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Original Research

Interaction of smoking and social status on the risk of respiratory outcomes in a Swedish adult population: A Nordic Epilung study

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ABSTRACT

Background: Evidence abounds on the independent roles of social class and smoking in relation to obstructive airway diseases, but data are sparse on the impact of their interaction. We evaluated whether and to what extent social class and smoking interact in relation to risk of respiratory diseases in adults.
Methods: Data from the population-based studies, West Sweden Asthma Study (WSAS, n = 23,753) and Obstructive Lung Disease in Northern Sweden studies (OLIN, n = 6519), were used, constituting randomly selected adults aged 20–75 years. Bayesian network analysis was used to estimate the probability for the interaction between smoking and socioeconomic status in relation to respiratory outcomes.
Results: Occupational and educational SES modified the association between smoking and the probability of allergic and non-allergic asthma. Former smokers who were at intermediate non manual employees and manual workers in service had higher probability of allergic asthma compared to professionals and executives. Furthermore, former smokers with primary education had higher probability of non-allergic asthma than those with secondary and tertiary education. Similarly, former smokers among professionals and executives had higher probability of non-allergic asthma than manual and home workers and primary educated. Likewise, allergic asthma due to former smoking was higher among highly educated compared to low educated.
Conclusions: Beyond their independent roles, socioeconomic status and smoking interact in defining the risk of respiratory diseases. Clearer understanding of this interaction can help to identify population subgroups at most need of public health interventions.

1. Introduction

Despite extensive research evaluating the impact of smoking and socioeconomic status (SES) on risk of respiratory diseases, evidence is conflicting regarding the role of SES. Low Socio-Economic Status (SES) based on occupation and education was associated with non-allergic asthma. In contrast, manual jobs were associated with a higher prevalence of allergic asthma compared to non-allergic asthma [1,2]. Part of this may be due to use of different indicators of socioeconomic status across studies [3]. Others may be due to variations in outcome

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assessment and definition. Furthermore, lack of consideration of sub-phenotypes when evaluating heterogenous diseases such as asthma and chronic obstructive pulmonary disease (COPD) can also contribute to the uncertainty in findings [3,4]. Different measures of social class may point to opposite directions when evaluating similar respiratory outcomes. For instance, joblessness and low SES was associated with asthma in some studies, while high SES, based on residential status, was a risk factor in other studies [1,5,6].

It is well known that smoking habits vary by SES: smoking rates are higher among those with low SES and socially disadvantaged groups defined by factors like housing, education and occupation. In England, smoking was found to be twice as high among manual workers compared to managerial and higher professionals [7]. Smoking is also a known risk factor for COPD, although its association with asthma is more equivocal [8,9].Yet, information is sparse on how SES and smoking may interact in relation to risk of respiratory diseases. In previous studies performed in the UK and Germany, beyond independent roles of smoking and SES, there was evidence of their interaction in relation to the risk of asthma and lower lung function. In particular, the risk was greater in smokers in the low SES category [10,11]. However, none of the studies showed whether the observed interaction between SES and smoking was related to phenotypes of respiratory diseases.

In the current study, by considering different measures of SES (including educational level and two different standard socioeconomic and occupational classification systems), we aimed to determine whether, and to what extent, SES and smoking interact in relation to the risk of respiratory diseases in adults. We used the Bayesian network framework in evaluating the potential interactive effect between smoking and SES, thereby estimating the conditional probability of the interaction on the respiratory outcomes.

2. Methods

2.1. Study sample and population

The West Sweden Asthma Study (WSAS) and Obstructive Lung Disease in Northern Sweden studies (OLIN) are two large epidemiological research programs with population-based cross-sectional studies conducted among randomly selected samples from adult populations (aged 20–75 years) living in the Västra Götaland region in western Sweden and the Norrbotten region in northern Sweden, respectively. In 2016, an identical validated postal questionnaire was sent to participants in the two studies using the same methods [12,13]. In WSAS, 23,753 participants (response rate 50.1%) responded while 6519 (response rate 56.4%) responded in OLIN. The OLIN and WSAS studies were approved by the regional ethical review boards in Umeå, Sweden, and Gothenburg, Sweden, respectively. All participants gave their written informed consent to participate in the study as they returned the postal questionnaire. Full information regarding WSAS cohort characteristics could be found in a previous publication [14].

2.2. Questionnaire

The questionnaire used was developed based on the British Medical Research Council and used in many other large-scale studies in Scandinavia and Estonia [15–21]. It included questions on respiratory symptoms, demographic characteristics like age and sex, smoking status, and social characteristics like education. It consisted of three parts: the first part was a modified version (29) of the Swedish OLIN study questionnaire [23] that has been used in several studies in northern Europe (24-27) and contained questions about asthma, rhinitis, chronic bronchitis/COPD/emphysema, respiratory symptoms, use of asthma medication and possible determinants of disease, such as smoking habits and family history of airway diseases. The second part included questions about occupation, airborne occupational and environmental exposures, socioeconomic status and health status. The third part consisted of the Swedish version of the GA2LEN questionnaire, which added detailed questions about rhinitis and eczema as well as height and weight.

2.3. Definition of exposure measures

2.3.1. Smoking habits

Smoking status was defined as [1] current smoker: those who reported smoking within the last 12 months of completing the questionnaire [2]; former smoker: those who reported quitting smoking at least 12 months before completing the questionnaire; and [3] never smokers.

