Reconstruction of Silica and Non-silica Exposures and Lung Burdens

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Background

The quantitative relationship between exposure to crystalline silica and development of silicosis is uncertain despite a number of studies.

- Exposure reconstructions based on sparse data.
- Lung burden reconstructions do not account for retention and clearance of inhaled dusts.
- Exposure reconstructions for silica do not account for simultaneous exposures to non-silica dusts.

Lung Overload

- Alveolar macrophages (AM) => clearance of deposited particles from alveoli.
- Ability of the AM to remove particles becomes impaired at high lung burdens - ‘overload’
- AM die => release acute inflammatory mediators =>chronic inflammation => fibrosis
- Seen in a number of studies with particles of relatively low cytotoxicity
- Overload occurs at ~ 1-3 mg/g of lung tissue, and is independent of the type of particle (at least for low toxicity particles).

Hypotheses

- A cumulative exposure metric, which includes both silica and non-silica dusts, is more related to the development of silicosis than cumulative silica exposure alone.
- The time to macrophage overload is a function of both silica and non-silica exposure, and is related to the development of silicosis

Goals of Study

- Estimate historical exposures for (a) silica and (b) non-silica dust for each job-code in the NC Dusty Trades program for each workplace for 1935-1980
- Calculate cumulative exposure (mg/m^3 x years) for silica and non-silica dusts
- Estimate lung burden (mg/kg) as a function of time from first exposure for each worker
- Estimate time to macrophage overload due to total (silica and non-silica) dust exposure for each worker

Goals of Study (continued)

- Conduct a case-control analysis for silicosis using the cumulative exposure and lung burden metrics
- Evaluate the influence of time to macrophage overload on the occurrence of silicosis with reference to the exposure and lung burden metrics

Previous Studies

- Rice, C., Harris, R.L., Lumsden, J., Symons, M.J.: Reconstruction of silica exposure in the North Carolina Dusty Trades. *American Industrial Hygiene Association Journal*, 45:689-696, 1984
- Rice, C., Harris, R.L., Jr., Symons, M.J. Checkoway, H.,: Factors affecting latency of silicosis in North Carolina, *Annals of Occupational Hygiene*, 32:673-680, 1988.
- Rice, C., Checkoway, H., Dosemici, M., Stewart, P., Blair, A.: Effects of exposure estimation procedures on the evaluation of exposure response relationships for silicosis, *Annals of Occupational Hygiene*, 41:485-490, 1997.

NC Dusty Trades Program 1935-1981

Industry 1, 2, .. 12 → Quarrying granite, Rock crushing, Foundry operations, Mining and milling of mica/feldspar, Kaolin, Lithium, Pyrophyllite, Tungsten, Quartz, Talc.

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Company A, B, …

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Location 1, 2, ….

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Job Codes a, b, c, …

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Tasks 1, 2, 3, …

Exposure Information

Work History	IH File
Worker ID	Industry
Date of birth, Race	Company
Industry	Work site location
Company	Job title
Work site location	Task
Job title	Engg. Controls
Start and end dates of job	Analytical result
	Date of sample

Health-Related Information

- Work History
- Chest Exam
- X-Ray
- Date of diagnosis
- Smoking

Available Measurements

- Task Exposure Measurements (15-min averages)
  - 1936-1979
  - Greenburg-Smith and Midget Impingers
  - Particle count concentration in mppcf
  - 85% of the ~15,000 measurements
- Job Exposure Measurements (8-hour TWA)
  - 1970-1981
  - Cyclone sampler
  - Particle mass concentration in mg/m^3
  - ~15% of all measurements

(mg/m^3)= mppcf x *0.09*

Imputation of Missing Data

- 7680 distinct jobs => Need measurements for 2447 distinct industry/company/worksite/task combinations for each 5-year time-interval between 1935 and 1980.
- Mean and variance => at least 7 measurements.
- Aggregate across worksites.
- Aggregate across worksites/5-year interval.
- Aggregate across worksites/tasks/5-year interval.
- Aggregate across company/worksite/task/5-year interval.
- Aggregate across industry/company/worksite/task/5-year interval.

