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Associations of adverse childhood experiences with smoking initiation in adolescence and persistence in adulthood, and the role of the childhood environment: Findings from the 1958 British birth cohort.

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Abstract

Adverse childhood experiences (ACEs) have been identified as a strong determinant of smoking. We aimed to examine the association between ACEs and early smoking initiation and subsequent persistence and the contribution of five pathways including family factors, parental involvement, material living conditions, social activities and conscientiousness.

Data are from 7 414 individuals born in 1958 in Great Britain included in the National Child Development Study. ACEs were measured at ages 7, 11, and 16. Smoking initiation was derived from smoking variables from ages 16 to 42 and persistent smoking was derived from smoking variables from ages 23 to 42. We modelled the relationship between ACEs and smoking, and further assessed the contribution of each pathway using multinomial logistic regressions.

During childhood, 20.9% of respondents experienced one ACE and 6.4% two or more. Those who experienced ACEs had a higher risk of initiating smoking by age 16 and of persistent smoking (RRR initiation by $_{16y} = 1.89$ [1.62; 2.20] for one ACE; RRR initiation by $_{16y} = 2.36$ [1.81; 3.08] for two or more ACEs, and RRR persistent smoking = 2.07 [1.73; 2.47] for one ACE, RRR persistent smoking = 2.59 [1.92; 3.49] for two or more ACEs). The factors that contributed most to explaining these associations were parental smoking, sibling order and conscientiousness. ACEs remained associated with persistent smoking after further adjusting for young adulthood variables.

Smoking prevention measures may need to be tailored when considering adolescents from communities where ACEs are more prevalent to curtail initiation, intensity and persistence.

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Keywords

Smoking; Social environment; Chronic stress exposure; Health behaviour; Cohort study; Social inequalities in health; Life course

1 Introduction

Tobacco smoking represents one of the most important and preventable causes of premature 2 mortality worldwide (1). On average, smokers die 10 years earlier than non-smokers from 3 4 tobacco related causes (2). Smoking is one of the most popular addictive behaviours initiated 5 and established during adolescence, with to date a substantial prevalence among adolescents worldwide (3). Early initiation of smoking is associated with the development of more severe 6 7 levels of nicotine addiction with persistent smoking thereafter (4). Understanding the factors 8 that contribute to the initiation and continuation of smoking is critical for public health and policy to develop more tailored smoking prevention interventions that will be effective in 9 10 reducing the prevalence of smoking.

Smoking is not only a consequence of an individual's intrinsic tendency towards addiction to 11 12 nicotine or cigarette smoking. Factors related to the social influences with which individuals evolve and interact, play an important part in determining smoking (5). Adverse childhood 13 14 experiences (ACEs) described as a set of psychological trauma, abuse, living conditions, out of 15 the child's control, that can generate chronic stress responses in the child's immediate environment (6), have been associated with poor health outcomes across the life course, 16 including chronic lung diseases (7) and lung cancer (8), partly through the adoption and 17 18 persistence of unhealthy behaviours (9), with a strong relationship with smoking (10).

In 1999, Anda et al. showed that individuals who had experienced more adverse childhood experiences were more likely to start smoking at younger ages and continue to do so over time (11). Since then, several studies have reported that ACEs are associated with an increased likelihood of smoking behaviours along the life course in adulthood (12–14,10,15–23) and more recently in adolescence (24,25) after various adjustments. Most of these studies controlled for age, sex and/or ethnicity, socioeconomic indicators and had additionally adjusted for other factors such as ethnicity, family factors, alcohol consumption, mood disorder, and marital status, showing a robust association between childhood adversity and smoking. Theintermediate processes linking adversity and smoking are not well understood.

In previous research, several factors were found to partially mediate the relationship between 28 29 ACEs and smoking including family factors (26,27), parenting practices (28,29), material living conditions (30,31), social activities (32-34), and conscientiousness (35,36). One of the 30 limitations of previous studies is the lack of simultaneous consideration of potential 31 32 intermediate or mediating factors identified in the risk of early initiation and subsequent persistence of smoking. It remains unclear whether these intermediate factors mediate the 33 association between ACEs and the risk of smoking initiation in adolescence and its maintenance 34 35 in adulthood, and which ones are the main drivers of the association.

In this study, we aimed (i) to assess the relationship between ACEs and early smoking initiation and persistence controlling for prior confounders and (ii) to comprehensively identify the contribution of all the above potential mediators in the association between ACEs and smoking initiation and continuation over the life course.

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41 Method

42 Study design and participants

We analysed data from the 1958 National Child Development Study (NCDS), a national birth 43 44 cohort study of 17 415 people born in 1958 in Great Britain. A full description of the study design and methods has been detailed elsewhere (37). There have been 12 waves of data 45 collection so far, at birth, ages 7, 11, 16, 23, 33, 42, 44/45, 46, 50, 55, and 62. Information on 46 47 multiple aspects of participants' lives was collected from a number of sources (i.e. parents, teachers, cohort members, medical personnel, health visitor). Detailed information on ethics 48 approval and informed consent across the different data collection waves is available from the 49 study website (38). We used information on participants up to age 42 when more detailed 50

information on smoking was collected. A total of 7 414 had complete exposure and outcome
data of whom 4 587 (38%) also had complete for all other covariates. The sample selection
strategy is described in Appendices Figure A.1.

