

# Exposure risk factors associated with beryllium sensitization in former NTS workers

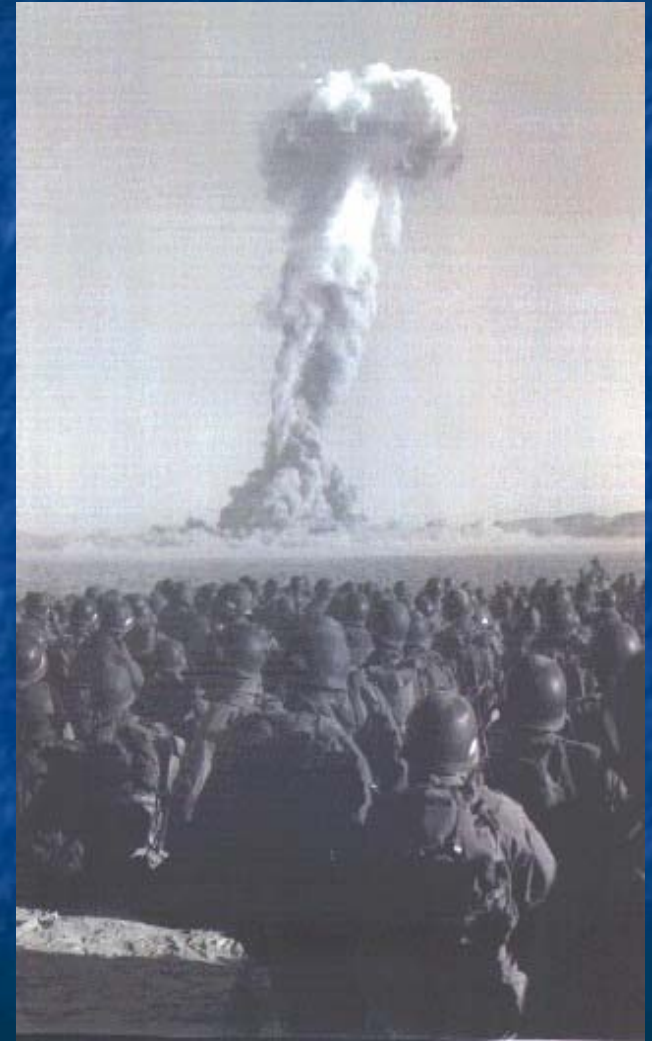
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From data developed by US DOE  
supported FWP

