Serial Evaluations at an Indium-Tin Oxide Production Facility

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Background *We evaluated the effectiveness of workplace changes to prevent indium lung disease, using 2002–2010 surveillance data collected by an indium-tin oxide production facility.*
Methods *We assessed pulmonary function using lower limits of normal. Blood indium concentration and personal air sampling data were used to estimate exposure.*
Results *Abnormalities were uncommon at hire. After hire, prevalence of spirometric restriction was 31% (n = 14/45), about fourfold higher than expected. Excessive decline in FEV1 was elevated at 29% (n = 12/41). Half (n = 21/42) had blood indium ≥5 μg/l. More recent hires had fewer abnormalities. There was a suggestion that abnormalities were more common among workers with blood indium ≥5 μg/l, but otherwise an exposure-response relationship was not evident. Peak dust concentrations were obscured by time averaging.*
Conclusions *Evolving lung function abnormalities consistent with subclinical indium lung disease appeared common and merit systematic investigation. Traditional measures of exposure and response were not illustrative, suggesting fresh approaches will be needed. Workplace changes seemed to have had a positive though incomplete impact; novel preventive interventions are warranted.* Am. J. Ind. Med. 56:300–307, 2013.

KEY WORDS: indium; indium-tin oxide; interstitial lung disease; occupational illness; surveillance

INTRODUCTION

Indium lung disease is a newly described disorder-affecting workers involved in the production, use, or reclamation of indium-tin oxide (ITO) [Omae et al., 2011]. Occurring as early as 1 year after first exposure, indium lung disease is marked by cough and dyspnea without a work-related pattern and abnormalities on pulmonary function tests and chest CT [Cummings et al., 2012]. Available evidence suggests that the disease begins with pulmonary alveolar proteinosis (PAP), progresses to include fibrosis and emphysema, and can cause premature death [Cummings et al., 2012]. Cross-sectional epidemiologic investigations have demonstrated an excess of lung abnormalities in workplaces where cases of indium lung disease occurred, indicating the presence of subclinical or undiagnosed disease [Chonan et al., 2007; Hamaguchi

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et al., 2008; Nakano et al., 2009]. A serum indium concentration of 3 μg/l or greater has been associated with adverse health effects [Nakano et al., 2009]. However, in previous studies, exposure assessments have been lacking, and the role of serial medical testing in disease detection and prevention has not been evaluated.

We previously reported two cases of PAP, including one fatality, among workers at a small ITO production facility [Cummings et al., 2010]. ITO production at this facility included multiple steps occurring in different areas (Fig. 1). The two cases of PAP occurred in the ITO tile-making area and the reclaim area. After the occurrence of the first case, the facility was purchased in 2002 by a company that made extensive workplace changes, including ventilation improvements, process enclosures, and the introduction of a respiratory protection program. Many of these changes were in place by 2007. In an effort to evaluate the effectiveness of these workplace changes at reducing exposures and preventing indium lung disease, we examined existing data from periodic medical and environmental evaluations conducted by the company. We attempted to gauge the burden of lung function abnormalities in the facility's workforce, examine the relationship between available exposure and disease estimates, and assess whether there was evidence that the company's efforts were impactful, recognizing the data were collected for other purposes.

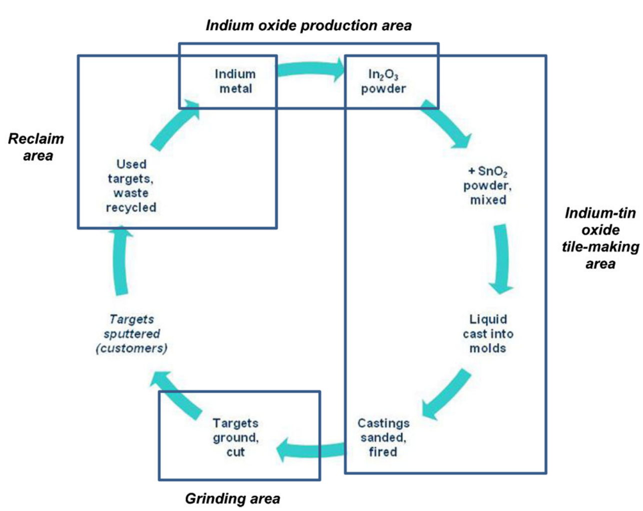

FIGURE 1. ITO production began with indium metal, which was used to make indium oxide powder. Indium oxide, tin oxide, and other compounds were mixed and the resulting liquid cast into molds to harden. The castings were sanded by hand and then fired. The sintered tiles, or targets, were ground and cut to the customer's specifications for sputtering. Indium metal was reclaimed from used targets and waste materials (cuttings, grindings, and rejected tiles) generated in the production process.

