

Validation of Autopsy Data for Epidemiologic Studies of Coal Miners

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Background South Africa has one of the largest miner autopsy databases, PATHAUT, dating back to 1925. The diagnoses recorded on this database have never been evaluated for coal miners. The objective was to determine the validity of the autopsy diagnoses for coal workers, specifically bronchitis, silicosis, tuberculosis, coal workers' pneumoconiosis and emphysema, from 1975 to 1997.

Methods Three pathologists experienced in miner respiratory pathology conducted the review. They were blinded to employment and medical histories as well as to previous pathological diagnoses on PATHAUT and reviewed 28 coal miners with mixed mining exposures, and 31 cases with exclusive coal mine exposure—all selected randomly. The reviewers' independent and consensus diagnoses were compared to PATHAUT. An additional 31 cases with available whole mount sections were reviewed for the diagnosis of emphysema. Kappa statistics were used to determine degrees of agreement among reviewers and between reviewers and PATHAUT.

Results There was good to excellent agreement between the reviewers and PATHAUT for silicosis, tuberculosis, and pneumoconiosis that had progressed beyond the stage of macules, among the mixed and exclusive coal exposure cases. There was good to excellent inter-reviewer agreement for all diseases except bronchitis (agreement = fair to very good). For emphysema, there was good to very good inter-reviewer agreement but fair agreement with PATHAUT.

Conclusions This, the first systematic review of PATHAUT autopsy diagnoses made on coal workers, showed that PATHAUT can be used with confidence to establish a diagnosis of moderate to severe grades of coal workers' pneumoconiosis. The grade of emphysema recorded on PATHAUT could be used for epidemiological purposes, when whole mount sections have been prepared. Am. J. Ind. Med. 47:83–90, 2005. © 2004 Wiley-Liss, Inc.

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INTRODUCTION

Autopsy examination of mine workers for diagnosing work-related respiratory disease and subsequent compensation has been practiced in several countries, including the United States, the United Kingdom, and Australia. Although the various databases have been analyzed for a number of diseases and exposures, only a few systematic autopsy evaluations of coal miners have been published [Leigh et al., 1982, 1994; Green et al., 1989, 1998].

In South Africa, the Occupational Diseases in Mines and Works Act No. 78 of 1973 places an obligation on physicians attending to deceased miners and ex-miners to remove, with family permission, the cardiorespiratory organs and submit them to the National Centre for Occupational Health (NCOH) in Johannesburg, regardless of the clinical cause of death [Goldstein and Webster, 1975]. Autopsy results are captured on a computerized Pathology Automation System (PATHAUT).

In addition to autopsy findings, the database also included demographic details, details about the mines by which the worker was employed, the type of processes and job descriptions of the worker, years worked in mines, cause of death, smoking history, and data from routine fitness medical assessments.

Until the mid-1990s medical data for black workers were not as detailed or as complete as those for whites. Most black workers were routinely assessed for fitness at the employing mine rather than the Medical Bureau of Occupational Diseases (MBOD) where whites underwent annual medical examinations, pulmonary function testing, and radiographs.

A key strength of the PATHAUT database is its comprehensive nature in capturing multiple variables on organs submitted for autopsy. Importantly, there are a limited number of pathologists who perform the autopsies and make the diagnoses; they are long-standing employees of the NCOH with extensive experience who follow a standard procedure. However, inter-observer consistency must be considered when analyzing the PATHAUT data.

To date only a cursory study of this database has been undertaken for the coal mining sector. A 1992 NCOH in-house report indicated that 54% of white miners and 21.6% of black miners autopsied from the coal industry over a 2 year period (1988/1989) suffered from emphysema [Mangena et al., 1992]. No other comprehensive study of this database has been undertaken among coal miners. This is in contrast to the numerous studies that have been conducted on South African gold miners [Sluis-Cremer, 1980; Becklake et al., 1987; Hnizdo et al., 1991, 1994; Murray et al., 1996; Hnizdo and Murray, 1998].

This report presents the findings of a validation study of autopsy diagnoses recorded by three pathologists highly experienced in the assessment of coal miner lung pathology. The overall objective for the present study was to determine

the validity of the diagnoses captured on PATHAUT, especially coal workers pneumoconiosis (CWP), silicosis and emphysema, among all coal miners on whom autopsies had been conducted and recorded in PATHAUT from 1975 to 1997.