2.3.2. Social and occupational groups

Previous reports indicate that different systems may have varying sensitivity in measuring occupational exposure in relation to respiratory diseases and symptoms [22]. The Swedish socio-economic classification system (SEI), published in 1982, categorizes individuals based on their occupation solely and does not take into account the education requirements for different occupations. Hence, it is more reflective of the material aspect of SES [23]. The Swedish standard classification of occupations 2012 (in Swedish" Svensk standard yrkesklassificering, SSYK"), an updated version of the international standard classification of occupations (ISCO) international system, takes into consideration the years of education required for different occupations and also better reflects the specific occupational exposures present in the workplace [24]. Socioeconomic (SE) groups were classified based on job titles according to two classification systems: the Swedish socioeconomic classification system (SEI); and the Swedish standard classification of occupations 2012 (in Swedish" Svensk standard yrkesklassificering, SSYK") [23,24].The results from the latter system will be presented in the supplementary material. Educational level was measured based on highest attained education: primary school, upper secondary school or tertiary education.

2.4. Definition of outcome measures

2.4.1. Current asthma

Current asthma was defined as an affirmative answer to having had a physician diagnosis of asthma and either recurrent wheeze or use of asthma medication during the last 12 months.

2.4.2. Allergic asthma

Allergic asthma was defined as having current asthma (defined above) and positive answer to having allergic rhino-conjunctivitis.

2.4.3. Non-allergic asthma

Non-allergic asthma was defined as having current asthma (defined above) and negative answer to having allergic rhino-conjunctivitis.

2.4.4. Chronic bronchitis and COPD or either of them (chronic bronchitis and/or chronic obstructive pulmonary disease (COPD)

Chronic bronchitis and/or COPD was defined as an affirmative answer to 1) chronic productive cough defined as coughing up mucus or having mucus in the chest that is difficult to be expectorated and 2) whether subjects have experienced mucus most days for periods lasting at least three months and 3) whether subjects had such periods for at least 2 years in row, plus/or 4) whether subjects reported use of COPD medications.

2.5. Covariates

Inclusion of covariates in the analyses was based on previous research [22,25,26]. These included participants' age; sex; body mass index (BMI, in kg/m^2) classified as underweight (<18.5), normal weight (18.5–25), overweight (25.0 to < 30), and obese (30 or above); vapor, gas, dust and fumes exposure at work; tobacco exposure at home; and comorbidities defined as receiving treatment for hypertension, diabetes, sleeping disorders and report of family history of either asthma, allergy or other lung disease. Information on how these variables were ascertained and defined is provided in detail in previous publications [25–27]. Three variables related to respiratory symptoms: having any respiratory symptom, respiratory symptoms without asthma, and asthmatic wheeze were included as covariates (See details in the supplementary material).

2.6. Statistical analysis

2.6.1. Descriptive analysis

Descriptive statistics were presented as proportions. Statistical differences between categories of variables were evaluated using Pearson's Chi-squared test.

2.6.2. Missing data and multiple imputation

Multiple imputation was used to impute missing data using delta adjustment method [28]. Sensitivity analysis was used to test for assumption of missingness. Missing rates in data was in general low ranging from 0.2% to 5%. The supplementary file contains detailed information on the applied multiple imputation method.

2.6.3. Bayesian analysis

A Bayesian network model was built to estimate the probability of the interaction of SES and smoking on the outcomes. The learned Bayesian Network model can reveal the complex nature of the data via learning its dependency structure. Particularly, this was identified via the Bayesian network using Directed Acyclic Graphs (DAGs), which are probabilistic graphical models. The leaned DAG demonstrates the underlying association structure between the variables and represents these as networks with directed connections. All the computational aspects of the Bayesian Network analysis was done using the bnlearn package [29]. A full reproducible environment was developed and can be accessed from the GitHub page available at here.

The network structure of the variables was learned using a hill-climbing algorithm with BIC-CG score (Bayesian Information Criterion score for mixed datasets). We conducted a bootstrap aggregation and model averaging to reduce the number of arcs that are incorrectly included in the network structure. Then, we fitted the Bayesian network model to learn the related parameters. Finally, we estimated the conditional probabilities by eliciting a sample of realizations of the model variables under specific conditions. We validated our model by running a cross-validation approach and simulating new data and comparing its statistical characteristics with the original data.

To compute conditional probabilities, we used the approximate inference using likelihood weighting sampling method. Results were presented in form of probabilities of outcome and their 95% credential intervals. We used the implementation of this method that exists in the bnlearn package. Further details on analysis method are provided in the supplementary material.

3. Results

3.1. Basic characteristics of the study cohorts (WSAS and OLIN)

The combined study sample was 30,123 (females 54%) participants. Compared to subjects without asthma, those with current asthma were mostly females (60.7%), highly educated and with high prevalence of comorbidities. Allergic asthma cases were mostly manual service workers (20.8%) with high hereditary lung diseases and home smoking exposure (23.3%). Non-allergic asthma subjects were mostly non-manual workers (19.5%) and manual service workers with high educational attainment. Those with COPD and/or chronic bronchitis were significantly older in age; working in industry, of low educational attainment and high prevalence of comorbidities and obesity (26.6%) compared to health ones, (Full results in Tables 1 and 2 in the main text).

3.2. Smoking and risk of study outcomes

Regarding independent association between smoking and the study outcomes, the results showed that the probability of having current asthma, allergic asthma, non-allergic asthma and chronic bronchitis and/or COPD was higher in former smokers, while the probability of having non-allergic asthma and chronic bronchitis and/or COPD was higher among current smokers, all compared to never smokers (see Fig. 1 in the main article and Table S1:2 in the supplementary material).

3.3. SEI, education, and risk of respiratory diseases

People who work in manual jobs in the service and industry sectors, as well as intermediate non-manual employees, were more likely to have allergic asthma and non-allergic asthma compared to professionals and executives. However, there were no associations between these socioeconomic groups and probability of current asthma or COPD and/or chronic bronchitis when compared with professionals and executives. Furthermores, the probability of having allergic asthma was higher for manual workers in service and intermediate employees, while the probability of having non-allergic asthma was lower among the same groups, but higher for manual workers in industry, all compared to professionals and executives. (See full results in Fig. 1 in the main article and tables from S2:3to S2:6 in the supplementary material).

