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PINE DUST, ATOPY AND LUNG FUNCTION: A CROSS-SECTIONAL STUDY IN NEW ZEALAND SAWMILL WORKERS

Jeroen Douwes[1,2], Dave McLean[1,2], Tania Slater[1,2], Noemie Travier[1,3], Soo Cheng[1,2], Neil Pearce[1,2]

[1]Centre for Public Health Research, Research School of Public Health, Massey University, Wellington, New Zealand

[2]Wellington Asthma Research Group, Otago University, Wellington, New Zealand

[3]Sleep/Wake Research Centre, Research School of Public Health, Massey University, Wellington, New Zealand

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Correspondence:

Dr Jeroen Douwes,

Private Box 756

Wellington, New Zealand

Tel: +64 4 3800617

Fax: +64 4 3800600

E-mail: j.douwes@massey.ac.nz

Short title: atopy and lung function in sawmill workers

ABSTRACT

Objectives: We have previously shown an increased risk of asthma symptoms in 772 pine sawmill workers. The current study assessed the association between dust exposure, lung function and atopy.

Methods: Subjects with (n=59) and without asthma symptoms (n=167) were randomly selected from the previous survey. Lung function and atopy were determined using spirometry and skin prick tests respectively. Inhalable dust was measured on the same day.

Results: The geometric mean dust concentration was 0.52 mg/m^3 (GSD, 2.66). Exposure to "dry" dust but not green dust was associated with asthma symptoms (OR, 2.1, CL 1.0-4.4). "Green" dust was associated with atopic sensitisation, particularly against outdoor allergens (OR 2.23, CL 1.02, 6.46); no association was found for "dry" dust. FVC, FEV_1, and PEF were significantly lower in high "green" dust (-350 ml; -260 ml; and -860 ml/s, respectively) and high "dry" dust exposed workers (-230 ml; -190 ml; and -850 ml/s, respectively). These associations were observed both in subjects with and without asthma symptoms. No associations with cross-shift changes in lung function were found.

Conclusions: Exposure to "green" pine sawdust may be a risk factor for atopy. Both "green" and "dry" dust were associated with obstructive as well as restrictive pulmonary effects.

Key words: asthma, atopy, lung function, occupational, sawmills, wood dust

INTRODUCTION

Wood and timber processing is a major industry world wide. Exposure to wood dust originating from a wide range of different tree species is associated with sinonasal cancer and respiratory health effects.[1] Most studies have been conducted in workers processing Western red cedar, showing associations between dust exposure and both symptoms and lung function.[2] In a previous study among 772 sawmill workers we demonstrated that pine sawmilling was associated with an increased prevalence of asthma and cough symptoms, and eye and nose irritations,[3] and several other studies (mainly in furniture workers) have shown similar results.[4][5][6] In furniture workers, associations between wood dust exposure and both base line lung function (FEV_1) [4] [7] and reduced cross-shift lung function (FEV_1) have also been described, with the effects being most pronounced among pine workers.[7][8]

Most of the reported respiratory health effects occurred at dust levels well below 5 mg/m^3, an occupational exposure limit (OEL) which is commonly used in many countries such as New Zealand, Australia and the US. The EU Scientific Committee on Occupational Exposure Limits (SCOEL) and the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) Committees have both recommended a substantially lower OEL of 1 mg/m^3, and some countries such as The Netherlands and Denmark have subsequently lowered the standard to 2 mg/m^3 with the Dutch OEL being based on inhalable dust compared to total dust in Denmark. Nonetheless, a safe level has so far not been established due to the lack of detailed information on dose-response associations. Currently it is not clear which components in wood dust cause these respiratory health effects. Abietic acid [9] in pine and plicatic acid [10][11] in Western red cedar may play a role, but

conclusive evidence is lacking. It is also not clear which mechanisms underlie these effects. Some studies found specific IgE against wood dust, but the proportion of symptomatic workers with a positive IgE test was small.[12][13]

In the current study, we randomly selected 167 sawmill workers with and 59 without asthma symptoms from our previous survey [3] and assessed the association between dust exposure and both baseline and cross-shift lung function. We also studied the association between dust exposure and atopic sensitisation against common allergens and pine pollen.

