THE LANCET
Public Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Syed S, Howe LD, Lacey RE, et al. Adverse childhood experiences in firstborns and mental health risk and health-care use in siblings: a population-based birth cohort study of half a million children in England. *Lancet Public Health* 2025; **10:** e111–23.

Table of content

eTable 1. Information on data sources used

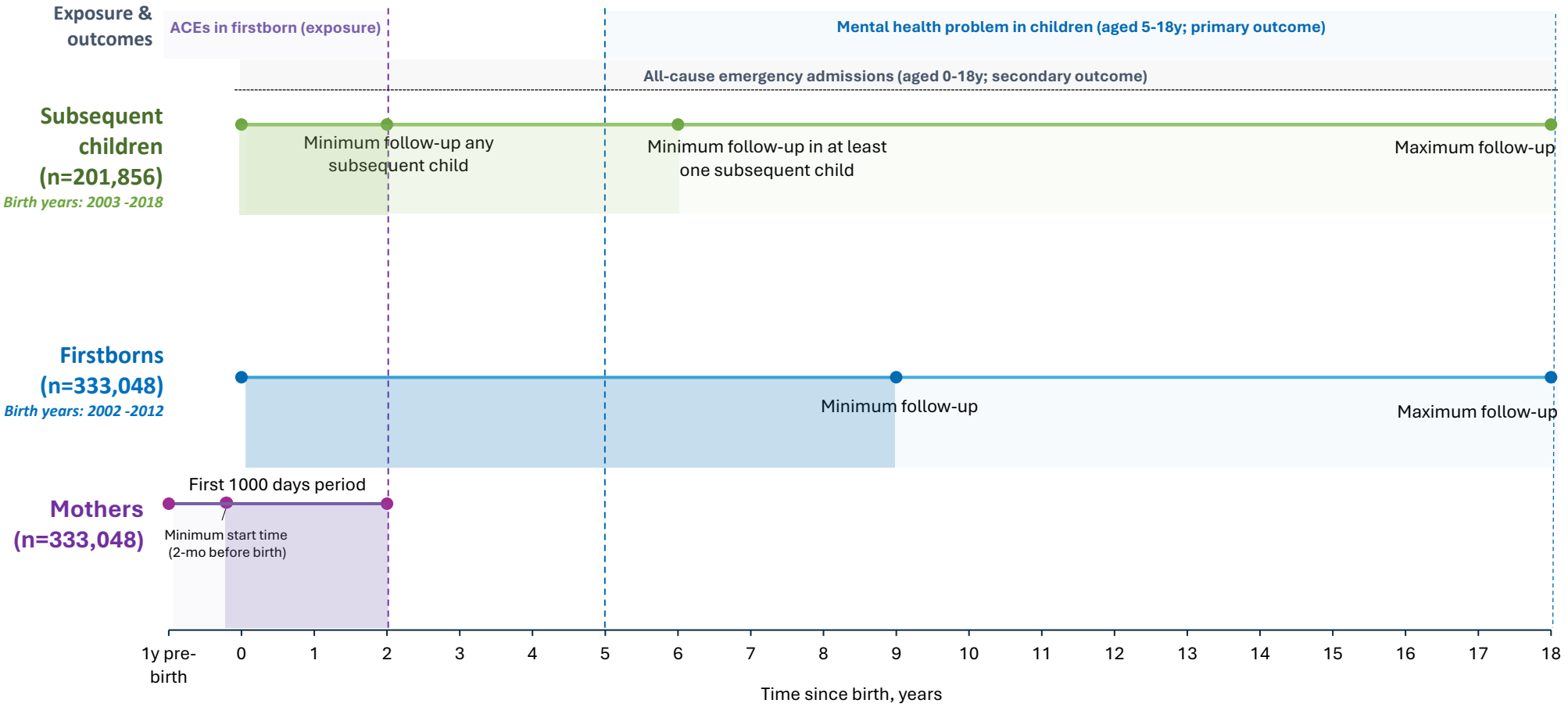
Data source & procedures	Description of the study population
Primary care: Clinical Practice Research Datalink (CPRD) GOLD[1] & Aurum,[2] CPRD Mother Baby Link (CPRD-MBL)[3-5]	We derived a population-based birth cohort of mothers and children using the mother-baby-link (MBL) from the Clinical Practice Research Datalink (CPRD). The CPRD GOLD[1] and CPRD Aurum[2] are primary care GP databases containing anonymised patient data from approximately 20%-25% of the UK population and broadly represent the general population. Over 99% of the English population are registered with a GP.[6] The data is recorded during routine visits or opportunistically during patient care.[3,7] Mothers and children in Aurum and GOLD are linked via practice-specific family IDs and birth and maternity variables. This *"mother-baby link"* forms a sub-cohort of CPRD (CPRD-MBL), with data refreshed every other year. This study used the CPRD-MBL GOLD (2022)[5] and the CPRD-MBL Aurum 2023.[4] We defined first-time mothers as those without a previous live birth recorded in the complete CPRD-MBL (births 1987-2020) or the HES-APC maternity file (1997-2020).
Coding system	CPRD data is recorded via SNOMED, Read codes (converted to *"medcodes"* by CPRD), Gemscript product codes (mainly medication/prescriptions), BNF codes, and additional data fields linked to a code, including birthweight, test results, data from self-report measures, referrals, quantities, frequency etc. We have previously developed cross-mapped code lists for ascertaining ACEs using Aurum data. We cross-compare tabulations of ACE indicators in CPRD GOLD vs Aurum, revealing consistent prevalences across both data sources.
Linkage	A subset of English general practices in the CPRD-MBL GOLD and Aurum has consented to link patient-level data to other existing data sources, including HES-APC, IMD 2015 and ONS. Most practices (1647/1755; 93.8%) and mother-child pairs (856,916/936,669; 91.5%) in the CPRD-MBL could be linked to HES and ONS data sources. **Follow-up restrictions** In the CPRD, patient follow-up is limited to the duration of their registration with a practice in the CPRD Aurum and GOLD databases.[1,2] This restriction means that follow-up time is limited to the patient's date of de-registration from the practice. As a result, follow-up time varied depending on the linked data source. All children were followed across all sources (CPRD-AURUM, CPRD-GOLD, HES A&E, HES OP, HES-APC, and ONS) from April 2007 (when children born in 2002 reached age 5) until March 2020 (the latest available HES A&E data). Follow-up using CPRD, HES APC, and ONS covered the whole study period, from April 1, 2001, to March 31, 2020.
Specific follow-up period	**Minimum follow-up period:** Mothers: 2 months before birth to 2-year post-birth Firstborns: within 6 months of birth to 9-years post-birth Subsequent child: within 6 months of birth to 2-years post-birth At least one subsequent child: within 6 months of birth to 6-years post-birth **Maximum follow-up period:** Mothers*:* 1-year before birth to 2-years post-birth Firstborns: birth to 18-years post-birth Subsequent child: birth to 18-years post-birth **Maximum date range of data:**