54 Smoking initiation and long-term smoking

The outcomes assessed in this analysis were smoking initiation and long-term smoking, derived 55 from information on smoking behaviour reported in questionnaires from ages 16 to 42. At each 56 57 age, "non-smokers" were defined as those who reported not smoking and "current smokers" were defined as follows: at 16y as those who reported smoking at least one cigarette per week, 58 at 23y as those who reported currently smoking cigarettes and those who reported smoking 59 60 cigars or pipes, at 33y as those who reported currently smoking cigarettes and as those who reported smoking at least one cigarette per month, at 42y as those who reported smoking 61 cigarettes every day. At 16 years, weekly cigarette consumption was also defined for 62 subsequent analyses in five categories: non-smoker, 1–19, 20–39, 40–59 and ≥ 60 63 cigarettes/week. From 23y to 42y, "former smokers" were defined as those who reported not 64 65 currently smoking but had previously smoked cigarettes. If the "never smokers" at any point in 66 the follow-up reported having smoked cigarettes regularly at an earlier age, we coded them as "former smokers". 67

From this set of smoking variables from 16 to 42 years we derived the smoking initiation variable as follows: "never smokers" were defined as those who had never smoked at ages 16 to 42; individuals who had "started smoking by age 16" were defined as those who reported smoking at 16y; and "smoking initiation after age 16" were defined as those who reported not having smoked in a previous sweep but who reported having smoked or being a former smoker at 23 or 33, or 42 years of age.

Similarly, long-term smoking was derived from smoking variables from ages 23 to 42 whereby
"non-smokers" were defined as those who never smoked from ages 23 to 42; "persistent

smokers" were defined as those who smoked from ages 23 to 42; and the last group of individuals was classified as those with a heterogeneous smoking consumption. A detailed description of the construction of the smoking variables is given in Appendices File A.1.

79 ACEs

The exposure of interest was adverse childhood experiences (ACEs) and was constructed 80 according to previous work carried out in the NCDS dataset (39). The NCDS has a wealth of 81 82 prospectively collected ACEs data collected from the child's parent, the health visitor or their 83 teacher. ACEs were measured by counting the number of positive responses across all three surveys at ages 7, 11, and 16 of the following categories: child in care, physical neglect, 84 85 offenders, parental separation, mental illness, and alcohol abuse (6,39). Based on the distribution of the cumulative ACEs score (1.69 % of participants were defined as having three 86 or more ACEs), a three-category variable was constructed (0 adversity/1 adversity/more than 87 one adversity). A full description of the six categories together with detailed information on 88 ACEs score construction is given in Appendices File A.1. 89

90 Covariates

Baseline variables, previously identified in the literature as confounders in the associations 91 between ACEs and the two main smoking outcomes (initiation by age 16 and long-term 92 93 smoking) and tested in bivariate analysis, were mother's age at birth, respondent's sex and birth weight. Socioeconomic background was also included since early childhood adversity is more 94 95 frequent among children growing up in disadvantaged socioeconomic conditions (30) and individuals from disadvantaged socioeconomic groups are more likely to smoke, to be heavy 96 smokers and to be more heavily dependent on smoking (4). Socioeconomic background was 97 measured using parental socioeconomic classification of occupations (SEC), based on a 98 questionnaire completed at birth by the parents (I-professional occupations & II-intermediate 99 occupations/III-skilled occupations (non-manual)/III-partly skilled occupations (manual)/IV-100 101 partly skilled occupations & V-unskilled occupations).

We considered five blocks of potential mediating variables in this study: family factors, parental 102 103 involvement, material living conditions, social activities, and conscientiousness. Family factors comprised sibling order at 7y (Single child/Elder/2nd place or more) and parental smoking at 104 105 16y (Smoker/Non-smoker). Parental involvement was derived from variables measured at age 7 including reading to the child, outdoor activities (Frequent/Occasionally, Hardly ever), and 106 107 father's role in the management of the child (Equal parental investment/Father less invested/ 108 Father not invested). Material living conditions at ages 7, 11, and 16 (Advantaged/Disadvantaged). Social activities at age 16 ranked from 0 to 4, where 4 indicates 109 a high participation in parties with friends. We also considered conscientiousness at age 16 110 111 measured with a score in which higher values indicated higher conscientiousness.

Other potential subsequent mediators during early adulthood were included in an additional analysis of long-term smoking, namely: education level at 23y (A level -12 years of education/O levels-10 years of education/ No qualifications), age of first child before 23y (No child/Child [18-23y]/Child <18y), Employment at 23y (With employment/Unemployed). See Appendices File A.1 for more a detailed description of the covariates.

117 Statistical analysis

We first carried-out either χ^2 test or the Wilcoxon signed-rank test to estimate bivariate 118 associations between the covariates and each outcome (smoking initiation or long-term 119 smoking). Second, we used multinomial logistic regression models to estimate relative risk 120 ratios (RRR) of smoking initiation or long-term smoking comparing participants who reported 121 one, or two or more ACEs to those who did not. We defined an adjusted model controlling for 122 baseline confounders and parental SEC (Model 1). Then we further adjusted for each block of 123 covariates to assess the contribution of each respective pathway and identify potential mediators 124 for future analyses. We defined a final model including all of the intermediate variables to 125 assess the residual effect of ACEs on smoking (Model 2) (40). 126