MATERIALS AND METHODS

Autopsies

The presence of compensable disease is established by macro- and microscopic examination of the lungs that, in most cases, are removed from the body, together with the heart, fixed in formalin and sent to the NCOH. Only if the death occurs within a 100 km radius of the NCOH is an autopsy conducted on the full body and the cardiorespiratory organs removed at the NCOH. In these cases, one lung is inflated and a paper mounted whole lung section is made, using the Gough–Wentworth technique. Once the histological slides have been examined they are archived.

Study Subjects

All cases on the PATHAUT database with a history of ever being employed in a coal mine, from 1975 to 1997 ($n = 7,760$), were identified and a subset of the cases based on the diagnoses of interest (emphysema, silicosis, and CWP) formed the sampling frame for this study. An initial sample of 30 coal miners with diagnoses of emphysema ($n = 15$), silicosis ($n = 10$), and/or CWP ($n = 16$) was randomly selected. Two cases were excluded because histologic slides could not be found.

Because 13 of the 28 cases had mixed exposures (histories of having worked in other mines besides coal; primarily gold mines) and given the likelihood of confounding effects of gold mining on outcomes, a second random sample of 31 miners with exclusive coal exposure was selected. Total years of mining experience in this group ranged from a few months to 40 years.

Because of the interest in assessing the validity of emphysema diagnoses arrived at by the best available methods, a third sample of 31 recent whole mount lung sections was selected, where these sections were still at the NCOH and had not yet been transferred to the MBOD, as is the usual procedure. Thus, these whole mount assessments were done on a convenience basis.

Three highly experienced, internationally recognized lung pathologists with long-term interests in pneumoconiosis and coal worker pathology reviewed the slides for accuracy of diagnoses. Although aware that all these cases had some degree of coal dust exposure, they were blinded to employment details and medical histories as well as previous pathological diagnoses. The pathologists reviewed the material independently and, with regard to emphysema, by consensus. Their independent and consensus findings were compared to the diagnoses on PATHAUT.

The following histological definitions were used by the three pathologists. These definitions were developed jointly by the NCOH and the National Institute of Occupational Safety and Health (NIOSH).

Coal workers' pneumoconiosis was assessed microscopically according to the presence of macules or nodules or both. A minimum of six sections of lung are examined. Slides are routinely stained with aldehyde fuchsin for elastic fibers with a hematoxylin and eosin counterstain. Occasionally pathologists request an additional reticulin stain (Gordon and Sweets' method). Macules are collections of coal dust laden macrophages in a size range of 0.5–6 mm within the walls of respiratory bronchioles and adjacent alveoli enmeshed within a fine network of reticulin and occasional collagen fibers, associated with focal emphysema. Nodules are lesions up to 10 mm (1 cm) in size with round, irregular, or serpiginous borders with a fibrotic stroma of collagen and reticulin containing dust laden macrophages. Only lesions in which there is a significant amount of collagen qualify for compensation (by the latter definition these lesions are "nodules"). Because they are not compensable, macules, even when observed, are often not recorded by the PATHAUT pathologists.

Silicosis was identified by the presence of nodular discrete lesions up to 10 mm in diameter, with smooth clear borders and concentrically arranged collagen fibers. The distinction between a silicotic nodule and the nodule of CWP may be arbitrary, but their distinction from a macule is important. For purposes of analysis, these two categories (CWP nodules and silicotic nodules) were combined.

Chronic bronchitis was assessed according to the mucous gland:wall ratio (Reid Index) of a main bronchus and was based on the average of three readings. A ratio of >0.5 was read as positive for chronic bronchitis.

Active tuberculosis was identified by the presence of granulomatous inflammatory lesions with caseous necrosis, epithelioid histiocytes, and Langhans giant cells.

Emphysema at autopsy is assessed on all lungs received because it is a compensable disease. However, because an accurate assessment of emphysema requires Gough–Wentworth sections, and formalin-fixed lungs are discarded after examination, the current study was confined to cases where

whole lung sections were available. Emphysema is graded, based on a score from 0% to 100%, as absent; insignificant (up to 33%); moderate (33%–66%); and marked ($>66%$). The grade is recorded on the PATHAUT database but the score is not. Emphysema is also categorized into four types, viz. panacinar, centrilobular/focal, irregular and combined panacinar and centrilobular.

