

1 **SUPPLEMENTARY MATERIAL**

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Occupational exposure to pesticides are associated with fixed airflow obstruction in middle-age

Authors

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1 **SUPPLEMENTARY METHODS**

2 **Definitions of confounders**

3 Having had asthma was defined by an affirmative response to the question “Have you ever had
4 asthma?” Current asthma was based on self-reported symptoms in the morning, day-time and
5 night-time or flare-ups in the last 12 months. Childhood asthma was defined as asthma reported
6 at age 7 and 12 by an affirmative response by the parents to the question “Has he/she at any
7 time of his/her life suffered from attacks of asthma or wheezy breathing?” Smoking status of
8 the participants was categorised as current, past and never-smokers. A current smoker was
9 defined as smoking status within last four weeks. Pack-years were calculated as the number of
10 cigarettes smoked per day divided by 20 multiplied by the number of years of smoking.(1)
11 Childhood and adulthood socioeconomic status were defined using Australian census data of
12 Socio-Economic Indexes for Areas (SEIFA indexes).(2) We used the Index of Education and
13 Occupation (IEO) variables that focused on the skills of the people required in different
14 occupations. A high IEO score indicated that individuals who lived in that area had high
15 qualifications and highly skilled jobs.

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17 **Additional statistical analysis**

18 We included 1,335 participants in the ever exposure analysis, but the participants with missing
19 or incomplete job history (n=80) were excluded in cumulative EU-years analysis (N=1,255).
20 Furthermore, we compared our complete-case analysis with multiple imputation by imputing
21 the missing confounding variables (Supplementary Table S3, S4, and S5). The missing data
22 ranged from 3% for pack-years to 0.3% for smoking, asthma, and socioeconomic status.
23 Multiple imputation method in two-stages was used as a sensitivity analysis. In the first stage,
24 the missing values were imputed by using chained equations (“mi impute chained” command)
25 for 20 imputations in stata. In the second phase, the logistic regression analyses were performed
26 in the imputed model including the same confounding variables that were included in the main
27 complete-case analyses. We also tested Spearman rank correlation matrix between the
28 exposures and the co-exposures were adjusted due to the presence of correlation.

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SUPPLEMENTARY RESULTS

The prevalence of occupational exposures to biological dust, mineral dust, gases/fumes, VGDF, all pesticides, herbicides, and insecticides are presented in Supplementary Table S2. The most common exposure was the combined measure to VDGF with 75% of participants having exposure at some point in their working life. Exposure to gases/fumes was also high at 71%, followed by biological dust (55%), mineral dust exposure (52%), and the all pesticides (15.8%).

1 **Table S1:** Comparisons of characteristics between responders and non-responders at
 2 of 2002-2008 follow-up study

Study characteristics	Laboratory attendees	Laboratory non-attendees	p-value*	Completed Postal survey only	p-value**
Sample size	N=1,397	N=990		N=3,350	
Age, years (mean, SD)	44.8 (0.8)	45.7 (0.9)	0.001	43.8 (0.1)	0.003
Sex, %			0.03		0.92
Men	684 (51.6)	509 (54.3)		1,574 (50.6)	
Women	651 (48.3)	417 (45.6)		1,558 (49.3)	
Smoking history					
Never, n (%)	586 (44.6)	323 (36.8)		1,366 (41.0)	
Past, n (%) Pack-years, median [IQR]	413 (29.6) 7.5[2-17.4]	259 (27.3) 11[2.3-22.5]	0.000	1,037 (30.9) 8 [2-18.8]	0.71
Current, n (%) Pack-years, median [IQR]	392 (25.7) 21[9.5-30]	395 (35.8) 23.3[13.5-33.7]		933 (28.0) 19.5[10-29.4]	
Currently employed, n (%)	1,182 (87.0)	802 (84.4)	0.16	2,868 (85.9)	0.28
Chronic bronchitis	256 (12.4)	204 (14.8)	0.03	35 (4.8)	0.000
Chronic cough	191 (8.7)	176 (11.2)	0.004	131 (3.2)	0.000
Chronic phlegm	174 (6.6)	139 (7.9)	0.000	84 (1.9)	0.000
Dyspnoea	242 (12.2)	207 (14.6)	0.01	283 (7.2)	0.000
Asthma	929 (39.8)	686 (44.2)	0.000	710 (11.7)	0.000
Child asthma	401 (15.2)	282 (15.3)	0.000	112 (1.3)	0.000

