ONLINE SUPPLEMENT

CHRONIC OCCUPATIONAL EXPOSURES TO IRRITANTS AND ASTHMA IN THE CONSTANCES COHORT

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ETHICS STATEMENT

The CONSTANCES cohort received ethical approval from the French National Data Protection Authority (authorisation no. 910486) and the Institutional Review Board of the National Institute for Medical Research (authorisation no. 01-011). All participants gave informed consent to participate.

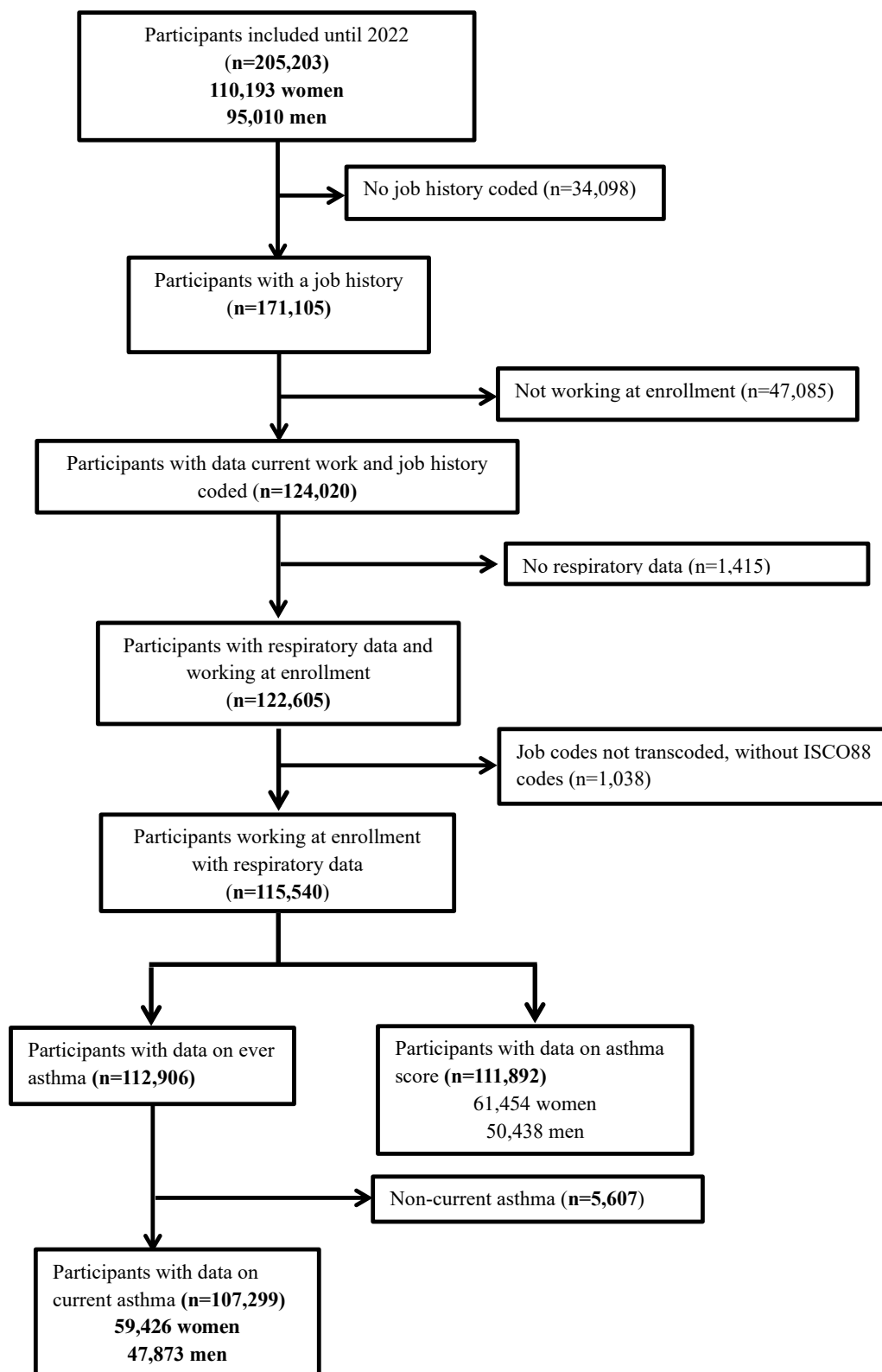Figure S1: Selection of study population

Table S1: List of individual agents classified in 3 large groups in the new occupational asthma-specific JEM (OAsJEM)