The reviewing pathologists recorded the types of emphysema and independently scored the grade. This was followed by an inter-reader comparison and weighted kappa statistics were used to determine agreement among the reviewers. Each case was given an overall reviewer grade of emphysema using the mean score of the three pathologists. This grading was compared to PATHAUT, and read as positive or negative agreement with PATHAUT.

For analysis, the pneumoconiosis was divided into two categories:

"Any" pneumoconiosis was defined as any combination of macules, silicotic nodules, CWP nodules, and PMF.

"Moderate or severe" pneumoconiosis included cases with any of the following: silicotic nodules, CWP nodules and PMF but excluded cases with macules only.

Kappa analysis was used to provide an estimate of the extent of agreement greater than chance among readers. A kappa of ≤ 0.2 indicated poor agreement, >0.2 – 0.4 fair agreement, >0.4 – 0.6 good agreement, >0.6 – 0.8 very good agreement, and >0.8 – 1 excellent agreement.

RESULTS

Coal miners ($n = 7,760$) comprised 10.3% of the entire PATHAUT database for the period 1975–1997.

Sample 1: 15 Cases With Exclusive Coal Mining Exposure; 13 With Mixed Dust Exposures

The numbers of positive diagnoses for each disease, as determined independently by the three pathologists, and recorded in the PATHAUT database, are shown in Table I. In all 10 cases in which pneumoconiosis was diagnosed, by the

TABLE I. Number of Cases of Pulmonary Disease in South African Coal Miners*, Diagnosed Independently by the Three Reviewers and Compared With the PATHAUT Data ($n = 28$)

Disease	Reviewer 1	Reviewer 2	Reviewer 3	PATHAUT
Bronchitis	13	19	20	14
Tuberculosis	5	5	5	4
Macules	18	21	20	8
Silicosis and/or nodules	12	14	14	13
Pneumoconiosis (any)	28	28	28	18
Pneumoconiosis (moderate/severe)	18	18	18	18

*Thirteen of the 28 cases had mixed exposures (exposures other than coal mining).

reviewing pathologists, on the basis of macules only, it was recorded as absent in the PATHAUT database. The explanation for this is that macules are not compensable so, even when observed, they are not recorded by the PATHAUT pathologists. For cases diagnosed as being moderate to severe ($n = 18$), there was excellent agreement between the reviewers and PATHAUT.

Inter-reviewer agreement

There was good to excellent agreement among the reviewers for all diseases except bronchitis, where agreement was from fair to very good (Table II).

Agreement with PATHAUT

For pneumoconiosis that had progressed beyond the stage of macules, the agreement between the reviewing pathologists and the PATHAUT database was near perfect

($K = 0.8-0.9$) as seen in Table II. For the compensable diseases (silicosis, tuberculosis, and pneumoconiosis that had progressed beyond the stage of macules) there was good to excellent agreement between the reviewers and the PATHAUT database. For bronchitis there was poor to fair agreement between the reviewers and the PATHAUT database.

Sample 2: 31 Cases With Exclusive Coal Mining Exposure

The numbers of positive diagnoses for each disease, as determined independently by the three pathologists, and recorded in the PATHAUT database, are shown in Table III.

Inter-reviewer agreement (Table IV)

As for the first sample, the reviewing pathologists were in perfect agreement for the diagnosis of “any” pneumoco-

TABLE II. Agreement for the Diagnoses of Pulmonary Diseases in South African Coal Miners,* Among Reviewers and Between Reviewers and PATHAUT, as Measured by Kappa Scores ($n = 28$)

	Kappa score (95% Confidence Interval)			
	Reviewer 1 versus 2	Reviewer 1 versus 3	Reviewer 2 versus 3	PATHAUT versus each reviewer^a
Bronchitis	0.5 (0.2–0.8)	0.4 (0.2–0.7)	0.7 (0.5–1.0)	0.1–0.2 (–0.1–0.5) (–0.1–0.3) (–0.1–0.2)
Tuberculosis	0.8 (0.4–1.1)	0.8 (0.4–1.1)	0.8 (0.4–1.1)	0.6–0.8 (0.6–1.1) (0.2–1.0) (0.6–1.1)
Macules	0.7 (0.4–1.1)	0.9 (0.6–1.2)	0.9 (0.5–1.3)	0.2–0.3 (–0.1–0.5) (0.02–0.4) (0.1–0.5)
Silicosis and/or nodules	0.6 (0.2–0.9)	0.9 (0.7–1.4)	0.7 (0.4–1.0)	0.6–0.9 (0.5–1.0) (0.3–0.9) (0.8–1.1)
Pneumoconiosis (any)	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	0.2 (–0.1–0.5) (–0.1–0.5) (–0.1–0.5)
Pneumoconiosis (moderate/severe)	0.8 (0.2–0.9)	0.9 (0.7–1.0)	0.8 (0.7–1.0)	0.8–0.9 (0.5–1.1) (0.3–0.9) (0.8–1.0)

*Thirteen of the 28 cases had mixed exposures (exposures other than coal mining).

