**Taskforce Statement on the Occupational Burden of Lung Disease:**

**The Occupational Burden of Pneumonias and Tuberculosis**

**Draft (Long Version) –September 2017**

**Introduction**

Certain occupational groups are at increased risk for pneumonias and tuberculosis (TB). While tuberculosis has been well documented as a work-related infection in the health care setting (Sepkowitz et al, 1994; Baussano et al., 2011) and among workers exposed to silica dust (Dharmadikhari et al., 2013; Chen et al., 2012), the occupational burden of pneumonia across a range of occupations has not been analyzed systematically to date.

**Literature Review**

Two systematic PubMed searches were performed, alternating “respiratory tract infections [MeSH Terms]” with “tuberculosis [MeSH Terms]” together with the following terms:

…. AND (occupation\*[All Fields] OR worker\*[All Fields] OR work-related\*[All Fields] OR (VGDF[All Fields] OR dust[All Fields] OR fume\*[All Fields] OR gas[All Fields])) AND (population attributable\*[All Fields] OR population based\*[All Fields] OR case series\*[All Fields] OR Cohort\*[All Fields]). For infections, this yielded 624 abstracts that were reviewed. Following exclusions of abstracts not relevant, 20 epidemiological papers and six case reports were retrieved for full text review, with a further two added from reference lists. A similar search for TB resulted in 701 abstracts, with 31 being reviewed.

We categorized the included publications into three types: cohort studies; case-control studies; and case reports, with the TB publications additionally stratified according to healthcare, silica or other exposure.

**Methods for Assessing the Population Burden**

There were limited population based studies that could assist in determing the population attributable fraction (PAF) of the occupational burden of tuberculosis, we used the method employed by Baussano et al (2011) among healthcare workers. In the Baussano review, the calculation of PAF was determined by comparing the incidence rates of TB in reported workplace studies with that of the general population of that country, as reported by the World Health Organisation (WHO, 2017). To determine the population at risk, the health workforce data was extracted from the WHO databases (WHO, 2014) for each country for the year in which the study was conducted. We extended this approach for silica exposed workers as well. We were able to obtain employment data for South African goldminers from the government databases and South African adult population data from the World Bank databases for the years in which these studies were conducted (World Bank, 2017).

**Occupational burden of Pneumonias**

**Cohort studies**

Although an early US study concluded that the incidence of pneumonia among ship-yard workers was not different from the general population (Collen 1944), later US and UK studies indicated an increased mortality for pneumonia among welders (Beaumont 1980, Newhouse 1985). Further studies from UK found that welders and other metal handling occupations had a striking excess of pneumonia, especially pneumococcal and unspecified lobar pneumonia, that seem to be restricted to workers in active age (Coggon 1994, Palmer 2009). In a Canadian study the risk for invasive pneumococcal disease was increased among welders (Wong 2010).

Dust exposed stone quarry workers had decreased pneumonia mortality risk, but coal miners showed an increased mortality from pneumonia (Graham 2004, Veiga 2006). A study from Korea showed increased risk for pneumonia among workers in cement, lime, plaster products, as well among males working with cast metals (Koh 2011).

Among male construction workers, exposure to inorganic dust and metal fumes was associated with increased mortality from infectious pneumonia, lobar pneumonia and pneumococcal pneumonia (Torén 2011). The exposures were overlapping; when analyzing the mortality from infectious pneumonia in non-overlapping exposure groups only exposure to inorganic dust was significantly increased.

Workers in ferroalloy plants or workers exposed to metal-working fluids were not at increased risk for pneumonia (Hobbesland 1997, Ramundstad 2002, (Youk 2013). Exposures to pesticides as well as exposure to styrene have been associated with increased mortality from pneumonia (Brown 1992, Amoateng-Adjepong 1995, Welp 1996).

Among British farmers the risk for self-reported pneumonia was increased among those having a pigeon loft and among those attending birth of piglets (Thomas 1994).

**Case-control studies**

A study from UK did not show any association with occupational exposures (Farr 2000). In another UK case-control study exposure to metal fumes, metal dust and oil mists the year before admittance were associated with an increased risk for pneumonia. When controlling for overlapping exposures all significant risks disappeared (Palmer 2003).

In Canada a general-population based case-control study was presented in two similar publications, and the history of occupational exposure to gas, fumes and chemicals was associated with a high risk for pneumonia (Loeb 2009, Neupane 2010a, b, Hnizdo 2010).

In a Spanish case-control study showed that exposure to dust during the last month and sudden change of temperature increased the risk for pneumonia (Almirall 2008, 2015).

In a Finnish study, pneumonic tularemia was associated with handling of hay (Rossow 2014).