MATERIALS AND METHODS

We obtained records pertaining to the company's medical surveillance program from healthcare providers and associated laboratories. We abstracted data including the following: responses to questions about chest symptoms from self-administered questionnaires used for respirator clearance; largest forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) from spirometry tests; total lung capacity (TLC) from helium dilution lung volume tests; diffusing capacity of the lungs for carbon monoxide (DLCO) from single breath diffusing capacity tests; indium concentration from blood (serum or plasma) analyses; and classification of chest radiographs by certified NIOSH B readers according to the International Labour Office (ILO) classification [ILO, 2002]. We obtained additional B readings such that each film had at least two independent classifications [ILO, 2002]. All data included in analyses were double-entered into a Microsoft Access database and reviewed for consistency.

We examined spirometry tests for quality on the basis of American Thoracic Society/European Respiratory Society (ATS/ERS) criteria of acceptability and repeatability [Miller et al., 2005]. We interpreted test results using reference values generated from the Third National Health and Nutrition Examination Survey (NHANES III) [Hankinson et al., 1999]. We defined obstruction as FEV1/FVC ratio and FEV1 below their respective lower limits of normal (LLN) (5th percentiles) with a normal FVC. We defined spirometric restriction as normal FEV1/FVC ratio with FVC below the LLN. We classified tests with FEV1/FVC ratio, FEV1, and FVC below their respective LLN as having a mixed pattern. We defined excessive decline in FEV1 as a greater than expected decrease in FEV1 between any two spirometry tests. The expected decrease in FEV1 was based on the LLN values from a large study of working males [Wang et al., 2006]. We compared the observed to expected proportion of workers with excessive decline in FEV1 using the Chi-square goodness-of-fit test.

For lung volume and diffusing capacity tests, we interpreted test results using reference values generated from a stratified random sample of a state's population [Miller et al., 1983]. We defined restriction as TLC below the LLN and low diffusing capacity as DLCO below the LLN. For chest radiographs, we considered a profusion score of 1/0 or greater to be abnormal. Final determination of the classification of each radiograph required agreement (defined as the same major profusion category or within one minor profusion category) between at least two of the readers. For radiographs with three readings that disagreed, we used the median profusion score.

For blood analyses, indium concentration in serum or plasma was determined using inductively coupled plasma mass spectrometry. The lowest calibration was 5 μg/l, and the laboratory did not report concentrations below this value. In some cases, a higher "reporting value," or threshold below which concentrations of indium were reported as "none detected," was used. We excluded 14 blood indium tests that had a result of "none detected" but used a reporting value above 5 μg/l. Included tests with a value of "none detected" were assigned half of the lowest calibrator value (2.5 μg/l) for calculations. We used contingency tables and the Chi-square test to examine the distributions of workers with blood indium concentrations ≥5 μg/l by worker characteristics.

The company provided reports of industrial hygiene evaluations conducted by its own staff and by consultants. We abstracted information on the sample type, location, fraction, length, analytical method, and concentration. We grouped samples from different years to determine geometric means and ranges of concentrations for dust, indium, and tin and to evaluate trends over time. In addition, in 2010, we collected full-shift area air samples for four work areas and conducted gravimetric analyses of total and respirable dusts and inductively coupled plasma atomic emission spectrometry analyses for tin and indium [NIOSH, 2003]. Particles ≤10 microns in diameter were measured using real-time personal dust monitors (Thermo Electron Corporation, PersonalDataRAM® model pDR-1000AN/1200, Franklin, MA).

