high-dose levodopa despite at least moderate severity of disease.
☐	7. Unequivocal cortical sensory loss (i.e., graphesthesia, stereognosis with intact primary sensory modalities), clear limb ideomotor apraxia, or progressive aphasia.
☐	8. Normal functional neuroimaging of the presynaptic dopaminergic system.
☐	9. Documentation of an alternative condition known to produce parkinsonism and plausibly connected to the patient's symptoms, or, the expert evaluating physician, based upon the full diagnostic assessment feels that an alternative syndrome is *more likely* than PD.
Red flags	
☐	1. Rapid progression of gait impairment requiring regular use of wheelchair within 5 years of onset.
☐	2. A complete absence of progression of motor symptoms or signs over 5 or more years unless stability is related to treatment.
☐	3. Early bulbar dysfunction: *severe* dysphonia/dysarthria (speech unintelligible most of the time) and/or severe dysphagia (requiring soft food, NG tube, or gastrostomy feeding) within first 5 years.
☐	4. Inspiratory respiratory dysfunction: either diurnal or nocturnal inspiratory stridor and/or frequent inspiratory sighs.
☐	5. Severe autonomic failure in the first 5 years of disease. This can include: (a) Orthostatic hypotension (Gilman et al., 2008)—orthostatic decrease of blood pressure within 3 min of standing by at least 30 mm Hg systolic or 15 mm Hg diastolic, in the absence of dehydration, medication, or other diseases that could plausibly explain autonomic dysfunction, or (b) Severe urinary retention or urinary incontinence in the first 5 years of disease (excluding long-standing or small amount stress incontinence in women), that is not simply functional incontinence. In men, urinary retention must not be due to prostate disease, and must be associated with erectile dysfunction.

Table 1 MDS Clinical Diagnostic Criteria for PD—Executive Summary/Completion Form—cont'd

☐ 6. Recurrent (>1/year) falls due to impaired balance within 3 years of onset.	
☐ 7. Disproportionate anterocollis (dystonic) and/or contractures of hand or feet within the first 10 years.	
☐ 8. Absence of any of the common nonmotor features of disease despite 5 years disease duration. These include sleep dysfunction (sleep-maintenance insomnia, excessive daytime somnolence, symptoms of REM sleep behavior disorder), autonomic dysfunction (constipation, daytime urinary urgency, symptomatic orthostasis), hyposmia, or psychiatric dysfunction (depression, anxiety, or hallucinations).	
☐ 9. Otherwise unexplained pyramidal tract signs, defined as pyramidal weakness and/or clear pathologic hyperreflexia (excluding mild reflex asymmetry and isolated extensor plantar response).	
☐ 10. Bilateral symmetric parkinsonism. The patient or caregiver reports bilateral symptom onset with no side predominance, *and* no side predominance is observed on objective examination.	
Criteria Application:	
1. Does the patient have parkinsonism, as defined by the MDS criteria?	Yes ☐ No ☐
If no, *neither* probable PD nor clinically established PD can be diagnosed. *If yes*:	
2. Are any absolute exclusion criteria present?	Yes ☐ No ☐
If "yes," *neither* probable PD nor clinically established PD can be diagnosed. *If no*:	
3. Number of red flags present	____
4. Number of supportive criteria present	____
5. Are there at least two supportive criteria *and* no red flags?	Yes ☐ No ☐
If yes, patient meets criteira for *clinically established PD*. *If no*:	
6. Are there more than two red flags?	Yes ☐ No ☐
If "yes," probable PD *cannot* be diagnosed. *If no*:	
7. Is the number of red flags equal to, or less than, the number of supportive criteria?	Yes ☐ No ☐
If yes, patient meets criteria for *probable PD*	

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