**Case reports**

Several case reports have described welders with lobar pneumonias (Wergeland 2001, Patterson 2015, Flodin 2017). There are number of reports describing outbreaks of Legionnaires’ diseases in different workplace setting (Fraser 1977, Isozumi 2005, Kusnetsov 2010).

*Rhodococcus equi* is a zoonotic gram-positive coccobacillus. Among immunocompromised persons occupational exposures seem to be an obvious risk (Yamshchikov 2010). The described exposures are various exposures to live stock environments (Golub 1967, Fischer 1998, Gallen 1999, Arya 2004).

**Occupational burden of Tuberculosis**

We were able to calculate the PAF for TB among silica exposed workers from four population-based case-control studies and seven cohort studies, the latter of which were all from South African mines. Three of the case-control studies extracted data from specific United States’ databases, two of which reviewed mortality data based on death certificates. Rosenman and Hall (1996), in reviewing the New Jersey TB Register, were able to determine occupational exposures and job descriptions. A PAR of 4.9 was found among those with any silica exposure. This was within the similar range for the two other American mortality studies for which PAR’s ranging from 3.2 – 3.6 was determined. The calculated PAR for the Iranian study was 36, strikingly higher than all other studies, however, a strong selection bias may be present in this study. The PAR for the cohort studies of various goldminers from South African mines ranged from 0.8 (Halsema et al., 2012) through to 7.9 (Churchyard et al., 2000), with a mean of 3.2.

A previous systematic review of occupational tuberculosis among health care workers stratified reports according to the reported TB incidence rates of the country (Baussano et al., 2011). The median PAR for low TB incidence countries was 0.36% (interquartile range: 0.13-2.24), while that of high TB incidence countries was 0.38% (IQR: 0.14-0.78). We excluded studies used in latter review. One cross-sectional, one case-control and sixteen cohort or registry review studies, were used to calculate PAR among health care workers. Among the cohort studies, the PAR showed little consistency, ranging from 0.09% (Jiamjarasrangsi et al., 2005) – 14.6% (Roche et al., 2008). This inconsistency may be due to the varying population burden of disease in the different countries, together with the sizes of healthcare population. In several low incidence countries, the incidence rates among health care workers were lower than that of the general population (eg. Netherlands (De Vries et al., 2006); United States (Ong et al., 2006; Lambert et al., 2012) and Finland (Raitio and Tala, 2000). In these instances, PAR was less than 0. Among studies in countries with higher incidence in the general population (eg. Ethiopia (Eyob et al., 2002), Nigeria (Kehinde et al., 2011), South Africa (Tudor et al., 2014 and Claassens et al., 2013)), the PAR ranged from 0.38 (Ethiopia) through to 3.7 (Nigeria). Surprisingly high PAR estimates were calculated for non-silica or non-health care workers in a variety of occupational settings: trucking and light truck drives in the US had estimates of 2 and 8.8 respectively (Rosenman and Hall, 1996), while sugar cane workers in Brazil had a PAR of 12.2 (Sacchi et al., 2013). The highest reported PAR (32.6%) was that of craft workers and machine operators from Estonia (Tekkel et al., 2002)

Several studies used TB mortality as an outcome among exposed workers, and calculated SMR’s from the general population. Marinaccio reported an SMR for TB among confirmed Italian silicotics of 2.89 (95% CI: 2.2-3.8) (Marinaccio et al., 2006). In a study of 74 040 Chinese workers from metal mines and potteries, nested case control studies for a variety of respiratory outcomes was performed, with carefully determined cumulative silica dust exposure for each worker. The SMR for TB mortality was reported as 4.9 (4.7-5.1) (Chen W et al., 2012). McKenna, in comparing TB mortality rates of workers against that of the general population of the United States, based on TB registries data from 29 states, found SMRs among HCWs similar to that of the general population. Specific jobs within this sector was associated with an increased risk, such as inhalation therapists (SMR: 2.9; 95%CI: 1.6-6.0) and lower paid health care workers (SMR: 1.3; 95%CI: 1.1-1.5). Other jobs not directly associated with health care or silica exposure, such as working with animals (SMR: 2.2; 2.0-2.4) and food services (SMR: 1.7; 1.1-1.4), being a farm-worker (SMR: 3.7; 3.4-4.1) was also associated with an increased risk of TB. (McKenna et al., 1997). **[SHOULD THIS BE RETAINED? –THESE SMR STUDIES DO NOT APPEAR IN THE TABLE]**

**Discussion**

The epidemiological studies show that occupational exposures are important risk factors for pneumonias, especially lobar pneumonias and pneumococcal pneumonias. Welders are probably at increased risk, but there is substantial confounding from inorganic dust, and the cause is probably a mixture of causes. Exposure to air pollution increase the risk for severe pneumonia among children, which support the relationship between occupational dust exposure and pneumonias (Smith 2011). The causal relation is further supported by mechanistic studies showing that inorganic dust affects the alveolar macrophages (Palmer 2006, Ghio 2014).