MATERIALS AND METHODS

Study design and population

Phase I of this study was a cross sectional questionnaire survey conducted in 772 sawmill workers selected from 5 large sawmills in New Zealand processing *pinus radiata* exclusively.[3] The sawmill process has been described in more detail previously.[14] Subjects with asthma symptoms were defined on the basis of having at least one positive response to any of the following questions: "*Have you been woken up with shortness of breath in the last 12 months?*"; "*Have you had wheezing in the chest in the last 12 months?*"; and, "*Are you currently taking asthma medication?*" [15]. All subjects with asthma symptoms (n=134) and a random sample of subjects without asthma symptoms (n=200) were invited to participate in the current Phase II study, one year after the first survey. The same three asthma questions were repeated at phase II, and those who no longer had symptoms (N=28) were excluded from the "asthma group", whereas those who had developed symptoms in the time between both studies (N=8) were included. An overview of the recruitment, exclusions, and refusals is presented in figure 1. Briefly, we excluded all night-shift workers and workers who were not available for testing at the time that we visited for other reasons (e.g. off-site work activities, no replacement available to take over the work load during the testing period, etc). Approximately 20% declined participation and a further 15% had left the work force since the Phase I study (these are estimates based on the information given to us by the site managers). Therefore, we were able to include only 59 workers with asthma symptoms, and after replacing 67 of the non-symptomatic workers who were excluded or declined participation with the next non-symptomatic person on the list, we were able to include 167 non-

symptomatic workers (figure 1). All subjects gave written informed consent and the study was approved by the Wellington Ethics Committee (protocol 99/93).

Exposure assessment

We assessed full-shift (8h) personal inhalable dust exposure in 205 workers on the same day that lung function and skin prick tests were done. Inhalable dust samples were taken at an airflow of 2 l/min using glass fibre filters mounted in IOM sampling heads. Filters were weighed before and after sampling in a climate controlled room. Due to technical errors we excluded 22 samples. We used job title based mean exposure levels since exposure levels are likely to vary less within job titles than within individuals,[16] although we also explored associations using individual exposure levels. Dust exposure categories were constructed by two qualified industrial hygienists with specific experience in this industry and were based on the workers' work area and job title [3]. Four 'crude' exposure categories were distinguished: 1) non-exposed: administration and other office workers; 2) low or intermittent exposure: yard, maintenance, dispatch, export workers and saw doctors; 3) high exposure to "green" dust: all workers in the green mill involved in sawing logs to green timber, and subsequently sorting, grading, trimming and stacking, and kiln drying the green timber; and 4) high exposure to "dry" dust: workers processing kiln dried timber in the planer mill, remanufacturing and moulding. We refer to "green" dust as dust (including chemicals such as resin acids and monoterpenes) associated with processing fresh timber before it is kiln dried; dust associated with processes that take place after kiln drying is referred to as "dry" dust.

Skin prick testing

Skin prick tests (Bayer Corporation, West Haven, CT, US) were carried out at the start of the work shift on 220 workers. Due to missing values for confounders (n=8) we used only 212 subjects in our adjusted analyses. Solutions containing the following allergens (Bayer Corporation) were tested: pine pollen mix (lodgepole and Western yellow pine; ED2204), cat pelt (TR4810), dog hair/dander (ED4084), cockroach (1661603/ED6585), grass mix (1659420/ED2631), mould mix (ED4956), New Zealand/Australian tree pollen mix (oak, beech, birch, plane and ash;1658343) and house dust mite (Der p; UP6692/1670858). We also tested a positive (histamine) and negative control (diluent). After 15 minutes the weals were read, and a positive reaction was defined as a weal with a diameter ≥ 3 mm, once any reaction to the negative control was subtracted. We also analysed the atopy data when the negative control was not subtracted, but this did not significantly change the results and we have therefore only reported the results involving subtraction of the negative control. Two subjects with no response to the positive control were excluded.

