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Two-year follow-up of exposure, engineering controls, respiratory protection and respiratory health among workers at an indium-tin oxide (ITO) production and reclamation facility

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Abstract

Objectives—To determine whether engineering controls and respiratory protection had measurable short-term impact on indium exposure and respiratory health among current indium-tin oxide production and reclamation facility workers.

Methods—We documented engineering controls implemented following our 2012 evaluation and recorded respirator use in 2012 and 2014. We measured respirable indium (In_{resp}) and plasma indium (In_P) in 2012 and 2014, and calculated change in In_{resp} (ΔIn_{resp}) and In_P (ΔIn_P) by the 13 departments. We assessed symptoms, lung function, serum biomarkers of interstitial lung disease (Krebs von den Lungen (KL)-6 and surfactant protein (SP)-D) and chest high-resolution CT at both time points and evaluated workers who participated in both 2012 and 2014 for changes in health outcomes (new, worsened or improved).

Results—Engineering controls included installation of local exhaust ventilation in both grinding departments (Rotary and Planar) and isolation of the Reclaim department. Respiratory protection increased in most (77%) departments. ΔIn_P and ΔIn_{resp} often changed in parallel by department. Among 62 workers participating in both 2012 and 2014, 18 (29%) had new or worsening chest symptoms and 2 (3%) had functional decline in lung function or radiographic progression, but

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Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study involves human participants and was approved by CDC NIOSH IRB protocol #10-DRDS-01. Participants gave informed consent to participate in the study before taking part.

average KL-6 and SP-D concentrations decreased, and no cases of clinical indium lung disease were recognised.

Conclusions—Increased engineering controls and respiratory protection can lead to decreased In_{resp}, In_P and biomarkers of interstitial lung disease among workers in 2 years. Ongoing medical monitoring of indium-exposed workers to confirm the longer-term effectiveness of preventive measures is warranted.

INTRODUCTION

Indium lung disease is a potentially fatal condition characterised by pulmonary alveolar proteinosis (PAP) that can progress to fibrosis with or without emphysema in workers exposed to indium-tin oxide (ITO) and other indium-containing compounds.[1,2] Most studies of ITO workers have been cross-sectional; such studies have demonstrated associations between biological exposure indices (indium measured in serum or plasma) and adverse health outcomes, including reduced diffusing capacity (DL_{CO}), pulmonary interstitial changes on high-resolution CT (HRCT), and elevated levels of biomarkers of interstitial lung disease such as Krebs von den Lungen (KL)-6 and surfactant protein (SP)-D).[3–5] Several cohorts in Japan followed for 5–9 years showed progression of emphysematous lesions on HRCT in workers with higher historical indium exposure, but serum indium, KL-6 and SP-D fell over time with reductions in exposure.[6,7] In addition to the risk of interstitial lung disease, the International Agency for Research on Cancer listed ITO as possibly carcinogenic to humans in 2017.[8]

In 2012, we conducted a cross-sectional study of workers at an ITO production and reclamation facility where two workers previously developed PAP, including one worker who died.[9] Despite participants' median facility tenure of just 2 years, we observed more dyspnoea, lower spirometric parameters, and increased KL-6 and SP-D associated with plasma indium concentrations as low as 1 µg/L.[10] Subsequently, we showed that respirable indium was correlated with plasma indium and also associated with respiratory health effects at cumulative exposures as low as 22 µg-year/m^3.[11] Following our 2012 evaluation, the facility introduced new engineering controls and more extensive use of respiratory protection. We hypothesised that these changes would lower worker exposures and result in improved respiratory health outcomes at 2 years' follow-up in 2014.

METHODS

All current workers at an ITO production and reclamation facility were invited to participate in the study. Participants provided informed consent for the industrial hygiene and health evaluations conducted in 2012 and 2014. Data collected during 2014 evaluations were largely the same as 2012, with slight differences as described in detail below.

Engineering controls and respiratory protection

We documented, by department, ventilation and non-ventilation engineering controls implemented following the 2012 evaluation. In 2012 and 2014, we observed respiratory protection and recorded use of N95 filtering facepiece respirator and powered air purifying respirator (PAPR) in task diaries and calculated average use by department (% of time used during observation).