No association was observed between educational level and the probability of COPD and/or chronic bronchitis. However, compared to low educational level, those who had higher education had higher probability of having current asthma and allergic asthma, but lower probability of non-allergic asthma (Full results in Table S3:1 to S3:4 in the supplementary material).

3.4. Interaction between SES and smoking in relation to the outcomes

3.4.1. Smoking and effect modification by SEI socioeconomic groups

3.4.1.1. Allergic asthma. The higher probability of allergic asthma among former smokers (5.95%, 95% credibility interval 5.84–6.06) was more profound among intermediate non-manual employees than among professionals and executives (5.68%, 5.58–5.79). Similarly, former smokers who were manual workers in service were of higher probability of allergic asthma (5.93%, 5.84–6.05) than among professionals and executives (5.68%, 5.58–5.79). (Full results are shown in Fig. 2 in the main article and Table S2:4 in the supplementary material and Fig. 2 in the main text).

3.4.1.2. Non-allergic asthma. The increased probability due to former smoking (3.09%, 3.02–3.17) among intermediate never manual employees was lower than it was among high professionals and executives (3.38%, 3.32–3.47). The increase in probability in former smokers was also lower among manual worker in service (3.11%, 3.05–3.19) compared to professionals and executives (3.38%, 3.32–3.47).

Former smoking was not associated with probability of non-allergic asthma in among manual worker in industry when compared to professionals and executives. (Full results are shown in Fig. 2 in the main article and Table S2:5 in the supplementary material and Fig. 2 in the main text).

3.4.1.3. Current asthma and COPD and/or chronic bronchitis. No moderation in the effect of smoking on probability of current asthma and COPD and/or chronic bronchitis was observed across SEI occupational classes (Full results in Table S2:1, S2:4 and Fig. S1:1 in the supplementary material).

3.4.1.4. Smoking and effect modification by educational level. Education modified the effect of smoking on the probability of allergic asthma.

Table 1
Baseline characteristics and distribution of known risk factors for respiratory outcomes among cases and non-cases of current, allergic, non-allergic asthma and COPD and/or chronic bronchitis.

’	Allergic asthma Yes N = 1701		Allergic asthma No N = 28422		P vlaue	Non-allergic asthma Yes N = 918		Non-allergic asthma No N = 29205		P value	Current asthma Yes N = 2678		Current asthma No N = 27445		P value	COPD and/or chronic bronchitis Yes N = 1449		COPD and/or chronic bronchitis No N = 28674		P value	
Variable	**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	n	**Percent ()**		**Total n**
Education n					***					***					***					***	
n missing n = (415)	19		396			14		401			35		380			27		388			
Primary 0	208	12.4	4778	17		179	19.8	4807	16.7		401	15.2	4585	16.9		329	23.1	4657	16.5		4986
Secondary 1	761	45.2	11096	39.6		378	41.8	11479	39.9		1168	44.2	10689	39.5		603	42.4	11254	39.8		11857
Tertiary 2	713	42.4	12152	43.4		347	38.4	12518	43.5		1074	40.6	11791	43.6		490	34.5	12375	43.7		12865
Socieconomic status recoded based on SEI groups n					***					***					***					***	
n missing = (1178)	49		1129			30		1148			79		1099			37		1141			
Professionals and executives 0	186	11.3	3484	12.8		106	11.9	3564	12.7		292	11.2	3378	12.8		115	8.1	3555	12.9		3670
Manual work in industry 1	215	13	3353	12.3		101	11.4	3467	12.4		324	12.5	3244	12.3		238	16.9	3330	12.1		3568
Manual work in service 2	343	20.8	4652	17		175	19.7	4820	17.2		534	20.5	4461	16.9		255	18.1	4740	17.2		4995
Assistant Non-manual employees 3	166	10	2807	10.3		97	10.9	2876	10.3		266	10.2	2707	10.3		138	9.8	2835	10.3		2973
Intermediate Non-manual employees 4	395	23.9	6886	25.2		173	19.5	7108	25.3		580	22.3	6701	25.4		289	20.5	6992	25.4		7281
Self-employed Non-professionals 5	58	3.5	843	3.1		27	3	874	3.1		86	3.3	815	3.1		42	3.0	859	3.1		901
Students and housewives 6	118	7.1	1603	5.9		69	7.8	1652	5.9		189	7.3	1532	5.8		81	5.7	1640	6.0		1721
Unclassified 7	171	10.4	3665	13.4		140	15.8	3696	13.2		328	12.6	3508	13.3		254	18.0	3582	13.0		3836
Socieconomic status recoded based SSYK classification system n										**					**						
n missing n = (1790)			701		1790	45					152		1638			72		1718			
	89							1745													
Jobs with high professional requirement	68	4.2	1397	5.2		41	4.7	1424	5.2		110	4.4	1355	5.3		210	15.3	5536	20.5		5746
Military jobs	2	0.1	63	0.2		2	0.2	63	0.2		4	0.2	61	0.2		2	0.1	63	0.2		65
Managerial job	323	20	5423	20.3		159	18.2	5587	20.3		492	19.5	5254	20.4		60	4.4	1405	5.2		1465
The professions with requirements for higher education or equivalent	187	11.6	3789	14.2		87	10	3889	14.2		276	10.9	3700	14.3		148	10.7	3828	14.2		3976
Occupations in administration and customer service	144	8.9	2206	8.3		80	9.2	2270	8.3		226	8.9	2124	8.2		114	8.3	2236	8.3		2350
Service Care and Sales Professionals	3.28	20.3	4509	16.9		173	19.8	4664	17		514	20.3	4323	16.8		224	16.3	4613	17.1		4837
Occupations in agriculture, garden, forestry, fishing	24	1.5	386	1.4		13	1.5	397	1.4		39	1.5	371	1.4		21	1.5	389	1.4		410
Occupations in construction and manufacturing	142	8.8	2451	9.2		70	8	2523	9.2		217	8.6	2376	9.2		163	11.8	2430	9		2593
Occupations in mechanical manufacturing and transport	135	8.4	1838	6.9		56	6.4	1917	7		195	7.7	1778	6.9		128	9.3	1845	6.8		1973
The professions with requirements for shorter education or introduction	65	4	865	3.2		43	4.9	887	3.2		110	4.4	820	3.2		55	4	875	3.2		930
Can not be classified	194	12	3794	14.2		149	17.1	3839	14		343	13.6	3645	14.1		252	18.3	3736	13.9		3988
Smoking status n										***										***	
n missing n = (311)	7		304			5		306			13		298			5		306			
Nonsmoker	1085	64	17793	63.3		526	57.6	18352	63.5		1643	61.7	17235	63.5		717	49.7	18861	64		18878
Former smoker	399	23.6	6866	24.4		261	28.6	7004	24.2		676	25.4	6589	24.3		393	27.2	6872	24.2		7265
Current smoker	210	12.4	3459	12.3		126	13.8	3543	12.3		346	13	3323	12.2		334	23.1	3335	11.8		3669
Sex n					***					***					***						
Female	1036	60.9	15216	53.5		554	60.3	15698	53.8		1625	60.7	14627	53.3		715	49.3	15537	54.2		16252
Male	665	39.1	13206	46.5		364	39.7	13507	46.2		1053	39.3	12818	46.7		734	50.7	3137	45.8		13871
Age categories n					***					**					***					***	
20–40 years	575	33.8	7524	26.5		245	26.7	7854	26.9		831	31	7268	26.5		312	21.5	7787	27.2		8099
40–60 years	688	40.4	10381	36.5		305	33.2	10764	36.9		1007	37.6	10062	36.7		445	30.7	10624	37.1		11069