Lung function testing

Lung function tests were carried out at the commencement and at the end of the work shift using portable spirometers (Alpha Spirometer, Vitalograph, Buckingham, UK) with the worker seated in an upright position. Subjects performed three acceptable reproducible (within 5%) manoeuvres following standard spirometry procedures.[17] From these, the Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1) and Peak Expiratory Flow (PEF) were determined. The highest values for FVC, FEV_1 and PEF were used in the analyses. Twelve technically unacceptable lung function tests were excluded. Nine subjects did not reach a maximum FVC,

whereas their FEV_1 and PEF were acceptable, so we excluded only their FVC values. In the adjusted analyses we used 197 and 206 subjects for FVC and FEV_1 respectively, due to missing values for confounders (n=8). The percentage of the predicted value was calculated using reference equations described for Caucasians in the US.[18] We also reported the actual lung function values adjusted for age, height, sex and ethnicity.

Analysis

The data were analysed using SAS statistical software (SAS institute, Cary, NC). Dust concentrations approximated a log-normal distribution, hence exposure measurements were log transformed and geometric means (GM) were presented with geometric standard deviations (GSD). Analysis of variance was applied to assess the explained variance in dust exposure by exposure categories and mill number. Chi-square and t-tests were performed to test differences in prevalence and mean levels respectively. Prevalence odds ratios were calculated by means of logistic regression analysis to describe the associations between exposure and atopy, and exposure and asthma symptoms. The association between exposure and lung function was calculated using linear regression analysis, with analyses adjusted for age, sex, current and ex-smoking, ethnicity and height. All analyses involving outcome variables other than asthma symptoms were also adjusted for the occurrence of asthma symptoms. Analyses were also stratified based on the occurrence of asthma symptoms to test for homogeneity.

RESULTS

The geometric mean dust concentration for all workers was 0.52 mg/m^3 (GSD, 2.66; n=183). The mean dust levels for each exposure group corroborated our previous exposure assessment based on expert judgement, however, the variance in exposure within each group was substantial (Table 1). Since the number of workers in the "non-exposed" group was very low (n=20) we combined them with the "low/intermittent" exposure group, resulting in a significant reduction of the explained variance (14% compared to 26%; Table 1). The "non/low and intermittent" group was subsequently used as the reference group for all further analyses.

Table 1. Dust concentrations stratified by job-title-defined exposure categories

	N	GM (mg/m^3)	GSD	Range (mg/m^3)
Non + low/intermittent exposed	92	0.38	2.80	0.02-4.51
Non-exposed	20	0.15	2.44	0.02-0.62
Intermittent/low exposed	72	0.49	2.48	0.06-4.51
High exposed to "dry" dust	48	0.62	2.23	0.08-3.11
High exposed to "green" dust	43	0.80	2.25	0.24-6.24

ANOVA explained variance including four exposure categories and mill number: 26%, $p<0.0001$;

ANOVA explained variance including three exposure categories (combining the non-exposed and low/intermittent exposed) and mill number: 14%, $P<0.0001$

Significant differences in age, smoking, ethnicity, time worked outdoors and use of respiratory equipment were observed among the "non/intermittent and low", "high

dry" and "high green" exposure groups (table 2). The population characteristics between subjects with and without asthma symptoms were very similar (Table 2).

Table 2. Characteristics of study population stratified by exposure and symptom status

	Exposure groups			Symptom status	
	Non and intermittent/low exposed N=117‡	**High exposed to "dry" dust N=53§**	**High exposed to "green" dust N=56¶**	**Subjects *without* asthma symptoms N=167**	**Subjects *with* asthma symptoms N=59**
Age (y,SD)	39.8 (11.0)	34.3 (10.3)**	35.3 (11.8)*	37.5 (11.2)	37.3 (11.5)
Duration of employment (y,SD)†	9.9 (8.5)	7.1 (7.2)*	8.1 (7.2)	8.8 (8.0)	8.9 (7.9)
Duration of employment (y,SD)††	5.1 (5.2)	4.6 (6.0)	4.7 (4.5)	5.0 (5.6)	4.5 (4.0)
Hours/week of work (SD)	44.8 (6.4)	43.7 (6.3)	44.2 (4.9)	44.5 (6.2)	44.3 (5.6)
Smokers	30.2 %	28.8 %	56.6 %**	37.4%	32.8%
Ex-smokers	31.0 %	23.1 %	20.8 %	28.8%	20.7%
Female workers	19.8 %	25.0 %	13.2 %	19.6%	19.0%
Māori[#]	19.0 %	35.3 %*	49.1 %**	31.3%	26.3%
Pacific Islander[#]	6.9 %	2.0 %	24.5 %**	9.2%	12.3%
European[#]	75.0 %	62.7 %	28.3 %**	60.7%	61.4%
Work >50% outdoors	22.4 %	17.3 %	9.4 %*	15.3%	25.9%
Daily use of respiratory equipment	6.9 %	15.4 %	18.9 %*	12.3%	10.3%