Exposure assessment and change in exposure from 2012 to 2014

Industrial hygiene evaluations included collecting full-shift personal and area samples to assess exposure to respirable indium, summarised by jobs or work area. Personal samples were collected for production departments; general area samples were collected for the administrative office area. In 2012, respirable samples were collected using the GK2.69 cyclone (BGI, Waltham, Massachusetts, USA) as described previously.[11] In 2014, the IOM sampler (SKC, Eighty Four, Pennsylvania, USA) with a MultiDust Foam Disk insert was used to assess both respirable and inhalable exposures. Side-by-side IOM and cyclone samples were collected from all the processes and a regression equation was developed to convert the IOM respirable concentration to cyclone-equivalent respirable concentration. The 2014 respirable exposure data were corrected using this equation to account for the slight differences observed between the samplers.[12] All personal samples in 2012 and 2014 were summarised for each job using the arithmetic mean (specifically, the minimum variance unbiased estimator) as previously described.[11] The job-specific mean was assigned to each participant to obtain a metric of respirable indium (In_{resp}) exposure in 2012 and 2014. The change in respirable indium (ΔIn_{resp}) was determined by subtracting the 2012 In_{resp} from the 2014 In_{resp}. Respirable indium concentrations represent measured exposures and are not adjusted for observed respiratory protection because information on respirator use for each participant was not available.

Blood collected during the health evaluations was used to measure plasma indium (In_P). The change in plasma indium (ΔIn_P) was calculated by subtracting 2012 In_P from 2014 In_P. ΔIn_P and ΔIn_{resp} were summarised by departments and presented as boxplots to compare the change in exposure metrics during 2012–2014.

We calculated a metric of cumulative respirable indium exposure occurring during participants' total tenure at the facility (hereafter, cumulative In_{resp}). All workers participating in the 2012 or 2014 survey who reported a job in 2012 or earlier in their work history were assigned the 2012 In_{resp} exposure associated with the job, which was then multiplied by the duration in years that job was performed and summed across all jobs held to obtain cumulative exposure until 2012. Workers who reported a job after 2012 (2014 survey participants) were assigned the 2014 In_{resp} exposure, which was multiplied by the duration and summed across jobs held during this period to obtain 2012–2014 interval cumulative exposure. The 2012–2014 interval cumulative exposure was then summed with the 2012 cumulative exposure to obtain cumulative exposure for the entire duration.

Longitudinal evaluation of workers in 2012 and 2014 surveys

The subset of workers who participated in both 2012 and 2014 surveys and had plasma or whole blood indium measured during the timeframe of each assessment was evaluated longitudinally over the 2-year study for new or worsening health outcomes. Health evaluations included an interviewer-administered questionnaire addressing respiratory symptoms and diagnoses, smoking history, work history including job and department details, and demographic information. Medical testing offered included spirometry, DL_{CO}, chest HRCT and blood collection to measure In_P and serum biomarkers of interstitial lung disease (KL-6 and SP-D). Detailed methods have been described previously.[10]

We defined new chest symptoms as those reported in 2014 but not in 2012. We defined worsening chest symptoms in the follow-up study as those reported in both 2012 and 2014, but that were reported to be more severe or frequent in 2014 than in 2012. Excessive decline in forced expiratory volume in 1 s (FEV_1) was defined as a decrease of at least 450 mL during the 2-year study window.[13] We excluded 2014 lung function testing results from one participant due to lung surgery that occurred between 2012 and 2014 evaluations and thought to be unrelated to indium exposure. For participants (n=6) who declined blood draw in either evaluation but released corporate medical surveillance records to NIOSH, we estimated In_P as two-thirds of the concentration of indium in whole blood measured during corporate medical surveillance within 5 months of our evaluation. This adjustment was based on the relationship between indium in plasma and whole blood that we described previously.[14] Two employees were excluded from analyses for blood-related variables due to a higher limit of detection of 10 μg/L that resulted in undetectable whole blood indium in 2012 corporate medical surveillance data. All analyses were conducted using SAS software V.9.3 and JMP software V.13.2.0 (SAS Institute). All p values reported are two sided. We considered $p \leq 0.05$ to be significant.

