

## **Executive Summary**

### **Objectives:**

The primary objective was to develop prediction models for determining the optimal intervals of chest radiographic surveillance for workers exposed to silica dust; the second primary objective is to assess the cost per case identification and compare the cost per life year gained under routine medical surveillance program with that under the recommended program for workers exposed to silica dust in China. In addition, the inter-rater agreement amongst three invited radiologists on rereading the chest radiographs and the agreement between the original diagnoses of silicosis (from routine reports) and the verified diagnoses reassessed by the three experts were also evaluated.

### **Methods:**

A total of 3492 male workers exposed to silica dust in an iron ore and 763 male workers in the tungsten ore during the period 1964 - 1974 were recruited into this retrospective cohort study. All cohort members were followed up through the end of 2008 to observe the occurrence of silicosis and the overall mortality. All 9084 chest X-ray films in the iron ore cohort and 10958 chest X-ray films in the tungsten ore cohort were reread by three radiologists who had been qualified as experts at the national level according to the Chinese National Diagnostic Criteria of Pneumoconiosis (GBZ70-2009). The diagnosis of silicosis made by the panel of these three invited experts was referred to the “verified diagnosis”.

Cohen's Kappa test was used to test inter-rater agreements of three invited readers on chest radiographs and the agreement on the diagnosis of silicosis obtained from routine medical surveillance (i.e., the original routine diagnosis) was compared with those verified by the 3 qualified readers (i.e., the verified diagnosis). The multivariate Cox's proportional hazard regression models were developed to predict the silicosis occurrence based on three selection approaches – entry of all predictors at the same time, backward stepwise selection, and Least Absolute Shrinkage and Selection Operator (LASSO) selection. The LASSO model showed the best model fit which was thus regarded as the final model for predicting a score chart.

Based on this practically used score chart, we then classified workers into three groups of different risk levels of silicosis (low, moderate, and high). We estimated the cumulative risk of silicosis over years of follow-up for these three groups of workers at different risk levels. We used 1 per thousand of cumulative risk for developing silicosis as a “benchmark” to determine the intervals of radiologic surveillance for workers with different risks of silicosis. Multi-state Markov model was used to calculate the transition probabilities of different states of silicosis and the analysis on cost and effectiveness was performed.

## **Results:**

By the end of 2008, the cumulative incidence rate of silicosis was 8.53% (298/3492) in the iron ore cohort and 38.93% in the tungsten ore cohort (297/763). Good inter-rater agreements were observed amongst three invited radiologists for rereading all the chest films.

Kappa value for the agreement between the original diagnoses and the verified diagnoses was 0.89 (95% confidence interval [95%CI], 0.88-0.91) in the iron ore cohort and 0.73 (95%CI, 0.68-0.77) in the tungsten ore cohort.

The model with the best fit was LASSO Cox model which showed a good discrimination with an area of 0.83 (95%CI, 0.81-0.86) under the receiver operating characteristic (ROC) curve. We classified workers into 3 risk groups according to the score chart obtained from the LASSO Cox model, and found the observed probabilities matched well to the predictions. According to 1 per thousand “benchmark”, we can determine that the initial interval of radiographic surveillance for workers in the low risk group was 11 years and a subsequent biyearly examination was recommended. The initial examination interval was 11 years and 5 years respectively for workers in the middle and high risk group, and then a yearly examination was recommended. For patients with silicosis, an annual radiological surveillance program was recommended regardless of the stage of pneumoconiosis.

According to results from multi-state model, we estimated that the yearly transition probability was 0.0198 for silica dust exposed workers from healthy state to the suspected silicosis cases (sojourn time = 47 years), 0.0338 from suspected silicosis cases to silicosis stage one (sojourn time = 23 years), 0.0516 from silicosis stage one to stage two (sojourn time = 9 years), 0.059 from silicosis stage two to stage three (sojourn time = 6 years), and 0.18 from silicosis stage three to death (sojourn time = 5 years).

During the period 1964 to 2008, the average direct medical cost spent on identifying one silicosis case was US\$ 21853.11 and the non-medical cost for identifying one case was US\$ 5993.30 per case. The estimated medical cost regarding per life year gained was US\$ 43.60 under the routine medical surveillance program and it would be US\$ 46.99 if the newly recommended surveillance program is adopted.

### **Conclusions:**

This study is the first to provide scientific evidence on determining the optimal intervals of radiographic surveillance for workers at different risk levels of silicosis based on the 'best' prediction model. Although our study revealed similar cost and effectiveness for using the recommended occupational health examination strategy compared with the routine program, this study is the first to provide scientific theory for guiding evidence-based occupational medical surveillance on workers exposed to silica dust in the world.