

Ever and cumulative occupational exposure and lung function decline in longitudinal population-based studies: a systematic review and meta-analysis

Supplementary material

Search terms

(1) 'Occupational Exposure' (MeSH) OR 'Occupational Pollutants' (MeSH) OR 'Occupational Endotoxin Exposure' (MeSH) OR 'Organic Dust Exposure' (MeSH) OR 'Dust Exposure' (MeSH) OR 'Inhalation Exposure' (MeSH) OR 'Occupational Air Pollutants' (MeSH) OR 'Occupations' (MeSH) OR 'Agriculture Workers Disease' (MeSH)

AND

(2) 'Pulmonary Disease' (MeSH) OR 'Chronic Obstructive' (MeSH) OR 'Lung Disease' (MeSH) OR 'Obstructive' (MeSH) OR 'Asthma' (MeSH) OR 'Asthma, Occupational' (MeSH) OR 'Occupational Asthma' (MeSH) OR 'Bronchitis' (MeSH) OR 'Bronchiolitis' (MeSH) OR 'Pulmonary Disease' (MeSH) OR 'Pulmonary Emphysema' (MeSH) OR 'Cough' (MeSH) OR 'Dyspnea' (MeSH) OR 'Pneumoconiosis' (MeSH) OR 'Bronchial Disease' (MeSH) OR 'Cystic Fibrosis' (MeSH) OR 'Chronic Airflow Obstruction' (MeSH) OR 'Obstructive Airway Disease' (MeSH) OR 'COPD' (MeSH) OR 'Occupational Lung Disease' (MeSH)

AND

(3) 'Lung Function' (text word) OR 'Pulmonary Function' (text word) OR 'Change in Lung Function' (text word) OR 'FEV₁ Decline' (text word) OR 'FVC' (text word) OR 'Longitudinal change in lung function' (text word) OR 'Job Exposure Matrix' (text word) OR 'Job Exposure Matrices' (text word) OR 'work' (text word).