RESULTS

The ITO production and reclamation process at this facility has been previously described.[5] A total of 111 workers at the ITO production and reclamation facility participated in at least one survey for a total of 173 observations: 87 workers in 2012 and 86 workers in 2014; 62 of these workers participated in both evaluations. Worker turnover was 29% of participants between 2012 and 2014 evaluations. Participation for eligible workers was 93% in 2012 and 86% in 2014. Cross-sectional comparison demonstrates exposure indices for these participants were similar in 2012 and 2014. Three participants in the 2014 survey with tenure <2 years at the facility had $In_P > 1$ μg/L.

Demographic, work and exposure characteristics, and health outcomes of the combined 2012 and 2014 study population at the time of most recent evaluation are described in table 1. Obstructive spirometry patterns were identified in 5% of workers, and restrictive patterns in 7% of workers. On HRCT, 6 (7%) workers had mild or moderate emphysematous changes, and 1 (2%) had evidence of early fibrosis (moderate). The median cumulative In_{resp} for all participants was 21 μg-year/m^3.

Engineering controls and respiratory protection

The facility focused engineering controls on three departments following the 2012 survey: Reclaim was isolated and segregated from the remainder of operations; primary control mist collectors were placed on Rotary Grinding units to remove contaminants; and Planar Grinding units were fitted with enclosed beds to serve as source control.

Figure 1 shows the per cent person-days with observed respirator use and number of person-days observed (A) and the average per cent time respirator use during observation for those who used a respirator (B) during 2012 and 2014 by department. The per cent of person-days with any observed respirator use (N95 filtering facepiece or PAPR) or the average per cent time respirator use increased for most (77%) departments (figure 1A,B). Rotary Grinding, QC Laboratory, Planar Grinding, ITO and Forming Preparation had increased or stable per cent person-days with any observed respirator use and increased average per cent time respirator use during 2014 compared with 2012. Reclaim had decreased per cent person-days with any observed respirator use during 2014, but the largest increase (45%) in average per cent time respirator use of any department in 2014 compared with 2012. Only Rotary Bond had decreased per cent person-days with any observed respirator use and decreased average per cent time respirator use during 2014 compared with 2012.

Exposure assessment and change in exposure from 2012 to 2014

For workers who participated in both evaluations, median In_P increased from 1.2 μg/L in 2012 to 1.6 μg/L in 2014; median ΔIn_P was 0.2 μg/L (table 2). ΔIn_P ranged from a decrease of close to 10 μg/L to an increase of nearly 7 μg/L during the 2 years; ΔIn_P was >0 (increased) in 41 (68%) of participants. ΔIn_P varied considerably by department (figure 2). In some departments none of the participating workers had ΔIn_P >0.2 μg/L (the median change), and in other departments all participating workers had an increase in In_P >0.2 μg/L. Median ΔIn_{resp} among participants was −0.2 μg/m^3 and ranged from a decrease of 58 μg/m^3 to an increase of 95 μg/m^3 from 2012 to 2014 (table 2). ΔIn_{resp} varied considerably by department (figure 2). We found the same correlation between cumulative In_{resp} and In_P updated with 2014 data as reported from 2012 data (Spearman's ρ=0.78). ΔIn_P and ΔIn_{resp} had a weak negative correlation (Spearman's ρ=−0.15).

Reclaim and Planar Bond were the only two departments with substantial ΔIn_{resp}>0 μg/m^3, and both departments also had ΔIn_P >0 μg/L for all three workers monitored in those departments. Some departments with ΔIn_{resp}<0 μg/m^3, had an average ΔIn_P <0 μg/L for workers in those departments, including Research and Development, Refinery, Planar Grinding and Maintenance and Facilities. ΔIn_{resp} and ΔIn_P did not change in parallel in other departments, however. ITO, Rotary Bond and Rotary Grinding had ΔIn_{resp}<0 μg/m^3, but workers in those departments had ΔIn_P >0 μg/L. The remaining departments had small ΔIn_{resp} and average ΔIn_P during 2012–2014.

Longitudinal evaluation of workers in 2012 and 2014 evaluations

Table 2 summarises symptoms and exposure characteristics of workers who participated in both surveys. No workers had new spirometric abnormalities in 2014. Eighteen (29%) participants reported a new or worsening chest symptom in 2014; new chest symptoms included usual phlegm or chest tightness and new or worsening symptoms included cough, shortness of breath or wheeze. One (2%) participant had excessive decline in FEV_1 (>450 mL) from 2012 to 2014. In addition, one (2%) developed mild emphysematous changes on HRCT in 2014. Participants with new or worsening chest symptoms, excessive decline in FEV_1 or new emphysematous changes in HRCT represented ITO (n=5), the QC laboratory (n=4) and nine other departments. During 2012–2014, KL-6 decreased by an average of 125 U/mL and SP-D decreased by an average of 36 ng/mL.