(*continued on next page*)

Table 1 (*continued*)

'	Allergic asthma Yes N = 1701		Allergic asthma No N = 28422		P vlaue	Non-allergic asthma Yes N = 918		Non-allergic asthma No N = 29205		P value	Current asthma Yes N = 2678		Current asthma No N = 27445		P value	COPD and/or chronic bronchitis Yes N = 1449		COPD and/or chronic bronchitis No N = 28674		P value	
Variable	**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	**n**	**Percent ()**		**n**	**Percent ()**	n	**Percent ()**		**Total n**
>60 years	438	25.7	10517	37		368	40.1	10587	36.3		840	31.4	10115	36.9		692	47.8	10263	35.8		10955
Body mass index n					***					***					***					***	
n missing n = (750)	36		714			18		732			56		694			43		707			
Normal weight	685	41.1	13088	47.2		352	39.1	13421	47.1		1052	40.1	12721	47.6		545	38.8	13228	47.3		13773
Under weight	16	1	358	1.3		12	1.3	362	1.3		30	1.1	344	1.3		18	1.3	356	1.3		374
Overweight	624	37.5	10330	37.3		334	37.1	10620	37.3		985	37.6	9969	37.3		535	38.1	10419	37.3		10954
Obese	340	20.4	3932	14.2		202	22.4	4070	14.3		555	21.2	3717	13.9		308	21.9	3964	14.2		4272
Diabetes n										***					***					***	
n missing n = (2217)	111		2106			84		2133			211		2006			164		2053			
Yes	89	5.6	1433	5.4		68	8.2	1454	5.4		163	6.6	1359	5.3		95	7.4	1427	5.4		1522
Hypertension n										***										***	
n missing n = (808)	56		752								100		708			76		732			
Yes	319	19.4	5820	21		228	25.9	5911	20.8		569	22.1	5570	20.8		371	27.0	5768	20.6		6139
Sleep disorders n					***					***					***					***	
missing N = (2166)	96		2070			74		2092			185		1981			143		2023			
Yes	193	12	2113	8		109	12.9	2197	8.1		306	12.3	2000	7.9		206	15.8	2100	7.9		2306
Hereditary lung disease n					***					***					***					***	
missing N= (169)	6		163			0		169			11		158			12		157			
Yes	1644	97	2952	10.4		856	93.2	3740	12.9		2553	95.7	2043	7.5		631	43.9	3965	13.9		4596
Exposure to dust, gases or smoke at work n					***					***					***					***	
missing N = (792)	39		753			13		779			58		734			38		754			
Yes	494	29.7	5730	20.7		252	27.8	5972	21		767	29.3	5457	20.4		529	37.5	5695	20.4		6224
Exposure to smoking at home n					***					***					***					***	
missing N = (746)	37		709	14		21		725			65		681			36		710			
Yes	387	23.3	4595	16.6		213	23.7	4769	16.7		610	23.3	4372	16.3		393	27.8	4589	16.4		4982
Having any respiratory symptom					***					***					***					***	
Yes	7807	26.70	734	80		7165	25.2	1376	80.90		6383	23.30	2158	80.60		1449	100	7092	24.7		8541
Respiratory symptom without asthma					***					***					***						
Yes	5563	19	0	0		5563	19.60	0	0		5563	20.30	0	0		851	58.7	4712	16.4		5563
Athmatic wheeze					***					***					***					***	
Yes	1675	5.70	295	32.10		1328	4.70	642	37.70		1009	3.70	961	35.90		442	30.5	1528	5.3		1970

Statistical significance markers: *p < 0.1; **p < 0.05; ***p < 0.01.

Table 2
Distribution of smoking status by socioeconomic groups.