4 *Definitions of abbreviations:* SD, Standard Deviation; IQR, Interquartile Range;

5 †The estimate prevalences were calculated using inverse-probability-of-inclusion
 6 weights to adjust for the enriched sample of the fifth decade follow-up survey

7 *compare lab attendees to non-attendees

8 ** compared postal survey participants to lab attendees

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1 **Table S2:** Adjusted prevalence of occupational exposures in the study population
 2 (n=1,335)

Study characteristics	Biological dust n(%)	Mineral dust n(%)	Gases/ fumes n(%)	VGDF n(%)	All pesticides n(%)	Herbicides n(%)	Insecticides n(%)
No exposure	579 (44.9)	628 (47.7)	375 (28.8)	322 (24.9)	1,109 (84.2)	1,148 (86.9)	1,151 (87.6)
Ever (low/high) exposure	756 (55.0)	707 (52.2)	960 (71.2)	1,013 (75.1)	226 (15.8)	187 (13.0)	184 (12.3)
Median [IQR] cumulative duration (years)	16.5 (6-30)	22 (8-48)	21.5 (9-38.5)	28 (12-76)	14.5 (4-28)	12 (6-27)	17.8 (8-34.5)

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1 **Table S3:** Associations between ever exposures and cumulative EU-years and fixed AO -
 2 LLN using complete case analysis and multiple imputation

Exposures	Fixed AO-LLN	
	Complete case RR (95%CI)	Imputed RR (95%CI)
Biological dust		
Not exposed	Ref.	Ref.
Exposed	1.56 (1.00-2.45)	1.56 (1.00-2.45)
Cumulative EU-years	1.03 (0.96-1.12)	1.05 (0.97-1.13)
Mineral dust		
Not exposed	Ref.	Ref.
Exposed	1.29(0.81-2.04)	1.29 (0.81-2.04)
Cumulative EU-years	1.03 (0.97-1.11)	1.05 (0.97-1.11)
Gases/fumes		
Not exposed	Ref.	Ref.
Exposed	1.47 (0.87-2.51)	1.48 (0.87-2.53)
Cumulative EU-years	1.02 (0.96-1.09)	1.02 (0.95-1.08)
VGDF		
Not exposed	Ref.	Ref.
Exposed	1.25 (0.72-2.15)	1.26 (0.73-2.17)
Cumulative EU-years	1.03 (0.97-1.08)	1.02 (0.97-1.08)
All pesticides		
Not exposed	Ref.	Ref.
Exposed	1.63 (0.91-3.07)	1.61 (0.91-2.87)
Cumulative EU-years	1.13 (1.00-1.29)	1.12 (0.99-1.24)
Herbicides		
Not exposed	Ref.	Ref.
Exposed	1.95 (1.08-3.49)	1.92 (1.08-3.44)
Cumulative EU-years	1.15 (1.00-1.36)	1.13 (0.98-1.31)
Insecticides		
Not exposed	Ref.	Ref.
Exposed	1.56 (0.84-2.90)	1.53 (0.83-2.84)
Cumulative EU-years	1.10 (0.96-1.26)	1.10 (0.97-1.24)

3 † Complete case-analysis; ± Multiple imputation

4 *Definitions of abbreviations:* LLN, Lower Limit of Normal; AO, Airflow Obstruction; RR, Relative Risk; CI,
 5 Confidence Interval; VGDF, Vapour, Gases, Dust and Fumes.

6 †Adjusted for sex, smoking, pack-years, childhood and adulthood socioeconomic status, childhood and
 7 adulthood asthma and sampling weights. The analyses with biological dust, mineral dust, gases/fumes, and
 8 VGDF were additionally adjusted for all pesticides, whereas the analyses with all pesticides, herbicides, and
 9 insecticides were additionally adjusted for VGDF exposure.