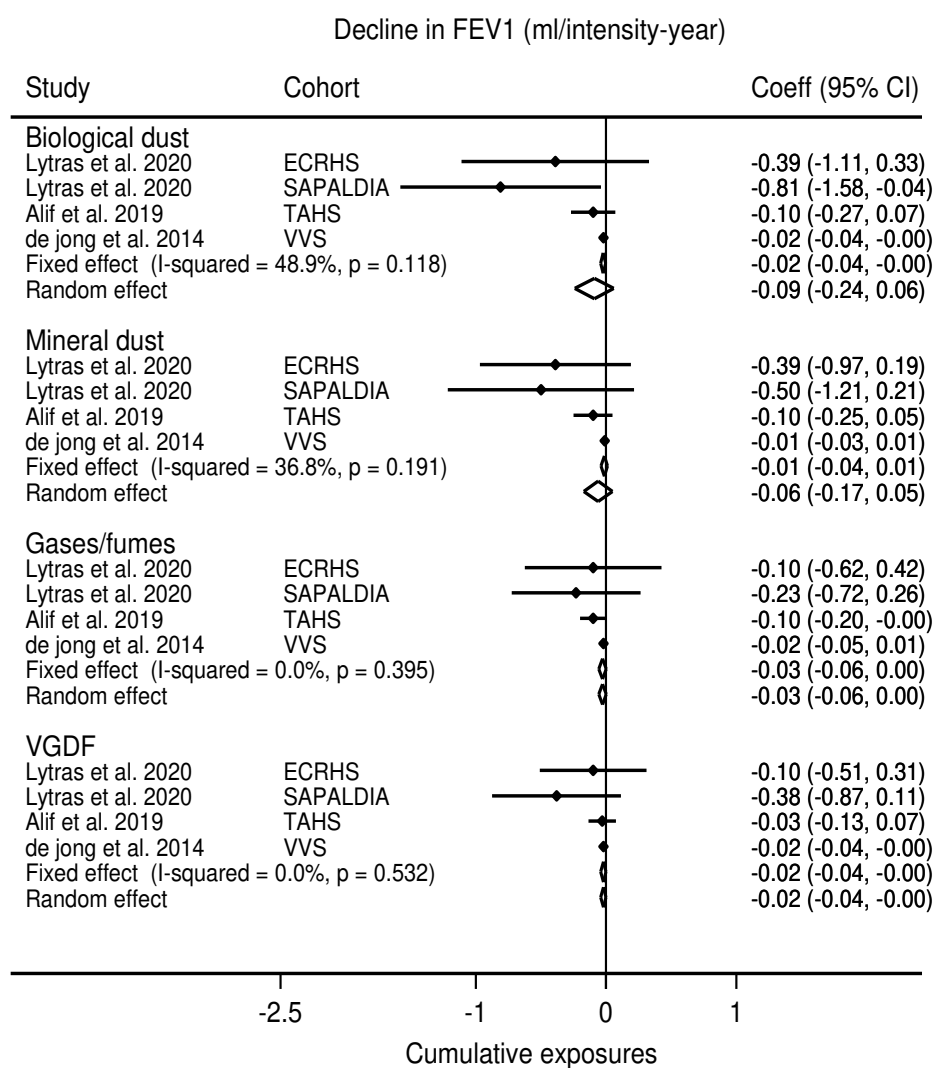


Figure S1. Forest plot showing the association between cumulative exposures to biological dust, mineral dust, gases/fumes and VGDF and FEV₁ decline.

(ECRHS; European Community Respiratory Health Survey study; SAPALDIA=Swiss Cohort Study on Air Pollution and Lung Disease in Adults; TAHS; Tasmanian Longitudinal Health Study, VVS; Vlagtwedde-Vlaardingen Study)

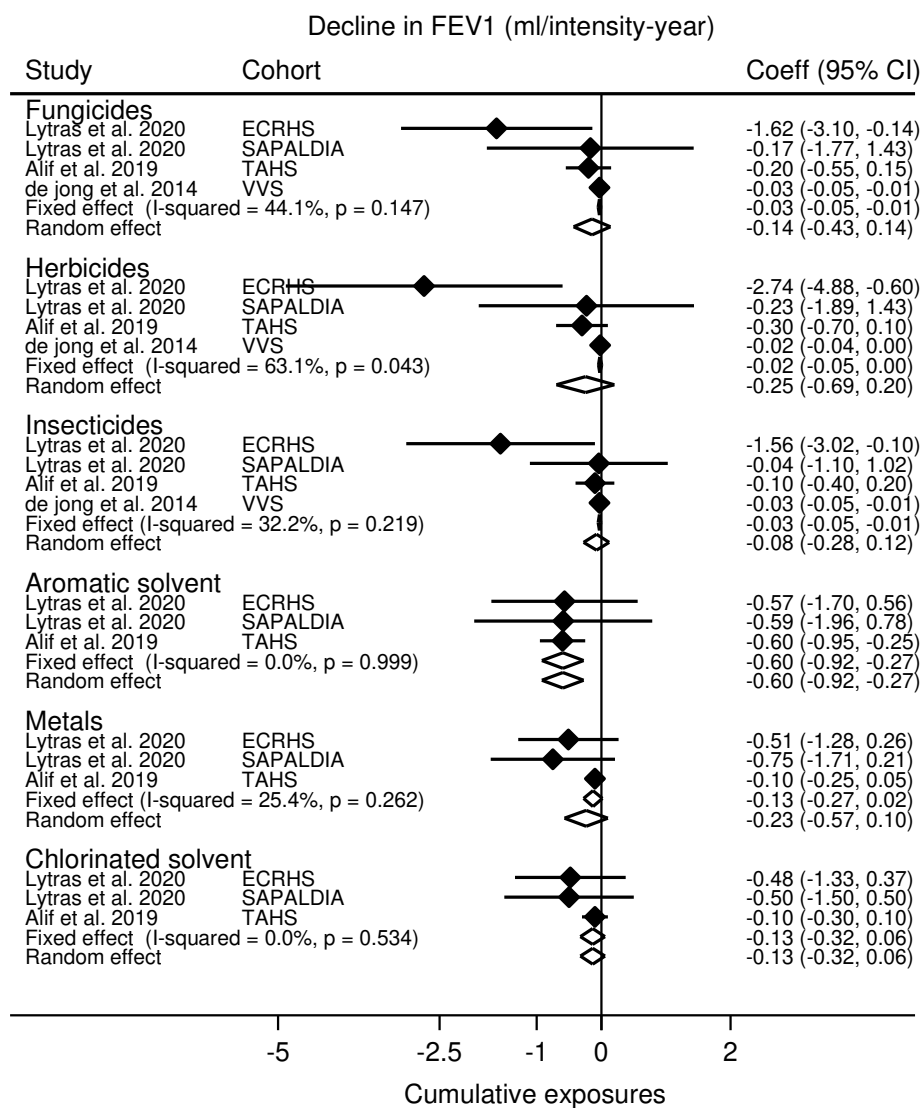


Figure S2. Forest plot showing the association between cumulative exposures to Fungicides, Herbicides, Insecticides, Aromatic solvents, Metals and Chlorinated Solvents, and FEV₁ decline.