Socioeconomic status based on SEI	Never smoker	Former smoker	Current smoker	Total	p value
	N = 18878	N = 7265	N = 3669	N = 29812	
	n (%)	n (%)	n (%)	n (%)	
n missing	805	173	139	1117	<0.001
Professionals and executives	2605 (14.4)	838 (11.8)	217 (6.1)	3660 (12.8)	
Manual work in industry	1993 (11.0)	1001 (14.1)	548 (15.5)	3542 (12.3)	
Manual work in service	2740 (15.2)	1294 (18.2)	936 (26.5)	4970 (17.3)	
Assistant Non-manual employees	1824 (10.1)	774 (10.9)	357 (10.1)	2955 (10.3)	
Intermediate Non-manual employees	5025 (27.8)	1651 (23.3)	576 (16.3)	7252 (25.3)	
Self-employed Non-professionals	553 (3.1)	246 (3.5)	98 (2.8)	897 (3.1)	
Students and housewives	1336 (7.4)	158 (2.2)	223 (6.3)	1717 (6.0)	
Unclassified	1997 (11.0)	1130 (15.9)	575 (16.3)	3702 (12.9)	
Occupational groups based on SSYK 2012					
n missing	1150	301	186	1637	<0.001
Managers	4119 (23.2)	1235 (17.7)	369 (10.6)	5723 (20.3)	
Military jobs	45 (0.3)	11 (0.2)	8 (0.2)	64 (0.2)	
Professions requiring advanced education	936 (5.3)	388 (5.6)	131 (3.8)	1455 (5.2)	
Professions requiring higher education	2737 (15.4)	891 (12.8)	333 (9.6)	3961 (14.1)	
Administration	1427 (8.0)	623 (8.9)	290 (8.3)	2340 (8.3)	
Service	2743 (15.5)	1265 (18.2)	809 (23.2)	4817 (17.1)	
Agriculture	261 (1.5)	99 (1.4)	48 (1.4)	408 (1.4)	
Building	1480 (8.3)	739 (10.6)	359 (10.3)	2578 (9.1)	
Manufacturing	1072 (6.0)	575 (8.3)	314 (9.0)	1961 (7.0)	
Elementary	497 (2.8)	208 (3.0)	220 (6.3)	925 (3.3)	
Others	2411 (13.6)	930 (13.4)	602 (17.3)	3943 (14.0)	
Education					
n missing	262	77	61	400	<0.001
Primary	2438 (13.1)	1620 (22.5)	852 (23.6)	4910 (16.7)	
Secondary	7110 (38.2)	2877 (40.0)	1749 (48.5)	11736 (39.9)	
Tertiary education	9068 (48.7)	2691 (37.4)	1007 (27.9)	12766 (43.4)	
Groups of number of cigarettes per day					
n missing	0	7221	102	7323	<0.001
0 cigarettes per day	18747 (99.3)	0 (0.0)	0 (0.0)	18747 (83.4)	
<5 cigarettes per day	49 (0.3)	25 (56.8)	1295 (36.3)	1369 (6.1)	
5-14 cigareetes per day	54 (0.3)	13 (29.5)	1532 (42.9)	1599 (7.1)	
>14 cigarettes per day	28 (0.1)	6 (13.6)	740 (20.7)	774 (3.4)	

With respect to primary education, former smoking among higher secondary and tertiary education were associated with higher probability of allergic asthma compared to never smokers in these classes. No effect of former smoking compared to never smoking on the probability of allergic asthma was observed among those with primary education.

Similarly, the increased in probability of non-allergic asthma due to former smoking compared to never smokers was higher among those with primary education compared to those with tertiary education.

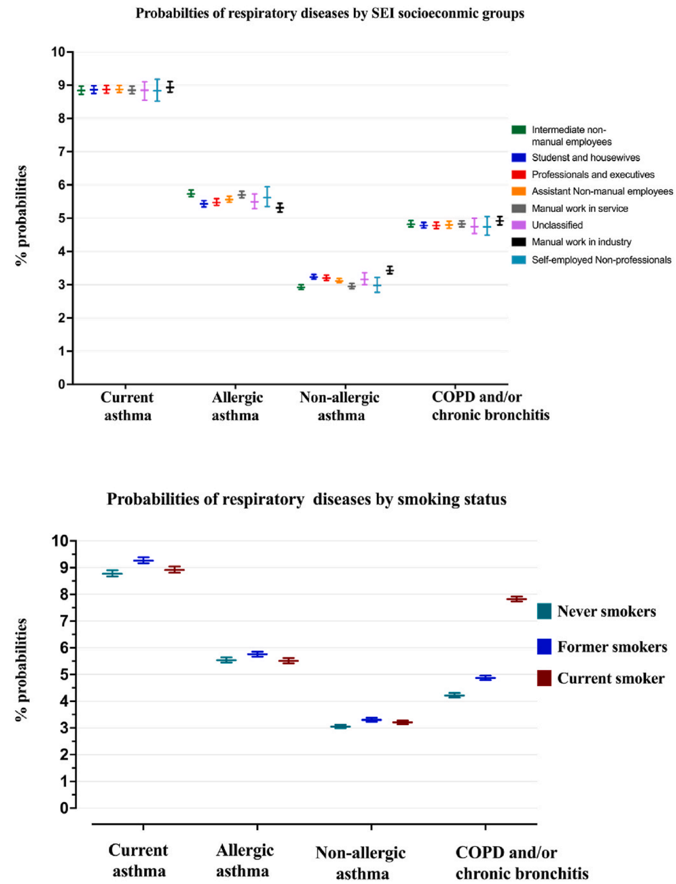

Fig. 1. Percentage probability and 95% credential intervals for the independent effect of socioeconomic status and smoking status on respiratory outcomes in adults.

Among the later, former smoking also predicted higher probability of non-allergic asthma compared to never smokers. The former smoking effect was, though, more profound among those with primary education. No significant variation of the effect of smoking across educational classes was observed concerning current asthma and COPD and/or chronic bronchitis. (Full results in Fig. 3 in the main text and Table S3:1 to S3:4 in the supplementary material).