† In current sawmill

†† In current job title

‡ there was 1 missing for some variables

§ there were 3 missings for some variables;

¶ there were 1-2 missings for some variables;

Question allowed for multiple ethnic identification

* $p<0.05$; ** $p<0.01$; compared to non-exposed group

High exposure to "dry" dust was associated with asthma symptoms (adjusted OR, 2.1, CL 1.0-4.4), whereas no association with high "green" dust exposure (adjusted OR, 1.4, CL 0.6-3.3) was found. Atopy defined as a positive skin prick test to one or more of the tested allergens was very common (80% in subjects with and 50% in those without asthma symptoms). Six percent of the subjects were sensitised against pine pollen and 20% against the tree pollen mix. No significant association between sensitisation against pine or other tree pollen (mix) and asthma symptoms was observed (data not shown). High exposure to "green" dust was significantly associated with atopic sensitisation against outdoor allergens (pine, grass mix or tree mix) and to a lesser extent with sensitisation against indoor allergens (mould, cockroach, dust mite, dog and cat) (Figure 2). The strongest association was found with atopy when defined as ≥ 2 or ≥ 3 positive SPTs with adjusted ORs of 2.6 and 3.1, respectively ($p<0.05$). High exposure to "dry" dust was not associated with atopy (Figure 2).

Subjects with asthma symptoms had a significantly lower FEV_1 and PEF than those without asthma symptoms, whereas their FVC was very similar (Table 3).

Table 3. Mean (SD) baseline lung function for subjects with and without asthma symptoms. Adjusted analyses were based on 197 subjects for FVC and 206 for FEV_1 and PEF.

	Subjects *without* asthma symptoms	Subjects *with* Asthma symptoms	Difference (95% CL)†
FVC in L	4.61 (1.04)	4.49 (1.12)	-0.04 (-0.25, 0.18)
FVC %-pred	91.72 (14.18)	89.50 (13.55)	-1.19 (-5.43, 3.04)

FEV_1 in L	3.59 (0.87)	3.24 (0.91)	-0.31 (-0.48, -0.14)**
FEV_1 %-pred	87.80 (13.85)	79.31 (14.91)	-7.86 (-11.85, -3.87)**
PEF in L/s	8.75 (2.28)	7.56 (2.04)	-1.12 (-1.65, -0.59)**
PEF %-pred	91.84 (18.99)	79.43 (17.06)	-11.61 (-17.17, -6.05)**

† adjusted for sex, age, ethnicity, smoking and height

**p<0.01

High exposure to both "dry" and "green" dust was significantly associated with a reduction in FEV_1 (-190 and -260 ml, respectively) and PEF (-850 and -860 ml/s, respectively) (Table 4). The FVC was also reduced (-230 and -350 ml, respectively), statistically significant in the "high green" exposure group and borderline significant for the "high dry" exposure group. Similar results were obtained when lung function was expressed as percentage predicted values (Table 4). Stratified analyses indicated that the effects in subjects with asthma symptoms for "high dry" exposure were somewhat stronger whereas they were somewhat weaker for "high green" exposure (Table 4). Nonetheless results were quite similar suggesting no strong heterogeneity, perhaps with the exception of the FVC in the high green dust exposed where the effect appears to be driven by the subjects with no asthma symptoms. Additional adjustments for use of personal respiratory protective equipment or mill number did not alter the results. Cross-shift changes (adjusted for height, age, sex and other confounders) in the FEV_1 and PEF were slightly lower in the high "dry" dust and "green" dust exposed workers (-40 ml, and -110 and -150 ml/s, respectively), but these differences were not statistically significant. We found no associations between exposure and FEV_1/ FVC, and exposure and the number of subjects with a FEV1/FVC

<70% (a key parameter for diagnosing COPD). Also, no associations with any of the lung function parameters were found using individual exposure measurements.