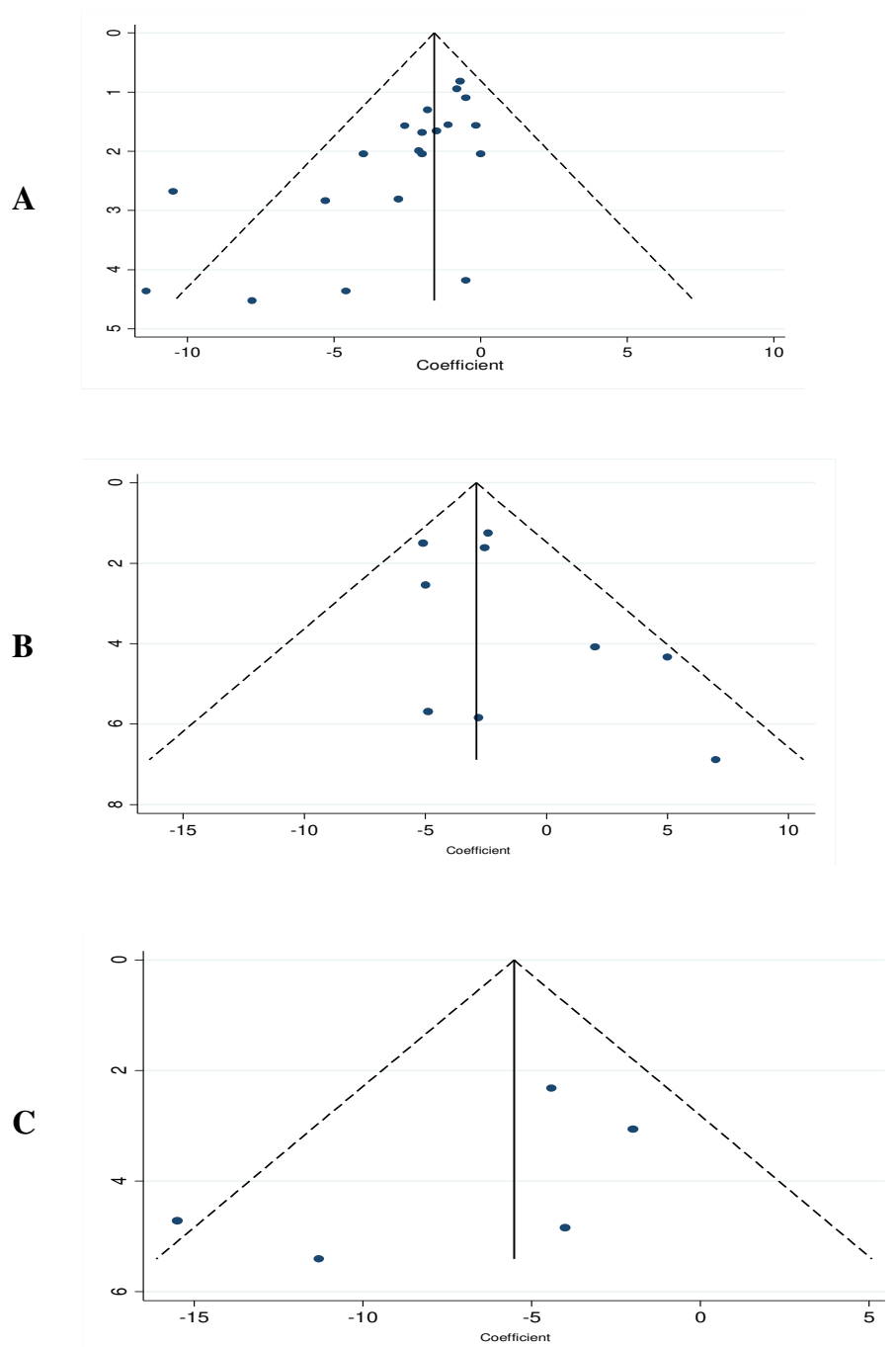


Figure S3. Funnel plot with Egger's test for assessing publication bias of the included studies; (A) Biological dust, Mineral dust, Gases/Fumes and VGDF (B) Fungicides, Herbicides and Insecticides (C) Aromatic solvents and Metals