	Main analysis: 2001-04-1 to 2020-03-31 *Sensitivity analysis:* 2012-04-01 to 2020-03-31.
Secondary care: Hospital Episode Statistics Admitted Patient Care (HES-APC)[8]	We linked CPRD GOLD and Aurum to the Hospital Episodes Statistics Admitted Patient Care (HES-APC). HES-APC contains data on all NHS-funded hospital admissions in England, including over 97% of all births.[8] The data is coded professionally using individual discharge summaries written by the treating clinician and compiled as a database.[9]
Coding system[9]	Discharge summaries are transferred to clinical hospital coders who convert the information into ICD-9/10 and OPCS-3/4 codes according to national clinical coding standards. HES-APC contains additional admission-specific data on birth characteristics (birth weight, parity etc.), maternal age, discharge destination (e.g. psychiatric inpatient unit, foster care, death etc.), etc.[8,9]
Ethnicity	HES-APC includes data on patient ethnicity, recorded for each hospital episode and categorised into broader groups.[8,10] Whilst most patients have consistent ethnicity across episodes, variations occur for some. CPRD provides linked HES-APC data with a single ethnicity per patient, derived by prioritising the most frequent recording (as detailed elsewhere).[10] This study combines CPRD and HES-APC data to refine ethnicity into five categories consistent with the National Office for Statistics formatting and National Census Ethnic group classification 6a in England.[11]
Specific follow-up period	**Minimum follow-up period:** 1 year before birth to 18 years post-birth (follow-up not dependent on GP registration) **Maximum follow-up period:** As above. **Maximum date range of data:** 2001-04-01 to 2020-03-31.
HES Accident & Emergency (A&E)[12]	We linked CPRD GOLD and Aurum to the HES Accident and Emergency (HES-A&E) and the HES Outpatient (HES OP) dataset.[12] HES-A&E contains data from all NHS-funded A&E services in England, including Type 1 (most resource-intensive with full resuscitation facilitates), Type 2, Type 3, Type 4 departments (less resource intensive) and urgent care centres with more than an average of 50 attendances per week.
Coding system[9]	HES&AE provides coded data directly entered by practitioners linked to the A&E attendance. The data includes diagnoses, treatments and investigations coded via ICD-10 codes A&E specific coding systems.[9] A smaller set of services also used Read and Snomed codes for some diagnoses. We used all the coded A&E data and have updated corresponding code lists at www.ACEsinEHRs.com to include relevant HES-A&E and HES-OP-specific codes.
Data quality	Overall data quality and consistency in HES-A&E increased over time (62%-74% attendances captured 2007-2011; 74%-86% attendances captured 2012-2016), as it was collected on an experimental basis until 2012. Data coverage in HES-A&E increased from 2018-19. However, the data completeness for several key fields (not used in this study) has been reduced since the phased introduction of the new Emergency Care Data Set (ECDS) commenced in October 2017.
Specific follow-up period	**Minimum/Maximum follow-up period:** 5 to 18-years post-birth (follow-up not dependent on GP registration) **Maximum date range of data collection:** 2007-04-01 to 2020-03-31
HES Outpatient (OP)[13] Coding system[9]	HES-OP contains individual records of all English NHS-funded outpatient appointments.[13]

Specific follow-up period	Each record details the attendance type, service speciality (e.g., *"Addiction Service*"; "*Adult Mental Health Service").*, primary diagnosis, main procedures and interventions.[9] **Minimum/ Maximum follow-up period:** 5 to 18-years post-birth (follow-up not dependent on GP registration) **Maximum date range of data collection:** 2003-04-01 to 2020-03-31
National English data sources:	The Index of Multiple Deprivation (IMD) 2019 is the official measure of relative deprivation for small areas in England. The IMD is derived from a composite score from seven domains (e.g. average income, crime rates etc.) for each Lower Layer Super Output Area (LSOA) in England (small areas/neighbourhoods). The IMD for each area is ranked against all other areas in England. Patients are linked to their corresponding *"small area"* and IMD by postcode. The ranked IMD for each area can be divided into IMD quantiles from 1 (least deprived) to 5 (most deprived).
Index of Multiple Deprivation (IMD) 2019[14]	
Specific follow-up period	**Minimum/maximum follow-up period:** NA **Maximum date range of data collection:** 2019 (Static)
Office for National Statistics (ONS) Death registrations[15,16]	The ONS mortality register contains records of all deaths and causes of death in England.[15,16]
Coding system	ICD-9 codes (<2001) or ICD-10 codes (>2000) are linked to a primary cause of death, with up to 15 other coded causes (and/or up to 8 neonatal causes of death).[15,16]
Specific follow-up period	**Minimum follow-up period:** 1 year before birth up to 18-years post-birth (follow-up not dependent on GP registration) **Maximum follow-up period:** 1 year before birth up to 18-years post-birth **Maximum date range of data collection:** 2001-04-01 to 2020-03-31
Resources & tools	
Cardiovascular disease research using linked bespoke studies and electronic health records (CALIBER)[17,18]	This study was carried out as part of the CALIBER© resource. CALIBER, led by the University College London Institute of Health Informatics, is a research resource providing validated electronic health record phenotyping algorithms and tools for national structured data sources. More information can be found at: https://portal.caliberresearch.org/
Adverse childhood experiences in Electronic health records (ACEsinEHRs).[19]	This study used validated domains, indicators, and code lists to identify adverse childhood experiences (ACEs) in electronic health records (EHRs). All accompanying code lists and algorithms are available at www.acesinehrs.com

Abbreviations: OPCS-4=Operating procedure codes, version 4; ICD-10/9=International classification of diseases, 10th/9th revision, BNF=British National Formulary Dictionary of Medicines and Devices

eFigure 1. Timeline of follow-up time and data availability for cohorts in the study



eFigure 1 shows the cohort's available follow-up time since birth. Firstborns were singleton first births between April 1, 2002, and April 2012, with a minimum of 9-year follow-up time and a maximum of 18 years of follow-up. Subsequent children were born between 2003 and 2018. Of these, at least one subsequent child had a minimum 6-year follow-up time. Mothers follow-up time ranged from one year (minimum two months) before birth to two years after birth. Follow-up time varied depending on the linked data source and the specific analysis (eTable 1). For the primary outcome (mental health problems): All children were followed across all sources (CPRD-AURUM, CPRD-GOLD, HES A&E, HES OP, HES-APC, and ONS) from April 2007 (when children born in 2002 reached age 5) until March 2020 (the latest available HES A&E data). For the main exposure (ACEs in firstborns): Follow-up was restricted to data available in CPRD, HES APC, and ONS, which covered the whole study period, from April 1, 2001, to March 31, 2020. For secondary outcomes relating to all-cause emergency admissions, children were followed from birth up to 18 years without any restrictions in HES-APC across the whole study period, from April 1, 2001, to March 31, 2020. ACEs=Adverse childhood experiences. HES-APC=Hospital Episode Statistics Admitted Patient Care.

eTable 2. Proportion of mothers with any child with MHP according to specific ACE domain and indicator in the firstborn