Table 4. Differences in base line lung function between high and non and low/intermittent exposed, presented for subjects with and without asthma symptoms combined and separately. Lung function is expressed both as absolute and percentage predicted values. Analyses are adjusted for symptom status (with exception of the stratified analyses), sex, age, ethnicity, smoking and height.

	High exposed to "dry" dust (95% CL)			High exposed to "green" dust (95% CL)		
	All† N/n¶=50/106	**Subjects without asthma symptoms‡ N/n¶=32/82**	**Subjects with asthma symptoms§ N/n¶=18/24**	**All† N/n¶=50/106**	**Subjects without asthma symptoms ‡ N/n¶=37/82**	**Subjects with asthma symptoms§ N/n¶=13/24**
FVC in L††	-0.23 (-0.46, 0.01)	-0.24 (-0.53, 0.06)	-0.11 (-0.57, 0.35)	-0.35 (-0.61, -0.10)**	-0.41 (-0.72, -0.10)*	-0.15 (-0.66, 0.36)
FVC %-pred††	-3.57 (-8.28, 1.13)	-3.70 (-9.46, 2.07)	-2.31 (-11.52, 6.90)	-6.33 (-11.33, -1.33)*	-8.08 (-14.18, -1.99)*	-1.07 (-11.33, 9.19)
FEV_1 in L	-0.19 (-0.37, 0.00)*	-0.14 (-0.36, 0.08)	-0.24 (-0.57, 0.10)	-0.26 (-0.46, -0.06)*	-0.21 (-0.44, 0.03)	-0.23 (-0.60, 0.15)
FEV_1 %-pred	-3.89 (-8.35, 0.57)	-2.90 (-8.16, 2.36)	-5.00 (-13.17, 3.16)	-5.72 (-10.56, -0.88)*	-5.18 (-10.88, 0.52)	-3.36 (-12.56, 5.83)
PEF in L/s	-0.85 (-1.43, -0.26)**	-0.79 (-1.53, -0.05)*	-0.96 (-1.89, -0.03)	-0.86 (-1.50, -0.23)**	-0.96 (-1.76, -0.16)*	-0.53 (-1.58, 0.52)
PEF %-pred	-8.04 (-14.21, -1.87)*	-7.03 (-14.84, 0.79)	-10.31 (-20.28, -0.34)*	-8.07 (-14.77, -1.38)*	-9.77 (-18.24, -1.30)*	-3.44 (-14.67, 7.79)

†The reference category consisted of all non and low/intermittent exposed workers (n=106)

‡The reference category consisted of all non and low/intermittent exposed subjects without asthma symptoms (n=82)

§The reference category consisted of all non and low/intermittent exposed symptoms with asthma symptoms (n=24)

¶ N=number of exposed/n=number of non and low/intermittent exposed

†† Nine subjects had missing values for FVC (see material and methods section)

* $p<0.05$, ** $p<0.01$

DISCUSSION

In this cross-sectional study, sawmill workers exposed to high levels of "green" pine dust were more likely to be atopic than those who were low or not exposed. In addition, both "dry" and "green" pine dust exposure was associated with reduced baseline lung function. No clear acute cross-shift lung function effects were observed.

As we over-sampled workers with asthma symptoms we effectively gave more weight to symptomatic workers, and the analyses for other health outcomes were therefore adjusted for "symptom status". The effect of over-sampling subjects with asthma symptoms was in fact very small, as demonstrated by the fact that exposure-related lung function deficits calculated separately for subjects with and without asthma symptoms were only moderately different (Table 4). In addition, when the analyses for exposure and atopy were stratified by "symptom status" there was no evidence of heterogeneity between subjects with and without asthma symptoms (data not shown).