127	- Model 1: Model 1 + baseline confounders (mother's age, birthweight, sex) + parental SEC
128	- Model 1A: Model 1 + family factors (sibling order, parental smoking)
129	- Model 1B: Model 1 + parental involvement (reading to the child, outdoor activities,
130	father's role in the management of the child)
131	- Model 1C: Model 1 + material living conditions
132	- Model 1D: Model 1 + social activities
133	- Model 1E: Model 1 + conscientiousness
134	- Model 2: fully adjusted model
135	For long-term smoking outcome, we further controlled for educational level, age at first child
136	and employment.
137 138	- Model 3: fully adjusted model + educational level + age of first child + employment
139	We imputed data for covariates with missing data using the multiple imputation by chained
140	equations method in the population with non-missing data for ACEs and smoking (n=7 414).
141	Forty-two imputations were conducted, using the two-step process recommended by von
142	Hippel to ensure replicable estimates of the standard errors (41,42), taking the missing at
143	random assumption for the covariates. Comparisons were made between complete-case
144	analyses and those run on estimates obtained by imputation to ensure that our results were not
145	biased by missing values (Appendices Table A.1 and Appendices Table B.1). Statistical
146	analyses were performed using STATA v17
147	
148 149	Data sharing Anonymised data from the 1958 NCDS are freely available and can be obtained by registering
450	

150 on the UK data service (https://ukdataservice.ac.uk/).

151 **Results**

A total of 7 414 participants were included for whom 37.91% had initiated smoking by 16y and
23.28% were smoking more than 20 cigarettes per week at 16 years. From ages 23 to 42, 17.16%
were persistent smokers. In addition, during childhood, 20.88% of the individuals experienced
one ACE and 6.41% two or more.
A higher proportion of individuals who experienced adversity, compared to those who did not,
had parents from a disadvantaged SEC, had older siblings, had a smoking parent, had fathers

158 who were absent in their family investment, had occasionally or rarely reading activities or

159 outdoor activities, lived in poor material conditions during childhood, attended a lot of parties,

and had a lower conscientiousness score (Table 1).

		None	One	Two or more	Total
		n=5391 (72.71%)	n=1548 (20.88%)	n= 475 (6.41%)	n=7414 (100%)
Variable	Level	n (%)	n (%)	n (%)	n (%)
Smoking initiation	Never smoked	1452 (26.93%)	300 (19.38%)	79 (16.63%)	1831 (24.70%)
	Initiation by 16y	1831 (33.96%)	730 (47.16%)	250 (52.63%)	2811 (37.91%)
	Initiation > 16y	2108 (39.10%)	518 (33.46%)	146 (30.74%)	2772 (37.39%)
Amount of smoking at 16y	Non-smoker	3560 (66.04%)	818 (52.84%)	225 (47.37%)	4603 (62.09%)
	1 to 19 cig./week	780 (14.47%)	234 (15.12%)	71 (14.95%)	1085 (14.63%)
	20 to 39 cig./week	492 (9.13%)	203 (13.11%)	71 (14.95%)	766 (10.33%)
	40 to 59 cig./week	324 (6.01%)	157 (10.14%)	61 (12.84%)	542 (7.31%)
	More than 60 cig./week	235 (4.36%)	136 (8.79%)	47 (9.89%)	418 (5.64%)
Long-term smoking	Never smoked	1452 (26.93%)	300 (19.38%)	79 (16.63%)	1831 (24.7%)
	Persistent smoking	794 (14.73%)	353 (22.8%)	125 (26.32%)	1272 (17.16%)
	Heterogeneous consumption	3145 (58.34%)	895 (57.82%)	271 (57.05%)	4311 (58.15%)
Sex	Men	2580 (47.86%)	766 (49.48%)	247 (52%)	3593 (48.46%)
	Women	2811 (52.14%)	782 (50.52%)	228 (48%)	3821 (51.54%)
Mother's age	\leq 23 y	1320 (24.49%)	439 (28.36%)	151 (31.79%)	1910 (25.76%)
	24-27 у	1500 (27.82%)	365 (23.58%)	119 (25.05%)	1984 (26.76%)
	27-31y	1207 (22.39%)	285 (18.41%)	76 (16%)	1568 (21.15%)
	> 31y	1222 (22.67%)	399 (25.78%)	107 (22.53%)	1728 (23.31%)
	Missing	142 (2.63%)	60 (3.88%)	22 (4.63%)	224 (3.02%)

Table 1. Descriptive statistics of variable of interest by ACEs in 7414 participants from the 1958 National Child Development Study.