DISCUSSION

We deployed serial industrial hygiene surveys and medical evaluations to evaluate the effects of engineering controls and respiratory protection use aimed at reducing exposures and protecting the health of workers at an ITO production and reclamation facility. Exposure indices (In_P and In_{resp}) often changed in parallel by department, suggesting reducing respirable exposure through targeted engineering controls aimed at isolating processes and reducing airborne indium levels, along with implementing stricter respiratory protection programmes, can lead to reduced plasma indium in a relatively short time period of 2 years and potentially prevention of severe adverse health outcomes. These findings provide additional support to our previous study that respirable indium is a valuable measurement to assess change in exposure.[15] Among workers evaluated in both 2012 and 2014, no participants developed clinical indium lung disease or spirometric abnormalities in 2014, excessive decline in lung function was uncommon, and nearly all (98%) lacked radiologic evidence of progressive interstitial or emphysematous abnormalities. Nonetheless, the increased burden of chest symptoms and observed cases of functional or radiographic changes suggest ongoing monitoring of indium-exposed workers is warranted.

The largest increase in both exposure indices (In_P and In_{resp}) occurred in Reclaim. Reclaim processes were isolated following the 2012 evaluation; the facility enclosed the area in an attempt to control the migration of indium from Reclaim to other parts of the facility and decrease indium exposure to workers in other departments. Although isolating Reclaim processes limited the migration of indium and lowered worker exposures in the other parts of the facility, the enclosure increased In_{resp} among workers in Reclaim. Such isolation measures need to be accompanied by other control measures such as increases in local exhaust ventilation to reduce worker exposures within the isolated area, and general exhaust ventilation to ensure air flows from low to high concentration areas. Participants from Reclaim also had the largest increase in In_P compared with participants in other departments during the 2-year study period. Of note, In_{resp} measurements in Reclaim likely overestimated exposure as the average per cent time respirator use in reclaim more than doubled from 2012 to 2014 (34%–79% of the time during observation as shown in figure 1A); nonetheless, the increase in In_P suggests ongoing exposure and/or historical lung burden. These results provide further evidence of the usefulness in assessing In_{resp}, particularly regarding any changes made in the production process or facility. Planar Bond also had parallel increases in In_{resp} and In_P measured from 2012 to 2014. However, these changes in airborne exposures were not accompanied by any process changes and could be attributable to increased production volumes or migration of indium from other departments.

Other departments had declines in both In_{resp} and In_P in participants from 2012 to 2014, including research and development, refinery, planar grinding and maintenance and facilities. All these departments increased respiratory protection use (N95 or PAPR) from 2012 to 2014, through increased per cent person-days any observed respirator use (Research and Development, Maintenance and Facilities), average per cent time respirator use (Refinery) or both (Planar Grinding). Planar rinding units were fitted with enclosed beds following the 2012 survey and declines in both exposure metrics indicated effective source control for the department. These results suggest that decreasing respirable indium exposure can result in a decrease in In_P over 2 years, consistent with prior longitudinal studies.[6 7]

ITO, Rotary Bond and Rotary Grinding showed substantial discrepancies between these exposure indices. For ITO and Rotary Bond, which are two of the largest production departments, In_{resp} was more than 20 μg/m^3 lower in 2014 than in 2012, yet In_P increased in most workers in these departments from 2012 to 2014, indicating reduction in measured exposure does not necessarily correspond to a reduction in In_P. It is possible that decreased In_{resp} with increased In_P could reflect changes in respiratory protection from 2012 to 2014. To that end, rotary bond was one the only department that had decreased per cent person-days with any observed respirator use and decreased average per cent time respirator use during 2014 compared with 2012; however, ITO had increased per cent person-days with any observed respirator use and increased average per cent respirator use in 2014, suggesting additional factors besides respirator use are contributing to the observed discrepancies. Furthermore, various forms of indium have different dissolution times from the lungs and blood that are further affected by tenure, indium stored in the lungs and other organs, and other factors which could in part account for these discrepancies.[16] For Rotary Grinding, the decrease in In_{resp} from 2012 to 2014 was modest and likely attributable in part to the engineering control of primary control mist collectors being added to each unit to remove contaminants, yet the average ΔIn_P was the second highest increase of any department; this discrepancy could reflect the small number of workers in Rotary Grind or historical exposure. Whereas interesting, consistent, and meaningful trends were observed between changes in exposure metrics, engineering controls, and respirator use in most departments, the respirator use data are often based on small sample size and should be interpreted with caution. Workers might have been more likely to wear respiratory protection during NIOSH surveys, however, observer bias unlikely influenced trends as it was most likely comparable during each survey.