We calculated frequencies of adverse health outcomes (chest symptoms, abnormal spirometric classification, excessive decline in FEV1, restriction, low diffusing capacity, and abnormal radiograph) and examined patterns over time. We determined prevalence ratios (PRs) of spirometric abnormalities from comparisons with the US adult population prevalence reported in NHANES III [DHHS, 1996] using indirect standardization for race (White, Black, or Mexican-American), sex, age (17–39 or 40–69 years), cigarette-smoking status (ever or never), and body mass index (normal, overweight, or obese). Workers for whom smoking status was unavailable were assumed to be ever smokers.

We used logistic regression to explore associations between adverse health outcomes derived from pulmonary function tests and chest radiography and the following exposure surrogates or metrics: workers' employment status (current or former), hire date, job title, blood indium concentration, and average total indium concentrations from historical personal air samples. In the few cases where a worker had changed jobs, we assigned the worker to the higher exposure job title. Analyses were conducted using SAS software Version 9.2 and JMP software Version 9.0.1 (SAS Institute Inc., Cary, NC). We considered two-sided $P \leq 0.05$ to be statistically significant.

Institutional review board approval was not required for this public health activity. As a public health agency conducting a health hazard evaluation, we obtained identifiable data without individuals' informed consent. Identifying information was maintained in accordance with the Federal Privacy Act, 5 U.S.C. § 552a, as amended.

RESULTS

Health

A total of 57 men, hired by September 30, 2009, participated in some aspect of the medical surveillance program from May 2002 through March 2010 and were included in our analyses (Table I). Most (n = 52; 91%) included workers had been hired since 2002. We included in our analyses: 70 questionnaires from 54 (95%) workers; 138 spirometry tests from 55 (97%) workers, including 41 (72%) workers who had at least two tests; 91 lung volume tests from 37 (65%) workers; 91 diffusing capacity tests from 37 (65%) workers; and 64 chest radiographs from 46 (81%) workers. Lung volume and diffusing capacity tests were added to the medical surveillance program in 2007, accounting for the lower numbers of these tests.

Table II shows the results of these tests. In adjusted comparisons with the US adult population, the prevalence of spirometric restriction at hire was not significantly elevated (4/27 [15%]; PR 2.1, 95% confidence interval [CI] = 0.8–5.4). The prevalence of spirometric restriction on the most recent test after hire was significantly elevated (14/43 [33%]; PR 4.0, 95% CI 2.4–6.7). Sensitivity analyses limited to spirometry tests that met ATS/ERS criteria for acceptability (9/22 [41%]; PR 5.3, 95% CI 2.8–10.1) and acceptability and repeatability (5/12 [42%]; PR 5.6, 95% CI 2.4–13.2) confirmed this finding. Prevalence of obstruction was not elevated (data not shown). Among workers with normal results on the first evaluation (at or after hire) who had subsequent evaluation, 2 (13%) of 15 developed chest symptoms, 6 (23%) of 26 developed a spirometric abnormality, 2 (7%) of 27 developed low TLC, 2 (7%) of 28 developed low DLCO, and 2 (8%) of 25 developed an abnormal chest radiograph during surveillance. Of 12 workers with spirometric restriction who had TLC measured, 7 (58%) had a low TLC, confirming restriction.

Among 41 workers with at least two spirometry tests, 12 (29%) had excessive decline in FEV1 during employment on the basis of LLN criteria, which was significantly higher than expected ($P < 0.0001$). Sensitivity analyses limited to spirometry tests that met ATS/ERS criteria for acceptability (5/22 [23%]) and acceptability and repeatability (5/10 [50%]) confirmed this finding.

Exposure

We included 101 blood indium tests from 51 (89%) workers. Of 19 workers, 1 (5%) tested at hire had an