Birth weight	Q1: Low weight	1082 (20.07%)	329 (21.25%)	118 (24.84%)	1529 (20.62%)
	Q2	1394 (25.86%)	405 (26.16%)	117 (24.63%)	1916 (25.84%)
	Q3	1327 (24.62%)	357 (23.06%)	110 (23.16%)	1794 (24.2%)
	Q4: High weight	1291 (23.95%)	351 (22.67%)	91 (19.16%)	1733 (23.37%)
	Missing	297 (5.51%)	106 (6.85%)	39 (8.21%)	442 (5.96%)
Parental SEC	I & II	1131 (20.98%)	195 (12.6%)	19 (4%)	1345 (18.14%)
	IIINM	536 (9.94%)	139 (8.98%)	35 (7.37%)	710 (9.58%)
	IIIM	2630 (48.79%)	748 (48.32%)	218 (45.89%)	3596 (48.5%)
	IV&V	914 (16.95%)	379 (24.48%)	171 (36%)	1464 (19.75%)
	Missing	180 (3.34%)	87 (5.62%)	32 (6.74%)	299 (4.03%)
Sibling order	Single child	478 (8.87%)	110 (7.11%)	22 (4.63%)	610 (8.23%)
Sising of del	Elder	1703 (31.59%)	367 (23.71%)	81 (17.05%)	2151 (29.01%)
	≥ 2	3022 (56.06%)	911 (58.85%)	312 (65.68%)	4245 (57.26%)
	– Missing	188 (3.49%)	160 (10.34%)	60 (12.63%)	408 (5.5%)
Parental smoking	Non smoker	1345 (24.95%)	223 (14.41%)	40 (8.42%)	1608 (21.69%)
	Smoker	3060 (56.76%)	977 (63.11%)	325 (68.42%)	4362 (58.83%)
	Missing	986 (18.29%)	348 (22.48%)	110 (23.16%)	1444 (19.48%)
Parental involvement	Mother = Father	3224 (59.8%)	709 (45.8%)	166 (34.95%)	4099 (55.29%)
	Mother > Father	1569 (29.1%)	407 (26.29%)	103 (21.68%)	2079 (28.04%)
	Father not	376 (6.97%)	173 (11.18%)	88 (18.53%)	637 (8.59%)
	Missing	222 (4.12%)	259 (16.73%)	118 (24.84%)	599 (8.08%)
Outdoor activities	Most weeks	4683 (86.87%)	1157 (74.74%)	310 (65.26%)	6150 (82.95%)
	Occasionally/hardly ever	506 (9.39%)	229 (14.79%)	110 (23.16%)	845 (11.4%)
	Missing	202 (3.75%)	162 (10.47%)	55 (11.58%)	419 (5.65%)
Reading activities	Most weeks	3126 (57.99%)	732 (47.29%)	160 (33.68%)	4018 (54.19%)
	Occasionally/hardly ever	2051 (38.04%)	651 (42.05%)	261 (54.95%)	2963 (39.96%)
	Missing	214 (3.97%)	165 (10.66%)	54 (11.37%)	433 (5.84%)
Housing deprivation	Advantaged	3714 (68.89%)	882 (56.98%)	200 (42.11%)	4796 (64.69%)
	Disadvantaged	1650 (30.61%)	664 (42.89%)	273 (57.47%)	2587 (34.89%)
	Missing	27 (0.5%)	2 (0.13%)	2 (0.42%)	31 (0.42%)
Leisure: parties	0: No parties	897 (16.64%)	214 (13.82%)	66 (13.89%)	1177 (15.88%)
	1	978 (18.14%)	244 (15.76%)	75 (15.79%)	1297 (17.49%)
	2	1333 (24.73%)	385 (24.87%)	114 (24%)	1832 (24.71%)
	3	1213 (22.5%)	350 (22.61%)	102 (21.47%)	1665 (22.46%)
	4: Lots of parties	642 (11.91%)	241 (15.57%)	73 (15.37%)	956 (12.89%)
	Missing	328 (6.08%)	114 (7.36%)	45 (9.47%)	487 (6.57%)
Conscientiousness	Score: med [p25-p75]	8 [6-10]	7 [5-9]	7 [5-9]	8 [6-10]
	Missing	275 (5.1%)	107 (6.91%)	24 (5.05%)	406 (5.48%)
Education level	A level	1450 (26.9%)	212 (13.7%)	30 (6.32%)	1692 (22.82%)
	O level	2292 (42.52%)	612 (39.53%)	151 (31.79%)	3055 (41.21%)
	No level	1591 (29.51%)	701 (45.28%)	288 (60.63%)	2580 (34.8%)
	Missing	58 (1.08%)	23 (1.49%)	6 (1.26%)	87 (1.17%)
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Employment	With employment	4174 (77.43%)	1075 (69.44%)	303 (63.79%)	5552 (74.89%)
	Unemployed	1163 (21.57%)	450 (29.07%)	166 (34.95%)	1779 (24%)
	Missing	54 (1%)	23 (1.49%)	6 (1.26%)	83 (1.12%)
Age 1st child	No child	4228 (78.43%)	1031 (66.6%)	276 (58.11%)	5535 (74.66%)
	Child [18-23y]	1039 (19.27%)	452 (29.2%)	174 (36.63%)	1665 (22.46%)
	Child < 18y	70 (1.3%)	42 (2.71%)	19 (4%)	131 (1.77%)
	Missing	54 (1%)	23 (1.49%)	6 (1.26%)	83 (1.12%)

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164 Individuals who had started smoking by age 16 or individuals with persistent smoking from 23 to 42 years were more likely to have experienced adversities during childhood, to have had 165 parents from a disadvantaged SEC (IIIM, IV&V), to have been younger siblings, to have had a 166 167 smoking parent, to have engaged occasionally or rarely in outdoor activities to have had fathers who were less involved in parenting than their mothers or even absent from family investment, 168 to have had occasionally or rarely reading activities, to have lived in poor material conditions 169 during childhood, to have attended a lot of parties and to have had a lower conscientiousness 170 score, compared to those who had never smoked. In addition, individuals with persistent 171 172 smoking from 23 to 42 years, compared to those who never smoked, generally had no level of education, were unemployed at 23y, and had a child born before 23y (Table 2A and Table 2B). 173