When we first evaluated this facility in 2009, it was in the context of two cases of severe lung disease attributable to indium exposure, one of which was fatal.[9] Our analysis of the company's medical records for 2002–2010 revealed high rates of post-hire spirometric restriction (31%), excessive decline in FEV_1 (29%) and elevated blood indium concentrations (50%).[5 10 17] In contrast, no cases of clinical indium lung disease were diagnosed among workers over the 2-year study to our knowledge. Among workers participating in both 2012 and 2014, HRCT abnormalities and progression were rare; one worker who reported being a smoker developed mild emphysematous changes on HRCT in our follow-up study. The few longitudinal studies that have been published on ITO workforces to date have shown dose-dependent progressive emphysematous changes in current or former workers exposed to relatively high levels of ITO as demonstrated by serum indium >20 μg/L or >22.5 μg/L[6 7]. For comparison, 2 of 60 participating workers in our cohort had In_P ≥20 μg/L in 2012 or 2014. Furthermore, we did not find evidence of clinical indium lung disease in any participants, likely due to lower exposures than other ITO workforces, as demonstrated by plasma and respirable levels of indium measured in both 2012 and 2014 in these participants. However, in 2 years nearly one-third (19 of 60) of participants had an interval In_{resp}>22 μg-year/m^3 (data not shown), indicating potential for exposure-related adverse health effects in these workers.[11] Additionally, four participants (two in ITO and two in Reclaim) in the 2014 survey who had started work at the facility following the 2012 survey had In_P≥1.0 μg/L (range: 1.0–1.9), indicating ongoing exposure in workers with tenure <2 years at plasma indium levels previously associated with adverse health outcomes.[10]

Overall, spirometric abnormalities were rare. Using the most recent spirometry results of all workers, prevalence of obstruction was 5% and prevalence of spirometric restriction was 7%, compared with 31% of the workers at this same ITO production and reclamation facility when we evaluated medical surveillance data from 2002 to 2010.[5] From the same surveillance data, 29% of workers had excessive decline in FEV_1, compared with only one worker in our follow-up study, likely in large part due to lower exposures in current workers than previously.

Our study includes several limitations. Although attempted, we were unable to model exposure and health with controls or respirator use as predictors given the few controls that affected small numbers of workers, and worker populations participating in the exposure assessments which included observed respirator use overlapped but were not the same as those participating in the health surveys. Additionally, we described interventions implemented by the company with the aim to reduce worker exposure; however, our study was not a formal intervention study and we were unable to assign appropriate control groups that only differed by the intervention for direct comparison. Furthermore, our evaluation did not include former workers at this facility. Workforce turnover at this facility during the 2-year study period was 29% and the reasons workers left employment at this facility are unknown. The healthy worker effect could have influenced our findings if workers included in the 2012 evaluations left the facility before the 2014 evaluations due to health problems, leaving a relatively healthier workforce with fewer adverse health outcomes in 2014.[18] We also only performed two medical and industrial hygiene evaluations, separated by just 2 years, a relatively short period of time. The adverse health effects we observed are best described as subclinical; the long-term impact of indium exposure at these levels on the risk of interstitial lung disease and cancer is unknown and merits further investigation.[8,19] Additionally, there are other factors that could contribute to adverse respiratory health effects, including smoking status as nearly half (49%) of the participating workers in our surveys reported being current or former smokers.