ACE domain and indicator associated with the firstborn child and their mother	Overall (n=333,048)	No MHP (n=267,107)	Any MHP (n=65,941)
Any ACE in firstborn	123573 (37.1%)	92527 (34.6%)	31046 (47.1%)
Adverse family environments (AFEs)	48,424 (14.5%)	36458 (13.6%)	11966 (18.1%)
Parental problems with daily living and work	10417 (3.1%)	7772 (2.9%)	2645 (4.0%)
Family disruptions and parental conflicts, NOS	9577 (2.9%)	6963 (2.6%)	2614 (4.0%)
Unwanted or concealed pregnancy (including attempted abortion)	6663 (2.0%)	5174 (1.9%)	1489 (2.3%)
Health visitors' increasing concern	5256 (1.6%)	3981 (1.5%)	1275 (1.9%)
Family is cause for concern	4543 (1.4%)	3288 (1.2%)	1255 (1.9%)
Housing problems effects of deprivation and refugees (excl homelessness)	2920 (0.9%)	2041 (0.8%)	879 (1.3%)
Family parental support referral	3253 (1.0%)	2441 (0.9%)	812 (1.2%)
Parental separation	3793 (1.1%)	2991 (1.1%)	802 (1.2%)
Parent with legal problems	2025 (0.6%)	1517 (0.6%)	508 (0.8%)
High-risk antenatal psychosocial presentation	1599 (0.5%)	1199 (0.4%)	400 (0.6%)
Psychosocial health problem with lower-level intervention	1230 (0.4%)	871 (0.3%)	359 (0.5%)
Parental learning or intellectual disability	442 (0.1%)	288 (0.1%)	154 (0.2%)
Vulnerable family NOS (incl. mother on CPA)	463 (0.1%)	331 (0.1%)	132 (0.2%)
Increased concerns regarding parental incapacity	436 (0.1%)	317 (0.1%)	119 (0.2%)
Maternal mental health problems (MHPs)	72075 (21.6%)	51736 (19.4)	20339 (30.8%)
Depression	50767 (15.2%)	35841 (13.4%)	14926 (22.6%)
Anxiety disorders	22245 (6.7%)	15911 (6%)	6334 (9.6%)
Referred/seen by a mental health professional	19039 (5.7%)	13184 (4.9%)	5855 (8.9%)
Mental health problems NOS	7827 (2.4%)	5703 (2.1%)	2124 (3.2%)
Sleep-wake disorders	3767 (1.1%)	2690 (1%)	1077 (1.6%)
Self-harm or suicide attempts	2799 (0.8%)	1900 (0.7%)	899 (1.4%)
Psychosis (incl. mental health sections)	2560 (0.8%)	1768 (0.7%)	792 (1.2%)
Personality disorders	1776 (0.5%)	1100 (0.4%)	676 (1.0%)
Eating disorders	1406 (0.4%)	955 (0.4%)	451 (0.7%)
Post-traumatic stress disorder (incl. Acute stress disorder)	1192 (0.4%)	829 (0.3%)	363 (0.6%)
Neurodevelopmental conditions and conduct disorders	418 (0.1%)	277 (0.1%)	141 (0.2%)
Maternal substance misuse (SM)	14,209 (4.3%)	10636 (4.0%)	3573 (5.4%)
Severe alcohol misuse	5033 (1.5%)	3735 (1.4%)	1298 (2.0%)
Moderate drug misuse (all other)	6863 (2.1%)	5406 (2.0%)	1457 (2.2%)
Severe drug misuse (likely dependence levels)	4221 (1.3%)	3735 (1.1%)	1298 (2.1%)
High-risk presentations of maltreatment in children	24794 (7.4%)	18264 (6.8%)	6530 (10.0%)
Non-attendance of child appointments (3 appts within 2 years)	15208 (4.6%)	11387 (4.3%)	3821 (5.8%)
Failure to thrive (eg, excessive thirst, suspected malnutrition)	3983 (1.2%)	2576 (1.0%)	1407 (2.1%)
Superficial injuries of head, neck or multiple body parts	3201 (1.0%)	2450 (0.9%)	751 (1.1%)
Bruising and contusions (multiple body parts)	2215 (0.7%)	1625 (0.6%)	590 (0.9%)
Child harm by undetermined intent and rare injuries and life-threatening events, incl. retinal haemorrhages, drownings, SUDI, injury by firearm etc	1488 (0.4%)	1059 (0.4%)	429 (0.7%)
Child maltreatment (CM)	6418 (1.9%)	4538 (1.7%)	1880 (2.9%)
CM NOS (incl physical or sexual abuse)	3608 (1.1%)	2527 (0.9%)	1081 (1.6%)
Social service involved (incl parental imprisonment criminal activity)	2244 (0.7%)	1656 (0.6%)	588 (0.9%)
Child protection safeguarding	1613 (0.5%)	1074 (0.4%)	539 (0.8%)
Intimate partner violence (IPV)	4264 (1.3%)	2664 (0.9%)	1600 (2.4%)

IPV NOS incl physical sexual abuse	2902 (0.9%)	2012 (0.8%)	890 (1.3%)
Mother assaulted NOS hospital admission only	2732 (0.8%)	1882 (0.7%)	850 (1.3%)

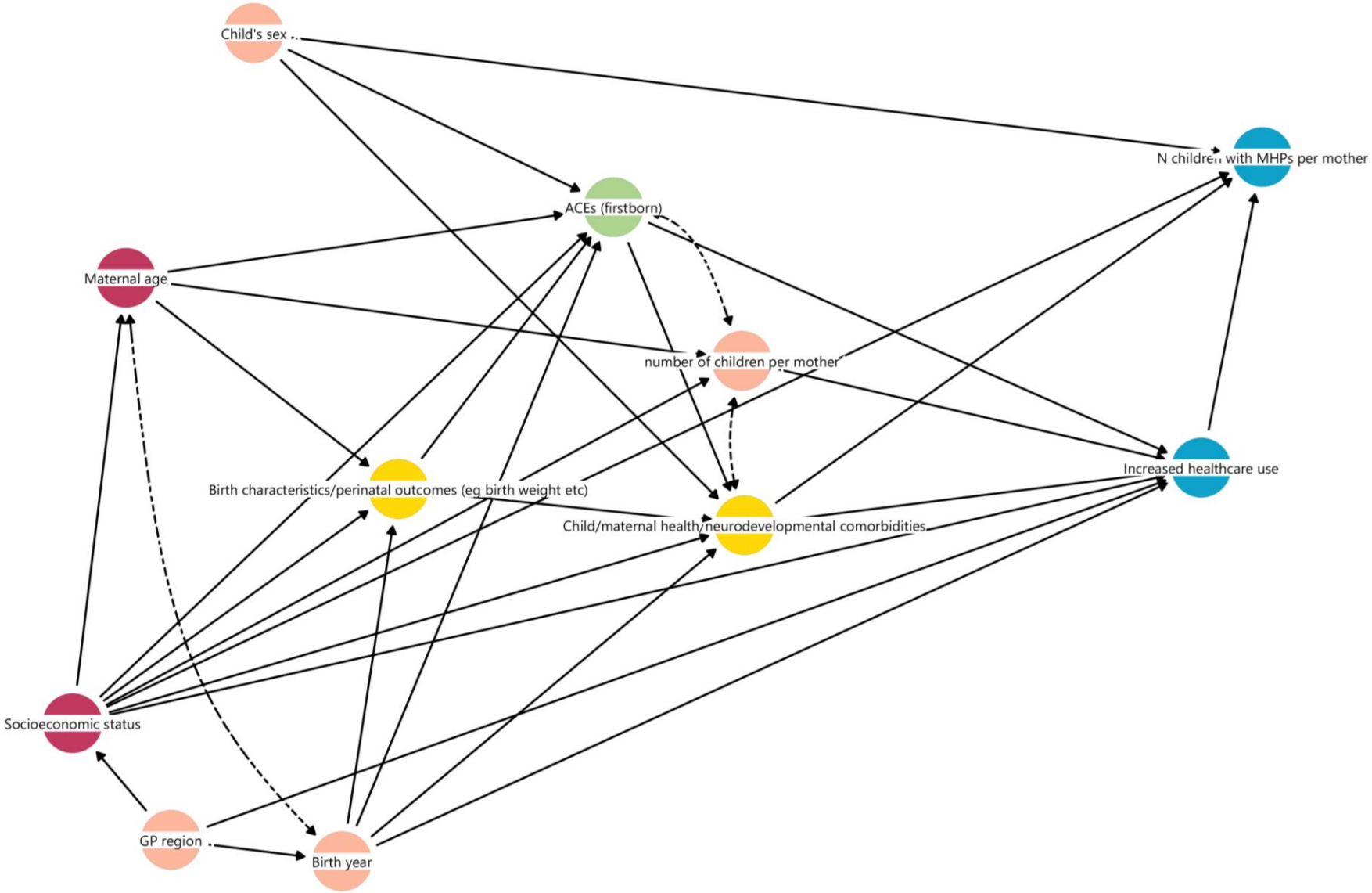
* Indicators were not mutually exclusive. Firstborns could be counted in multiple indicators, but only once per indicator or domain. We restricted disaggregation of ACE domain-specific indicators to indicators present in 100 or more unique firstborns and first-time mothers. Indicators are ordered by ascending prevalence, high to low. †Neurodevelopmental disorders include ADHD, autism spectrum disorders, and conduct disorders. ‡Medications, interventions, and psychiatric symptoms were combined into appropriate disorder clusters using validated algorithms.[19] §Indicators are defined by multiple rule-based algorithms, including age restrictions in years (upper age cut-off denoted in brackets), exclusions of accidental injuries, genetic predispositions (eg, bone diseases), traumatic birth injuries, transmissions of diseases from mother to child during birth, or need to meet higher cut-off score on a validated self-report instrument. All code lists and algorithms are freely available online (www.ACEsinEHRs.com).[19] ACEs=adverse childhood experiences, AFE= Adverse family environment, CM=Child maltreatment, CPA=Care programme approach, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse, SUDI=Sudden unexpected death in infancy, NOS=Not otherwise specified.