TABLE I. Characteristics of 57 Indium-Tin Oxide (ITO) Production Workers

	Employment status[a]		
	Current (N = 30)	Former (N = 27)	All (N = 57)
	n (%)	n (%)	n (%)
Age (years)			
At hire, mean (range)	38 (20–56)	35 (19–55)	37 (19–56)
At latest test, mean (range)	43 (23–60)	37 (21–58)	40 (21–60)
Tenure (years)[b]			
Mean (range)	4.8 (<1–34)	2.2 (<1–7.2)	3.6 (<1–34)
Surveillance time (months)[c]			
Mean (range)	38 (0–93)	13 (0–66)	26 (0–93)
Hire date			
<2007	14 (47)	17 (63)	31 (54)
2007–2009	16 (53)	10 (37)	26 (46)
Smoking status[d]			
Ever	22 (73)	13 (48)	35 (61)
Never	5 (17)	1 (4)	6 (11)
Unknown	3 (10)	13 (48)	16 (28)
Body mass index (BMI)[e]			
Under/normal weight	5 (17)	4 (15)	9 (16)
Overweight	15 (52)	17 (65)	32 (58)
Obese	9 (31)	5 (19)	14 (26)
Job title			
IO producer	3 (10)	2 (7)	5 (9)
ITO tile-maker	13 (43)	9 (33)	22 (39)
Grinder	3 (10)	5 (19)	8 (14)
Reclaimer	3 (10)	4 (15)	7 (12)
Other[f]	8 (27)	7 (26)	15 (26)

[a]As of March 2010, the end of surveillance study period.
[b]Defined as time between hire and March 18, 2010 for current workers and time between hire and termination for former workers.
[c]Defined as time between first medical surveillance test of any kind and most recent medical surveillance test of any kind. Workers with only one testing interval were assigned a surveillance time of 0 month.
[d]Determined from spirometry reports. "Ever" includes current and former smokers. "Unknown" refers to workers for whom no smoking information was available.
[e]Determined from the most recent spirometry reports. BMI $\leq$ 24.9 kg/m^2 = under/normal weight; 25–29.9 kg/m^2 = overweight; $\geq$30 kg/m^2 = obese.
[f]Other jobs included: process control technician, laboratory technician, maintenance electrician, maintenance technician, plant electrician, mould maker, mould maker assistant, shipper/receiver, production planner/scheduler, health and safety manager, engineering manager, and controller.

indium concentration $\geq$5 µg/l. Of 42 workers, 21 (50%) tested after hire ever had indium concentrations $\geq$5 µg/l. Among 14 workers with indium concentrations <5 µg/l on the first evaluation (at or after hire) who had subsequent testing, 6 (43%) developed indium concentrations $\geq$5 µg/l during surveillance. Results appeared to vary by some worker characteristics (Table SI, Online Supplement). A significantly higher proportion (19/27 [70%]) of

TABLE II. Results of Medical Surveillance of 57 ITO Production Workers

	Test		
Result	At hire n/N (%)	After hire, latest n/N (%)	After hire, ever n/N (%)
Chest symptoms reported	2/32 (6)	4/34 (12)	4/34 (12)
Abnormal spirometry			
Obstruction	2/28 (7)	4/45 (9)	5/45 (11)
Restriction	5/28 (18)	14/45 (31)	18/45 (40)
Mixed	0/28 (0)	1/45 (2)	1/45 (2)
Low total lung capacity	1/12 (8)	6/35 (17)	8/35 (23)
Low diffusing capacity	0/12 (0)	6/35 (17)	8/35 (23)
Abnormal chest X-ray	0/25 (0)	2/28 (7)	2/28 (7)[a]

[a]In addition, two workers had abnormal chest radiography apart from the periodic surveillance after respiratory symptoms prompted investigation.

workers hired before 2007 ever had indium concentrations $\geq$5 µg/l after hire compared with workers hired more recently (2/15 [13%]) ($P < 0.001$).

Air sampling was conducted on 13 occasions from 2004 to 2010. A total of 84 personal samples and 30 area samples were collected, some of which reflected short-duration, task-specific activities. We included partial- to full-shift personal samples for total dust (n = 37), total indium (n = 38), and total tin (n = 30) in our analyses. Concentrations were highest in the indium oxide production and reclaim areas (Fig. 2). Figure 3 shows the trends in total indium concentration over time. Four general area samples collected in 2005 used four-stage cascade impactors to assess particle size distribution. By mass, the respirable fraction of the total airborne particulate matter was less than 20% in each area sampled (≈16% in the grinding area, ≈10% in the ITO tile-making area, and ≈3% in the reclaim area).