Agents, n=30	HMW sensitizer	LMW Sensitizer	Irritant
Animals	1		
Fish/shellfish	1		
Flour	1		
Foods	1		
Plant-related dusts	1		
House dust mites	1		
Storage mites	1		
Plant mites	1		
Enzymes	1		
Latex	1		
Textiles	1		1
Moulds			1
Endotoxin			1
Drugs	1	1	
High-level chemical disinfectants		1	1
Aliphatic amines		1	1
Isocyanates		1	1
Acrylates		1	1
Epoxy resins		1	1
Persulfates/henna		1	1
Wood		1	1
Metal		1	1
Metal working fluids		1	1
Herbicides			1
Insecticides			1
Fungicides			1
Indoor cleaning			1
Bleach			1
Organic solvents			1
Exhaust fumes			1

Table S2: Description of included and excluded populations

	Included n = 115,540	Missing asthma status n =1,415	Missing BMI or smoking status n = 6,027	Missing -job transcoded codes (ISCO88) n = 1,038
Age, Mean, (sd)	43.1 (10.7)	46.5 (13.7)*	44.3 (10.8)*	43.0 (11.0)
Women	55.1	51.7*	54.7	34.3*
BMI		*		
<25	60.9	46.3	.	39.6
25-29.9	28.6	32.5	.	25.5
≥30	10.5	21.2	.	35.0
Education		*	*	
< High school	17.6	44.6	21.2	42.5
High school	14.9	15.4	14.9	23.2
2-3 years post-secondary	29.3	18.5	26.9	23.0
4-5 years post-secondary	38.0	21.1	36.8	11.0
Other	0.2	0.4	0.2	0.3
Smoking habits		*		*
Non smoker	48.3	52.0	.	39.5
Former smoker	31.9	32.0	.	25.5
Current smoker	19.8	16.0	.	35.0
Asthma symptoms score				
0	69.6	.	68.3	68.6
1	18.7	.	19.8	18.1
2	6.7	.	6.9	7.4
3	2.8	.	2.8	3.1
4	1.4	.	1.3	2.0
5	0.8	.	0.9	0.8
Current asthma	10.2	.	9.4	11.2

Data are presented as % unless otherwise stated;
BMI = Body Mass Index;
*p<0.05 for chi square test/Student test

Supplemental material

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Table S3: Associations between lifetime occupational exposure to irritants and current asthma or asthma symptom score, after excluding exposures also classified as potential LMW sensitizers

| | **Current asthma** | | | | | **Asthma symptom score** | | | | |
| | Men (n = 47,873) | | Women (n = 59,426) | | | Men (n = 50,438) | | Women (n = 61,454) | | |
	n	Odds Ratio (95% CI)	n	Odds Ratio (95% CI)	p inter	n	Mean Score Ratio (95% CI)	n	Mean Score Ratio (95% CI)	p inter
Ref	26922	1	37157	1		28504	1	43315	1	
Irritants without LMW sensitizers	45985		57549			48451		59483		
Exposed	19063	0.96 [0.90-1.02]	20392	**1.07 [1.01-1.13]**	<0.001	19947	**1.12 [1.08-1.16]**	20996	**1.10 [1.07-1.14]**	0.35
Medium	12732	0.97 [0.91-1.04]	11149	1.02 [0.95-1.10]	0.31	13399	**1.09 [1.05-1.13]**	11564	1.03 [0.99-1.07]	0.01
High	6331	0.93 [0.85-1.02]	9243	**1.14 [1.06-1.22]**	<0.001	6548	**1.16 [1.09-1.22]**	9432	**1.19 [1.15-1.24]**	0.61

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Table S4: Associations between lifetime occupational exposures and current asthma according to age of onset in men