4. Discussion

4.1. Summary of key findings

This study found putative interactions between smoking and different measures of SES in relation to the probability of having respiratory diseases. Education and occupational classification, as different measures of SES, presented different patterns of smoking association with asthma, when the latter is divided by allergic status. Former smokers had higher probability of both allergic asthma and non allergic asthma than never smokers. The harmful effect of smoking towards allergic asthma was more profound among lower occupational groups of manual workers in service and intermediate non manual employees than in high professionals and executives. Yet, it was higher among highly educated groups than lower educated. In the other hand, smoking detrimental effect towards non-allergic asthma was more observed among high occupational classes of professionals and executives compared to manual and homer workers. It was, however, higher among low educated groups compared to highly educated.

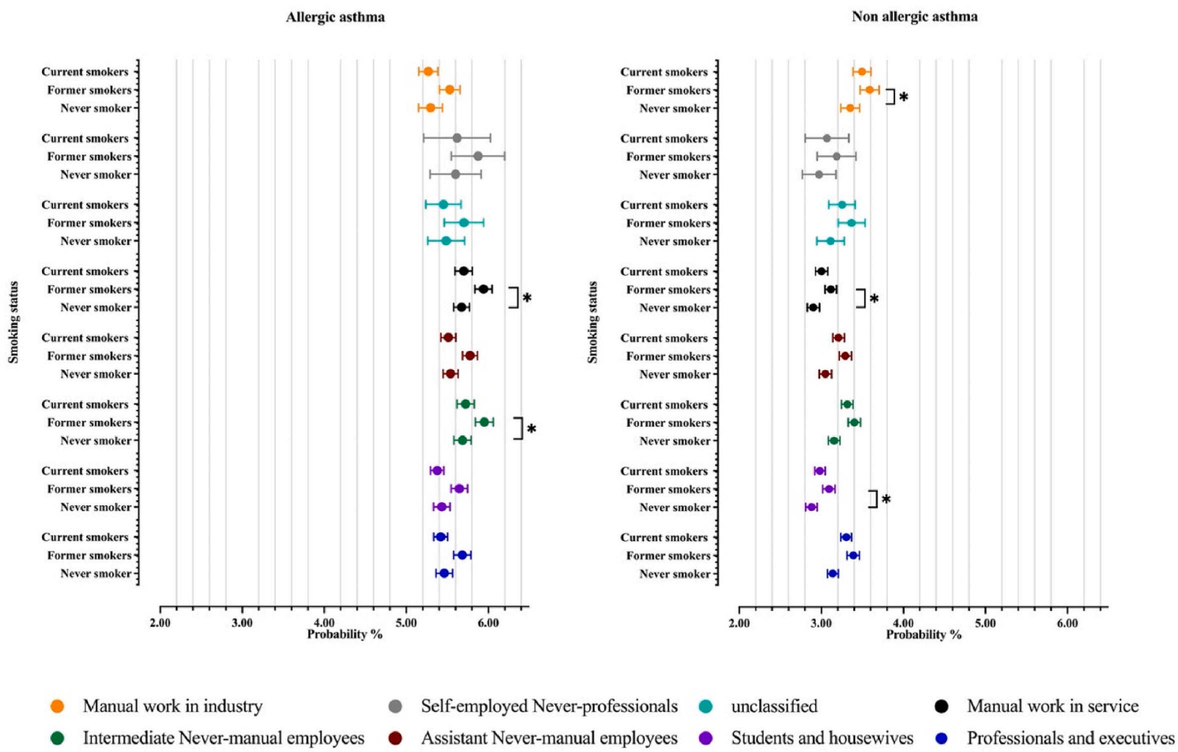

Fig. 2. The percentage probability and 95% credential interval of the probability of allergic and non-allergic asthma by smoking status as modified by SEI socio-economic groups.

4.2. Strength and limitations

Although only few previous studies assessed the association between multiple measures of SES and risk of respiratory outcomes, this is the first study, to our knowledge, to evaluate the interaction between smoking and multiple measures of SES in relation to respiratory outcomes. The large sample size enhanced the precision of the study, so that we could explore interactive effects despite the multi-categories of smoking and SES variables. The study population, being a random sample, is representative of the Swedish adult population and thus the results are generalizable to the source population. The questionnaire used to collect the study data has been validated and used in several previous international studies [22,25,26]. A limitation of this work lies in its cross-sectional design, so that we cannot infer a causal relationship between the smoking-SES interaction and long-term respiratory outcomes. Besides, the retrospective data collection via subjects' self-report of both exposures, outcomes, and covariates can introduce a risk of recall bias [13–15,21]. Defining COPD and bronchitis based on spirometry measures would have been more accurate to capture differences between the two outcomes with respect to our study aim. However, as this study was only based on questionnaire survey, spirometry data was unavailable. Given this shortcoming in the study, it seems helpful to combine COPD and/or chronic bronchitis using self-report of symptoms with self-reported medication use to define possible COPD and/or chronic bronchitis. Although we acknowledge that this definition is still loose, in the recent update of 2023 GOLD, more attention was brought into the importance of symptom presentation into defining COPD [9]. Such definition is also inclusive and less distinguishing from subjects with severe asthma. Since conducting a sensitivity analysis among such group of asthmatics was not feasible in the context of our work due to unavailable data, we notice the importance of such consideration when interpretating results from our study. Furthermore, allergic rhinitis was used as a marker of sensitization among asthmatics, but it is less sensitive among older asthmatics; however, we conditioned for age in our analysis model to account for any variation in effect by age group.

4.3. Comparison of findings with previous studies

The SEI and SSYK occupational classification systems classify subjects based on professional environment, exposures, and, to an extent, power and income. Previous research using these two classification systems found higher levels of exposure to vapors, gas, dust and fumes among certain occupational groups, particularly, manual workers in industry using the SEI system and agriculture, building and manufacturing workers using the SSYK system [22].