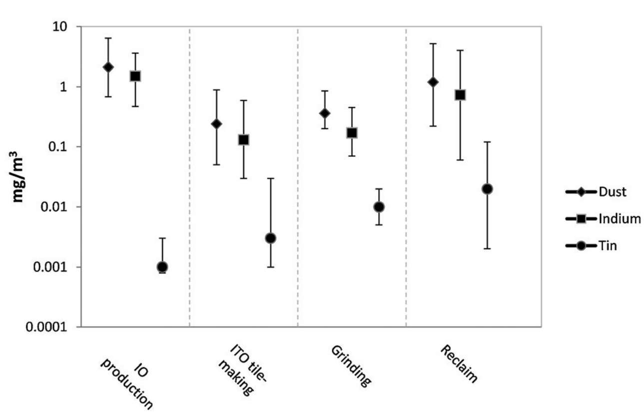

FIGURE 2. Geometric means and ranges of total dust, indium, and tin concentrations in air by work area. Numbers of partial- to full-shift personal samples (dust, indium, and tin) were as follows: IO production (n = 4, 5, and 3); ITO tile-making (n = 15, 15, and 12); grinding (n = 8, 8, and 7); reclaim (n = 10, 10, and 8).

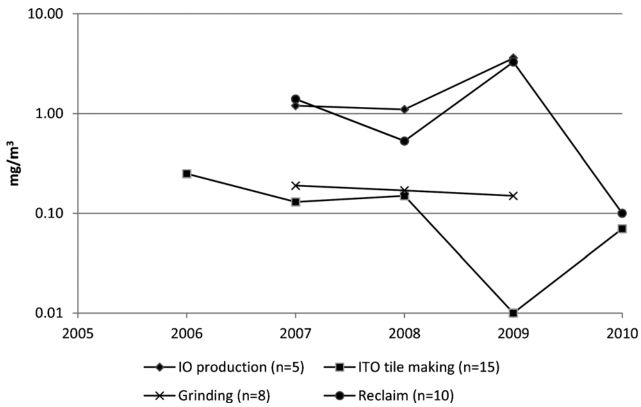

FIGURE 3. Trends in total indium concentration in air by work area. Geometric means were calculated from a total of 38 partial- to full-shift personal samples.

Area air samples that we collected in April 2010 revealed lower dust, indium, and tin concentrations than the historical personal samples (Table SII, Online Supplement). Real-time dust monitoring demonstrated short-term peak concentrations that were not reflected in time-averaged estimates of exposure (Fig. S1, Online Supplement).

Exposure-Response

Abnormalities on after-hire medical tests were significantly more common among workers hired before 2007 than workers hired more recently ($P < 0.01$) (Table III). Abnormalities on after-hire medical tests also appeared to be more common among workers with blood indium concentration ≥ 5 μg/l than workers with blood indium concentration <5 μg/l, but this difference was not statistically significant ($P = 0.07$). There was no association between abnormalities on after-hire medical tests and job title (data not shown), employment status, or average airborne indium concentration.

DISCUSSION

Existing data collected as part of a workplace medical surveillance program suggested that abnormalities on after-hire tests were more common than expected. While not all included workers were tested at hire, the available evidence is consistent with a temporal relationship between employment and respiratory impairment. At hire, few workers reported chest symptoms or had abnormal pulmonary function, and all had normal chest radiographs. After hire, 40% ever had spirometric restriction and nearly a quarter each ever had restriction by helium dilution or a diffusing capacity defect. Using the last after-hire test, the prevalence of spirometric restriction was at least four times higher than expected. Robust comparisons with the US adult population are not possible for TLC and DLCO measurements; however, given our use of LLN to define abnormal, the expected prevalence in a healthy non-smoking population would be 5%, several fold lower than observed. The available serial results also suggest temporality, by pointing to the development of new chest symptoms, pulmonary function abnormalities, and radiographic changes during employment in those with normal

TABLE III. Abnormal Medical Surveillance Results Ever After Hire, by Worker Characteristics and Exposure Categories