Most cases of indium lung disease reported in the literature have occurred in workers involved in ITO production or reclamation, however, one worker at a mobile phone manufacturing facility developed the disease, suggesting potential risk in other downstream industries that consume ITO.[1,3,20] In Korea, display panel manufacturing workers were exposed to respirable indium as high as 34.2 μg/m^3, which is greater than the average 2014 exposure of 22 μg/m^3 (data not shown) in our cohort and above the Japanese standard of 0.3 μg/m^3 and the ACGIH TLV for indium of 0.0001 mg/m^3 (0.1 μg/m^3).[3,21–24] In the USA, air sampling performed in downstream industries measured indium levels above those previously associated with health effects.[25] Our findings therefore have implications for a broader group of workers beyond the primary ITO production and reclamation industry where the risk of indium lung disease has been clearly established, as lower exposures that might reflect conditions in downstream industries could still lead to adverse health effects over a relatively short period of time.

Our follow-up study in this population of ITO production and reclamation workers determined exposure indices (In_P and In_{resp}) often changed in parallel by department, suggesting reducing respirable exposure and improved respiratory protection can lead to reduced In_P in a relatively short time period of 2 years. The ITO production and reclamation industry as well as downstream industries that may have similar workplace exposures, must continue to assess the need for engineering and administrative controls to further reduce worker exposure to indium. Also, once workplace changes are implemented, air sampling to determine In_{resp} is likely the most practical exposure metric to determine effectiveness of such changes, while measuring indium in the blood should be included in medical surveillance programmes to monitor cumulative exposure to indium.

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Data availability statement

No data are available. Due to restrictions imposed under the US Privacy Act and the limitations of what participants consented to, the data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html.

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Key messages

What is already known on this topic

- Previous longitudinal studies showed indium-tin oxide (ITO) workers with high indium exposure levels had progression of emphysematous changes on chest imaging over time, despite improvements in serum indium and biomarkers of interstitial lung disease.

What this study adds

- In this study of a workplace with relatively lower indium exposures, interventions to reduce respirable indium exposure including targeted engineering controls and increased respiratory protection resulted in a decrease in average plasma indium in 2 years. Among participating workers evaluated in both 2012 and 2014, none developed clinical indium lung disease or new spirometric abnormalities in 2014, average serum biomarkers of interstitial lung disease improved, and functional decline or radiographic progression was uncommon.

How this study might affect research, practice and/or policy

- The ITO production and reclamation industry as well as downstream industries that may have similar workplace exposures, must continue to assess the need for engineering and administrative controls to further reduce worker exposure to indium. Also, once workplace changes are implemented, air sampling to determine In_{resp} is likely the most practical exposure metric to determine effectiveness of such changes, while measuring indium in the blood should be included in medical surveillance programmes to monitor cumulative exposure to indium.

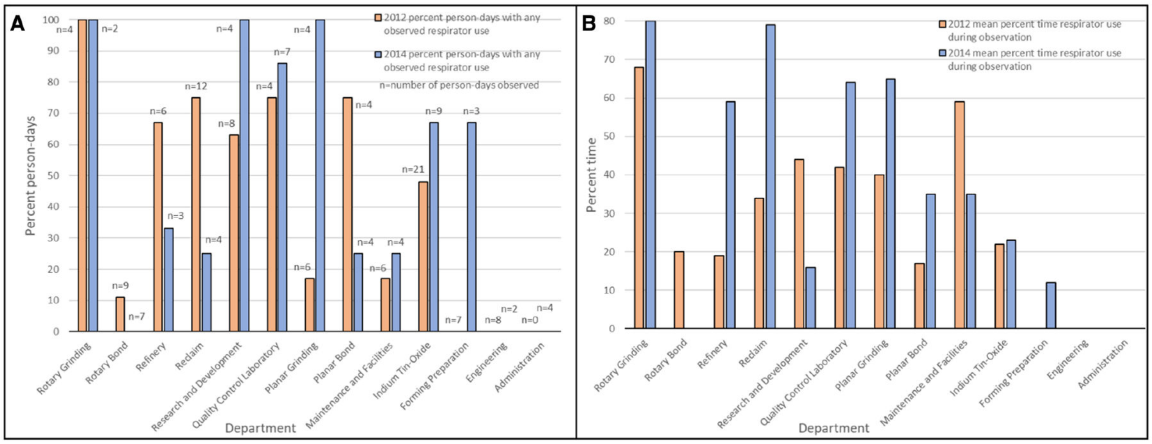

Figure 1.