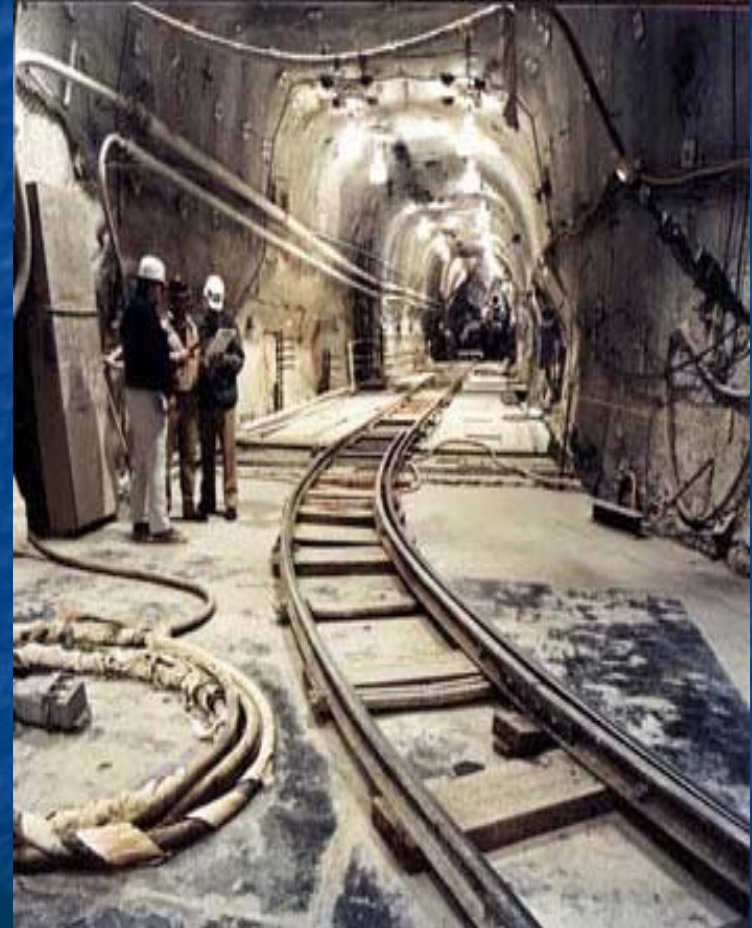
# Background-Nevada Test Site

- Atomic Energy Commission's proving ground
- 928 nuclear weapons tests conducted from 1951 to 1992
  - One hundred atmospheric and remainder underground
- Approximately 15,000 workers employed at peak of testing
- Radiation and beryllium exposures of re-entry crews



# Beryllium exposure

- 1950's: above-ground dispersal tests
- 1957-1992: underground "line-of-sight" pipes (pre-shot grinding, post-shot exposures)
- 1960-1973: tested nuclear reactors and engines at NRDS (machining, fuel exhaust)
- 1973-1992: Atlas Facility in North Las Vegas (machining)



# Beryllium epidemiology

- Relying on historic exposure assessment
  - Difficult to quantify past exposures
    - Limited industrial hygiene measurements
    - Must use questionnaire information
    - Temporal variability of exposure
    - Many workers unaware of exposure
  - Few studies in non-traditional low-level exposure settings

# Objectives

- To apply data reduction methods to categorize individual worker exposure to beryllium using questionnaire data
- To identify job factors associated with beryllium sensitization
- To estimate the risk of beryllium sensitization associated with job factors

# Hypotheses

- Those who worked in underground tunnels, NRDS, or the Atlas facility have an increased risk of beryllium sensitization
- The risk of beryllium sensitization is associated with total years worked at NTS

# Study Population

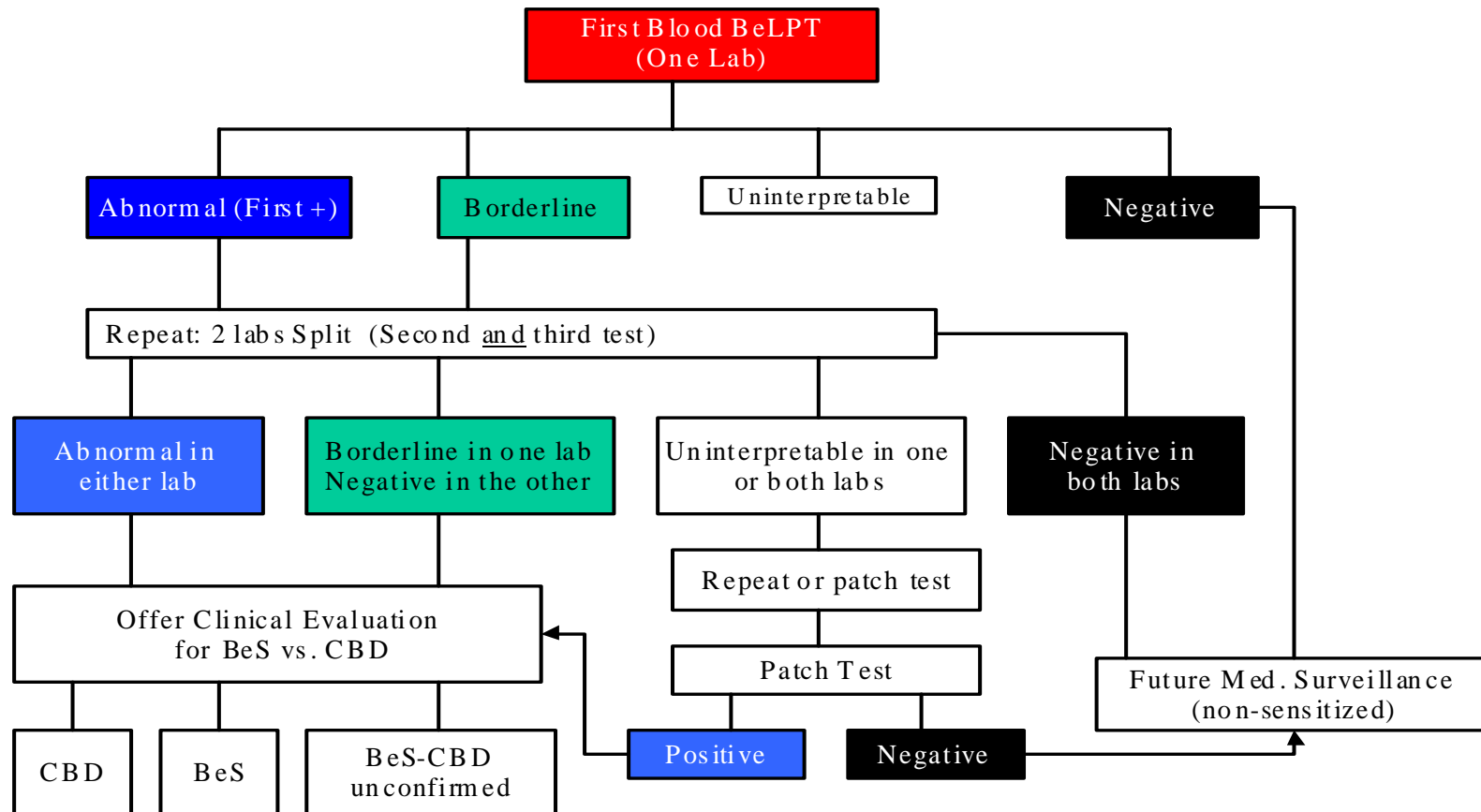
- Worked at NTS between 1951 and 1992
- Selected from larger group part of DOE medical screening program
  - based on responses to phone questionnaire about location and time period worked
- Screened from March 2001 to December 2004

