

Silicosis Diagnostic Rule

Description of diagnostic rule and impact of misclassification error

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Setup

Packages used

```
if (!require("pacman", quietly = TRUE)) {  
  install.packages("pacman")  
}  
  
pacman::p_load(  
  tidyverse, # Used for basic data handling and visualization.  
  gt,        # Used to print html tables.  
  report     # Used to cite packages used in this session.  
)
```

Session and package dependencies

R version 4.4.1 (2024-06-14 ucrt)
Platform: x86_64-w64-mingw32/x64
Running under: Windows 11 x64 (build 22631)

Matrix products: default

locale:

[1] LC_COLLATE=Spanish_Mexico.utf8 LC_CTYPE=Spanish_Mexico.utf8
[3] LC_MONETARY=Spanish_Mexico.utf8 LC_NUMERIC=C
[5] LC_TIME=Spanish_Mexico.utf8

time zone: Europe/Berlin
tzcode source: internal

attached base packages:

[1] stats graphics grDevices utils datasets methods base

other attached packages:

[1] report_0.5.8 gt_0.10.1 lubridate_1.9.3 forcats_1.0.0
[5] stringr_1.5.1 dplyr_1.1.4 purrr_1.0.2 readr_2.1.5
[9] tidyr_1.3.1 tibble_3.2.1 ggplot2_3.5.1 tidyverse_2.0.0
[13] pacman_0.5.1

Description

A diagnostic prediction model to **rule out** pneumoconiosis in construction workers was developed and published in 2007.¹ The study population consisted of Dutch natural stone and construction workers age 30 years and older.

Outcome

The diagnosis of pneumoconiosis was defined as a chest x ray (CXR) indicative for pneumoconiosis (ILO profusion category 1/1), for which the ILO international classification of radiographs of pneumoconioses 2000 version was used. The most up-to-date version of this guideline is the 2022 revised edition.² The ILO score is assigned upon examination of small opacities on CXR, in comparison to standardized CXR images, and is composed of a major category, which is followed by a subcategory. For instance, a score of 1/0 means that 1 was assigned as the major category, while 0 was strongly considered as the alternative. Conversely, a score of 0/1 means that the radiologist assigned 0 as the major category, but strongly considered 0 as suitable. A score 1/1 means that the CXR is consistent with the standardized CXR graded as 1.

As mentioned earlier, an ILO score 1/1 was considered as the reference standard for pneumoconiosis to develop the prediction rule. This contrasts with standard recommendations at the time mentioning that an ILO category 1/0 or higher should be considered consistent with the presence of pneumoconiosis.³ This decision was made under the rationale that a 1/0 cutoff would lead to greater misclassification. Furthermore, three different radiologists provided a score and the median score was used. Out of the 1291 workers included for analysis, a total of 37 (2.9%) had a score 1/1, whereas 131 (10.1%) were graded 1/0.

Predictors

Lung function measured with a pneumotacometer on the same day of CXR obtention and worker questionnaire variables were assessed as potential predictors of pneumoconiosis. Seven candidate predictors were identified in univariable analysis:

- Age
- Smoking status
- Job title
- Time working in the construction industry
- Feeling unhealthy
- Cumulative exposure to silica index
- Standardized residual FEV1

Continuous variables were dichotomized and modeled both as continuous and binary. Since there were no differences in the AUC of a prediction model with continuous vs binary predictors, the latter was kept for simplicity.

The final model included five predictors:

Predictor	Value	Score	Beta
Age	40 years	1.0	0.72
Smoking habit	Current smoker	1.0	0.70
Job title	High exposure job title	1.5	1.14
Work duration in construction industry	15 years	1.5	1.00
Self-related health	Feeling unhealthy	1.25	0.84
Standardized residual FEV1	-1.0	1.25	0.91

Diagnostic accuracy

The uncorrected AUC of the model was 0.81 (95%CI: 0.75 to 0.86). The corrected AUC was 0.76. A cutoff point of 3.75 is suggested as optimal, with the following classification measures:

	CXR +	CXR -	
Rule +	33	534	567
Rule -	4	720	724
	37	1254	1291

- Sensitivity: 89.2%,
- Specificity: 57.4%,
- Negative Predictive Value: 99.4%,
- Positive Predictive Value: 85.2%

Misclassification error of CXR

CXR based on Meijer, et al.⁴

A subset of 180 participants enrolled in the study used for the development of the diagnostic prediction rule were invited for further examination with chest high resolution computed tomography (HRCT), of which a total of **n=79** participants underwent HRCT.⁴ However, a final diagnosis of silicosis was not made based on HRCT and consensus by radiologists, and the study limited to report HRCT findings with their frequencies among different ILO thresholds.