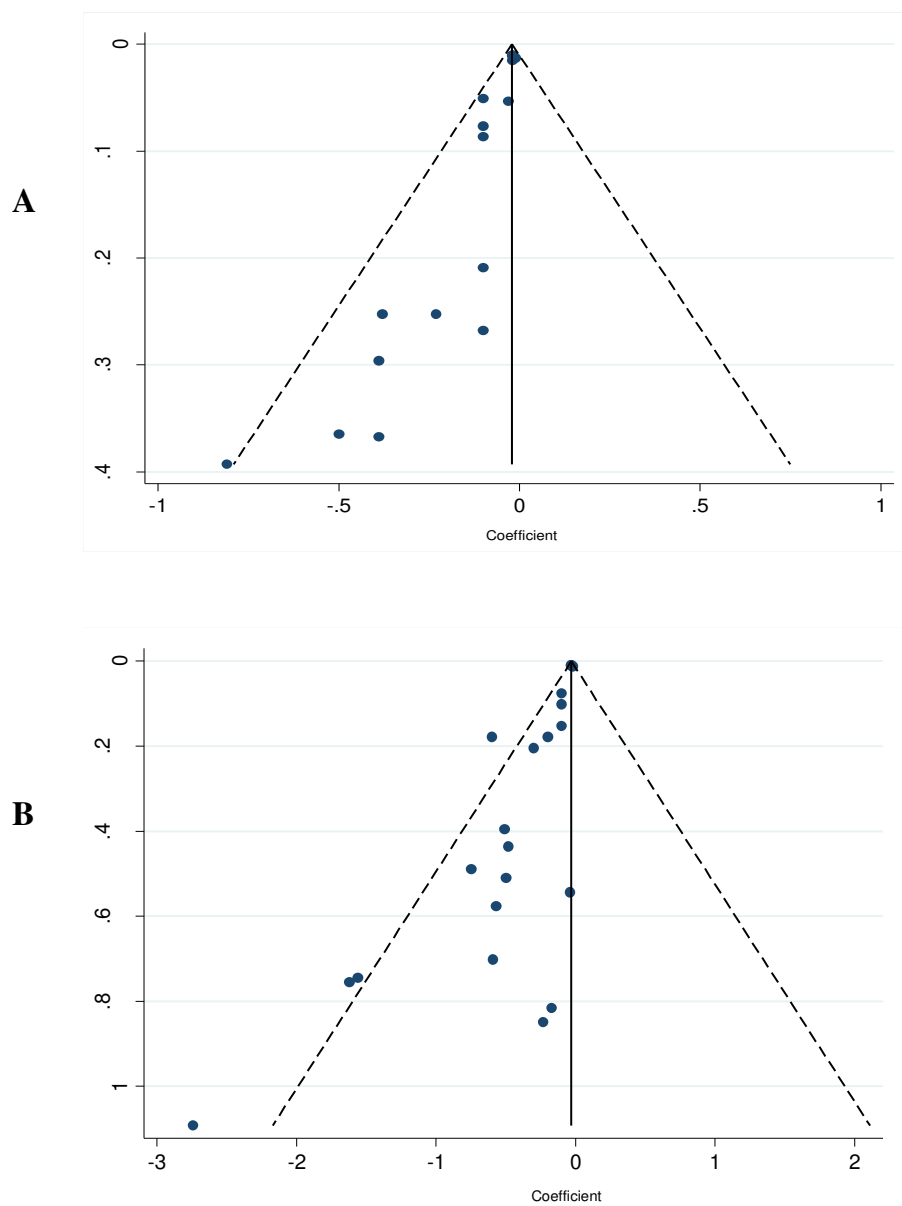


Figure S4. Funnel plot with Egger's test for assessing publication bias of the included studies (cumulative exposures); (A) Biological dust, Mineral dust, Gases/Fumes and VGDF (B) Fungicides, Herbicides, Insecticides, Aromatic solvents, Chlorinated solvents and Metals

Table S1 Lung function decline in the studies included in systematic review.