# Data Collection

- Initial contact form
  - Personal information (dob, residence, etc.)
  - Work history (job tasks, years, etc.)
- Study Questionnaire
  - Work history (dates worked, job tasks, etc.)
  - Medical history
  - Smoking history
- Clinical tests
  - Beryllium lymphocyte proliferation test (BeLPT), chest X-ray, and spirometry

# BeLPT Protocol

Workplace Medical Surveillance Beryllium Algorithms: One Lab, Then Two Lab Split



# Table 1: BeLPT results for tested participants

BeLPT result	n Subjects	% tested
Total screened for Be	3259	47.1
Sensitized	21	1.4
Single borderline	16	1.0
Single positive	16	1.0
Normal	1449	94.5
Uninterpretable	32	2.1
Total tested for Be	1534	

# Table 2: Study population characteristics

		All Subjects n = 1470	Normal n = 1449	Sensitized n = 21	p-value
Age, mean (sd)		62.1 (10.7)	62.1 (10.7)	63.3 (8.9)	0.59 <sup>a</sup>
Years at NTS, mean (sd)		13.0 (9.8)	12.9 (9.8)	17.6 (10.7)	0.03 <sup>a</sup>
Gender, n (%)	male	1391 (94.6)	1370 (94.5)	21 (100)	0.62 <sup>b</sup>
	female	79 (5.5)	79 (5.5)	0	
Smoking status, n (%)	current	281 (19.1)	276 (19.0)	5 (23.8)	0.43 <sup>b</sup>
	former	653 (44.4)	642 (44.3)	11 (52.4)	
	never	452 (30.7)	447 (30.8)	5 (23.8)	
	missing	84 (5.7)	84 (5.8)	0	
Pack-years, mean (sd)		22.1 (26.5)	22.4 (13.1)	13.1 (13.4)	0.38 <sup>c</sup>
median		13.5	13.5	10.8	

<sup>a</sup> two-sample t-test was used

<sup>b</sup> chi-square test was used

<sup>c</sup> Wilcoxon test was used

# Table 3: Comparison of clinical test results

	Normal n = 1425	Sensitized n = 21	P-value
<b>Spirometry<sup>a</sup></b>			
FEV1 % predicted, mean (sd)	88.44 (31.51)	95.62 (16.48)	0.06
FVC % predicted, mean (sd)	95.96 (30.8)	98.00 (15.6)	0.57
FEV1 / FVC, mean (sd)	0.73 (0.11)	0.77 (0.08)	0.10
<b>X-Ray (B-reading)<sup>b</sup></b>			
Normal-0/1, n (%)	1334 (93.6)	20 (95.2)	1.00
1/0+, n (%)	78 (5.5)	1 (4.8)	