	Result n/N (%)				
Characteristic	Spirometric restriction	Excessive decline in FEV1	Low TLC	Low DLCO	Abnormal Chest X-ray[a]
Employment status[b]					
Current	9/27 (33)	8/27 (30)	7/27 (26)	5/27 (19)	1/20 (5)
Former	9/18 (50)	4/14 (29)	1/8 (13)	3/8 (38)	1/8 (13)
Hire year					
<2007	13/25 (52)	8/22 (36)	5/15 (33)	4/15 (27)	2/19 (11)
2007–2009	5/20 (25)	4/19 (21)	3/20 (13)	4/20 (20)	0/9 (0)
Blood [In]					
<5 μg/l	6/19 (32)	3/16 (19)	2/15 (13)	4/15 (27)	0/10 (0)
≥5 μg/l	9/20 (45)	7/19 (37)	4/14 (29)	4/14 (29)	2/16 (13)
Air [In][c]					
Lower	10/25 (40)	9/22 (41)	3/18 (17)	6/18 (33)	0/16 (0)
Higher	3/9 (33)	1/9 (11)	2/8 (25)	1/8 (13)	2/6 (33)

FEV1, forced expiratory volume in 1 s; TLC, total lung capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; [In], indium concentration.
[a]Numerator does not include two workers who had abnormal chest radiography apart from the periodic surveillance after respiratory symptoms prompted investigation.
[b]At end of surveillance period.
[c]Determined by average total indium concentrations from historical personal air sampling and assigned by job title. Indium oxide producers and reclaimers comprised the "higher" group and ITO tile makers and grinders comprised the "lower group." Air sample results were not available for other job titles.

results on first evaluation. Particularly notable are the high incidences of new spirometric abnormality and excessive decline in FEV1 during employment.

The existing data offered a unique opportunity to evaluate exposure, which in published epidemiologic studies has been limited primarily to cross-sectional investigations of blood indium concentrations [Chonan et al., 2007; Hamaguchi et al., 2008; Nakano et al., 2009]. Despite the use of an insensitive test, serial blood indium concentrations indicated work-related exposure to some form of indium in at least half of included workers. The prevalence of blood indium concentration ≥ 5 μg/l after hire among production workers ranged from 57% (grinders) to 75% (indium oxide producers) and was 0% among workers in other jobs. Although small numbers in sub-groups were limiting, ITO tile makers had a more limited range of indium concentrations than other production jobs, suggesting lower indium exposures than for other production workers. Historical and our own air sampling results indicated a range of indium exposures by work area, with the lowest exposures in the ITO tile-making area.

There was some evidence that indium exposures decreased over time, with a lower proportion of workers hired since 2007 having blood indium concentrations ≥ 5 μg/l compared with workers hired before 2007. Such trends were difficult to corroborate with the existing historical sampling data. With the exception of the most recent exposure estimates for the ITO tile-making area (Fig. 3), none of the average indium exposures from historical sampling was below the NIOSH recommended exposure limit (REL) for total indium of 0.1 mg/m^3 [NIOSH, 2005]. It is important to note that this REL was established before the widespread use of ITO and the recognition of indium lung disease in workers. A lower standard for respirable indium of 3×10^{-4} mg/m^3 set in Japan in 2010 on the basis of animal studies of indium oxide and ITO toxicity [MHLW, 2010] will be challenging to meet. Miyauchi et al. [2012] recently documented a decline in indium exposures at an indium recycling facility following the installation of local exhaust ventilation, but exposures remained above the 2010 standard.