First Author (Year)	Exposure categories	Occupational exposures	Measurements of lung function decline		
			FEV ₁ ml/year or %predicted, β (95% CI)	FVC ml/year or %predicted, β (95% CI)	FEV ₁ /FVC %/year, β (95% CI)
Skaaby et al. (2021) ¹ Copenhagen City Heart Study	Only high exposure	Biological dust	2.8 (-2.7; 8.3)	-	-0.4 (-1.3; 0.6)
		Mineral dust	-2.1 (-6.0; 1.8)	-	-1.0 (-0.8; 0.5)
		Gases/fumes	-5.3 (-10.9; 0.2)	-	0.5 (-0.5; 1.4)
		VGDF	-2.0 (-5.3; 1.3)	-	-1.0 (0.6; 0.5)
Skaaby et al. (2021) ¹ Copenhagen General Population Study	Only high exposure	Biological dust	0.5 (-1.7; 2.6)	-	-0.1 (-0.5; 0.3)
		Mineral dust	0.8 (-1.0; 2.7)	-	0.01 (-0.3; 0.3)
		Gases/fumes	1.1 (-2.0; 4.1)	-	0.4 (-0.2; 0.9)
		VGDF	0.7 (-0.9; 2.3)	-	-0.1 (-0.4; 0.2)
Faruque et al. (2020) ²	Only high exposure	Biological dust	-4.0 (-8.0; 0.0)	-4.0 (-9.0; 2.0)	-0.02 (-0.09; 0.05)
		Mineral dust	-2.0 (-6.0; 2.0)	-8.0 (-13.0; -2.0)	0.09 (0.02; 0.16)
		Gases/fumes	0.0 (-4.0; 4.0)	-4.0 (-9.0; 1.0)	0.07 (-0.00; 0.14)
		Fungicides	5.0 (-3.0; 14.0)	3.0 (-8.0; 15.0)	0.10 (-0.5; 0.25)
		Herbicides	7.0 (-7.0; 20.0)	-2.0 (-20; 17)	0.19 (-0.05; 0.43)
		Insecticides	2.0 (-6.0; 10.0)	0.0 (-11; 10)	0.07 (-0.7; 0.21)
		Aromatic solvents	-4.0 (-13; 6.0)	-3.0 (-16; 10)	-0.07 (-0.23; 0.10)
		Chlorinated solvents	-4.0 (-11; 2.0)	-7.0 (-15; 2.0)	0.00 (-0.11; 0.12)
Alif et al. (2019) ³	Combined high and low exposures defined as ever exposures	Biological dust	0.5 (-7.7; 8.7)	-9.3 (-22.2; 3.6)	0.05 (-0.1; 0.2)
		Mineral dust	-4.6 (-13.1; 4.0)	3.7 (-9.7; 3.6)	-0.2 (-0.3; -0.02)
		Gases/fumes	-11.4 (-20.0; -2.9)	-4.9 (-18.6; 8.6)	-0.2 (-0.4; -0.1)
		Fungicides	-2.4 (-13.3; -8.4)	-3.0 (-20.1; 14.1)	0.04 (-0.2; 0.2)
		Herbicides	-4.9 (-16.0; 6.3)	-6.5 (-24.1; 11.1)	0.1 (0.1; 0.3)
		Insecticides	-2.8 (-14.3; 8.6)	-6.5 (-24.6; 11.6)	0.2 (-0.1; 0.4)
		Aromatic solvents	-15.5 (-24.8; -6.3)	-14.1 (-28.8; -0.7)	-0.05 (-0.2; 0.1)
		Chlorinated solvents	-11.6 (-21.5; 1.6)	-3.8 (-19.6; 12.1)	-0.1 (-0.3; 0.04)
		Metals	-11.3 (-21.9; -0.7)	-17.5 (-34.3; -0.8)	-0.1 (-0.3; 0.1)
VGDF	-7.8 (-16.7; 1.0)	-5.8 (-19.8; 8.3)	-0.22 (-0.4; -0.06)		
Liao et al. (2015) ⁴	High exposure	Dust	-4.5 (-7.83; -1.17)	-	-
de Jong et al. (2014) ⁵	Only high exposure	Biological dust	-1.50 (-4.74; 1.74)	-	-
		Mineral dust	-0.16 (-3.23; 2.90)	-	-
		Gases/fumes	-2.58 (-5.66; 0.50)	-	-
		VGDF	-1.8 (-4.4; 0.7)	-	-
		Fungicides (Pesticide)	-5.1 (-8.0; -2.1)	-	-
		Herbicides	-2.56 (-5.73; 0.60)	-	-
		Insecticides	-4.99 (-7.94; -2.03)	-	-
Sunyer et al. (2005) ⁶	Only high exposure (only female)	Biological dust	-8.78 (-15.89; -1.67)	-	-
		Mineral dust	-7.38 (-14.30; -0.46)	-	-
		Gases and fumes (Low exposure)	-3.00 (-5.08; -0.92)	-	-
Humerfelt et al. (1993) ⁷	Sulphur dioxide	Gases	-58.7 (-63.99; -53.41)	-	-
	Chromium/nickel/platinum	Metals	-56.8 (-60.52; -53.08)	-	-
	Asbestos and quartz	Mineral dust	-53.0 (-55.35; -50.65) and -55.4 (-59.12; -51.68)	-	-
Krzyzanowski et al. (1985) ⁸	Exposed (only male)	Dust	-6.9 (-12.78; -1.02)	-	-