Due to practical issues we were able to recruit only 59 (52%) of the 114 eligible symptomatic workers (Figure 1), potentially introducing non-response bias. However, we consider the potential for non-response bias to be minimal because (1) no significant differences in symptom severity, exposure, age, smoking and ethnicity were found between workers with asthma symptoms included in the first and second phases of the study (data not shown); (2) Similar associations between wood dust exposure and lung function were found for workers with and without asthma symptoms; and (3) in those workers that we were able to contact for the second phase of the study the response rate was high (approximately 80%). Similarly, the response

rate was high for the non-symptomatic workers who we were able to contact for the phase II study (Figure 1).

Group-mean exposure categories have previously been shown in the wood processing industry to result in less biased exposure estimates.[8] [13] [16] Nonetheless, in our study, the exposure categories were relatively crude with a relatively large variance in concentrations within each exposure group (Table 1). Due to low numbers in the "non-exposed" group we were also forced to combine this group with the intermittent/low exposure group, further reducing the contrasts among the exposure categories. This could explain why, compared to our previous survey (in which we used a reference group of exclusively "non-exposed" workers [3]), we found weaker relationships between exposure and asthma symptoms. We also used *current* exposures to estimate group averages whereas cumulative or past exposures may have been more relevant. Unfortunately we were not able to explore this since we had no detailed information on past exposures and/or job titles. Duration of employment in the current sawmill was inversely associated with lung function, but compared to current group-mean based exposures (based on job title and work area) the effects were small (data not shown). Job title and area may therefore, in this study, be a better predictor of cumulative exposure than duration of employment. Finally, dust may not be the best marker of the true causal exposures as abietic acid, monoterpenes or microbial agents may be more important.[19] All the above issues may have resulted in random exposure misclassification, but this is likely to produce a bias towards the null and is unlikely to explain our positive findings.[20]

We adjusted for potential confounders in the multivariate analyses and this did not change the results, with the exception of ethnicity. Since Polynesians (Māori and Pacific Islanders) have lower mean lung function,[21][22] and the adjusted and unadjusted analyses differed, we performed a further check by repeating the analyses of lung function excluding all non-European New Zealanders. These analyses showed similar results i.e. lung function was lower in both the high dry dust exposure group (FVC -370 ml [95%CL -670,-70; p=0.018]; FEV1 -320 ml [95%CL -540,-100; p=0.005]; PEF -1460 ml [95%CL-2100,-820; p=0.0001]) and high green dust exposure group (FVC -220 ml [95%CL -640,210; p=0.320]; FEV1 -140 ml [95%CL -450,180; p=0.396]; PEF -620 ml [95%CL-1550,300; p=0.178]). This indicates that our results were not due to confounding by ethnicity. The lack of statistical significance for the associations with green dust can be explained by the low number of subjects after excluding all Polynesians.

Baseline lung function in the reference group was lower than expected based on the predicted values. This may be because the reference group was also exposed to significant levels of dust (Table 1), or the fact that a significant proportion was Polynesian who are known to have a lower lung function than Caucasians (see above). Also, the predicted values were based on a US population [18] which may not reliably predict lung function for New Zealanders. In any case, we found consistent associations that were highly comparable with the results based on the actual lung function indicating that the results reported are valid.

Elevated exposures to both “dry” and “green” pine dust were associated with a significant deficit in baseline lung function, both of an obstructive (FEV_1 and PEF)

and restrictive (FVC) nature. This is consistent with previous findings in saw mill workers processing western red cedar [2] [23] and pine,[5] although some studies in pine sawmill workers showed no effects on FVC and FEV_1.[24][25] Reduced FEV_1 and FVC have also been reported for furniture workers exposed to "dry" pine dust. [4] [7] Pine dust exposure in furniture making was shown to be more potent in affecting lung function than other types of wood.[7] In our study the effect of dry dust exposure on the FVC appeared to be driven mainly by the subjects without asthma symptoms (Table 4); the reasons for this are not clear. In contrast to other studies,[7][8] we found no significant effects on cross-shift lung function. Small changes in cross-shift lung function may not have been detectable in our study because of the already substantially reduced baseline lung function in the high exposed subjects.