Per cent person-days with any observed respirator use and number of person-days observed by department (A) and mean per cent time respirator use during observation by department (B) among 46 workers and 98 observations during 2012 and 38 workers and 57 observations during 2014.

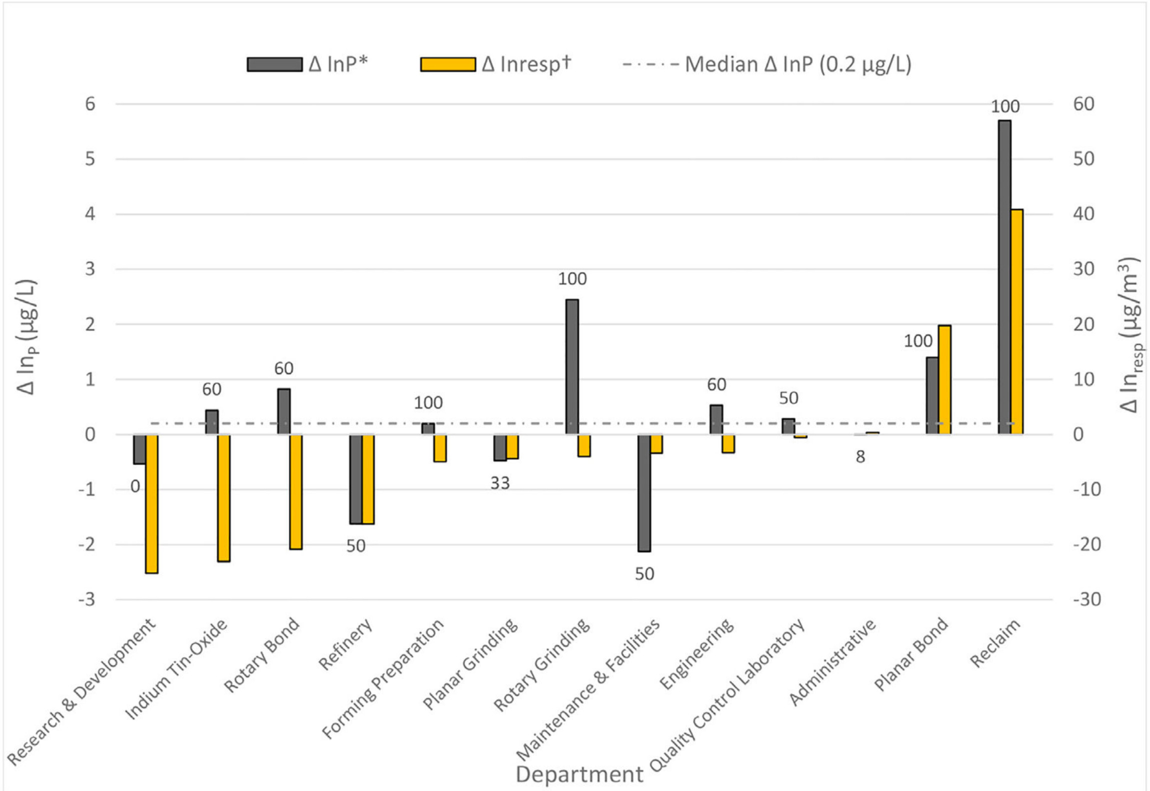

Figure 2.

2012–2014 ΔIn_P and ΔIn_{resp} by department at an ITO production facility and percentage of workers with ΔIn_P >0.2 μg/L in each department, N=60. ITO, indium-tin oxide.

Table 1

Most recent demographic, work and exposure characteristics, and health outcomes of participants at an indium-tin oxide (ITO) production and reclamation facility, 2012–2014, N=111

Characteristic	**n (%)**
Median age(range) (years)	43 (19–66)
Male	96 (86)
Race/ethnicity	
White	71 (68)
Asian	11 (10)
Hispanic	16 (15)
Black	6 (6)
Smoking status	
Never	57 (51)
Current	28 (25)
Former	26 (23)
Median tenure (range) (years)	3.1 (<1–38)
Department	n (%)
Administrative	23 (21)
Engineering	11 (11)
Forming Preparation	4 (4)
ITO	20 (18)
Maintenance and facilities	6 (5)
Planar bond	3 (3)
Planar grinding	3 (3)
Quality control laboratory	12 (11)
Research and development	5 (5)
Reclaim	5 (5)
Refinery	4 (4)
Rotary bond	10 (9)
Rotary grinding	3 (3)
HRCT findings	
Emphysema (at least mild)	6 (7)
Fibrosis (at least moderate)	1 (1)
Spirometry *	
Obstruction	5 (5)
Restriction	7 (7)
Mixed	0
% predicted FEV, (mean±SEM)	97±1.4
% predicted FVC (mean±SEM)	99±1.2