	No asthma (ref)	Childhood onset asthma (≤16 years)		Adult onset asthma (>16 years)	
	n=43,115	n=3,282	Odds ratio (IC95%)	n=1,141	Odds ratio (IC95%)
Irritants	42,736	3,249		1,122	
Ref.	24,232	1,869	1	649	1
Exposed	18,504	1,380	0.97 [0.90-1.04]	473	0.91 [0.81-1.03]
Medium	11,404	881	0.99 [0.91-1.07]	300	0.95 [0.83-1.09]
High	7,100	499	0.94 [0.85-1.04]	173	0.85 [0.71-1.00]
DCPs	30,352	2,410		824	
Ref.	24,232	1,869	1	649	1
Exposed	6,120	541	*1.09 [0.99-1.21]*	175	1.03 [0.87-1.22]
Medium	3,860	363	**1.13 [1.00-1.27]**	113	1.08 [0.88-1.32]
High	2,260	178	1.03 [0.88-1.21]	62	0.96 [0.73-1.25]
Organic solvents	34,640	2,587		915	
Ref.	24,232	1,869	1	649	1
Exposed	10,408	718	0.93 [0.85-1.02]	266	0.90 [0.78-1.05]
Medium	9,654	663	0.93 [0.84-1.02]	250	0.92 [0.79-1.06]
High	754	55	1.00 [0.75-1.32]	16	0.74 [0.45-1.22]
HMW Sensitizers	29,759	2,363		812	
Ref.	24,232	1,869	1	649	1
Exposed	5,527	494	**1.11 [1.00-1.23]**	163	1.07 [0.90-1.27]
Medium	3,453	318	*1.13 [0.99-1.28]*	87	0.92 [0.73-1.15]
High	2,074	176	1.09 [0.92-1.28]	76	**1.32 [1.04-1.69]**
LMW Sensitizers	35,435	2,653		956	
Ref.	24,232	1,869	1	649	1
Exposed	11,203	784	0.94 [0.86-1.03]	307	0.97 [0.84-1.11]
Medium	8,464	598	0.94 [0.85-1.03]	229	0.96 [0.82-1.12]
High	2,739	186	0.94 [0.80-1.10]	78	0.98 [0.77-1.25]

Logistic regressions adjusted for age, BMI and smoking status

n=335 participant with missing age of asthma onset

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Table S5: Associations between lifetime occupational exposures and current asthma according to age of onset in women

	Current asthma (n=47,538)				
	No asthma (réf)	Childhood onset asthma (≤16 years)		Adult onset asthma (>16 years)	
	n=53,243	n=3,296	Odds ratio (IC95%)	n=2,292	Odds ratio (IC95%)
Irritants	52,854	3,276		2,281	
Ref.	33,435	2,000	1	1,374	1
Exposed	19,419	1,276	1.01 [0.94-1.09]	907	*1.08 [0.99-1.17]*
Medium	11,205	723	0.98 [0.90-1.07]	472	1.01 [0.91-1.13]
High	8,214	553	1.06 [0.96-1.17]	435	**1.16 [1.04-1.30]**
DCPs	49,594	3,061		2,145	
Ref.	33,435	2,000	1	1,374	1
Exposed	16,159	1,061	1.01 [0.93-1.09]	771	**1.09 [1.00-1.20]**
Medium	9,122	575	0.94 [0.85-1.04]	387	1.02 [0.91-1.15]
High	7,037	486	1.10 [0.99-1.22]	384	**1.18 [1.05-1.33]**
Organic solvents	40,790	2,478		1,718	
Ref.	33,435	2,000	1	1,374	1
Exposed	7,355	478	1.02 [0.92-1.13]	344	1.05 [0.93-1.19]
Medium	6,402	428	1.06 [0.95-1.18]	307	1.08 [0.95-1.22]
High	953	50	0.79 [0.59-1.05]	37	0.88 [0.63-1.24]
HMW Sensitizers	45,923	2,822		1,943	
Ref.	33,435	2,000	1	1,374	1
Exposed	12,488	822	1.02 [0.94-1.11]	569	1.06 [0.96-1.17]
Medium	5,794	382	0.96 [0.86-1.08]	251	1.02 [0.89-1.18]
High	6,694	440	1.07 [0.96-1.20]	318	1.08 [0.96-1.23]
LMW Sensitizers	45,752	2,748		1,950	
Ref.	33,435	2000	1	1,374	1
Exposed	12,317	748	0.96 [0.88-1.05]	576	1.08 [0.98-1.19]
Medium	11,010	667	0.97 [0.89-1.06]	518	1.08 [0.98-1.20]
High	1307	81	0.89 [0.70-1.12]	58	1.04 [0.79-1.36]