10 The bolded text identifies results reaching statistical significance (p≤0.05)

Table S4: Association between Ever Exposure and Fixed Airflow Obstruction, Chronic Bronchitis and Respiratory Symptoms using complete case analysis and multiple imputation

Exposures	Fixed AO-GOLD		Chronic bronchitis		Chronic cough		Chronic phlegm		Dyspnoea	
	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)
Biological dust										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.58 (1.01-2.48)	1.57 (1.00-2.48)	0.99 (0.67-1.48)	0.92 (0.61-1.38)	1.24 (0.83-1.84)	1.24 (0.83-1.85)	0.98 (0.66-1.46)	0.99 (0.66-1.47)	1.32 (0.95-1.85)	1.32 (0.94-1.86)
Mineral dust										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.29 (0.81-2.04)	1.30 (0.82-2.06)	1.10 (0.72-1.67)	1.06 (0.68-1.64)	1.62 (1.06-2.48)	1.66 (1.09-2.51)	1.51 (1.00-2.30)	1.58 (1.03-2.40)	1.57 (1.10-2.23)	1.55 (1.08-2.21)
Gases/fumes										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.50 (0.88-2.54)	1.49 (0.88-2.55)	0.91 (0.58-1.45)	0.88 (0.55-1.40)	1.25 (0.80-1.98)	1.27 (0.81-2.01)	1.20 (0.76-1.90)	1.23 (0.78-1.95)	1.31 (0.89-1.91)	1.31 (0.90-1.92)
VGDF										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.29 (0.73-2.17)	1.27 (0.74-2.19)	0.95 (0.58-1.55)	0.91 (0.55-1.50)	1.69 (1.01-2.84)	1.72 (1.03-2.87)	1.31 (0.80-2.17)	1.34 (0.82-2.22)	1.29 (0.86-1.93)	1.29 (0.86-1.92)
All pesticides										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.74 (1.00-3.07)	1.72 (0.99-3.04)	1.81 (1.12-2.93)	1.76 (0.99-3.14)	1.77 (1.04-3.01)	1.86 (1.09-3.13)	2.06 (1.23-3.47)	2.18 (1.30-3.66)	1.95 (1.23-3.09)	2.01 (1.27-3.18)
Herbicides										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	2.09 (1.18-3.70)	2.06 (1.16-3.64)	1.81 (1.08-3.02)	1.71 (0.96-3.05)	1.79 (1.04-3.09)	1.89 (1.10-3.25)	1.62 (0.93-2.83)	1.74 (1.01-3.03)	1.44 (0.89-2.34)	1.49 (0.92-2.42)
Insecticides										
Not exposed	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Exposed	1.70 (0.93-3.10)	1.66 (0.91-3.03)	1.64 (1.00-2.72)	1.51 (0.83-2.76)	1.74 (1.00-3.05)	1.84 (1.05-3.18)	1.62 (0.93-2.84)	1.73 (1.00-3.00)	1.58 (0.97-2.57)	1.64 (1.01-2.68)

Definitions of abbreviations: GOLD, Global Obstructive Lung Disease; AO, Airflow Obstruction; RR, Relative Risk; CI, Confidence Interval; VGDF, Vapour, Gases, Dust and Fumes

† Adjusted for sex, smoking, pack-years, childhood and adulthood socioeconomic status, childhood and adulthood asthma and sampling weights. The analyses with biological dust, mineral dust, gases/fumes, and VGDF were additionally adjusted for all pesticides, whereas the analyses with all pesticides, herbicides, and insecticides were additionally adjusted for VGDF exposure.

The bolded text identifies results reaching statistical significance ($p \leq 0.05$)

Table S5: Association between Cumulative EU-years and Fixed Airflow Obstruction, Chronic Bronchitis and Respiratory Symptoms using complete-case analysis and multiple imputation