Bui et al. (2019) ⁹	Any exposures (post-BD)	VGDF	-8.3 (-13.6; -3.1)	5.6 (- 0.4; 11.6)	-0.11 (-0.19; -0.02)
		Aromatic solvents	-1.0 (-5.6 ; 3.5)	-2.6 (-8.7; 3.4)	0.03 (-0.04; 0.11)
	Any exposures (pre-BD)	VGDF	-10.5(-16.1; -4.9)	-9.3 (- 14.9; -3.7)	-0.08 (-0.13; -0.03)
		Aromatic solvents	-4.4 (-8.3 ; -0.5)	-3.1 (-9.7; -3.5)	0.05 (-0.04; 0.14)
Tagiyeva et al. (2017) ¹⁰ *Effect estimates reported as %predicted	Any exposures	Any VGDFFiM	-1.26 (-4.35; 1.82)	-1.90 (-4.93; 1.13)	-
		Biological dust	-3.24 (-5.92; 0.55)	-1.15 (-3.8; 1.51)	-
		Mineral dust	-2.24 (-5.04; 0.57)	-1.92 (-4.69; 0.85)	-
		Gases	-0.51 (-3.33; 2.31)	-1.22 (-3.99; 1.55)	-
		Dust	-2.24 (-5.12; 0.65)	-1.74 (-4.58; 1.10)	-
		Vapors	-3.30 (-5.94; -0.66)	-1.88 (-4.49; 0.73)	-
		Fumes	-1.29 (-4.38; 1.8)	-4.43 (-7.46; -1.41)	-
		Diesel fumes	-4.08 (-7.60; -0.56)	-5.96(-9.41; -2.51)	-
Harber et al. (2007) ¹¹ *Effect estimates reported as %predicted (no CIs)	Any exposures	Fumes	-0.25	-	-
		Dust (male only)	-0.12	-	-

Significant association (p<0.05) highlighted in bold

Table S2 Association between cumulative exposure (per intensity-year) and lung function decline in the selected studies included in systematic review.

First author (year)	Name of Cohort	Occupational exposure	Lung function measurement		
			FEV ₁ ; (ml/year) β (95% CI)	FVC; (ml/year) β (95% CI)	FEV ₁ /FVC; (%/year) β (95% CI)
Alif et al. (2019) ³	TAHS	Biological dust	0.1 (-0.04; 0.3)	0.1 (-0.1; 0.4)	-0.0 (-0.003; 0.003)
		Mineral dust	0.1 (-0.1; 0.2)	0.2 (-0.03; 0.4)	-0.0 (0.003; 0.002)
		Gases/fumes	-0.1 (-0.3; -0.1)	-0.2 (-0.1; 0.1)	-0.0 (0.002; 0.002)
		Fungicides	0.2 (-0.2; 0.5)	0.7 (0.2; 1.3)	-0.0 (-0.006; 0.006)
		Herbicides	0.3 (-0.1; 0.7)	0.6 (-0.03; 1.3)	0.003 (-0.005; 0.1)
		Insecticides	0.1 (-0.2; 0.4)	0.6 (0.1; 1.1)	-0.0 (-0.006; 0.005)
		Aromatic solvents	-0.6 (-1.0; -0.3)	-0.9 (-1.6; -0.4)	0.003 (-0.004; 0.01)
		Chlorinated solvent	-0.1 (-0.3; 0.1)	-0.1 (0.4; 0.2)	-0.001 (0.004; 0.001)
		Metals	-0.1 (-0.2; 0.1)	-0.1 (-0.3; 0.3)	-0.002 (-0.004; 0.001)
		VGDF	-0.03 (-0.14; 0.07)	0.02 (-0.14; 0.19)	-0.001(0.002; 0.001)
de Jong et al. (2014) ⁵	Vlagtwedde-Vlaardingen	VGDF	-0.02 (-0.04; 0.00)	-	-
		Biological dust	-0.02 (-0.04; 0.00)	-	-
		Mineral dust	-0.01 (-0.04; 0.01)	-	-
		Gases/fumes	-0.02 (-0.05; 0.01)	-	-
		Fungicides	-0.03 (-0.05; -0.01)	-	-
		Herbicides	-0.02 (-0.04; 0.01)	-	-
Lytras et al (2020) ¹²	ECRHS	Biological dust	-0.39 (-1.13; 0.31)	0.47 (-0.41; 1.30)	-0.03 (-0.04; -0.008)
		Mineral dust	-0.39 (-0.96; 0.20)	0.90 (0.21; 1.59)	-0.04 (-0.05; -0.02)
		Gases/fumes	-0.10 (-0.62; 0.43)	0.98 (0.37; 1.58)	-0.02(-0.04; -0.01)
		VGDF	-0.10 (-0.51; 0.32)	0.95 (0.46; 1.44)	-0.03 (0.04; 0.02)
		Fungicides	-1.62 (-3.10; -0.14)	-1.21 (-3.0; 0.60)	-0.02 (-0.06; 0.01)
		Herbicides	-2.74 (-4.82; -0.54)	-2.94 (-5.47; -0.38)	-0.02 (-0.07; 0.03)
		Insecticides	-1.56 (-3.03; -0.11)	-0.99 (-2.76; 0.74)	-0.03 (-0.06; 0.01)
		Aromatic solvent	0.57 (-0.56; 1.70)	1.52 (0.15; 2.86)	-0.02 (-0.05; 0.01)
		Chlorinated solvent	-0.48 (-1.34; 0.37)	0.19 (-0.83; 1.20)	-0.02 (-0.04; 0.002)
		Metals	-0.51 (-1.28; 0.27)	0.49 (-0.46; 1.41)	-0.03 (-0.05; -0.01)
Lytras et al. (2020) ¹²	SAPALDIA	Biological dust	-0.81 (-1.59; -0.05)	0.61 (-0.23; 1.44)	-0.04 (-0.06; -0.02)
		Mineral dust	-0.5 (-1.22; 0.21)	0.42 (-0.38; 1.20)	-0.02 (-0.04; -0.003)
		Gases/fumes	-0.23 (-0.89; 0.42)	0.90 (0.16; 1.63)	-0.03 (-0.04; -0.01)
		VGDF	-0.38 (-0.87; 0.12)	0.72 (0.18; 1.28)	-0.03(-0.04; -0.01)
		Fungicides	0.17 (-1.45; 1.75)	0.56 (-1.17; 2.25)	-0.01 (-0.05; 0.04)
		Herbicides	0.23 (-1.45; 1.88)	0.57 (-1.25; 2.33)	-0.01 (-0.05; 0.04)
		Insecticides	0.04, (-1.03; 1.10)	0.23 (-0.97; 1.39)	-0.001(-0.03; 0.03)
		Aromatic solvent	-0.59 (-1.97; 0.78)	0.20 (-1.25; 1.65)	0.02 (-0.05; 0.02)
		Chlorinated solvent	-0.50(-1.50; 0.50)	-0.18 (-1.28; 0.91)	-0.01 (-0.04; 0.02)
	Metals	-0.75 (-1.71; 0.21)	-0.13 (-1.15; 0.89)	-0.02 (-0.05; 0.01)	
	WHEASE		Short	-4.79 (-8.15; -6.28 (-9.60; -2.97)	-