174 Table 2. Characteristics of study participants by (A) smoking initiation and (B) long-term smoking (n=7414).

		A. Smoking initiation			B. Long term smoking		
		Never smoked	Initiation by 16y	Initiation > 16y	Never smoked I	Persistent smokin	ng Heterogeneous
Variable	Level	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ACEs	None	1452 (79.3%)	1831 (65.14%)	2108 (76.05%)	1452 (79.3%)	794 (62.42%)	3145 (72.95%)
	One	300 (16.38%)	730 (25.97%)	518 (18.69%)	300 (16.38%)	353 (27.75%)	895 (20.76%)
	Two or more	79 (4.31%)	250 (8.89%)	146 (5.27%)	79 (4.31%)	125 (9.83%)	271 (6.29%)
Sex	Men	801 (43.75%)	1409 (50.12%)	1383 (49.89%)	801 (43.75%)	581 (45.68%)	2211 (51.29%)
	Women	1 030 (56.25%)	1402 (49.88%)	1389 (50.11%)	1 030 (56.25%)	691 (54.32%)	2 100 (48.71%)
Mother's age	≤ 23 y	443 (24.19%)	786 (27.96%)	681 (24.57%)	443 (24.19%)	382 (30.03%)	1085 (25.17%)
	24-27 y	496 (27.09%)	751 (26.72%)	737 (26.59%)	496 (27.09%)	347 (27.28%)	1141 (26.47%)
	27-31y	406 (22.17%)	555 (19.74%)	607 (21.9%)	406 (22.17%)	249 (19.58%)	913 (21.18%)
	> 31 y	441 (24.09%)	628 (22.34%)	659 (23.77%)	441 (24.09%)	257 (20.2%)	1030 (23.89%)
	Missing	45 (2.46%)	91 (3.24%)	88 (3.17%)	45 (2.46%)	37 (2.91%)	142 (3.29%)
Birth weight	Q1: Low weight	408 (22.28%)	589 (20.95%)	532 (19.19%)	408 (22.28%)	298 (23.43%)	823 (19.09%)
	Q2	507 (27.69%)	672 (23.91%)	737 (26.59%)	507 (27.69%)	323 (25.39%)	1086 (25.19%)
	Q3	414 (22.61%)	670 (23.83%)	710 (25.61%)	414 (22.61%)	304 (23.9%)	1076 (24.96%)

	Q4: High weight	406 (22.17%)	702 (24.97%)	625 (22.55%)	406 (22.17%)	272 (21.38%)	1055 (24.47%)
	Missing	96 (5.24%)	178 (6.33%)	168 (6.06%)	96 (5.24%)	75 (5.9%)	271 (6.29%)
Parental SEC	I & II	362 (19.77%)	432 (15.37%)	551 (19.88%)	362 (19.77%)	162 (12.74%)	821 (19.04%)
	IIINM	178 (9.72%)	241 (8.57%)	291 (10.5%)	178 (9.72%)	98 (7.7%)	434 (10.07%)
	IIIM	882 (48.17%)	1368 (48.67%)	1346 (48.56%)	882 (48.17%)	624 (49.06%)	2090 (48.48%)
	IV&V	353 (19.28%)	648 (23.05%)	463 (16.7%)	353 (19.28%)	332 (26.1%)	779 (18.07%)
	Missing	56 (3.06%)	122 (4.34%)	121 (4.37%)	56 (3.06%)	56 (4.4%)	187 (4.34%)
Sibling order	Single child	197 (10.76%)	188 (6.69%)	225 (8.12%)	197 (10.76%)	93 (7.31%)	320 (7.42%)
	Elder	608 (33.21%)	677 (24.08%)	866 (31.24%)	608 (33.21%)	320 (25.16%)	1223 (28.37%)
	≥ 2	928 (50.68%)	1796 (63.89%)	1521 (54.87%)	928 (50.68%)	789 (62.03%)	2528 (58.64%)
	Missing	98 (5.35%)	150 (5.34%)	160 (5.77%)	98 (5.35%)	70 (5.5%)	240 (5.57%)
Parental smoking	Non smoker	466 (25.45%)	437 (15.55%)	705 (25.43%)	466 (25.45%)	164 (12.89%)	978 (22.69%)
	Smoker	1044 (57.02%)	1766 (62.82%)	1552 (55.99%)	1044 (57.02%)	842 (66.19%)	2476 (57.43%)
	Missing	321 (17.53%)	608 (21.63%)	515 (18.58%)	321 (17.53%)	266 (20.91%)	857 (19.88%)
Parental involvement	Mother = Father	1052 (57.45%)	1496 (53.22%)	1551 (55.95%)	1052 (57.45%)	646 (50.79%)	2401 (55.69%)
	Mother > Father	500 (27.31%)	802 (28.53%)	777 (28.03%)	500 (27.31%)	383 (30.11%)	1196 (27.74%)
	Father not	147 (8.03%)	274 (9.75%)	216 (7.79%)	147 (8.03%)	123 (9.67%)	367 (8.51%)
	Missing	132 (7.21%)	239 (8.5%)	228 (8.23%)	132 (7.21%)	120 (9.43%)	347 (8.05%)