CXR based on ILO 1/0 cut-off from Hoy, et al.⁵

A recent study has estimated misclassification error of CXR using ILO categories against HRCT as the reference standard.⁵ Using the standardized cut-off of 1/0, CXR diagnostic performance against HRCT was as follows:

	HRCT +	HRCT -	
CXR +	25	2	27
CXR -	15	68	83
	40	70	110

Sensitivity (%): 62.5

Specificity (%): 97.1

False Positive Rate (%): 2.9

Positive Predictive Value; (%): 92.6

Negative Predictive Value; (%): 81.9

Likelihood Ratio (+): 21.87

Likelihood Ratio (-): 0.39

Accuracy (%): 84.5

Diagnostic Odds Ratio: 56.67

CXR based on ILO 1/1 cut-off from Hoy, et al.⁵

Using the summary data reported by Hoy, et al.⁵ for different ILO scores, a 2x2 table can be recreated for the 1/1 ILO threshold:

	HRCT +	HRCT -	
CXR +	23	2	27
CXR -	17	68	83
	40	70	110

Sensitivity (%): 57.5

Specificity (%): 97.1

False Positive Rate (%): 2.9

Positive Predictive Value; (%): 92

Negative Predictive Value; (%): 80

Likelihood Ratio (+): 20.12

Likelihood Ratio (-): 0.44

Accuracy (%): 82.7

Diagnostic Odds Ratio: 46

Accounting for misclassification error

Corrected ROC curve analysis of prediction models can be done by taking into account misclassification error for binary outcomes, provided that disease prevalence and misclassification rates are known.⁶

```
source("scripts/Zawistowski_misclassification_functions.R")
```

```
source("scripts/Diagnostic_rule_AUC_misclassification.R")
```

Results

Main prediction model (ILO 1/1),¹ misclassification based on ILO 1/0 by Hoy, et al.⁵

Outcome	Mean	Median	Q1	Q3	Min	Max
True	0.741	0.742	0.716	0.767	0.552	0.862
Misclassified	0.595	0.596	0.571	0.620	0.442	0.721

Absolute difference in AUC: 0.146

References

1. Suarathana E, Moons KGM, Heederik D, Meijer E. A simple diagnostic model for ruling out pneumoconiosis among construction workers. *Occupational and Environmental Medicine*. 2007;64(9):595-601. doi:[10.1136/oem.2006.027904](https://doi.org/10.1136/oem.2006.027904)
2. International Labour Organization. *Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconioses*. revised ed.; 2023:37. <https://www.ilo.org/publications/guidelines-use-ilo-international-classification-radiographs-pneumoconioses-1>
3. Wagner GR, World Health Organization. Screening and surveillance of workers exposed to mineral dust. Published online 1996:68.
4. Meijer E, Tjoe Nij E, Kraus T, et al. Pneumoconiosis and emphysema in construction workers: results of HRCT and lung function findings. *Occupational and Environmental Medicine*. 2011;68(7):542-546. doi:[10.1136/oem.2010.055616](https://doi.org/10.1136/oem.2010.055616)
5. Hoy RF, Jones C, Newbiggin K, et al. Chest x-ray has low sensitivity to detect silicosis in artificial stone benchtop industry workers. *Respirology*. 2024;29(9):785-794. doi:[10.1111/resp.14755](https://doi.org/10.1111/resp.14755)
6. Zawistowski M, Sussman JB, Hofer TP, Bentley D, Hayward RA, Wiitala WL. Corrected ROC analysis for misclassified binary outcomes. *Statistics in Medicine*. 2017;36(13):2148-2160. doi:[10.1002/sim.7260](https://doi.org/10.1002/sim.7260)