*Tagiyeva et al. (2017) ¹⁰	cohort	Vapors		-1.44		
			Medium	-3.89 (-7.10; -0.68)	0.11 (-3.05; 3.28)	-
			Long	-1.23 (-4.45; 1.99)	-0.10 (-3.28; 3.07)	-
		Biological dust	Short	-1.71 (-5.26; 1.84)	-1.68 (-8.25; 1.88)	-
			Medium	-7.42 (-10.8; -4.04)	-1.39 (-4.78; 2.00)	-
			Long	-0.41 (-3.83; 3.01)	-1.42 (-4.85; 2.01)	-
		Diesel fumes	Short	-1.94 (-7.01; 3.18)	-2.68 (-7.66; 2.31)	-
			Medium	-3.67 (-7.95; 0.61)	-6.41 (-10.6; -2.20)	-
			Long	-7.16 (-12.1; -2.24)	-9.50 (-14.3; -4.66)	-

Significant associations ($p < 0.05$) highlighted in bold; *= Estimates are odds ratio (OR) and %predicted as unit.

Quality assessment

All studies ascertained the exposure using self-reported work histories and scored three out of four in the selection of study group. In terms of comparability, we predetermined that to receive a full score studies should adjust for age, sex, smoking status and pack-years and additional confounding variables would be asthma or history of respiratory infection or other lung diseases and co-exposures. Two studies performed the analysis with adjustment for at least two key confounders and additional confounding variables which awarded two stars (***) for comparability ^{3, 12}. Seven studies performed the analysis with the adjustment for at least two key confounders but did not adjust for additional confounders, those awarded single star (*) for comparability ^{4-8, 10, 11}. However, one study performed the analysis with adjustment for only one key confounder and did not adjust additional confounders and was therefore awarded a zero score in the comparability criterion ⁹.