Outdoor activities	Most weeks	1536 (83.89%)	2272 (80.83%)	2342 (84.49%)	1536 (83.89%)	1027 (80.74%)	3587 (83.21%)
	Occasionally/hardly ever	194 (10.6%)	386 (13.73%)	265 (9.56%)	194 (10.6%)	173 (13.6%)	478 (11.09%)
	Missing	101 (5.52%)	153 (5.44%)	165 (5.95%)	101 (5.52%)	72 (5.66%)	246 (5.71%)
Reading activities	Most weeks	1061 (57.95%)	1421 (50.55%)	1536 (55.41%)	1061 (57.95%)	626 (49.21%)	2331 (54.07%)
	Occasionally/hardly ever	664 (36.26%)	1230 (43.76%)	1069 (38.56%)	664 (36.26%)	572 (44.97%)	1727 (40.06%)
	Missing	106 (5.79%)	160 (5.69%)	167 (6.02%)	106 (5.79%)	74 (5.82%)	253 (5.87%)
Housing deprivation	Advantaged	1233 (67.34%)	1685 (59.94%)	1878 (67.75%)	1233 (67.34%)	719 (56.53%)	2844 (65.97%)
	Disadvantaged	590 (32.22%)	1117 (39.74%)	880 (31.75%)	590 (32.22%)	550 (43.24%)	1447 (33.57%)
	Missing	8 (0.44%)	9 (0.32%)	14 (0.51%)	8 (0.44%)	3 (0.24%)	20 (0.46%)
Leisure: parties	0: No parties	424 (23.16%)	236 (8.4%)	517 (18.65%)	424 (23.16%)	128 (10.06%)	625 (14.5%)
	1	382 (20.86%)	367 (13.06%)	548 (19.77%)	382 (20.86%)	168 (13.21%)	747 (17.33%)
	2	479 (26.16%)	661 (23.51%)	692 (24.96%)	479 (26.16%)	306 (24.06%)	1047 (24.29%)
	3	316 (17.26%)	806 (28.67%)	543 (19.59%)	316 (17.26%)	340 (26.73%)	1009 (23.41%)
	4: Lots of parties	128 (6.99%)	541 (19.25%)	287 (10.35%)	128 (6.99%)	234 (18.4%)	594 (13.78%)
	Missing	102 (5.57%)	200 (7.11%)	185 (6.67%)	102 (5.57%)	96 (7.55%)	289 (6.7%)
Conscientiousness	Score: med [p25-p75]	9 [8-11]	7 [5-8]	9 [7-10]	9 [8-11]	7 [5-9]	8 [6-10]
	Missing	89 (4.86%)	165 (5.87%)	152 (5.48%)	89 (4.86%)	69 (5.42%)	248 (5.75%)
Education level	A level	588 (32.11%)	323 (11.49%)	781 (28.17%)	588 (32.11%)	138 (10.85%)	966 (22.41%)

	O level	788 (43.04%)	1040 (37%)	1227 (44.26%)	788 (43.04%)	463 (36.4%)	1804 (41.85%)
	No level	453 (24.74%)	1365 (48.56%)	762 (27.49%)	453 (24.74%)	670 (52.67%)	1457 (33.8%)
	Missing	2 (0.11%)	83 (2.95%)	2 (0.07%)	2 (0.11%)	1 (0.08%)	84 (1.95%)
Employment	With employment	1469 (80.23%)	1910 (67.95%)	2173 (78.39%)	1469 (80.23%)	865 (68%)	3218 (74.65%)
	Unemployed	362 (19.77%)	818 (29.1%)	599 (21.61%)	362 (19.77%)	407 (32%)	1010 (23.43%)
	Missing	0 (0%)	83 (2.95%)	0 (0%)	0 (0%)	0 (0%)	83 (1.93%)
Age 1st child	No child	1492 (81.49%)	1819 (64.71%)	2224 (80.23%)	1492 (81.49%)	796 (62.58%)	3247 (75.32%)
	Child [18-23y]	320 (17.48%)	830 (29.53%)	515 (18.58%)	320 (17.48%)	438 (34.43%)	907 (21.04%)
	Child < 18y	19 (1.04%)	79 (2.81%)	33 (1.19%)	19 (1.04%)	38 (2.99%)	74 (1.72%)
	Missing	0 (0%)	83 (2.95%)	0 (0%)	0 (0%)	0 (0%)	83 (1.93%)

Multivariate multinomial logistic regression results between ACEs and smoking initiation and 177 178 long-term smoking on the imputed data are presented in Figure 1. In all settings, individuals who had experienced one, or two or more ACEs had gradually a higher risk to initiate smoking 179 in adolescence and to have a persistent consumption in adulthood. The associations between 180 ACEs and smoking outcomes were maintained after adjustment for socioeconomic background 181 and confounding factors: participants who reported one, or two or more ACEs had consistently 182 higher risk to initiate smoking by age 16 (RRR= 1.89 [1.62; 2.2] for one ACE; RRR= 2.36 183 [1.81; 3.08] for two or more ACEs, Model 1) compared to those who have not experienced any 184 adversity. Similarly, participants who had experienced one ACE, or two or more had 185 186 consistently higher risk to be persistent smokers between 23 and 42 years old (RRR= 2.07 [1.73; 2.47] for one ACE, RRR= 2.59 [1.92; 3.49] for two or more ACEs, Model 1), compared to 187 those who had not experienced any adversity. 188

For both smoking outcomes, controlling for family factors or conscientiousness had the largest effect while controlling for parenting, material deprivation and social life had little effect on RRRs. Graded associations were observed across ACEs categories, only results for two or more ACEs will be detailed here.

The associations between ACEs and risk for smoking by 16y and persistent smoking between 193 ages 23 and 42 were similar in effect size and observed consistently after controlling for 194 intermediate factors of parenting, material deprivation or social life (RRR initiation by 16y=2.22 195 [1.69; 2.9], Model 1 + parental involvement; RRR initiation by 16y=2.27 [1.74; 2.96], Model 1 + 196 material living conditions; RRR initiation by 16y=2.38 [1.81; 3.13], Model 1 + social activities and 197 RRR persistent smoking =2.44 [1.8; 3.31], Model 1 + parental involvement; RRR persistent smoking =2.45 198 [1.81; 3.3], Model 1 + material living conditions; RRR persistent smoking =2.56 [1.89; 3.47], Model 199 200 1 +social activities).