Cumulative exposures*	Fixed AO-GOLD		Chronic bronchitis		Chronic cough		Chronic phlegm		Dyspnoea	
	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)	Complete case RR (95%CI)	Imputed RR (95%CI)
Biological dust	1.05 (0.97-1.13)	1.05 (0.97-1.13)	1.06 (0.99-1.13)	1.00 (0.92-1.07)	1.07 (1.00-1.15)	1.05 (0.99-1.13)	1.01 (0.94-1.09)	0.98 (0.91-1.06)	0.99 (0.92-1.06)	0.99 (0.93-1.06)
Mineral dust	1.03 (0.97-1.10)	1.04 (0.97-1.11)	1.04 (0.98-1.11)	0.99 (0.92-1.06)	1.00 (0.93-1.07)	1.00 (0.94-1.08)	1.03 (0.96-1.10)	1.04 (0.98-1.12)	1.05 (1.00-1.11)	1.06 (1.00-1.12)
Gases/fumes	1.02 (0.96-1.09)	1.03 (0.96-1.10)	1.03 (0.97-1.09)	0.97 (0.91-1.04)	0.97 (0.91-1.04)	0.98 (0.91-1.04)	1.03 (0.98-1.10)	1.05 (0.99-1.12)	1.05 (1.00-1.10)	1.05 (0.99-1.11)
VGDF	1.02 (0.97-1.08)	1.03 (0.97-1.09)	1.05 (1.00-1.10)	0.99 (0.93-1.04)	1.03 (0.97-1.08)	1.03 (0.97-1.08)	1.03 (0.98-1.08)	1.04 (0.99-1.09)	1.02 (0.98-1.07)	1.03 (0.98-1.08)
All pesticides	1.12 (1.00-1.25)	1.13 (1.01-1.26)	1.16 (1.10-1.30)	1.07 (0.95-1.20)	1.12 (1.00-1.28)	1.09 (1.00-1.22)	1.13 (1.00-1.30)	1.03 (0.92-1.16)	0.94 (0.82-1.08)	0.97 (0.86-1.09)
Herbicides	1.16 (1.00-1.32)	1.16 (1.00-1.32)	1.22 (1.05-1.41)	1.08 (0.93-1.25)	1.12 (0.97-1.30)	1.09 (0.96-1.24)	1.10 (0.93-1.31)	1.00 (0.86-1.16)	0.91 (0.77-1.09)	0.97 (0.83-1.12)
Insecticides	1.10 (0.98-1.24)	1.12 (0.99-1.26)	1.15 (1.02-1.29)	1.06 (0.93-1.20)	1.06 (0.92-1.22)	1.05 (0.92-1.18)	1.13 (0.99-1.30)	1.05 (0.93-1.19)	0.94 (0.83-1.09)	0.97 (0.85-1.10)

Definitions of abbreviations: GOLD, Global Obstructive Lung Disease; AO, Airflow Obstruction; RR, Relative Risk; CI, Confidence Interval; VGDF, Vapour, Gases, Dust and Fumes

† Adjusted for sex, smoking, pack-years, childhood and adulthood socioeconomic status, childhood and adulthood asthma and sampling weights. The analyses with biological dust, mineral dust, gases/fumes, and VGDF were additionally adjusted for all pesticides, whereas the analyses with all pesticides, herbicides, and insecticides were additionally adjusted for VGDF exposure.

The bolded text identifies results reaching statistical significance ($p \leq 0.05$)

Table S6: Correlations between the exposures as no, low, and high exposure (0/1/2) in the TAHS cohort

	Dusts				Pesticides		
Correlation	Biological Dust	Mineral Dust	Gases and Fumes	VGDF	All pesticides	Herbicides	Insecticides
Biological Dust		0.47	0.56	0.64	0.39	0.35	0.34
Mineral Dust			0.61	0.59	0.40	0.37	0.37
Gases and Fumes				0.90	0.28	0.25	0.24
VGDF					0.25	0.22	0.22
All pesticides						0.88	0.87
Herbicides							0.84

Table S7: Overview of number of workers with high exposure to all pesticides

ISCO-88 job description	ISCO-88	n (%)
<i>High exposure to all pesticides (n=151)</i>		
Farm-hands and labourers	9211	37 (24.5%)
Gardeners, horticultural and nursery growers	6113	31 (20.5%)
Market oriented crop and animal producer	6130	29 (19.2%)
Forestry labourers	9212	27 (17.8%)
Mixed crop growers	9322	27 (17.8%)

Table S8: Association between Ever (low and high) Exposure and Fixed Airflow Obstruction, Chronic Bronchitis and Respiratory Symptoms