^aThis column shows kappa score ranges of the three reviewers and PATHAUT; 95% CI for reviewer 1 versus PATHAUT; 95% CI for reviewer 2 versus PATHAUT; 95% CI for reviewer 3 versus PATHAUT.

TABLE III. Number of Cases of Pulmonary Disease in South African Coal Miners,* Diagnosed Independently by the Three Reviewers and Compared With the PATHAUT Data (n = 31)

Disease	Reviewer 1	Reviewer 2	Reviewer 3	PATHAUT
Bronchitis	18	14	18	13
Tuberculosis	6	6	6	6
Macules	22	27	27	13
Silicosis and/or nodules	13	13	11	14
Pneumoconiosis (any)	31	31	31	19
Pneumoconiosis (moderate/severe)	19	19	19	19

*Exclusive coal mining exposure.

TABLE IV. Agreement for the Diagnoses of Pulmonary Diseases in South African Coal Miners,* Among Reviewers and Between Reviewers and PATHAUT, as Measured by Kappa Scores (n = 31)

	Kappa score (95% Confidence Interval)			
	Reviewer 1 versus 2	Reviewer 1 versus 3	Reviewer 2 versus 3	PATHAUT versus each reviewer ^a
Bronchitis	0.3 (-0.1-0.6)	0.4 (0.1-0.7)	0.4 (0.0-0.7)	-0.01-0.1 (-0.3-0.3) (-0.3-0.4) (-0.4-0.01)
Tuberculosis	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	1.0 (1.0) (1.0) (1.0)
Macules	0.2 (-0.01-0.5)	0.2 (-0.01-0.5)	1.0 (0.6-1.4)	0.07-1.0 (-0.2-0.4) (-0.1-0.2) (-0.1-0.2)
Silicosis and/or nodules	0.6 (0.3-0.9)	0.7 (0.4-1.0)	0.7 (0.4-0.9)	0.5-0.8 (0.3-0.9) (0.7-1.0) (0.5-1.0)
Pneumoconiosis (any)	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	0.2 (-0.1-0.5) (-0.1-0.4) (-0.1-0.4)
Pneumoconiosis (moderate/severe)	0.7 (0.3-0.9)	0.8 (0.5-1.0)	0.9 (0.7-1.1)	0.7-0.9 (0.3-0.9) (0.7-1.0) (0.5-1.0)

*Exclusive coal mining exposure.

^aThis column shows kappa score ranges of the three reviewers and PATHAUT; 95% CI for reviewer 1 versus PATHAUT; 95% CI for reviewer 2 versus PATHAUT; 95% CI for reviewer 3 versus PATHAUT.

TABLE V. Classification of Emphysema Type on Whole Mount Lung Sections of South African Coal Miners (n = 31)

	Reviewer 1	Reviewer 2	Reviewer 3	PATHAUT	Cases with global ^a inter-reviewer agreement	Cases with global reviewer and PATHAUT agreement ^b
None	6	2	4	7	1	2
Centrilobular/focal only	8	11	6	7	4	1
Panacinar only	3	7	4	6	1	0
Irregular only	0	0	0	3	0	0
Two or more types	13	11	17	4	5	3

^aAll three reviewers listed the same types.

^bAll three reviewers and PATHAUT listed the same types.

niosis. Apart from bronchitis, the inter-reviewer agreement for all diseases ranged from good to excellent (Table IV).

Agreement with PATHAUT

Again, there was excellent agreement between the reviewers and PATHAUT for pneumoconiosis that had progressed beyond the stage of macules, and all 12 cases recorded as absent in PATHAUT were diagnosed by the reviewers as pneumoconiosis in the presence of macules only. For the compensable diseases, there was good to excellent agreement between the reviewers and PATHAUT (Table IV). The agreement with PATHAUT for the diagnoses of macules was only fair.