Logistic regressions adjusted for age, BMI and smoking status

n=595 participant with missing age of asthma onset

Table S6: Associations between current occupational exposure and current asthma or asthma symptom score

| | Current Asthma | | | | | Asthma symptom score | | | | |
| | Men (n = 47,873) | | Women (n = 59,426) | | | Men (n = 50,438) | | Women (n = 61,454) | | |
	n	Odds Ratio (95% CI)	n	Odds Ratio (95% CI)	p Inter	N	Mean Score Ratio (95% CI)	n	Mean Score Ratio (95% CI)	p Inter
Ref	34,863	1	43,996	1		36,863	1	45,550	1	
Irritants	47,310		58,564			49,846		55,589		
Exposed	12,447	**0.93 [0.87-1.00]**	14,568	0.98 [0.92-1.04]	0.13	12,943	**1.07 [1.03-1.12]**	15,004	1.01 [0.97-1.04]	0.001
Medium	8,298	0.94 [0.87-1.02]	9,173	0.96 [0.89-1.04]	0.48	8,701	**1.06 [1.02-1.11]**	9,530	**0.92 [0.89-0.97]**	<0.001
High	4,149	0.90 [0.81-1.01]	5,395	1.00 [0.91-1.10]	0.07	4,282	**1.10 [1.04-1.17]**	5,474	**1.14 [1.09-1.20]**	0.39
DCPs	38,538		56,148			40,701		58,075		
Exposed	3,675	1.08 [0.97-1.20]	12,182	0.98 [0.92-1.05]	0.27	3,838	**1.11 [1.03-1.17]**	12,525	1.02 [0.98-1.05]	0.02
Medium	2,315	*1.13 [0.99-1.29]*	7,357	0.96 [0.89-1.04]	0.04	2,434	**1.08 [1.00-1.17]**	7,646	**0.93 [0.89-0.97]**	<0.001
High	1,360	0.99 [0.83-1.19]	4,825	1.02 [0.93-1.12]	0.17	1,404	**1.14 [1.03-1.26]**	4,879	**1.16 [1.10-1.22]**	0.80
Organic solvents	41,196		48,012			43,457		49,642		
Exposed	6,333	**0.89 [0.81-0.97]**	8,150	0.93 [0.84-1.04]	0.31	6,594	**1.05 [1.00-1.11]**	4,092	**1.05 [1.00-1.12]**	0.93
Medium	6,079	**0.89 [0.81-0.97]**	3,910	0.96 [0.86-1.08]	0.11	6,344	1.05 [0.99-1.10]	3,694	**1.06 [1.00-1.13]**	0.79
High	254	0.91 [0.60-1.40]	379	**0.68 [0.47-0.98]**	0.23	250	1.20 [0.95-1.50]	398	0.98 [0.83-1.17]	0.14
HMW Sensitizers	38,174		53,633			40,339				
Exposed	3,311	**1.15 [1.03-1.29]**	9,637	0.94 [0.87-1.01]	0.004	3,476	**1.06 [1.00-1.14]**	10,017	**0.94 [0.91-0.98]**	0.002
Medium	2,151	**1.17 [1.02-1.33]**	4,500	**0.88 [0.79-0.98]**	0.04	2,259	1.07 [0.99-1.16]	4,692	**0.93 [0.88-0.99]**	0.004
High	1,160	1.13 [0.94-1.36]	5,137	0.99 [0.90-1.09]	0.94	1,217	1.06 [0.95-1.18]	5,325	0.96 [0.91-1.01]	0.10
LMW Sensitizers	41,551		53,110			43,836		55,064		
Exposed	6,688	**0.91 [0.84-1.00]**	9,174	0.93 [0.87-1.01]	0.48	6,973	**1.05 [1.00-1.10]**	9,514	**0.95 [0.91-0.99]**	0.002
Medium	5,468	**0.90 [0.82-0.99]**	8,491	0.95 [0.88-1.02]	0.08	5,717	1.02 [0.97-1.08]	8,798	**0.96 [0.92-1.00]**	0.04
High	1,220	0.97 [0.80-1.18]	683	**0.77 [0.59-1.00]**	0.14	1,256	**1.15 [1.03-1.28]**	716	**0.88 [0.77-1.00]**	0.002

Logistic regressions and binomial negative regressions adjusted for age, BMI and smoking habits