Atopy is not generally used as an outcome variable in occupational asthma studies. Nonetheless, several recent studies have shown that certain exposures may offer protection against atopy (e.g. occupational endotoxin exposure; [26]), whereas others have shown that exposures such as diesel exhaust may increase the risk of atopy [27]. Our study is the first to show a positive association between pine dust exposure and atopy. A previous study in Western red cedar workers showed a lower prevalence of atopy compared to non-exposed controls.[23] Qualitative and quantitative differences in exposures may explain these contradictory findings. Several studies have demonstrated IgE responses against various types of wood including pine.[12][13] However, in most of these studies only few workers were positive.[12] Allergy to pine dust is therefore unlikely to explain the elevated prevalence of atopy in the high "green" dust exposed workers. Also, it is unlikely to be related to pollen exposure since the pine pollen SPT results were not associated with exposure (data not shown).

Since we only found an association with “green” dust it is more likely to be related to agents such as resin acids or monoterpenes which are present at elevated levels in pine processing, particularly in areas where fresh wood is sawn.[28] These agents may either be allergenic themselves after oxidation [29] or may possibly act as an adjuvant increasing the risk of becoming allergic to other agents. Microbial agents present in sapwood of fresh pine logs may also play a role.[30]

Whether atopic mechanisms can explain the increased risk of asthma symptoms and adverse lung function effects is unclear. It is of interest to note that in the current study the effect on asthma symptoms was found in the “high dry” exposure group whereas the effect on atopy was observed in the “high green” exposure group, while effects on baseline lung function were found both in the “high green” and the “high dry” dust exposure categories. This suggests that in this population the underlying mechanisms and/or causal exposures might be different for atopy, asthma symptoms and lung function.

The effects observed in the current study occurred at mean levels well below (0.6-0.8 mg/m^3; Table 1) the current occupational exposure standard (5 mg/m^3) used in most countries. This finding is in line with other studies [7][8] and suggests that the standard might be too high as suggested previously.[1]

In conclusion, exposure to pine wood dust, and/or specific components therein, may increase the risk of atopy and obstructive and restrictive pulmonary effects.

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Figure 1. Flow diagram describing subject recruitment, exclusion and refusals. † phase II participants were approached through the sawmill site managers directly; the number of workers in each category were therefore estimated based on the information provided by the site managers. ‡ We excluded all night-shift workers and workers who were not available for testing at the time that we visited for other reasons (e.g. off-site work activities, no replacement available to take over the work load during the testing period, etc).