eTable 3. Odds ratios for variables used to calculate inverse probability weights to account for selection bias and censoring (n=1,195,933 first-time mothers and firstborns)*

Predictor of loss-to-follow-up	Odds ratio (95% CI)	Robust Std	z
Birthweight, g	1.00 (1.00-1.00)	0.0000	-4.41
Gestational age, weeks	0.99 (0.99-1.00)	0.0013	-5.39
Number of days mother enrolled before first birth	1.00(1.00-1.00)	0.0000	-211.14
Older maternal age, years	0.96 (0.96-0.96)	0.0004	-100.51
Congenital anomaly (yes/no)	1.15 (1.09-1.24)	0.0390	4.33
Firstborn being male	1.00 (1.00-1.01)	0.0048	0.86
Index of multiple deprivation			
1 (least deprived)	Ref		
2	1.17 (1.15-1.19)	0.0087	20.84
3	1.30 (1.28-1.32)	0.0099	34.88
4	1.41 (1.39-1.43)	0.0108	44.44
5	1.50 (1.48-1.52)	0.0118	51.34
Region of general practice			
East midlands	Ref		
East of England	0.90 (0.87-0.93)	0.0182	-6.03
London	0.47 (0.46-0.50)	0.0169	-5.65
North East	0.43 (0.41-0.44)	0.0103	-34.25
North West	0.60 (0.58-0.62)	0.0080	-45.55
South Central	0.62 (0.59-0.64)	0.0112	-27.31
South West	0.48 (0.46-0.50)	0.0118	-25.31
West Midlands	0.64 (0.61-0.67)	0.0090	-39
Yorkshire & The Humber	0.88 (0.85-0.92)	0.0142	-20.02
ACEs in firstborn			
Adverse family environments	1.14 (1.12-1.15)	0.0074	19.58
Maternal mental health problems	1.03 (1.01-1.04)	0.0060	4.23
Maternal substance misuse	1.14 (1.11-1.16)	0.0121	11.89
Child maltreatment	1.22 (1.16-1.28)	0.0306	8.02
Intimate partner violence	1.13 (1.09-1.17)	0.0198	6.90

*We modelled all estimates using inverse probability weights (IPWs),[20,21] to account for potential selection bias from excluding 862,885 first-time mothers with a firstborn with less than nine years follow-up, mother-child pairs who registered with a GP later than two months before birth, mother-child pairs who could not be followed to their second birthday (see figure 1 in main paper). eTable 3 shows the predictor and auxiliary variables used to calculate IPWs to predict any of the above listed exclusion criteria.

eFigure 2. Directed acyclic graph (DAG) of hypothesised associations between ACEs in firstborns and the number of children with MHPs per mother



This DAG provides an overview of the hypothesised causal relationships between ACEs in firstborns (exposure; green node) and the number of children with MHPs per mother (primary outcome; blue node) and increased healthcare use (secondary outcomes; blue node). The DAG does not represent an exhaustive list of variables and shows only variables considered in our primary analysis. Yellow nodes indicate associations blocked by adjustment for other variables (red and light red nodes).[22] Solid arrows represent direct associations, while dashed arrows indicate bidirectional associations.

eMethods 1. Supplementary information on statistical analyses, model adjustments and assumptions

As shown in the directed acyclic graph (DAG, eFigure 2), our primary analysis examined the association between ACEs in firstborns (exposure; green node) and the number of children (aged 5-18 years) with MHPs per mother (primary outcome; blue node) using weighted and adjusted negative binomial regression models. We repeated the analysis in the sibling-sub cohort (efigure 1) to estimate secondary outcomes, including the total number of mental health-related healthcare contacts and all-cause emergency admissions among children stratified by different ages.

Model adjustments

All models in the primary analysis were adjusted for the following variables (represented by light red nodes in the DAG):

- Firstborn's birth year: To account for variations of health care professionals' recording practices of ACEs and prevalences and trends of MHPs over time.
- Region of general practice (GP): To control for regional variations in healthcare access, service provision, and recording and prevalence of ACEs.[23,24]
- Firstborn's sex: To adjust for potential differences in ACE exposure and MHP risk between boys and girls.
- Number of children per mother: to adjust for larger family sizes, which may influence the likelihood of ACEs (due to family resource strain), having a child with MHPs and more interactions with healthcare services, increasing the chances of recordings (e.g. surveillance bias).
- Total person-years contributed by all children per mother: To account for varying observation time and calculate the incidence rate of MHPs, adjusting for differences in family size and follow-up time.

In a second adjustment step, we included the following variables (represented by red nodes in the DAG eFigure 2):

- Socioeconomic status (index of multiple deprivation, IMD): to explore the extent to which upstream factors explain the observed associations in the primary analysis. Lower socioeconomic status is a well-established risk factor for ACEs and child mental health problems,[25] and it's a variable hypothesised to be associated with both the exposure (ACEs) and the outcome (child MHPs). In this study, we used the index of multiple deprivation (IMD) as an indicator of neighbourhood deprivation and wider systemic risk factors that influence access to resources, quality of parenting, and exposure to family stressors etc.
- Maternal age at first birth: we added maternal age as an additional adjustment to control for socioeconomic factors and covariates related to maternal age (teenage pregnancies, or risk of adverse perinatal outcomes in older mothers),[26] as the IMD represent neighbourhood deprivation and not a measure of direct measure of the mother's social deprivation.

Other variables not directly adjusted for

The yellow nodes show hypothesised variables blocked by model 1 and 2 adjustments, including birth characteristics and adverse perinatal outcomes (e.g. low birth weight, congenital anomalies, low gestational age). Maternal mental health problems and child neurodevelopmental conditions can be both a consequence of ACEs (e.g. substance use during pregnancy associated with increased incidence of neurodevelopmental conditions) and a risk factor for further MHPs in the family.

Statistical model assumptions

We used a negative binomial regression model over a Poisson model due to overdispersion to analyse primary and secondary outcomes relating to incidence rate ratios and estimated marginal means. We checked the Poisson model assumption of no overdispersion by examining the distribution of the primary outcome using histograms. The variance (SD= 0.455) of the primary outcome was larger than the mean (0.216), suggesting overdispersion in the data. We then compared the model fit of a Poisson model with a negative binomial model using a likelihood ratio test. The likelihood ratio test (χ^2 = 306.85, p<0.001) showed that the negative binomial model better fit the data.

For the secondary analysis (i.e. unit of analysis was children) in the sibling-sub cohort (children with siblings only), we used adjusted and weighted Cox-proportional hazard models to examine the association between firstborns with ACEs and time to first recorded MHP in any child. We checked Model assumptions for Kaplan-Meier estimates were checked using log-log plots and Schoenfeld's residuals, which showed the proportional hazards assumption was met based on Schoenfeld's residuals (range for different ACE domains: $\chi2(1)$=0.52 to 3.64, range p=0.469 to 0.057).