Job exposure estimation

- Arithmetic mean task exposure is estimated from measurements and imputation.
- Job exposures are estimated using task exposures

$$E(job) = \sum_{i=1}^{N} E(task_i)\, t(task_i)$$

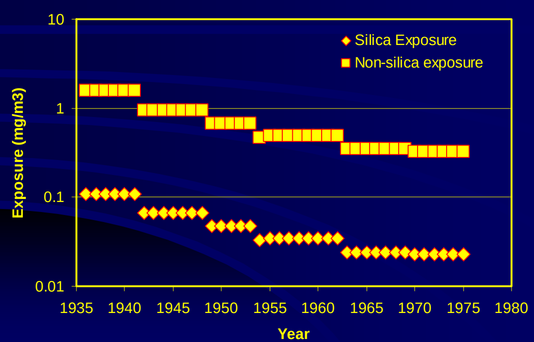
- where *Ei* is task exposure and *ti* is the time fraction spent on each task within a job.
- The variance for the job exposure is estimated as

$$Var(job) = \sum_{i=1}^{N} \mathrm{var}(task_i)\, [t(task_i)]^2$$

Average fractional silica content by industry

Industry	% silica
Granite	0.261
Mica/feldspar	0.200
Rock crushing	0.293
Foundry operations	0.065
Kaolin	0.303
Lithium	0.232
Pyrophyllite	0.346
Tungsten	0.134
Quartz	0.501
Talc	0.015

Job Exposure history for Crane Operator in Foundry Industry



Lung Burden Modeling Example

Exposure History

1935 to 1945	0.5 mg/m3
1945 to 1955	1.1 mg/m3
1955 to 1965	1.2 mg/m3
1965 to 1975	0.3 mg/m3

Model Assumptions

- Worker worked 5 days/week, 48 weeks/year
- Breathing rate for the worker is 20 L/min (12-25 L/min)
- Breathing rate for rat is 0.1 L/min
- Human lung weighs 1 kg (0.6–1.5 kg)
- Rat lung weighs 2 g
- Lung accumulation rate = 2-3 (µg/mg m^{-3})/day (for rats from animal studies)
- Lung accumulation rate is 6-15 (µg/mg m^{-3})/day (for humans by extrapolation from limited human data).
- Accounts for clearance during periods of no exposure

Lung Burden Calculation

Year	Dust retained	Lung burden
1935 to 1945	1920 mg	1.92 mg g-1
1945 to 1955	4224 mg	6.14 mg g-1
1955 to 1965	4608 mg	10.74 mg g-1
1965 to 1975	1152 mg	11.89 mg g-1
Cumulative Lung Burden		11.89 g
Time to overload		= ~ 10 years

Cumulative exposures for cases/controls

		Cases	Controls
Total silica exposure mg/m^3*years	N	214	631
	Mean	**22.46**	**13.54**
	Median	**13.79**	**3.59**
	25th %ile	3.81	1.39
	75th %ile	35.21	14.18
Total non-silica dust exposure mg/m^3*years	N	214	631
	Mean	**81.1**	**51.79**
	Median	**44.61**	**22.73**
	25th %ile	15.90	12.48
	75th %ile	121.01	47.12

Lung burdens for cases/controls

		Cases	Controls
Silica (mg/g of lung tissue)	N	214	631
	Mean	**8.61**	**5.19**
	Median	**5.29**	**1.38**
	25th %ile	1.37	5.30
	75th %ile	13.52	5.41
Non-silica (mg/g of lung tissue)	N	214	631
	Mean	**31.09**	**19.86**
	Median	**17.13**	**8.71**
	25th %ile	6.11	4.75
	75th %ile	46.47	18.09

Time to lung overload for cases/controls

		Cases	Controls
Months from first employment to overload (2 mg/g of lung tissue)	N	205	595
	Mean	**143.2**	**204.9**
	Median	**121.0**	**188.0**
	25th %ile	54.0	111.0
	75th %ile	196.0	285.0

Preliminary Conclusions

- Cases have a higher cumulative silica and non-silica dust exposures than the controls.
- Median silica exposures for cases were 4 times higher than for controls.
- Time to overload is lower in the cases (121 vs 188 months).
- Non-silica exposures and time to overload appear to be related to the development of silicosis.

Further Analysis

- Use of experts judgments along with empirical modeling and historical information about workplace conditions. **(PRIORS)**
- Use Bayesian framework with priors and sparse data to obtain refined estimates of exposure **(POSTERIORS)**