

Occupational Beryllium Exposure & High ILO Profusion Score Linked with Declining FVC

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Abstract:

Background: Manufacturing nuclear weapons exposed workers to beryllium, asbestos, and other toxins. Beryllium causes lung fibrosis in sensitized individuals; fibrosis is evaluated by chest X-ray (CXR), which is read with the International Labor Organization's (ILO) Profusion Scale. Some question the ILO classifications' clinical relevance. **Hypotheses:** 1) Increasing ILO scores correlates with decreased Forced Vital Capacity (FVC), independent of age, smoking status, and gender. 2) Beryllium exposure correlates with decreased FVC. **Methods:** A cohort of 729 beryllium-exposed former nuclear weapons workers (FWs) received CXR and spirometry. CXRs were read by three physicians blinded to each other's readings; the highest ILO rating was used. Beryllium exposure level was determined by an industrial hygienist. Statistical analyses were conducted in Epi Info® and SAS 9.1v®. **Results:** In linear regression models controlling for age, smoking status, beryllium exposure, and gender, increasing ILO scores correlated with decreasing FVC (Spearman= -0.1867; Pearson= -0.1768). In models controlling for age, gender, and smoking status, both beryllium exposure (p=0.0318) and abnormal ILO scores (p=0.0020) independently correlated with decreasing FVC. Normal ILO scores had average FVC of 88.40% and abnormal ILO scores had average FVC of 75.64%; this difference was statistically significant. ANOVA/ANCOVA analyses showed beryllium and ILO scores to both be independently associated with decline in FVC (R²=0.0543). There was no significant interaction between ILO scores and beryllium. **Conclusion:** Correlation of ILO scores to FVC validates use of the ILO Scale for CXR evaluation. Exposure to beryllium and other metals was associated with lower FVC. The ILO Profusion Scale is an objective method to quantify lung damage.

Introduction:

- From 1949-1975, Line 1/Division B manufactured nuclear weapons at the Iowa Army Ammunition Plant (IAAP) in Middletown, IA.
- FWs were exposed to potentially harmful substances such as beryllium, solvents, biological agents, acids, and possibly radiation. Beryllium causes an immunological response in susceptible individuals, leading to pulmonary fibrosis.
- In 1993, Congress passed a law requiring the Department of Energy to provide medical screenings for all former Atomic Energy Commission (AEC) workers. Screenings for Line 1 FWs began in 2001 through The University of Iowa Former Worker Program (UI-FWP).
- Screening includes CXR, spirometry, Beryllium Lymphocyte Proliferation Test (BeLPT), Hemocult stool testing, blood tests, and urinalysis.
- FWs with occupational lung diseases and radiogenic cancers may be eligible for compensation under the Energy Employees Occupational Illness Compensation Program Act (EEOICPA), passed by Congress in 2001.

Figure 1: Former Worker Smoking Status

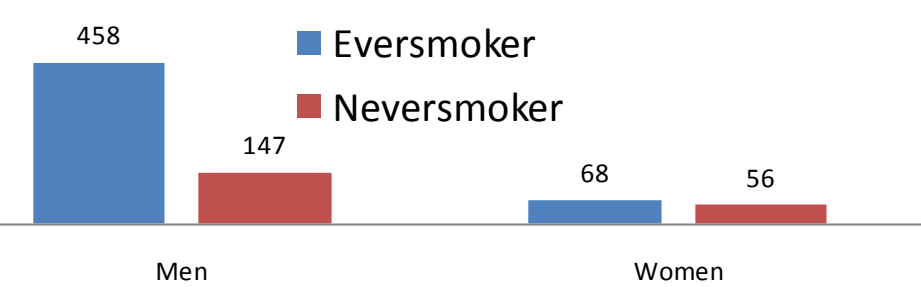
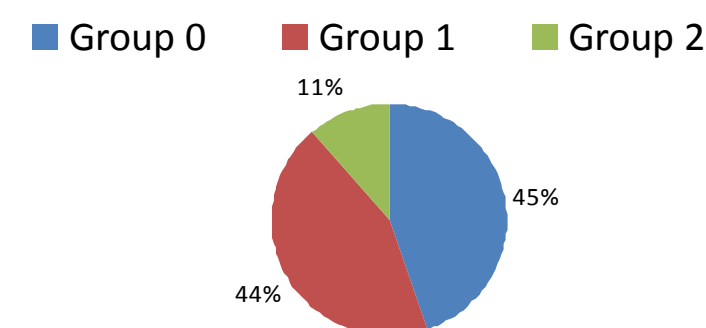