Secure server. We conducted all analyses on UCL's secure analytic server (Data Safe Haven; certified to ISO27001 information security standards) using Stata 18 and R (version 4.4.0; complete list of R packages available online).

Theoretical models

Theoretical models underpinning our analytic predictions and variable selections have been described in previous linked studies[19,26,27] and are available at www.acesinehrs.com, with an overview of risk and protective factors of ACEs available at CDC.

eTable 4. Number of children born to mothers in the primary birth cohort by ACE exposure in firstborn

	Overall cohort (n=333,048 families)	Firstborn number of ACEs				
		No ACE (n=209,475)	Any ACE (n=123,573)	1 ACE (n=87,337)	2 ACEs (n=27,380)	≥3 ACEs (n=8,856)
Total number of children						
Median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)
Range (min-max)	1.0-9.0	1.0- 9.0	1.0-8.0	1.0-8.0	1.0-8.0	1.0-7.0
Mean (SD)	1.6 (0.7)	1.6 (0.7)	1.6 (0.7)	1.6 (0.7)	1.6 (0.8)	1.6 (0.8)
1 child	171897 (51.6%)	106030 (50.6%)	65867 (53.3%)	46056 (52.7%)	14879 (54.3%)	4932 (55.7%)
2 children	127277 (38.2%)	82803 (39.5%)	44474 (36.0%)	32279 (37.0%)	9444 (34.5%)	2751 (31.1%)
≥3 children	33874 (10.2%)	20642 (9.9%)	13232 (10.7%)	9002 (10.3%)	3057 (11.2%)	1173 (13.2%)

eTable 5. Prevalences of child-specific mental health problems (aged 5-18 years) among first-time mothers (n=333,048) with and without a firstborn exposed to ACEs

Mental health problem*	Overall (n=333,048 mothers)	Firstborn without ACEs (n=209,475)	Firstborn with ACEs (n=123,573)	Age of onset years, median (IQR)
Any mental health problem	65941 (19.8%)	34895 (16.7%)	31046 (25.1%)	8.67 (5.16)
Referred to or seen by a mental health professional (tier≥ 3 services)	41127 (12.3%)	21404 (10.2%)	19723 (16.0%)	12.27 (3.90)
Mental health problems not otherwise specified (NOS)	16331 (4.9%)	7514 (3.6%)	8817 (7.1%)	7.29 (3.54)
Any anxiety or trauma-related disorder	17293 (5.2%)	9333 (4.5%)	7960 (6.4%)	11.65 (5.70)
Anxiety disorder, NOS†	16199 (4.9%)	8661 (4.1%)	7538 (6.1%)	13.73 (5.81)
Obsessive-compulsive disorders†	995 (0.3%)	556 (0.3%)	439 (0.4%)	13.44 (4.88)
Panic disorder (including agoraphobia or health anxiety)	835 (0.3%)	416 (0.2%)	419 (0.3%)	14.87 (3.66)
Post-traumatic stress disorder (including acute stress disorder)†	632 (0.2%)	307 (0.1%)	325 (0.3%)	14.12 (6.31)
Neurodevelopmental conditions and conduct disorders (with an associated mental health-related referral or intervention)‡	17773 (5.3%)	8815 (4.2%)	8958 (7.2%)	7.50 (3.92)
Autism spectrum disorder	8892 (2.7%)	4466 (2.1%)	4426 (3.6%)	7.67 (3.87)
ADHD or conduct disorder	6572 (2.0%)	3118 (1.5%)	3454 (2.8%)	8.26 (3.96)
Depression†	6118 (1.8%)	3164 (1.5%)	2954 (2.4%)	14.38 (2.56)
Self-harm or suicide attempts	6138 (1.8%)	3289 (1.6%)	2849 (2.3%)	14.73 (3.25)
Sleep-wake disorders†	4747 (1.4%)	2337 (1.1%)	2410 (2.0%)	8.90 (6.67)
Substance use any	3823 (1.1%)	1926 (0.9%)	1897 (1.5%)	15.39 (2.49)
Moderate drug misuse (all other)	1811 (0.5%)	956 (0.5%)	855 (0.7%)	14.63 (2.00)
Severe drug misuse (likely dependence)	3108 (0.9%)	1522 (0.7%)	1586 (1.3%)	14.94 (1.93)
Severe alcohol misuse (including self-report measures of ≥35/≥50 alcohol units per week)†	279 (0.1%)	161 (0.1%)	118 (0.1%)	15.78 (2.53)
Eating disorders	2858 (0.9%)	1574 (0.8%)	1284 (1.0%)	11.62 (5.96)
Anorexia nervosa	1670 (0.5%)	951 (0.5%)	719 (0.6%)	12.56 (7.23)
Eating disorders, NOS (excluding Anorexia nervosa)	1422 (0.4%)	771 (0.4%)	651 (0.5%)	13.98 (6.53)
Personality disorders (eg, borderline personality disorder)	220 (0.1%)	100 (0.0%)	120 (0.1%)	15.02 (1.65)
Psychosis (including mental health sections NOS)	675 (0.2%)	337 (0.2%)	338 (0.3%)	14.62 (5.24)

*Indicators are not mutually exclusive. A child could be counted in multiple indicators, but only once per indicator and only once for any mental health problem. We restricted the disaggregation of specific mental health problems to indicators present in 100 or more children. Estimates are ordered by ascending prevalence, high to low. †Mental health indicators are defined by multiple rule-based algorithms, including the need to meet a higher cut-off score on a validated self-report instrument or the need for the presence of symptoms combined with an intervention or referral and minimum age restrictions to minimise misclassification (self-harm ≥7 years, personality disorders ≥12 years, psychosis ≥10 years, substance use ≥12 years). Medications, interventions, and psychiatric symptoms were combined into appropriate disorder clusters using validated algorithms.[19] ‡ Recorded neurodevelopmental conditions only retained when also associated with a mental health-related referral or intervention (i.e. could not alone meet criteria for a mental health problem). All code lists and algorithms are freely available online (www.ACEsinEHRs.com)[19] ADHD=Attention-deficit hyperactivity disorder, NOS=Not otherwise specified.

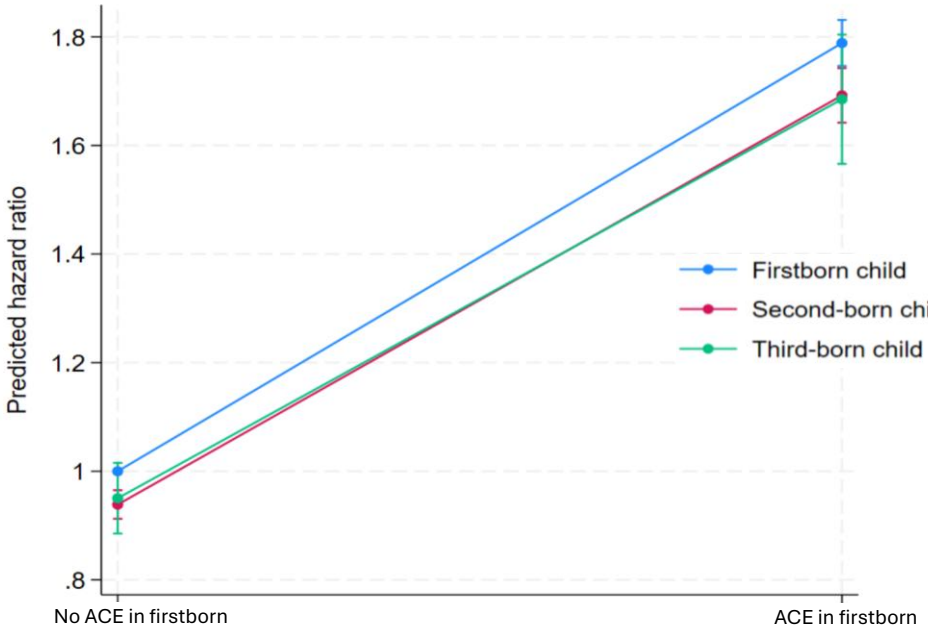
eTable 6. Incidence rate ratios and the mean number of subsequent children with mental health problems per mother (excluding firstborns in the outcome) by firstborn exposure to ACEs (n=333,048)