<sup>a</sup> two-sample t-test was used

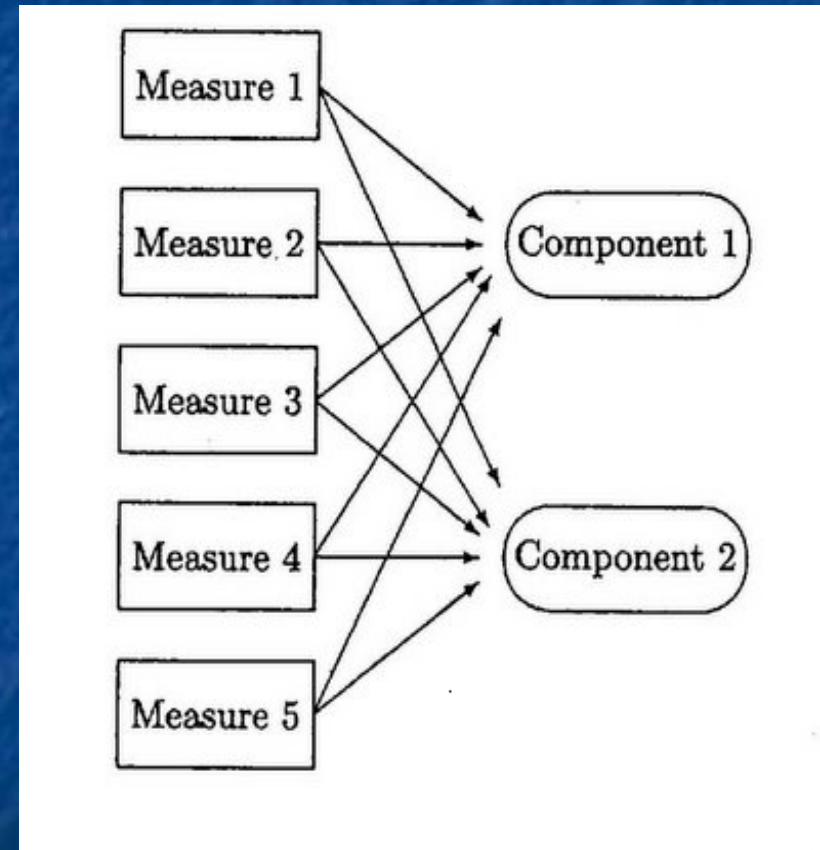
<sup>b</sup> Fisher's exact test was used

# Objectives

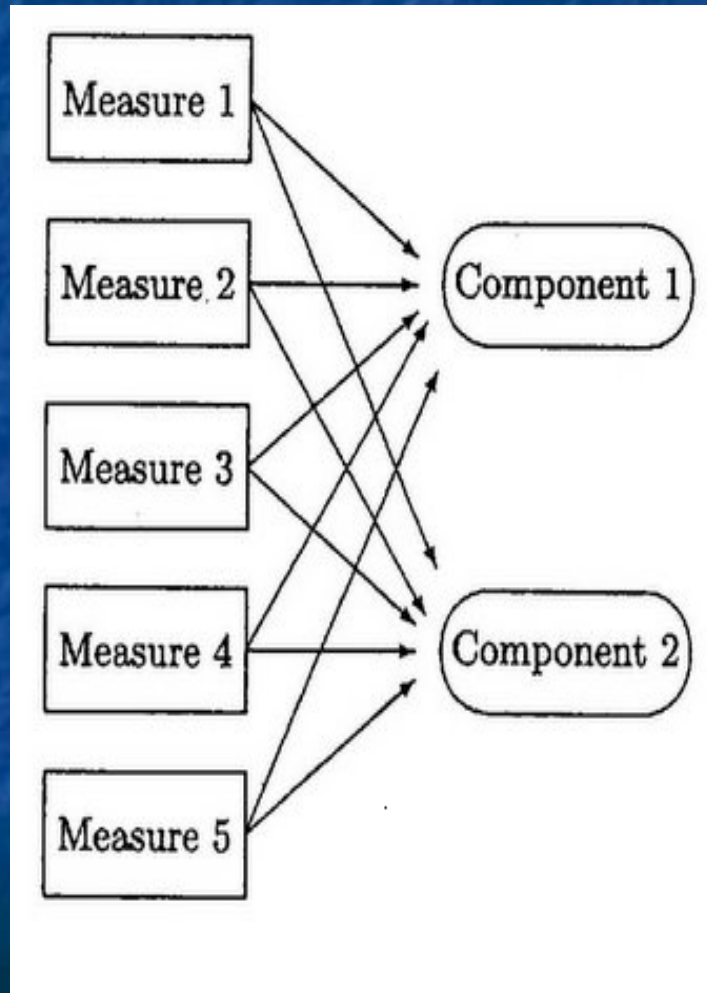
- Use data reduction methods to categorize individual worker exposure to beryllium using questionnaire data
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# Statistical Analysis