Figure 2: Beryllium Exposure by Occupational Category



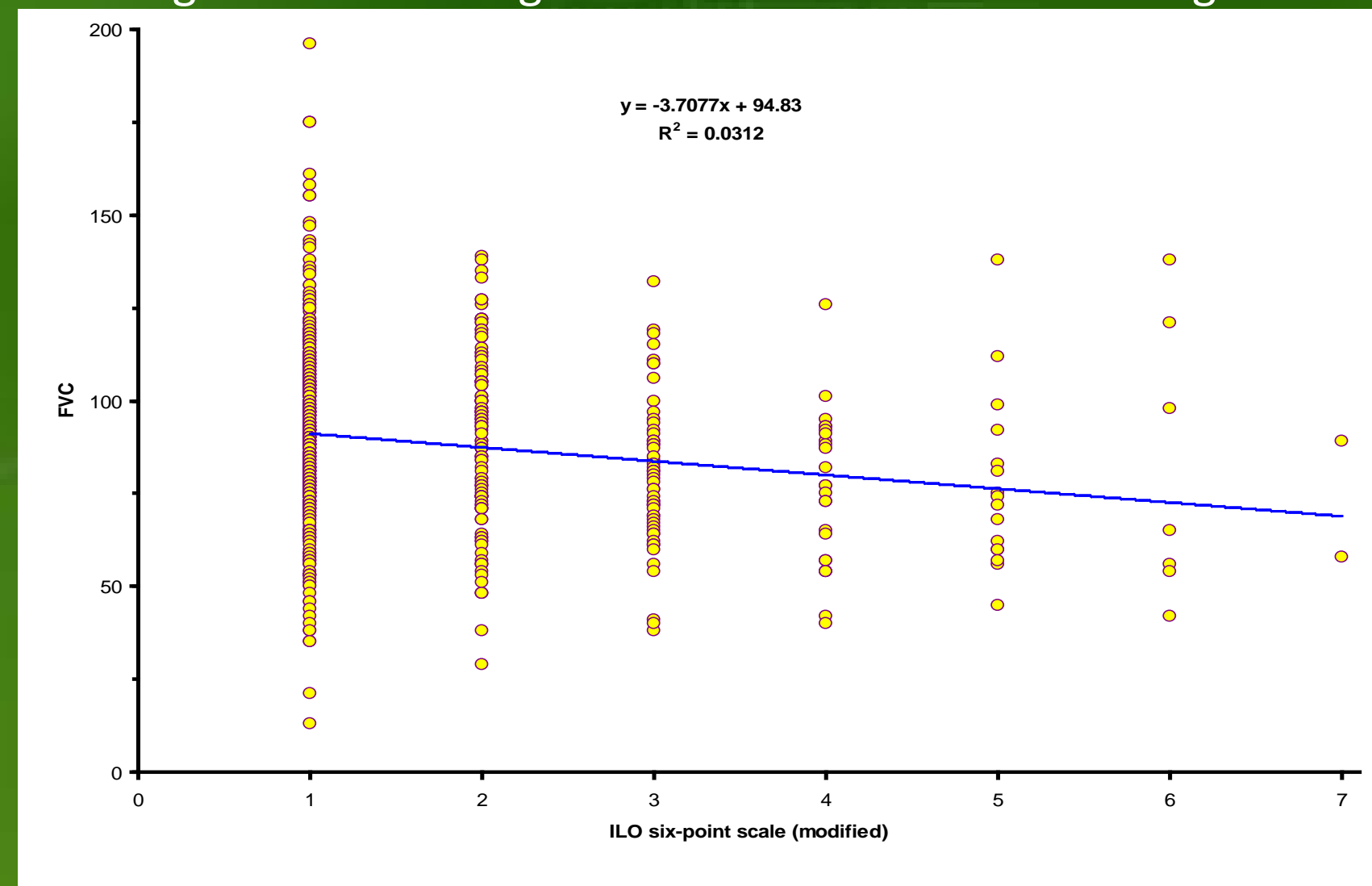
Methods:

- Cohort selection was based on records from IAAP, contractors' records, & employment validation by other FWs.
- Participants were recruited from 2001-2008 by mail, telephone, press releases, and word-of-mouth (n=729).
- Conducted spirometry to determine the Forced Vital Capacity (FVC) of the lungs: the total amount of air expelled during the test.
- CXR were graded using International Labor Organization's (ILO) Chest X-ray Profusion scale and grouped according to system defined in Miller et al 1996 (see Table 1).
- Three occupational medicine physicians read each CXR. They were blinded to each other's readings, smoking status, occupation, and age of subjects.
- ILO Profusion Scores greater than ≥1/0 were considered abnormal.
- Smoking status was reported as: smoker, ex-smoker or never smoker.
- Beryllium exposure data was based on self-reported job data and assigned an exposure code based on an industrial hygienist's job dictionary created for the project (see Table 2 & Figure 2).
- Epi Info® and SAS v9.1® were used for statistical analyses.

Hypotheses:

1. An increase in ILO scores correlates with decreased FVC on spirometry. This relationship is independent of age, smoking status, and gender. This demonstrates the clinical and epidemiological relevance of the scale.
2. Occupational beryllium exposure correlates with decreased FVC due to the knowledge that beryllium causes pulmonary fibrosis in sensitized individuals.

Figure 3: Increasing ILO scale linked with decreasing FVC



Results:

- No statistically significant association between smoking status (ever smokers vs. never smokers) and FVC % predicted (classes: ≥80, 50-79, 30-49, <30). Chi-squared test for linear trend=2.659 (p=0.102, n=729).
- In a linear regression of workers who reported Be exposure controlling for age, smoking status, beryllium exposure, and gender, we found increasing ILO profusion statistically significantly associated with decreasing FVC % predicted (Pearson partial correlation= -.1867, Spearman partial correlation= -0.1768).
- FVC % predicted mean for men (n=605) was 84.87% and women (n=124) was 84.87%.
- Higher ILO profusion score (≥1/0) was associated with lower mean FVC % predicted in both men and women. ILO score groups 0-1 (Table 1) average FVC % predicted of 90.28% and groups 2-6 average 79.3% (ANOVA/ANCOVA analysis R²=0.036, n=729, P < 0.0001).
- In ANOVA/ANCOVA model controlling for sex, ILO scale, smoking status, age, and beryllium exposure, both ILO score (p=0.0020) and beryllium exposure (p=0.0318) were significantly associated with decreasing FVC % predicted. ILO score groups 0-1 FVC % predicted mean was 88.40% and groups 2-6 FVC % predicted mean was 75.64% (p=0.0001, R²=0.0565, n=609).
- There was no significant interaction between ILO scale and Be exposure (p=0.69, R²=0.0469).
- In a model with only ILO score (p<0.0001) and beryllium (p=0.0311) exposure, both were significantly associated with decline in FVC % predicted (p<0.0001, R²=0.0543, n=609).

Discussion & Conclusions:

- Beryllium exposure is also associated with a decrease in FVC % predicted. In the lungs of sensitized individuals, an immunological response occurs leading to fibrosis. The relationship of Be exposure to FVC % predicted demonstrates that the health of FWs is affected due to their occupational exposure to Be.
- Increasing ILO score is associated with decline in FVC % predicted as shown by both linear regression and ANOVA. The average FVC % predicted is significantly lower for former workers with abnormal ILO readings (ILO groups 2-6).
- The association of ILO score to FVC % predicted is independent of age, gender, smoking status, and Be exposure. Both Be exposure and ILO are independently affecting the decrease in FVC % predicted.
- Accounting for beryllium exposure and ILO scale only improves the predictability of FVC % predicted by 5.43%. More research needs to be done on the genetic and other unaccounted for factors that influence the decrease in FVC % predicted in this former worker cohort.
- Overall, this validates the use of the ILO profusion scale to evaluate chest X-rays for epidemiological and clinical purposes.

Table 1: Groups for ILO readings

Group 0	0/-, 0/0
Group 1	0/1
Group 2	1/0
Group 3	1/1
Group 4	1/2
Group 5	2/1, 2/2, 2/3
Group 6	3/2, 3/3, 3/+

Grouped according to Miller et al 1996.

Beryllium Exposure by Occupation

Group 0	Group 1	Group 2
Security	QC	Machinist
Medical	Inspection	Tool
Administration	Production	Millwright
Office	Electrician	Weld
Chemistry	Component Operator	
Engineering	Pipefitter	
Food service	Iron worker	
Labor	Melt	
Construction	Changehouse	
Carpentry	Laundry	
Storage	Custodial	
Railroad	Maintenance	

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