	MHPs in children (primary outcome)		MHPs in children, excluding firstborns (secondary outcome)	
	Mean n children with MHP per 100 mothers (95% CI)	**IRR (95% CI)**	**Mean n children with MHP per 100 mothers (95% CI)**	**IRR (95% CI)**
Firstborn exposure				
No Ace	17.3 (17.2-17.5)	Ref	5.93 (5.85-6.01)	Ref
Any ACE	29.8 (29.4-30.1)	1.7 (1.7-1.7)	9.64 (9.5-9.79)	1.63 (1.59-1.66)
AFEs	28.9 (28.4-29.4)	1.4 (1.4-1.4)	9.78 (9.55-10.01)	1.44 (1.4-1.47)
Maternal MHPs	33.5 (33.1-34.0)	1.8 (1.8-1.8)	10.93 (10.73-11.13)	1.73 (1.7-1.77)
Maternal SM	32.6 (31.5-33.6)	1.5 (1.4-1.4)	9.52 (9.08-9.95)	1.33 (1.27-1.4)
HRP-CM	31.8 (31.0-32.5)	1.5 (1.5-1.6)	9.8 (9.48-10.12)	1.39 (1.35-1.44)
CM	38.3 (36.7-39.9)	1.8 (1.7-1.9)	12.47 (11.73-13.2)	1.75 (1.64-1.85)
IPV	37.8 (36.0-39.6)	1.8 (1.7-1.9)	12.34 (11.55-13.12)	1.72 (1.62-1.84)
Number of ACEs in firstborn				
0	17.3 (17.1-17.5)	Ref	5.92 (5.84-6.01)	Ref
1	26.3 (26.0-26.7)	1.5 (1.5-1.5)	8.72 (8.56-8.88)	1.47 (1.44-1.51)
2	35.7 (34.9-36.4)	2.0 (2.0-2.1)	11.58 (11.24-11.92)	1.95 (1.89-2.02)
≥3	45.3 (43.8-46.8)	2.6 (2.5-2.7)	13.67 (13-14.33)	2.31 (2.19-2.43)

Data are adjusted and inverse probability weighted incidence rate ratios and mean number of children with MHPs by ACEs in firstborn. Means are expressed as the number of children per 100 first-time mothers. All estimates were adjusted for birth year, practice region, firstborn's sex, and number of children per mother.
ACEs=adverse childhood experiences, AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

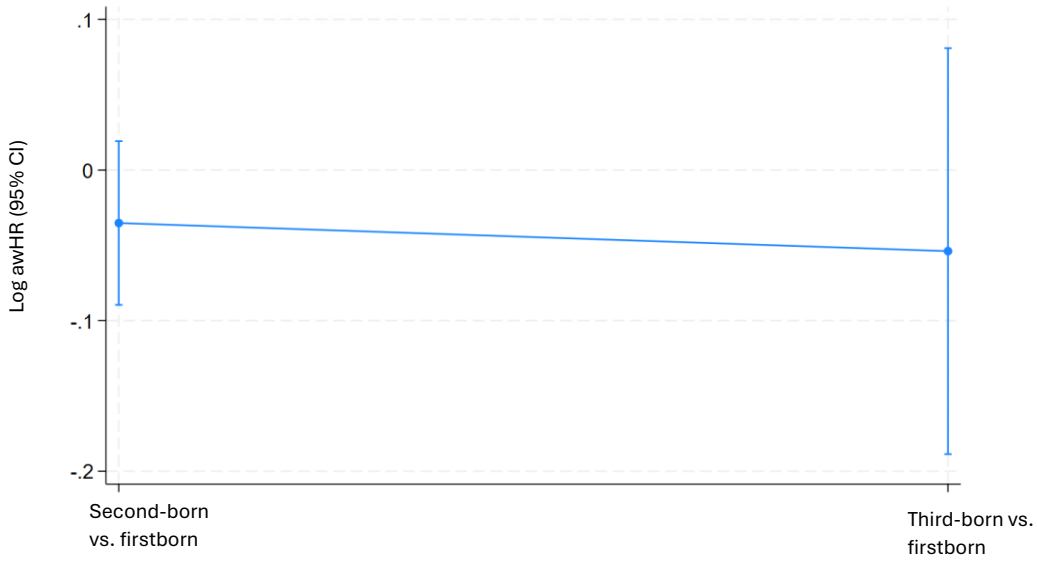
eFigure 3. Marginal plots comparing MHP risk between different siblings considering firstborn exposure to ACEs in the sibling-sub cohort (n=355,898)

(A) Marginal interaction plot showing the predictive margins of the adjusted hazard ratios for mental health problems in children and ACEs in firstborns



	Predicted marginal awHR (95 %CI)*
Firstborn child	1.79 (1.75-1.83)
Second-born child	1.69 (1.64-1.74)
Third-born child	1.69 (1.57-1.80)

(B) Marginal effects plot showing the estimated relative difference in the log-adjusted weighted hazard ratio between second-born vs firstborn child (left), and third-born vs firstborn child (right)



Comparison	Predicted marginal awHR (95 %CI)*	P-value for comparison
Second-born vs. firstborn	0.965 (0.914-1.019)	0.205
Third-born vs. firstborn	0.948 (0.828-1.084)	0.434

eFig 3A shows the margins plot of interaction for the predicted marginal awHRs of MHPs in second-born and third-born children when firstborns were exposed to ACEs compared to those who were not. The relatively parallel lines suggest that the effect of having a firstborn exposed to ACEs is relatively consistent across different birth orders. The vertical lines represent 95% confidence intervals.

eFig 3B shows the estimated margins of the relative difference[28] in log the awHR (log[HR]) of MHP between second-born vs. first-born and third-born vs. first-born children in families where the firstborn experienced ACEs using the sibling-sub cohort (n=355,898). Vertical lines represent 95% confidence intervals. *Predictive margins of the adjusted weighted hazard ratios (awHR) and corresponding 95% confidence intervals for each sibling comparison.

Interpretative text eFig3 B. *Second-born vs. firstborn. the hazard ratio of 0.965 suggests that the hazard of MHP for second-born children is slightly lower (by 3.5%) than that of firstborn children in families where the firstborn experienced ACEs. However, the confidence interval (0.914, 1.019) includes 1, indicating no statistically significant difference. Third-born vs. firstborn: Similarly, the hazard ratio of 0.948 suggests a slightly lower hazard of MHP for third-born children compared to firstborn children (a 5.2% reduction). Again, the confidence interval (0.828, 1.084) includes 1, signifying no statistically significant difference. Overall, results suggest that there was a similar MHP risk across siblings in families with a firstborn with ACEs.*

All estimates were adjusted for birth year, practice region, birth year, firstborn's sex and number of children per mother. ACEs=adverse childhood experiences, awHZ= adjusted and inverse probability weighted hazard ratios.

eTable 7. (A) Mental health-related healthcare contacts and (B) all-cause emergency admissions among children aged 0-18 years to mothers with and without a firstborn with ACEs by sibling order (firstborn, second born, third-born)