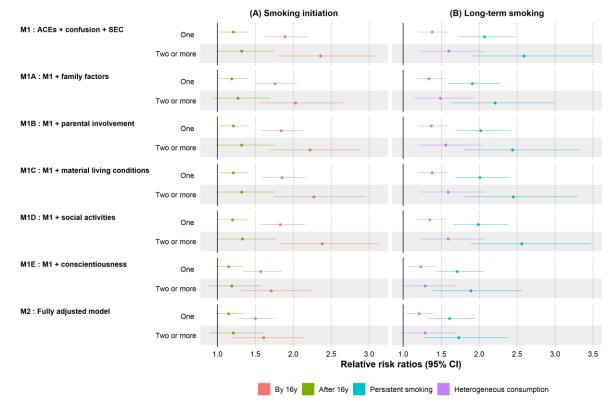
Observed RRRs between ACEs and both smoking outcomes were smaller in size after
controlling for family factors or personality variables (RRR initiation by 16y=2.03 [1.55; 2.66],
Model 1 + family factors; RRR initiation by 16y=1.71 [1.29; 2.26], Model 1 + conscientiousness ;
and RRR persistent smoking =2.21 [1.63; 2.99], Model 1 + family factors ; RRR persistent smoking =1.89
[1.38; 2.57], Model 1 + conscientiousness).
When all potential confounders and mediators were controlled for, ACEs remained associated
with smoking initiation by 16y and with persistent smoking (Model 2: RRR initiation by 16y = 1.5)

208 [1.27; 1.77] for one ACE; RRR initiation by $_{16y}$ = 1.61 [1.2; 2.15] for two or more ACEs; RRR

209 persistent smoking =1.61 [1.33; 1.95] for one ACE. RRR persistent smoking =1.73 [1.26; 2.38] for two or

210 more ACEs).

Figure 1: Relative risk ratios for (A) smoking initiation and (B) long-term smoking in 7 414 participants from the NCDS 58. Estimates are from multinomial logistic regression model where the never smoker group is the reference category. Models are adjusted for sex, mother's age, birthweight, parental SEC and each block of variables.



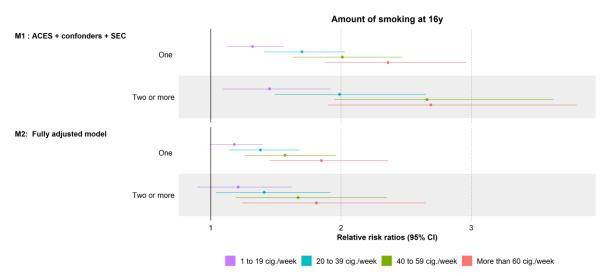
The additional analysis of the association between ACEs and the amount of smoking at 16y is presented in Figure 2. Individuals who experienced one, two or more adversities were more 217 likely to smoke a higher number of cigarettes, after adjustment for socioeconomic background 218 and baseline confounders. ACEs remained associated with smoking consumption \geq 20 219 cig./week when all potential confounders and mediators were controlled for.

Figure 2: Relative risk ratios for amount of smoking at 16y in 7 414 participants from the

221 NCDS 58. Estimates are from multinomial logistic regression model where the never smoker

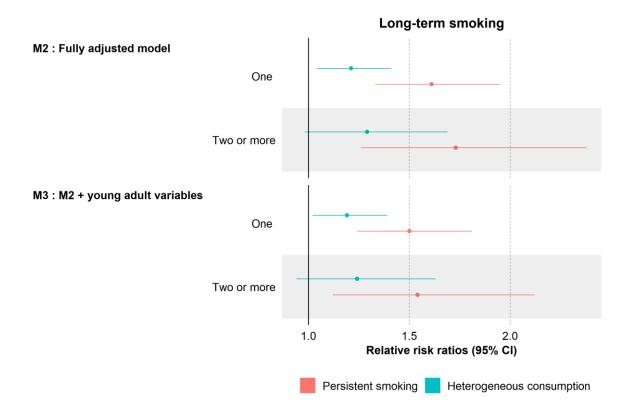
group is the reference category. Models are adjusted for sex, mother's age, birthweight, parental

223 SEC and each block of variables.



The additional analysis between long-term smoking and ACEs is presented in Figure 3. The association was attenuated when variables from the young adulthood life stage were added to the model, namely a low level of education, unemployment, a child born before 23y. However, ACEs remained associated with persistent smoking (Model 3, RRR _{persistent smoking} =1.50 [1.24; 1.81] for one ACE; RRR _{persistent smoking} = 1.54 [1.12; 2.12] for two or more ACEs).

Figure 3: Relative risk ratios for additional models adjusting for variables from the young adulthood life stage between ACEs and long-term smoking. Estimates are from multinomial logistic regression model where the never smoker group is the reference category. Models are adjusted for sex, mother's age, birthweight, parental SEC and each block of variables.



Supplemental Tables C.1; D.1; E.1 and F.1 in Appendices contain the results of these figurespresented in table format.