Characteristic	n (%)
FEV_1/FVC ratio	80 (74–84)
% predicted V_A (mean±SEM)	93±1.1
% predicted DL_{CO} (mean±SEM)	88±1.4
KL-6>466 U/mL	39 (38)
KL-6 (U/mL), mean (range)	404 (305–576)
SP-D (ng/mL), mean (range)	135 (89–214)
	Median (IQR)
In_p (µg/L)	0.9 (0.2; 2.4)
Cumulative In_{resp} (µg-year/m^3)	21 (5.3; 116)

*Spirometry: We defined obstruction as an FEV1/FVC ratio less than the lower limit of normal with FEV1 less than the lower limit of normal; restriction as a normal FEV1/FVC ratio with FVC less than the lower limit of normal; and mixed obstruction and restriction as having FEV1, FVC and FEV1/FVC ratio all less than the lower limit of normal.

DL_{CO}, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; HRCT, high-resolution CT; In_p, plasma indium; In_{resp}, respirable indium; KL-6, Krebs von den Lungen-6; SP-D, surfactant protein-D; V_A, alveolar volume.

Table 2

Symptoms, lung function testing, biomarkers and exposure indices in 2012, 2014 and change from 2012 to 2014 in workers who participated in both 2012 and 2014 surveys at an indium-tin oxide production and reclamation facility, N=62

Symptoms, n (%)	**Both years**	**Resolved**	**New in 2014**
Usual cough	7 (11)	2 (3)	5 (8)
Usual phlegm	3 (5)	3 (5)	4 (6)
Shortness of breath	5 (8)	8 (13)	5 (8)
Wheeze	4 (6)	8 (13)	2 (3)
Chest tightness	3 (5)	1 (2)	5 (8)
Lung function testing, mean (range)	2012	2014	Δ2012–2014
FEV_1 (L)	3.47 (1.49–5.89)	3.43 (1.42–5.78)	−50 mL (–594 to 353)
% predicted FEV_1	96 (58–117)	96 (59–119)	–
FVC (L)	4.45 (2.20–6.63)	4.46 (2.25–6.46)	−47 mL (−751 to 393)
% predicted FVC	98 (74–134)	99 (79–134)	–
FEV_1/FVC	78 (49–97)	77 (49–96)	n/a
DL_{CO} (mL/min/mm Hg)	27.2 (15.3–44.9)	26.2 (16.9–42.2)	−0.9 mL/min/mmHg (−8.3; 5.0)
% predicted DL_{CO}	91 (62–132)	89 (62–123)	–
V_A (L)	5.56 (3.58–9.06)	5.75 (3.78–7.89)	113 mL (−1262, 693)
% predicted V_A	91 (70–122)	94 (71–119)	–
Biomarkers, mean (range)*	2012	2014	Δ2012–2014
KL-6 (U/mL)	722 (201–2779)	605 (201–2992)	−125 (−1209; 1665)
SP-D (ng/mL)	209 (41–836)	172 (17–998)	−36 (−589; 523)
Exposure indices, median (IQR)	2012	2014	Δ2012–2014
In_{p*}	1.2 (0.4–2.9)	1.6 (0.6–4.3)	0.2 (−0.1 to 0.9)
In_{resp}	4.9 (3.4–26.3)	4.9 (1.2–34.0)	−0.2 (−5.8 to 1.4)
Cumulative In_{resp}	48.8 (5.8–131.3)	73.3 (12.8–228.1)	n/a

* two employees removed from analyses from blood-related variables (biomarkers and InP); therfore, N=60 for these analyses

DL_{CO}, diffusing capacity of the lungs for carbon monoxide; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; In_P, plasma indium; In_{resp}, respirable indium; KL-6, Krebs von den Lungen-6; n/a, not available; SP-D, surfactant protein-D; V_A, alveolar volume.