Similar studies using the same classification systems also revealed high prevalence of respiratory symptoms among manual workers in service and industry and intermediate employees. It also revealed high prevalence of current asthma among workers in health care and science while high risk of non-allergic asthma among service workers [22].

Our observation of higher probability of respiratory diseases among former smokers compared to never and current smokers in low socioeconomic groups is not unexpected. Previous studies of smoking effect in relation to trend of respiratory outcomes reported consistent results concerning former smokers having higher risk than current smokers concerning respiratory outcomes [25,30,31]. The observed higher probability of respiratory diseases among smokers in lower socioeconomic groups compared to higher socioeconomic groups is consistent with previous findings showing higher risk of COPD, chronic bronchitis among groups of combined exposure to occupational dust, fumes and vapors and smoking.De Meer et al. [28] similarly found that smokers who were exposed to mineral dust at work were at higher risk of chronic bronchitis and lower FEV_1/FCV ratios than the expected risk of smoking and mineral dust separately [32,33]. Van der Plaat et al. [34] in turn, found an interaction between vapor, gas dust and fumes exposure and smoking on the risk of COPD [34]. Further, despite, using different measures of respiratory impairment, Hisinger-Mölkänen et al. [35] observed that odds of chronic rhinitis, nasal symptoms and runny nose were the highest among the group with combined exposure to active or

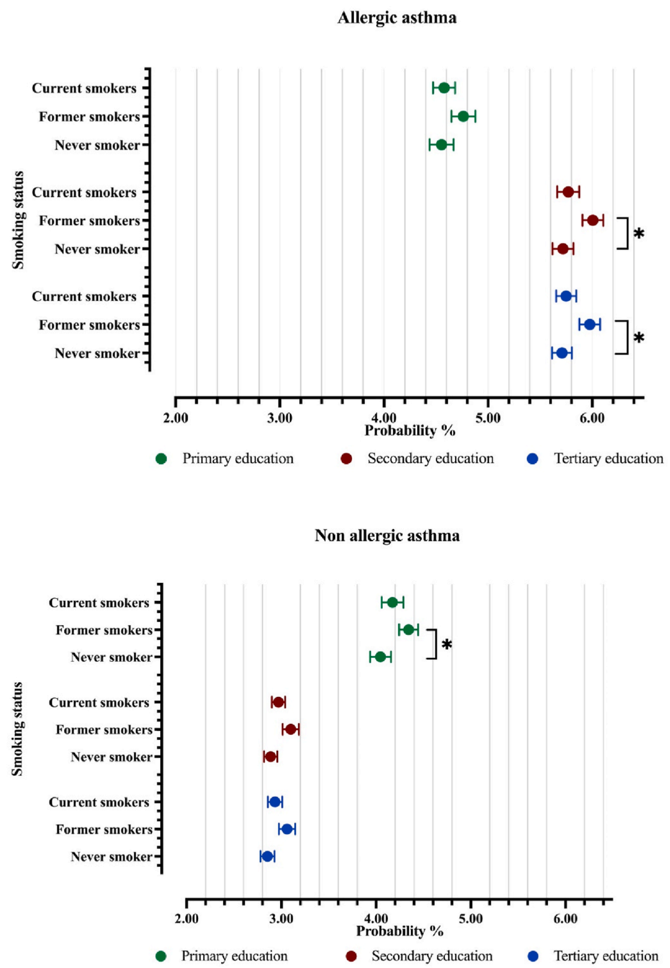

Fig. 3. The probability and 95% credential interval of allergic and non-allergic asthma by smoking status as modified by educational levels.

environmental smoking and occupational irritants compared to exclusive exposure to occupational irritants among Finnish subjects [35]. Although our study did not capture the combined effect of smoking and occupational exposure towards COPD and/or chronic bronchitis specifically, the combined effect of smoking and occupational exposures lasted towards allergic asthma and non allergic across different occupations.

4.4. Possible mechanisms for the observed findings

Our observed combined detrimental effect of smoking and occupational exposures towards the probability of allergic asthma in low socioeconomic groups is conceivable through either the direct damage each of the two causes to airways, or through their exertion of a sensitization effect. Beyond the known fact that occupational exposure may exert their adverse respiratory effects through increasing allergic sensitization, smoking may also act via increasing airway sensitivity to such hazardous agents [36,37]. Smoking effect on allergic sensitization is not very clear, with some studies linking it to increased risk of allergic diseases [38,39] while others are suggestive of its role in preventing atopy and allergic sensitization [40,41]. Smoking has been shown to have an adjuvant effect on producing airways allergic inflammatory mediators like immunoglobulin E (IgE), immunoglobulin G (IgG) antibodies and histamine, which is possibly due to its induced airway mucosal damage [42]. Zetterström et al. [42] studied two different populations of workers in pharmaceutical and coffee production professions and found that smokers had excess sensitization in form of higher means of total serum IgE concentration and skin prick test to specific allergen compared to non-smokers [42].

On the other hand, considering the sensitization independent harmful effect, studies from Sweden, Norway and Spain have reported higher risk of adult onset asthma in association with long term exposure to low dose of non-sensitizing irritants among workers in metal, wood, plastic processing industries and workers in jobs of construction, plumbing, welding, mining and asphalt roof working [37]. Such effect may add up to the direct damage exerted by smoking on airways toward increasing probability of respiratory diseases. Shirkaw et al. [36] stated that smoking has a potentiating effect, i.e., marked combined effect when joined with other irritants, such as heavy metals, even if such substances might have no independent effect [36,43].

Our observation of higher probabilities of allergic asthma among former smokers in highly educated compared to low educated further align with the notion of smoking interplay through a sensitization path that is further enhanced in hygienic settings [44].