235 Discussion

In this prospective UK cohort, in which 20.9% of individuals experienced one adversity in 236 childhood and 6.4% two or more, we found evidence that these exposures were associated in a 237 graded fashion with smoking outcomes. Children who experienced one, or two or more 238 adversities had a consistently higher risk of initiating smoking in adolescence, to smoke heavily 239 at 16y and to smoke persistently thereafter. These findings are consistent with a previous study 240 where adverse childhood experiences were strongly associated with smoking initiation, heavy 241 smoking and subsequent persistence (11). The associations between ACEs and risk for smoking 242 initiation, amount of smoking at 16y and persistent smoking were weaker when adjusting for 243 childhood mediating factors. Family factors and conscientiousness were the strongest 244 245 contributors to the risk of smoking initiation and persistence associated with ACEs. ACEs remained associated with persistent smoking after adjusting for education level, age at first 246

child and employment. These findings suggest that ACEs should be examined as an important
upstream determinant of initiation and maintenance of smoking. Our results offer several
insights with respect to previous studies.

250

251 Growing evidence indicates that exposure to toxic stress early in life can lead to mood dysregulation in childhood which can in turn result in the initiation and persistence of smoking. 252 253 Anxiety, anger, or depression, may induce early smoking initiation, as smoking provides an immediate pharmacological or psychological benefit in coping with the strain of life's stressors. 254 using the reward circuit and dopamine delivery (6,43). Beyond the benefit of dopamine, 255 nicotine intake can lead to structural modifications of the brain that are also strongly implicated 256 in the mechanisms of addiction (4). Early smoking initiation during adolescence, which may be 257 258 a period when the physiological effects of nicotine are exacerbated (44) and brain systems exhibit plasticity, can have lasting effects into adulthood leading to nicotine dependence and 259 260 persistent smoking. In addition, exposure to toxic stress early in life may result in alterations in 261 various biological systems and neural circuits (45), including emotional processing of threat and reward, and may therefore induce increased nicotine susceptibility (46). Therefore, early 262 smoking combined with exposure to toxic stress in early life can cumulatively lead to a higher 263 overall susceptibility to nicotine addiction (46). Additionally, nicotine intake can increase the 264 onset of anxiety disorders (47) in turn, reinforcing the need for nicotine to reduce them, while 265 worsening these anxiety disorders over time in a vicious circle of interdependence (48). 266 Subsequently, individuals with anxiety or stress disorders are less likely to overcome craving 267 and smoking withdrawal symptoms, which promotes the maintenance of smoking addiction 268 269 (49).

Our *a priori* assumption was that early life socioeconomic position could modulate the effects
of ACEs on smoking behaviour, since disadvantaged socioeconomic background has been

identified as a determinant of smoking behaviour (50). Our results highlighted that socioeconomic background plays a minimal role in the association between ACEs and the smoking (Appendices Table G.1) in agreement with previous studies (51,52).

Among the five blocks of variables investigated in the present study, the most important potential pathways identified were family factors and conscientiousness. To establish mechanisms and mediation, further analyses using causal inference approaches are required.

Later in the life course, early parenthood, low level of education and unemployment, played a role in explaining the association between persistent smoking and ACEs, consistent with previous findings (50). Based on our results, we hypothesize that these factors may contribute to a chain of risk exposing individuals to chronic stress with consequences for their wellbeing in adulthood. The association between ACEs and persistent smoking were maintained after adjustment for early adulthood variables.

284

285 There are several limitations in this study. First, the measurement of ACEs may be limited as it only considers the child's circumstances at ages 7, 11, and 16, combining different indicators 286 with different potential effects. However, this measure captures severe circumstances that we 287 288 hypothesized as being chronically stressful. Misclassification bias may have occurred in relation to adversity categories, namely when considering the sensitive nature of the questions. 289 290 For this reason, we constructed the ACEs variable conservatively. Second, attrition is a problem in cohort studies, increasing the potential for selection bias in the remaining sample. We dealt 291 with this by carrying out multiple imputation of missing data, a recommended method to avoid 292 293 the interpretation of biased results. Third, it is also possible that we misclassified individuals when constructing the smoking initiation and long-term smoking variables due to the self-294 reported nature of the data. Furthermore, the construction of the smoking variable at age 23 295

took into account those who smoked cigars, pipes, and resulted in a heterogeneous group of 296 individuals in the current smoking category. However, sensitivity analyses showed similar 297 results for this group, justifying their inclusion. We used parental occupation at birth to control 298 299 for socioeconomic background. Other results could have been obtained using other socioeconomic variables. However, additional analyses (not reported here) showed that other 300 301 socioeconomic measures, such as parental education and family income, had little effect in the association between ACEs and smoking. Finally, we may have overlooked variables or 302 assumptions contributing to the relationship between ACEs and smoking initiation and long-303 term smoking. Therefore, it is probable that residual confounding factors are present, and that 304 305 our estimates of the impact of ACEs on smoking are overestimated.

The strengths of this study lie in its prospective design, with a large sample size and data collected in great detail and across the life course, allowing us to control for numerous confounding and mediating variables to understand the causal sequence of events. While many studies examine early adversity using retrospective questions, which are subject to recall bias, we used prospective information on ACEs.

311

Using longitudinal prospective data covering 42 years of the life course, in a large sample from a representative cohort study, we provide evidence that stressful events during childhood are strong determinants of smoking initiation and long-term smoking, independently of the socioeconomic background. Our results emphasize the importance of considering ACEs in smoking prevention and the need for targeted prevention for adolescents, from all socioeconomic groups, who have experienced adversity.

318

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- 323

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