- Principal Component Analysis
  - Data reduction
  - Identify uncorrelated components
- Multiple Logistic Regression Model



# Exposure Questions for PCA Analysis



## Component 1

- Pre-shot work in LOS
- Post-shot work in LOS
- Modified flanges in LOS
- Cut LOS pipe
- Disposed LOS pipe

## Component 2

- Disassembled nuclear reactors
- Worked in MAD building
- Clean up machining areas

## Component 3

- Worked in Atlas facility

# Regression Model

$$\ln OR = \beta_0 + \beta_1 * \text{age} + \beta_2 * \text{yrswork} + \beta_3 * \text{pack-yrs} \\ + \beta_4 * \text{atlas} + \beta_5 * \text{lospipe} + \beta_6 * \text{nrds} + \epsilon$$

component 1

pre-shot LOS  
post-shot LOS  
flanges LOS  
cut LOS  
disposed LOS

component 2

disassembled nuclear reactors  
MAD building during NRD era  
clean up machining areas

## Table 4: Univariate regression analyses

Variable	Univariate OR (95% CI)
Age	1.01 (0.97, 1.05)
Years worked	1.04 (1.00, 1.09)
Pack-years	0.98 (0.96, 1.01)
Atlas	2.09 (0.80, 5.44)
LOS pipe	0.98 (0.64, 1.50)
NRDS	1.49 (1.03, 2.16)

## Table 4: Univariate regression analyses

Variable	Univariate OR (95% CI)
Age	1.01 (0.97, 1.05)
Years worked	1.04 (1.00, 1.09)
Pack-years	0.98 (0.96, 1.01)
Atlas	2.09 (0.80, 5.44)
LOS pipe	0.98 (0.64, 1.50)
NRDS	1.49 (1.03, 2.16)

# Table 5: Results from regression analyses

Variable	Univariate OR (95% CI)	Multivariate* OR (95% CI)
Age	1.01 (0.97, 1.05)	1.03 (0.97, 1.08)
Years worked	1.04 (1.00, 1.09)	1.03 (0.99, 1.08)
Pack-years	0.98 (0.96, 1.01)	0.98 (0.96, 1.00)
Atlas	2.09 (0.80, 5.44)	1.55 (0.54, 4.45)
LOS pipe	0.98 (0.64, 1.50)	0.94 (0.61, 1.46)
NRDS	1.49 (1.03, 2.16)	1.45 (0.94, 2.23)

\*Adjusted for start date at NTS, as well as other variables in the model

# Conclusions

- Principal component scores can be used to categorize individual worker exposure
- Working at the NRDS and total years worked at NTS may be used to identify workers at higher risk
- Workers on the NRDS have a 45% increased risk of beryllium sensitization

# Limitations

- Small sample size
- Potential recall bias
  - But subjects unaware of disease status at time of monitoring
- Exposure misclassification
  - Workers' recall of task can be fairly accurate (Reeb-Whitaker et al. 2002)
  - NTS workers unsure of exposures and tasks performed

# Next Steps

- Refine Exposure measure
  - Validate PCA exposure measures using limited area and personal sampling data
  - Conduct intensive interviews with cases and sample of controls
  - Identify high short-term exposures
- Collaborate with other cohorts with atypical low-level exposures to study relationship with sensitization and disease
  - Evaluate gene-environment interactions

# Acknowledgments

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# Factor vs. Principal Component Analysis

- Based on different models and assumptions
- FA assumes that the measured responses are based on the underlying factors
- PCA assumes that the principal components are based on the measured responses