Exposure	Fixed AO-GOLD			Chronic bronchitis			Chronic cough			Chronic phlegm			Dyspnoea		
	No 1,222	Yes 113	RR (95%CI) †	No 1,075	Yes 246	RR (95%CI)	No 1,131	Yes 185	RR (95%CI)	No 1,146	Yes 171	RR (95%CI)	No 1,107	Yes 226	RR (95%CI)
Biological dust															
No exposure	541	37	Ref.	484	87	Ref.	516	53	Ref.	507	60	Ref.	504	75	Ref.
Low exposure	434	46	1.63 (1.01-2.65)	396	82	0.73 (0.46-1.14)	414	60	1.20 (0.78-1.84)	425	51	0.83 (0.53-1.29)	389	90	1.24 (0.86-1.78)
High exposure	247	30	1.47 (0.81-2.69)	196	77	1.59 (0.96-2.64)	227	44	1.35 (0.79-2.31)	226	44	1.35 (0.80-2.27)	214	62	1.56 (1.00-2.48)
Mineral dust															
No exposure	585	42	Ref.	522	98	Ref.	564	54	Ref.	565	54	Ref.	544	84	Ref.
Low exposure	287	24	1.01 (0.57-1.79)	251	58	1.11 (0.67-1.83)	254	53	2.08 (1.32-3.29)	264	43	1.49 (0.92-2.41)	256	55	1.27 (0.84-1.93)
High exposure	350	47	1.60 (0.94-2.72)	303	90	1.08 (0.66-1.77)	339	50	1.13 (0.67-1.90)	329	58	1.54 (0.93-2.55)	307	88	2.05 (1.33-3.15)
Gases/fumes															
No exposure	352	22	Ref.	314	57	Ref.	336	32	Ref.	335	33	Ref.	327	48	Ref.
Low exposure	515	46	1.47 (0.83-2.58)	454	101	0.88 (0.54-1.44)	479	76	1.42 (0.88-2.28)	485	69	1.22 (0.75-1.98)	465	95	1.21 (0.81-1.82)
High exposure	355	45	1.53 (0.82-2.84)	308	88	0.97 (0.56-1.70)	342	49	0.95 (0.54-1.69)	338	53	1.16 (0.66-2.03)	315	84	1.55 (0.97-2.46)
VGDF															
No exposure	300	21	Ref.	273	45	Ref.	294	22	Ref.	289	26	Ref.	281	41	Ref.
Low exposure	411	32	1.20 (0.65-2.22)	363	76	0.88 (0.51-1.52)	379	58	1.90 (1.09-3.29)	387	42	1.34 (0.78-2.32)	371	72	1.05 (0.67-1.63)
High exposure	511	60	1.31 (0.71-2.41)	440	125	1.03 (0.60-1.78)	484	77	1.48 (0.83-2.65)	482	77	1.29 (0.73-2.26)	455	114	1.72 (1.08-2.75)
All pesticides															
No exposure	1,024	85	Ref.	916	183	Ref.	977	116	Ref.	977	116	Ref.	940	169	Ref.
Low exposure	68	7	0.92 (0.35-2.44)	58	17	1.61 (0.72-3.57)	62	13	1.95 (0.92-4.16)	59	15	2.41 (1.11-5.17)	55	20	2.41 (1.27-4.56)
High exposure	130	21	1.78 (1.01-3.27)	102	46	1.82 (1.08-3.07)	118	28	1.68 (0.92-3.09)	122	24	1.81 (1.04-3.15)	112	38	1.75 (1.03-2.95)
Herbicides															
No exposure	1,061	87	Ref.	947	191	Ref.	1,011	121	Ref.	1,008	124	Ref.	966	182	Ref.
Low exposure	66	11	2.02 (0.95-4.28)	57	20	1.62 (0.76-3.44)	59	17	2.37 (1.19-4.71)	63	13	1.58 (0.74-3.34)	60	17	1.65 (0.86-3.10)
High exposure	95	15	2.15 (1.05-4.42)	72	35	1.95 (1.03-3.72)	87	19	1.35 (0.66-2.78)	87	18	1.68 (0.83-3.39)	81	28	1.29 (0.70-2.36)
Insecticides															
No exposure	1,060	91	Ref.	947	194	Ref.	1,012	123	Ref.	1,009	125	Ref.	970	181	Ref.
Low exposure	34	2	0.65 (0.14-2.90)	28	8	1.07 (0.38-3.02)	28	8	2.48 (0.97-6.33)	30	6	1.77 (0.64-4.92)	26	10	1.91 (0.82-4.41)
High exposure	128	20	2.02 (1.07-3.79)	101	44	1.83 (1.04-3.19)	117	26	1.59 (0.87-2.90)	119	24	1.60 (0.87-2.90)	111	36	1.50 (0.88-2.54)

- Adjusted for sex, smoking, pack-years, adult and childhood socio economic status, adult and child asthma and sampling weight. Additionally, all pesticides was adjusted for the analysis with biological dust, mineral dust, gases/fumes, VGDF while VGDF was adjusted for all pesticides, herbicides and insecticides

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