Attenuation of the harmful effect of smoking on the probability of non-allergic asthma among both low occupational and educational groups in oppose to higher likelihood among high professionals, however, was an interesting finding in our results. In general, understanding of non-allergic asthma pathophysiology, risk factors and their interaction compared to allergic asthma is in the rear. Let alone, evidence on how smoking affect asthma among atopic and non atopic is quite conflicting. Some studies pinpointed smoking as a risk factor for adult's onset asthma among atopics. Other linked smoking to atopic asthma varying effect by gender and smoking habits [45–47]. The effect of smoking on non-allergic asthma was lesser among manual workers in industry and home workers possibly due to those who are not atopic in these groups being less sensitive to harmful effect of smoking. Such desensitization is plausibly a result of occupational exposures in these occupational settings [48]. Those in lower occupational settings and high educational classes where non-allergic asthma was less among smokers could possibly present certain smoking behavioural patterns related to amount, quitting and frequency of smoking that were also reported to be associated to non-allergic asthma [48] Overall, such variation in smoking effect across SE groups and the further variation by each SE measure indicates that exposures at different occupational settings operate differently in inducing airways damage, allergic sensitization and sensitivity to occupational irritants. Further, exposures in different socioeconomic settings may further interact with host immunogenic, genetic, psychosocial factors and smoking status diversly [17,18].

The healthy smoker effect is one possible explanation for our finding of higher probability of having respiratory diseases among former smokers than among current and never smokers. Increased probability of respiratory disease was observed among former smokers perhaps because asthma patients who had previously smoked might have quit smoking due to increase of respiratory symptoms, severity and deterioration of lung function [49].

Another possible explanation is the difference in duration and age at which former smokers began smoking versus never and current smokers. Studies on characterization of asthma and COPD patients have frequently reported that former smokers are usually older, with longer duration of smoking and higher decline in lung function than current and never smokers [50]. Even when the comparison was conducted among subjects with new onset asthma, Jaakkola et al. concluded that the marked impairment among former smokers is suggestive of the negative effect of smoking that starts even before the occurrence of asthma [51,52]. It is also possible that former smokers may have quit smoking due to other comorbidities, which might have contributed to the increased outcome probabilities. Although the questionnaire included the age they began smoking and age they quit smoking, we only asked for number of cigarettes they smoked per day currently and not in the past thus, we could not estimate the amount of smoking in former smokers.

4.5. Future research and public health implications

Our findings show that socio-occupational classifications are useful in defining SES in a population setting and capturing variant patterns of respiratory diseases in different SES levels. The SES classifications used in our study represent reliable systems for capturing their interactions with smoking in relation to respiratory diseases, being also sensitive in presenting different effects of smoking on allergic and non-allergic asthma phenotypes by socioeconomic groups. Future studies might benefit by replicating the current study by using similar SES systems.

Our findings on how smoking interacted with each SES measure in relation to respiratory diseases suggest that certain high-risk social/occupational groups may benefit more from tailored smoking cessation interventions than others. Our work encourages further studies on the different effect of smoking on allergic and non-allergic asthma by SES. Although smoking cessation is widely acknowledged as a primary health intervention for chronic obstructive lung disease, there is need for additional research to fully comprehend the mechanism of interaction between smoking and occupational exposures towards risk of possible occupational induced allergic sensitizations and airways hyper-responsiveness in different socio-occupational settings. Studies are required to elucidate the mechanisms through which the combined effect of smoking and socioeconomic exposures act on lung health.

In conclusion, this study showed that beyond the independent role of smoking and SES in respiratory diseases, in high income countries such as Sweden, SES as measured using different socioeconomic classification systems and smoking interact in defining the risk of respiratory diseases in adults. Better understanding of this interaction can be of help when identifying social and occupational risk groups at higher need of preventive intervention.

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Availability of data and material

Code availability.

Ethical approval

The studies were approved by the regional ethical review board in Gothenburg, Sweden and Umeå, Sweden.

Consent to participate

Not applicable.

CRediT authorship contribution statement

Muwada Bashir Awad Bashir: processed the experimental, Data curation, performed the, Formal analysis, Writing – original draft, and designed the figures. **Rani Basna:** designed the model and the computational framework and, Formal analysis, Data curation, processed the experimental, Writing – original draft. **Linnea Hedman:** revised the, Project administration, the main conceptual ideas and proof outline, processed the experimental, Data curation, performed the, Formal analysis, Writing – original draft. **Helena Backman:** revised the, Project administration, the main conceptual ideas and proof outline. **Linda Ekerljung:** revised the, Project administration, the main conceptual ideas and proof outline. **Heidi Andersén:** revised the, Project administration, the main conceptual ideas and proof outline, implementation of the research, to the, Formal analysis, of the result. **Göran Wennergren:** revised the, Project administration, the main conceptual ideas and proof outline, contributed to the design and implementation of the research, to the, Formal analysis, of the result. **Laxmi Bhatta:** revised the, Project administration, the main conceptual ideas and proof outline. **Anne Lindberg:** revised the, Project administration, the main conceptual ideas and proof outline, implementation of the research, to the, Formal analysis, of the result. **Bo Lundbäck:** revised the, Project administration, the main conceptual ideas and proof outline, implementation of the research, to the, Formal analysis, of the result. **Hannu Kankaanranta:** revised the, Project administration, the main conceptual ideas and proof outline, designed the figures, processed the experimental, Data curation, performed the, Formal analysis, Writing – original draft, Supervision. **Eva Rönmark:** revised the, Project administration, the main conceptual ideas and proof outline, implementation of the research, to the, Formal analysis, of the result. **Bright I. Nwaru:** revised the, Project administration, the main conceptual ideas and proof outline, processed the experimental, Data curation, performed the, Formal analysis, Writing – original draft, designed the figures, Supervision.

Declaration of competing interest

All authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2023.107192.

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