There is, however, shaky evidence to present attributable risks, but data indicate that the attributable fraction is substantial (Table 3). It has been argued that welder should be vaccinated, but the obvious intervention is exposure control, i e reduce exposure to gas, dust and fumes at workplaces (Pamer 2012a,b, Lie 2006).

Case reports have less value than epidemiological studies in providing data relevant to risk estimation, but can contribute top knowledge regarding rare disease, such pneumonias due to different microorganisms. An obvious such case is *Rhodococus equi* – an emerging risk that has to be highlighted. There is need for larger studies on transplanted patients.

The epidemiological evidence for occupational burden of tuberculosis is somewhat stronger, but varies according to the population incidence of the disease. In countries with low incidence, there is limited evidence that healthcare environments increase the population burden, while in countries with high incidence the PAR can be as high as 3.7%. Among silica exposed workers, determining the PAR is challenging because of the absence of population based studies. When data is available, as in the case of South Africa, a substantial amount of disease may be attributable to exposure.

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| **Table 1. Summary of cohort studies of occupationally exposed groups and pneumonia as the outcome** | | | | | | | | |
| Author, Year, Country | Number of cases | Time frame | Cohort and main exposure | Risk estimate | | | | |
| All pneumonias | | Lobar | | Pneumo-coccal |
| Beaumont, 1980,  US | 8679 | Employed 1950-73 | Trade union members  Welders | 1.67 (n=19) | |  | |  |
| Newhouse, 1985,  UK | 10? | Employed 1940-68 | Shipyard workers  Welders | 184 (100-314) | |  | |  |
| Brown,  1992,  US | 14? | Males  Employed before 1965 | Organo-chlorine pesticide plants  Aldrin, dieldrin | 1.7 (0.95-2.9) | |  | |  |
| Thomas,  1994, UK | 14 | 1991 | Farmers  Pigeon loft | 7.4 (1.9-28.0) | |  | |  |
|  |  | Attending birth of piglets | 6.6  (2.0-21.4) | |  | |  |
| Coggon, 1994, UK | 55  20  18  14 | 20-64  65-74  20-64  65-74 | National mortality registers  Welders  Moulders and  coremakers |  | | 255 (192-332)  107 (65-165)  292 (173-461)144 (79 – 241) | | |
| Amoateng-Adjepong  1995, US |  | Ever worked 1952-82. Extension of Brown, 1992 | Organo-chlorine pesticide plants  Aldrin, dieldrin, ever hourly | 189  (110-302) | |  |  | |
|  |  | Aldrin, dieldrin, never hourly | 91  (19-266) | |  |  | |
| Welp,  1996, Europe | 3  8  7  7 |  | 660 European factories for reinforced plastics  Styrene  (ppm)  <60  60-119  120-199  >200 | 1.0  2.1(0.5-8.0)3.2  (0.8-13.0)  6.1  (1.4-25.8) | |  |  | |
| Hobbesland, 1997, Norway | 14 730 men | Employes 1933-1990 | Ferroalloy plants  FeSi/Si  FeMn/SiMn | 0.88  (0.66-1.16)  1.03  (0.75-1.38) | |  |  | |
| Ramund-stad, 2002,  Norway | 2562 men | The plants started 1913, 63 and 65. Follow-up 1962 – 1996 | Silicon carbide smelters | 0.8 (n=24)  (0.5-2.1) | |  |  | |
| Graham, 2004, US | 5408 | Employed 1950-1996 | Vermont granite workers  All workers  Quarry  Shed | 0.65 (n=42)  (0.47-0.88)  0.28 (n=4)  (0.08-0.70)  0.76 (n=38)  (0.54-1.05) | |  |  | |
| Veiga, 2006 | 3224 | Employed 1942-97 | Underground coalmine workers  All  Empl.<1970  Empl.>1969  Underground | 263 (n=16)  (160-429)  292  (152-562)  144  (36-577)  253 (n=11)  (140-257) | |  |  | |
| Palmer, 2009 | 54 | 16-74 yrs | National registers  Metal work |  | | 198  (149-258) |  | |
| 32 |  | Welders |  | | 242  (166-342) |  | |
| 5 |  | Moulders |  | | 300  (97-701) |  | |
| 13 |  | Sheet metal  Workers |  | | 268  (143-459) |  | |
| Wong, 2010,  Canada |  | 19-65 | National registers  Welders  Electricians  Day-care |  | |  | 2.7 (n=18)  (1.7-4.2)  1.4 (n=6)  (0.6-3.1)  1.2 (n=8)  (0.6-2.4) | |
| Koh,  2011, Korea |  | 20-69 | National cohort of workers from health sur-veillance  Glass  Ceramics  Cement  Non- metallic mineral products  Iron and steel  No-ferrous metals  Cast metals | Males Females  1.3 (0.8-1.8) N.a.  1.0 1.7 (0.8-3.1)  1.5 (1.1-2.1) 3.2 (1.4-6.4)  1.0 N.a.  1.1 (0.9-1.3) 2.2 (0.8-4.8)  1.0 N.a.  1.6 (1.3-2.1) N.a. | | |  | |
| Torén,  2011 |  | 20-64 | Con-struction workers  Inorganic  dust  Chemicals  Metal fume  Wood dust  Any exposure  Inorganic dust (non-overlapping)  Metal-fumes (non-over lapping) | 1.9  (1.2-2.9)  1.9  (1.4-3.2)  2.3  (1.4-4.0)  0.9  (0.4-2.2)  1.8  (1.2-2.8)  1.7  (1.03-2.6)  No cases | 3.4  (1.3-8.6)  4.5  (1.6-12.6)  3.7  (1.3-10.1)  N.a.  3.5  (1.4-8.7)  No cases | | 4.3  (1.3-13.9)  5.8  (1.6-20.9)  5.8  (1.5-21.7)  N.a.  4.2  (1.3-13.7)  No cases | |