	Overall				No ACE in firstborn			ACE in firstborn		
	Firstborn (N=161151)	**Second born (N=161,126)**	**Third-born (N=33,621)**	**All children (n=355,898)**	**Firstborn (n=103,445)**	**Second born (N=103,428)**	**Third born (N=20,502)**	**Firstborn (N=57,706)**	**Second born (N=57,698)**	**Third born (N=13,119)**
Total person-years at-risk*										
CPRD (primary care)	2,207,588.8	1,675,992.9	278,757.8	3,747,526.3	1,313,399.7	976,698.4	148,245.4	710,020.7	511,097.1	880,64.9
HES (secondary care, hospital data)	2,023,420.4	1,487,795.5	236,310.3	4,162,339.5	1,432,067.2	1,098,118.0	174,216.2	775,521.7	577,874.9	104,541.6
(A) Mental health related										
Number of children with at least one contact										
Any GP or hospital	27422 (17.0%)	14138 (8.8%)	1703 (5.1%)	43263 (12.2%)	14622 (14.1%)	7633 (7.4%)	881 (4.3%)	12800 (22.2%)	6505 (11.3%)	822 (6.3%)
GP consultations	23914 (14.8%)	11771 (7.3%)	1328 (3.9%)	37013 (10.4%)	12602 (12.2%)	6233 (6.0%)	668 (3.3%)	11312 (19.6%)	5538 (9.6%)	660 (5.0%)
Any hospital contact	11116 (6.9%)	5961 (3.7%)	788 (2.3%)	17865 (5.0%)	5860 (5.7%)	3289 (3.2%)	413 (2.0%)	5256 (9.1%)	2672 (4.6%)	375 (2.9%)
Hospital admissions	5342 (3.3%)	3014 (1.9%)	469 (1.4%)	8825 (2.5%)	2651 (2.6%)	1633 (1.6%)	245 (1.2%)	2691 (4.7%)	1381 (2.4%)	224 (1.7%)
A&E attendance	4463 (2.8%)	3511 (2.2%)	640 (1.9%)	8614 (2.4%)	2297 (2.2%)	1894 (1.8%)	318 (1.6%)	2166 (3.8%)	1617 (2.8%)	322 (2.5%)
Outpatients	5473 (3.4%)	2668 (1.7%)	290 (0.9%)	8431 (2.4%)	2873 (2.8%)	1468 (1.4%)	147 (0.7%)	2600 (4.5%)	1200 (2.1%)	143 (1.1%)
Children's total number of healthcare contacts										
Any GP or hospital	189280	73957	8148	271385	91156	37734	4135	98124	36223	4013
GP consultations	141684	55066	6024	202774	68930	27538	2972	72754	27528	3052
Any hospital contact	65578	26318	2870	94766	30538	14013	1544	35040	12305	1326
Hospital admissions	12263	6107	943	19313	4936	3229	576	7327	2878	367
A&E attendance	5610	3930	673	10213	2797	2120	327	2813	1810	346
Outpatients	49510	18767	1815	70092	23637	9981	913	25873	8786	902
(B) All-cause emergency admissions by age groups										
Number of children with at least one admission										
0-18y	91572 (56.8%)	81258 (50.4%)	16209 (48.2%)	189039 (53.1%)	55108 (53.3%)	49661 (48.0%)	9287 (45.3%)	36464 (63.2%)	31597 (54.8%)	6922 (52.8%)
0-5y	68126 (42.3%)	66972 (41.6%)	14302 (42.5%)	149400 (42.0%)	39651 (38.3%)	40207 (38.9%)	8070 (39.4%)	28475 (49.3%)	26765 (46.4%)	6232 (47.5%)
5-12y	41392 (25.7%)	28644 (17.8%)	4331 (12.9%)	74367 (20.9%)	24651 (23.8%)	17623 (17.0%)	2542 (12.4%)	16741 (29.0%)	11021 (19.1%)	1789 (13.6%)
12-18	12937 (8.0%)	3484 (2.2%)	153 (0.5%)	16574 (4.7%)	7951 (7.7%)	2271 (2.2%)	100 (0.5%)	4986 (8.6%)	1213 (2.1%)	53 (0.4%)
Children's total number of admissions										
0-18y	258259	210526	42916	511701	139265	123897	24172	118994	86629	18744
0-5y	147082	148678	33887	329647	77428	85591	18719	69654	63087	15168
5-12y	84904	55473	8753	149130	46691	34211	5318	38213	21262	3435
12-18	26273	6375	276	32924	15146	4095	135	11127	2280	141

* Follow-up time varied by data source (eTable 1). For CPRD (primary care), follow-up began at birth and ended at the earliest practice deregistration, last data collection date, death, study end date, or 18th birthday, whichever came first. For any of the HES data sources (hospital data, secondary care), follow-up began at birth and ended at the earliest of death, study end date, or 18th birthday, whichever came first. When combining CPRD and HES data, follow-up ended at the earliest date as per CPRD criteria. Follow-up time in CPRD is determined by the child's registration with a practice, while HES data captures all NHS-funded hospital admissions, A&E visits, and outpatient appointments.

eTable 8. Adjusted weighted IRRs and mean number of primary and secondary care mental health-related health care contacts among children aged 5-18 years born to mothers with firstborns exposed to ACEs (sibling sub cohort, n=355,898 children)