Sample 3: Review of 31 Whole Lung Sections for Emphysema

The reviewing pathologists classified the type of emphysema into the four major categories (Table V). Grade of emphysema, based on the reviewing pathologists' mean score is shown in Table VI.

Inter-reviewer agreement

There was agreement among the reviewers for 11 of the 31 cases (35%) for any or all types of emphysema. For a

further five cases, there was agreement on at least one type. In the other 20 cases, two of the three pathologists agreed. As shown in Table VII, there was good to very good agreement between each pair of readers ($K = 0.6-0.7$) for the grade of emphysema.

Agreement with PATHAUT

In six of the cases (20%) there was exact agreement with PATHAUT for type of emphysema (Table V). In 23 of the 31 cases (75%), there was complete agreement between the reviewers and PATHAUT (Table VI) for grade. The agreement between the mean grade of all the reviewers and PATHAUT was fair ($K = 0.4$) as shown in Table VII.

DISCUSSION AND CONCLUSIONS

Although the PATHAUT dataset has been in existence for several decades, and has been used extensively for examining health outcomes primarily among gold miners, there has been limited systematic analysis of the data on coal miner autopsies. Apart from a single published report reviewing the quality of the data in the late eighties [Hessel et al., 1987] (which did not look at validity of diagnoses) no independent evaluation of the database or validation of the diagnoses has been conducted. The reviewers selected for this study were carefully chosen for having years of

TABLE VI. Reviewer Classification of Emphysema Grade on Whole Mount Lung Sections of South African Coal Miners (n = 31) (Shaded Areas Reflect Identical Reading)

		PATHAUT grading			
		Absent	Insignificant	Moderate	Marked
Grading based on reviewers' mean score	Absent	0	0	0	0
	Insignificant	0	17	2	0
	Moderate	0	3	6	3
	Marked	0	0	0	0

TABLE VII. Agreement for the Grade of Emphysema From Review of Whole Mount Lung Sections Among Reviewers and Between Reviewers and PATHAUT, as Measured by Kappa Scores (n = 31)

Kappa score (95% CI)			
Reviewer 1 versus 2	Reviewer 1 versus 3	Reviewer 2 versus 3	PATHAUT versus overall reviewer grade
0.6 (0.4–0.9)	0.6 (0.3–0.9)	0.7 (0.4–1.1)	0.4 (0.1–1.1)

Overall reviewer grade was derived from the mean emphysema score of all three reviewers.

experience with mine workers, especially coal-exposed pathology. The reviewers were aware that all of the selected cases had coal dust exposure, and this could have impacted on their classification of the nodular lesions as being either coal related or silicotic. For purposes of the review, silicotic and coal nodules were combined.

Based on the review of the histological specimens and the comparison with the diagnoses captured on the PATHAUT database, the reviewers concluded that PATHAUT can be used with confidence to establish a diagnosis of coal workers nodules and silicosis. However, there was poor agreement with PATHAUT for coal workers macules. The most likely reason is that macules are not compensable and, consequently, are often not recorded by the pathologists even when they are observed. This will restrict any epidemiological studies based on PATHAUT diagnoses to the more advanced part of the CWP spectrum. In particular, it will reduce the number of available cases based CWP case selection and limit the gradient of outcome to none/nodular as opposed to none/macular/nodular.

For many of the key respiratory outcomes, such as silicosis, tuberculosis, and pneumoconiosis that had progressed beyond the stage of macules, the agreement between reviewers and PATHAUT was good to excellent (kappa = 0.5–1.0) (Tables II and IV). This implies a high degree of validity of the data in PATHAUT. Although there was less agreement between reviewers and PATHAUT for some diagnoses, these are mostly reflective of the different criteria used for borderline disease. The consistently high degree of agreement between the pathologist who had acted as a PATHAUT pathologist as well as a reviewer in this study (reviewer number 1) and the two external reviewers, lent confidence to the findings between the reviewers and PATHAUT.

The whole mount lung section assessment for grade and type of emphysema showed reasonable agreement among the reviewers and between the reviewers and PATHAUT. Where whole lung sections were not available, the reviewers felt that it was not possible to assess the grade and type of emphysema from histological preparations. The reviewers recommended that, even for epidemiological studies, strong preference

should be given to cases with the properly prepared whole lung sections.

In summary, the good to excellent agreement on many microscopic analyses offers assurance about the validity of PATHAUT. Similarly, the good agreement for emphysema grading for appropriately prepared sections, allows for this subset of PATHAUT to be used for epidemiological purposes.

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