Figure 1

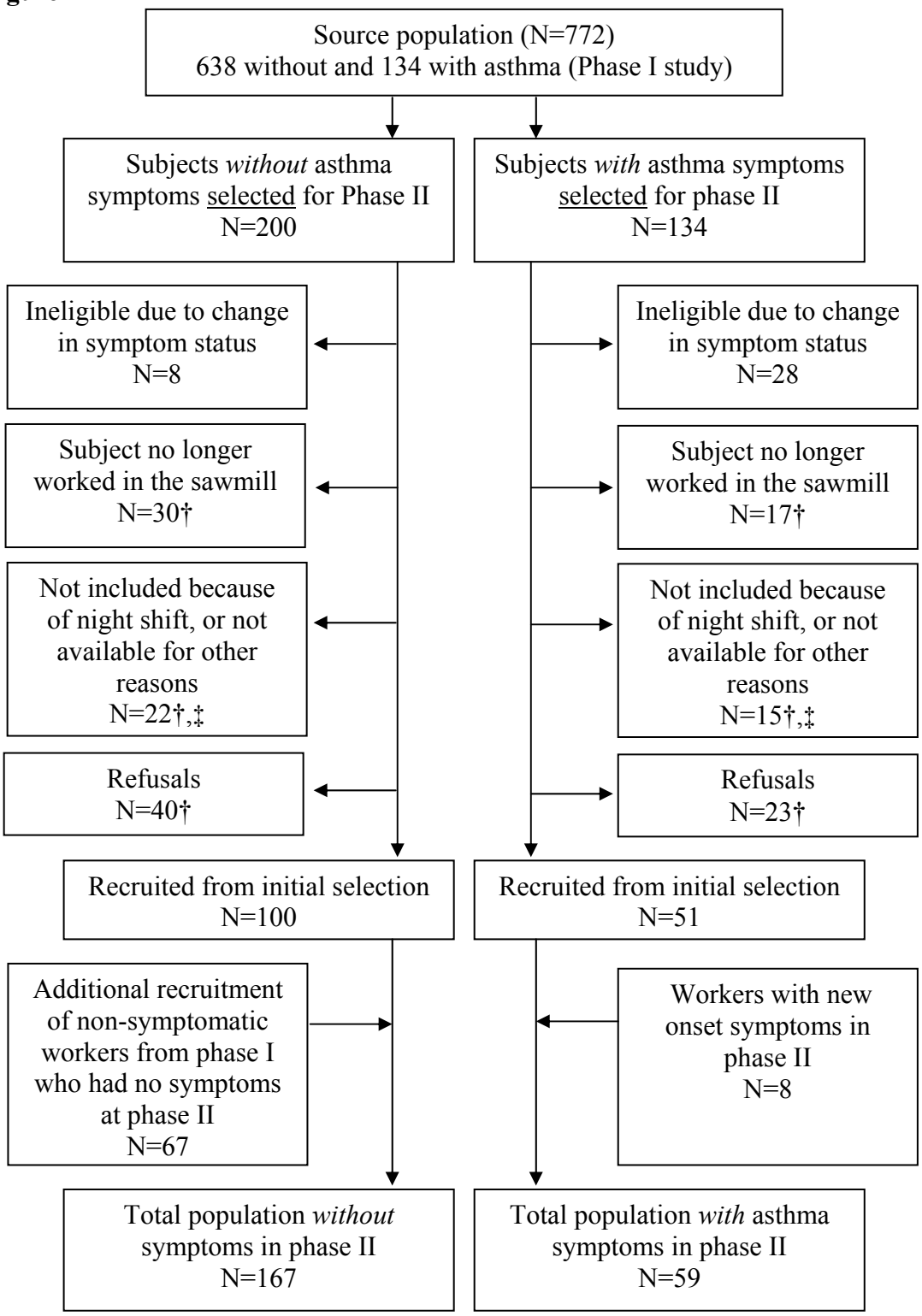
Source population (N=772)
638 without and 134 with asthma (Phase I study)
Subjects *without* asthma symptoms selected for Phase II N=200
Subjects *with* asthma symptoms selected for phase II N=134
Ineligible due to change in symptom status N=8
Ineligible due to change in symptom status N=28
Subject no longer worked in the sawmill N=30†
Subject no longer worked in the sawmill N=17†
Not included because of night shift, or not available for other reasons N=22†,‡
Not included because of night shift, or not available for other reasons N=15†,‡
Refusals N=40†
Refusals N=23†
Recruited from initial selection N=100
Recruited from initial selection N=51
Additional recruitment of non-symptomatic workers from phase I who had no symptoms at phase II N=67
Workers with new onset symptoms in phase II N=8
Total population *without* symptoms in phase II N=167
Total population *with* asthma symptoms in phase II N=59

Figure 2. The association between exposure and several definitions of atopy. 'Indoor' and 'outdoor' atopy were defined as any positive skin prick test (SPT) against any of the indoor allergens (mould mix, cockroach, dust mite, dog, cat) or outdoor allergens (Pine, grass mix, tree mix), respectively. Odds Ratios (ORs) were adjusted for symptom status, sex, age, ethnicity, and smoking. N=212 for analyses regarding indoor atopy, outdoor atopy and atopy defined ≥1 SPT, N=161 for the analysis regarding atopy defined ≥2 SPT, and N=133 for the analysis regarding atopy defined ≥3 SPT. *p<0.05

Figure 2