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| **Table 2. Summary of case-control studies of pneumonia associated with occupational exposures** | | | | | |
| Author, Year | Cases,  n | Age,  Years | Exposures | Risk estimates by outcome | |
| All  OR (95% CI) | Lobar |
| Farr,  2000,  UK | 66 | 15-79 | BirdsDusty occupations  Animals | 0.95 (0.4-2.2)  1.7 (0.96-3.0)  0.6 (0.3-0.99) | N.a.  N.a.  N.a. |
| Palmer,  2003,  UK | 525 | 20-64 | Metal fume  Metal fume  Metal dust  Wood dust  Cement dust  Oil mist  Iron,  without alloys  Any metals | 1.4 (0.8-2.3)  (adjusted)  1.6 (1.1-2.4)  1.2 (0.7-1.8)  0.8 (0.5-1.4)  1.1 (0.7-1.9)  1.3 (0.8-2.2) | 1.8 (1.0-3.3)  3.0 (1.4-6.7)  1.8 (1.0-3.3) |
| Loeb, 2009,  Canada | 717 | >65 | Gases, fumes, chemicals  Dusty work | 3.7 (2.4-5.8)  2.6 (2.1-3.2) |  |
| Neupane,  2010, Canada | N? | >65 yrs | Gas, fumes, chemicals | 5.8 (4.2-7.9) |  |
| Almirall, 2008, 2014,  Spain | 1336 | >15 years | Vapor, gas, fume  Dust  Inorganic fibers  Animals excrement | 0.9 (0.6-3.2)  1.7 (1.2-2.3)  1.1 (0.6-2.0)  1.8 (1.0-3.2) |  |
|  | Δ work temperature | 3.3 (2.2-4.8) |  |
| Rossow,  2014,  Finland | 20 |  | Exposure to hay | 7.1 (1.5-32.9) |  |

**Table 3. Summary of population attributable fraction (PAF) and attributable fraction (AF) in all pneumonias and lobar pneumonia/pneumococcal pneumonias with regard to exposure to vapor, gas, dust, fumes and welding/metal fumes.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author** | **All pneumonias** | | **Lobar/pneumococcal pneumonias** | |
|  | **PAF** | **AF** | **PAF** | **AF** |
|  | **Vapor, gas, dust, fumes** | | | |
| Farr, 2000 | 0.16 |  |  |  |
| Almirall, 2008, 2014 | 0.03 |  |  |  |
| Graham, 2004 |  | <0 |  |  |
| Veiga, 2006 |  | 0.6 |  |  |
| Torén, 2011 |  | 0.44 |  | 0.76 |
| Loeb, 2009 | 0.26 |  |  |  |
|  |  |  |  |  |
|  | **Welding, welding fumes, metal fumes** | | | |
| Beaumont, 1980 |  | 0.41 |  |  |
| Newhouse, 1985 |  | 0.46 |  |  |
| Torén, 2011 |  | 0.57 |  | 0.83 |
| Coggon, 1994 |  |  | 0.62 |  |
| Palmer, 2003 | 0.03 |  | 0.58 |  |
| Palmer, 2009 |  |  |  | 0.5 |
| Wong, 2010 |  |  |  | 0.63 |
|  |  |  |  |  |
|  |  |  |  |  |