Nine studies sufficiently assessed outcomes by objective measurement of lung function test, follow-up was long enough to obtain the outcomes of interest and reported loss of follow-up and were awarded three stars (***) for outcomes. ^{2, 3, 6-12} However, two studies awarded two stars (**) for outcomes because they did not report the loss of follow-up. ^{4, 5}

Table S3 Assessment of study quality of cohort study by Newcastle-Ottawa Scale

Cohort Studies		Skaaby et al. ¹	Lytras et al. ¹²	Faruque et al. ²	Alif et al. ³	Bui et al. ⁹	Tagiyeva et al. ¹⁰	Liao, et al. ⁴	de Jong et al. ¹³	Harber et al. ¹¹	Sunyer et al. ⁶	Hum erfelt et al. ⁷	Krzyzano et al. ⁸	
Selection	1) Representative of the exposed cohort													
	a) truly representative	★General population in Danish	★Multicentre, General population	★General people of northern three provinces of Netherlands	★ School children born in 1961 in Tasmania, Australia	★ School children born in 1961 in Tasmania, Australia	★ School children at aged 10-15 years in Aberdeen, UK	★General people live in Farmingham, Massachusetts, USA	★General population in Netherlands	N/A	★ General People (living in 27 centre of EU)	★All men living in Bergen, Norway in January 1,1964 (born between 1914-1943)	General People (aged 19-70 living Carcow, Poland)	
	b) somewhat representative	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	★Participants (with COPD and current smoker) in 10 study centres in USA and Canada	N/A	N/A	N/A	
	c) selected group of users	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		N/A	N/A	N/A	
	d) no description of derivation of the cohort	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
	2) Selection of non-exposed cohort										★			
	a) drawn from the same community as the exposed cohort	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community	★ Drawn from the same community
	b) drawn from a different source	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	c) no description of the derivation of the non-exposed cohort	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	3) Ascertainment of exposure												
	a) secure record (eg surgical records)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	b) structured interview	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	c) written self-report	Self-reported work history at last follow-up	Self-reported work history at last follow-up	Self-reported current or last held job at baseline	Self-reported work history at baseline	Self-reported work history at baseline	Self-reported work history at last follow-up	Self-reported work history at last follow-up	Self-reported work history at last follow-up	Self-reported work history at follow-up	Self-reported work history at last follow-up	Self-reported work history at last follow-up	Self-reported work history at baseline and last follow-up
	d) no description	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	4) Demonstration that outcome of interest was not present at start of study												
	a) yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes	★Yes
	b) no	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1) Comparability of study on the basis of the design or analysis												
Comparability	a) Age, sex, smoking status and/ or pack-years	★ Adjusted for Sex, smoking height, education, weights and baseline FEV ₁	★ Age, sex, height, smoking status (current, lifetime, pack-year), SES,	★ Adjusted for age, sex, smoking, pack-years,	★ Adjusted for sex, smoking status and pack-years but not age at baseline	Adjusted for sex and SES at baseline	★ Adjusted for sex, age at baseline, smoking and pack-years	★ Adjusted for sex, age at baseline, smoking and pack-years at baseline	★ Adjusted for sex, age, and pack-years of smoking at last measurement	Adjusted for age and smoking status (cigarette per day, yes/no)	★ Adjusted for age, smoking and number of cigarettes	Adjusted for age and smoking	★ Adjusted for age and smoking
	b) Asthma or previous respiratory infection or other lung	Not Adjusted	★ Current asthma, asthma (maternal, paternal,	Not Adjusted	★ Adjusted for childhood asthma, current asthma and	Not adjusted	Not adjusted	Not adjusted	Adjusted for co-exposure only	Not adjusted	Not adjusted	Not adjusted	Not adjusted

	disease and co-exposure		childhood)		co-exposure								
Outcome	1) Assessment of outcome												
	a) independent blind assessment	Lung ★ function test	★ Lung function test	★ Lung function test	★ Lung function test	Lung★ function test	Lung ★ function test	Lung function test ★	★ Lung function test	★ Lung function test	Lung function test	★ Lung function test	★ Lung function test
	b) record linkage	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	N/A
	c) self-report	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	N/A
	d) no description	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2) Was follow-up long enough for outcomes to occur												
	a) yes	★ 9 years	★ 16.3 years	★ 4.5 years	★ 06 years	★ 08 years	★ 25 years	★ 17 years	★ 25 years	05 Years ★	★ 8.9 Years	★ 23 Years	13 Years ★
	b) no	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	3) Adequacy of follow up of cohorts												
	a) complete follow up	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	b) subjects lost to follow up unlikely to introduce bias	11% sample was included in the analysis	★ 60.6% completed both visit	★ 25% completed lung function test at last follow-up	★ 61.1% completed lung function test at last follow-up	74.5% ★ completed lung function test at last follow-up	57% ★ completed lung function test at last follow-up	NG	NG	★ 93 % were still at last follow- up	★ 76% complete d lung function test at last follow-up	★ 60% completed lung function test at last follow-up	★ 61% were present at last follow-up
	c) follow up rate	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
d) no statement	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	

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