We found evidence of possible differential health risks by potential exposure surrogates and exposure metrics. After hire, workers hired since 2007 had a lower proportion of abnormal results across all lung function and radiographic indices, compared with workers hired before 2007. Such an observation would be expected if the more recently hired workers had lower exposures to indium compounds, as suggested by blood indium concentrations. Indeed, adverse health outcomes appeared to be less common in workers with blood indium concentrations <5 μg/l than in those with indium concentrations ≥ 5 μg/l. However, our ability to discern an exposure-response relationship from the existing data was limited. The relationship between historical airborne indium concentrations and health appeared discrepant, in that higher exposures were not associated with greater lung function and radiographic abnormalities. For instance, indium oxide producers had among the highest airborne indium exposures and serum indium concentrations, but virtually no respiratory impairment, while ITO tile makers had the lowest airborne indium exposures and apparently lower serum indium concentrations, but a large burden of respiratory abnormalities. Given the small size of sub-groups, it is possible that this discrepancy is explained by chance alone, but it may be related to the inability of a non-specific exposure index like indium concentration (whether measured in air or blood) to account for potential differential toxicity of the various indium compounds involved in ITO production. Thus, while indium oxide producers have high indium exposure, they likely have low exposure to ITO, which appears to have a higher relative toxicity than other indium compounds [Lison et al., 2009; Nagano et al., 2011]. Indium concentration alone cannot distinguish the form of indium (i.e., indium metal, indium hydroxide, indium oxide, or ITO) to which a worker has been exposed, nor can it capture properties such as surface chemistry and solubility that may be relevant to differential toxicity [Stefaniak et al., 2011]. In addition, our observation of high peak dust exposures that were obscured by time averaging calls into question the sole reliance on average exposure metrics that may not capture all biologically relevant exposures.

There are several limitations to our analyses. Caution is appropriate in making inferences from these observational data. The data were collected for practical purposes in an evolving preventive effort rather than as part of a comprehensive study. As a result, some workers were not tested at hire, so a full description of baseline respiratory health was not possible. However, the fact that the vast majority of included workers were hired during the surveillance period mitigates concerns about the impact of distant exposures to indium compounds on health. Historical air samples were not collected in a systematic way to make estimates of exposure by job title. Rather, sampling was primarily intended to identify areas with higher indium concentrations and assess the local effects of workplace changes. This limitation may also have contributed to the aforementioned discrepancies in exposure and health outcomes. The small size of some sub-groups limited our ability to examine differential risk. Testing did not continue after termination of employment, precluding a description of outcomes following complete cessation of exposure. Thus, while we did not find evidence of a healthy worker effect using the existing surveillance data, it is possible that such a phenomenon would be evident with the benefit of post-employment evaluations. Finally, the quality of the medical tests reflected the typical community experience [Kreiss et al., 2011], with spirometry tests not consistently meeting strict criteria for acceptability and repeatability, most commonly due to lack of time-volume plateau. However, examination of the expiratory curves revealed generally good starts and terminations that approached plateau, indicating that the tests were usable [Miller et al., 2005], particularly for FEV1, and were unlikely to grossly underestimate FVC. Indeed, sensitivity analyses confirmed that the frequency of abnormalities could not be explained by variable test quality.

Our observations using existing data are consistent with the occurrence of subclinical or undiagnosed indium lung disease in this workforce, as has been found in epidemiologic studies of other workforces using indium compounds [Chonan et al., 2007; Hamaguchi et al., 2008; Nakano et al., 2009]. The available evidence suggests that the company's extensive workplace changes had a positive impact in terms of exposure reduction and disease prevention, similar to the experience in Japan [Nakano et al., 2009; Miyauchi et al., 2012]. However, up to a quarter of the more recently hired workers appeared to have abnormal lung function after hire, suggesting that continued monitoring and additional preventive interventions are needed.

Further systematic study is necessary to confirm these findings, advance our limited understanding of the relationship between workplace exposures and indium lung disease, and identify effective strategies for prevention. The insensitivity of self-reported chest symptoms elicited in the context of respirator clearance is not unexpected, and the insensitivity of chest radiographs for detecting indium lung disease has been shown previously [Chonan et al., 2007]; inclusion in future surveillance efforts is unlikely to be impactful. Conversely, our evaluation highlighted the potential utility of changes in FEV1 for identifying possible indium lung disease. Given the recognition that disease onset can occur within a year of hire [Cummings et al., 2010, 2012] more frequent spirometric surveillance early in employment and attention to declines within the normal range may be useful. The incorporation of promising blood biomarkers of lung inflammation such as KL-6 may ultimately reduce the need for surveillance chest CT and its resultant radiation exposure [Kobayashi and Kitamura, 1995; Nakano et al., 2009]. A better understanding of exposure through the use of more sensitive blood indium tests, novel exposure metrics, and physicochemical characterization that differentiates between the various indium compounds is also needed and will play a crucial role in the control of this emerging occupational health hazard.

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