Any data source: GP, hospital admissions, A&E, outpatient (children aged 5-18y)				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACE	61.86 (59.51-64.22)	48.8 (46.04-51.55)	40.22 (33.69-46.76)	56.64 (54.84-58.43)
Any ACE	128.02 (122.91-133.14)	94.03 (88.52-99.53)	69.57 (58.72-80.42)	114.33 (110.39-118.27)
AFEs	127.63 (119.76-135.5)	87.98 (80.48-95.48)	78.83 (60.9-96.75)	112.42 (106.45-118.4)
Maternal MHPs	147.68 (140.31-155.05)	111.8 (103.94-119.66)	84.06 (67.78-100.34)	132.95 (127.29-138.61)
Maternal SM	158.56 (136.81-180.31)	91.18 (76.59-105.77)	50.41 (26.95-73.87)	131.57 (116.44-146.71)
HRP-CM	152.61 (138.56-166.65)	97.26 (84.65-109.86)	67.9 (46.97-88.83)	130.52 (120.21-140.83)
CM	194.58 (161.71-227.44)	152.09 (119.16-185.02)	127.13 (52.71-201.55)	177.57 (152.34-202.8)
IPV	171.85 (142.67-201.02)	138.63 (108.4-168.86)	79.95 (30.25-129.64)	156.09 (134.48-177.7)
Number of ACEs in firstborn				
1	107.62 (102.41-112.84)	83.2 (77.3-89.1)	58.13 (47.15-69.12)	97.53 (93.45-101.62)
2	167.67 (155.03-180.32)	117.57 (104.91-130.23)	94.88 (66.3-123.46)	148.24 (138.58-157.9)
≥3	228.39 (194.61-262.17)	158.57 (130.85-186.28)	128.16 (72.98-183.35)	201.36 (176.85-225.87)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	2.07 (1.96-2.19)	1.52 (1.41-1.63)	1.12 (0.96-1.32)	2.07 (1.96-2.19)
AFEs	1.63 (1.52-1.75)	1.12 (1.02-1.23)	1.01 (0.80-1.27)	1.63 (1.52-1.75)
Maternal MHPs	2.12 (2.00-2.25)	1.60 (1.48-1.74)	1.21 (0.99-1.47)	2.12 (2.00-2.25)
Maternal SM	1.92 (1.67-2.21)	1.10 (0.94-1.30)	0.61 (0.38-0.97)	1.92 (1.67-2.21)
HRP-CM	1.90 (1.73-2.10)	1.21 (1.06-1.39)	0.85 (0.62-1.16)	1.90 (1.73-2.10)
CM	2.33 (1.96-2.77)	1.82 (1.46-2.27)	1.52 (0.85-2.74)	2.33 (1.96-2.77)
IPV	2.04 (1.72-2.43)	1.65 (1.32-2.06)	0.95 (0.51-1.77)	2.04 (1.72-2.43)
Number of ACEs in firstborn				
1	1.75 (1.64-1.86)	1.35 (1.24-1.47)	0.94 (0.78-1.15)	1.75 (1.64-1.86)
2	2.72 (2.50-2.97)	1.91 (1.70-2.14)	1.54 (1.14-2.09)	2.72 (2.50-2.97)
≥3	3.71 (3.18-4.32)	2.58 (2.15-3.08)	2.08 (1.35-3.21)	3.71 (3.18-4.32)
Primary care only: CPRD Aurum & CPRD GOLD (general practice; children aged 5-18y)				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACE	47.05 (45.08-49.02)	35.55 (33.37-37.74)	28.3 (23.15-33.45)	42.43 (40.96-43.9)
Any ACE	94.9 (90.96-98.84)	70.88 (66.26-75.51)	51.37 (42.58-60.15)	85.04 (81.94-88.14)
AFEs	96.94 (90.44-103.45)	67.81 (61.32-74.29)	63.2 (47.14-79.27)	85.73 (80.78-90.68)
Maternal MHPs	109.55 (104.02-115.09)	83.49 (77-89.99)	62.83 (49.73-75.92)	98.75 (94.4-103.1)
Maternal SM	116.07 (101.79-130.35)	73.57 (60.52-86.62)	39.97 (18.48-61.46)	98.41 (87.79-109.04)
HRP-CM	109.48 (99.31-119.64)	72.77 (61.87-83.67)	44.19 (28.36-60.01)	94.84 (86.95-102.72)
CM	147.75 (123.01-172.49)	119.37 (90.35-148.38)	99.29 (38.09-160.49)	136.06 (116.22-155.91)
IPV	131.41 (108.36-154.47)	114.76 (86.69-142.84)	53.29 (12.92-93.66)	122.14 (104.31-139.98)
Number of ACEs in firstborn				
1	46.8 (44.84-48.76)	35.69 (33.5-37.89)	29.02 (23.73-34.3)	42.39 (40.92-43.86)
2	79.73 (75.56-83.9)	61.59 (56.74-66.43)	40.92 (32.77-49.06)	72.08 (68.82-75.34)
≥3	125.25 (115.2-135.3)	89.87 (78.96-100.77)	74.69 (49.8-99.58)	111.47 (103.72-119.22)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	2.02 (1.9-2.14)	1.51 (1.39-1.63)	1.09 (0.91-1.3)	2.02 (1.9-2.14)
AFEs	1.65 (1.53-1.78)	1.16 (1.04-1.28)	1.08 (0.83-1.39)	1.65 (1.53-1.78)
Maternal MHPs	2.08 (1.96-2.22)	1.59 (1.45-1.73)	1.19 (0.96-1.48)	2.08 (1.96-2.22)
Maternal SM	1.87 (1.65-2.12)	1.18 (0.99-1.42)	0.64 (0.38-1.1)	1.87 (1.65-2.12)
HRP-CM	1.77 (1.6-1.95)	1.17 (1.01-1.37)	0.71 (0.5-1.02)	1.79 (1.62-1.97)
CM	2.36 (1.99-2.8)	1.9 (1.49-2.44)	1.58 (0.85-2.94)	2.36 (1.99-2.8)
IPV	2.08 (1.74-2.49)	1.82 (1.42-2.33)	0.84 (0.4-1.8)	2.08 (1.74-2.49)
Number of ACEs in firstborn				
1	1.7 (1.59-1.82)	1.32 (1.2-1.44)	0.87 (0.71-1.07)	1.7 (1.59-1.82)
2	2.68 (2.44-2.93)	1.92 (1.69-2.19)	1.6 (1.14-2.24)	2.68 (2.44-2.93)
≥3	3.54 (3.08-4.06)	2.76 (2.26-3.38)	2.14 (1.32-3.47)	3.54 (3.08-4.06)

Data are adjusted and inverse-probability-weighted incidence rate ratios and mean number of children with mental health problems (MHPs) per 100 mothers by ACEs in firstborn. Adjusted for birth year, practice region, firstborn sex, and number of children per mother. AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 9. Adjusted weighted IRRs and mean number of hospital-related mental health-related contacts among children aged 5-18 years born to mothers with firstborns exposed to ACEs (sibling sub-cohort, n=355,898 children)

Hospital contact only: Hospital admission, A&E attendance, OP attendance (children aged 5-18y)				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACE	19.97 (18.84-21.1)	18.71 (16.95-20.47)	16.72 (12.56-20.89)	19.45 (18.51-20.38)
Any ACE	45.22 (42.01-48.42)	33.88 (30.74-37.01)	26.37 (19.76-32.98)	40.92 (38.48-43.36)
AFEs	43.19 (39.16-47.22)	29.79 (26.18-33.4)	22.36 (16.5-28.22)	38.09 (35.09-41.1)
Maternal MHPs	51.83 (47.02-56.63)	40.53 (36.06-45)	31.3 (20.78-41.81)	47.42 (43.86-50.98)
Maternal SM	59.35 (41.66-77.04)	24.97 (19.04-30.9)	19.32 (10.19-28.45)	46.83 (34.94-58.72)
HRP-CM	58.39 (48.54-68.25)	33.04 (26.6-39.47)	25.02 (15.56-34.48)	49.03 (41.9-56.15)
CM	63.75 (42.4-85.11)	50.33 (33.12-67.54)	39.42 (2.15-76.68)	58.5 (43.11-73.89)
IPV	55.49 (37.23-73.76)	33.5 (23.37-43.63)	31.85 (4.36-59.33)	47.54 (35.06-60.02)
Number of ACEs in firstborn				
0	19.89 (18.77-21.01)	18.76 (17-20.53)	17.07 (12.82-21.33)	19.43 (18.49-20.37)
1	37.81 (34.72-40.89)	31.51 (27.91-35.1)	24.62 (16.4-32.83)	35.33 (32.83-37.83)
2	59.82 (52.47-67.16)	41.3 (34.83-47.77)	31.63 (18.84-44.42)	52.95 (47.35-58.55)
≥*3*	82.97 (56.45-109.49)	41.16 (31.71-50.6)	35.99 (15.32-56.65)	68.11 (50.37-85.85)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	2.26 (2.07-2.48)	1.70 (1.51-1.90)	1.32 (1.02-1.71)	2.26 (2.07-2.48)
AFEs	1.63 (1.47-1.82)	1.13 (0.98-1.29)	1.13 (0.98-1.29)	1.63 (1.47-1.82)
Maternal MHPs	2.24 (2.02-2.49)	1.76 (1.55-1.99)	1.76 (1.55-1.99)	2.24 (2.02-2.49)
Maternal SM	2.15 (1.59-2.09)	0.90 (0.71-1.15)	0.90 (0.71-1.15)	2.15 (1.59-2.90)
HRP-CM	2.20 (1.85-2.62)	1.25 (1.02-1.53)	1.25 (1.02-1.53)	2.20 (1.85-2.62)
CM	2.27 (1.61-3.18)	1.79 (1.27-2.53)	1.79 (1.27-2.53)	2.27 (1.61-3.18)
IPV	1.96 (1.40-2.73)	1.18 (0.87-1.61)	1.18 (0.87-1.61)	1.96 (1.40-2.73)
Number of ACEs in firstborn				
1	1.90 (1.72-2.10)	1.58 (1.39-1.81)	1.24 (0.88-1.74)	1.90 (1.72-2.10)
2	3.01 (2.62-3.45)	2.08 (1.75-2.46)	1.59 (1.05-2.40)	3.01 (2.62-3.45)
≥*3*	4.17 (3.02-5.76)	2.07 (1.63-2.62)	1.81 (1.01-3.23)	4.17 (3.02-5.76)
Hospital admissions only (children aged 5-18y)				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACE	3.53 (3.19-3.87)	3.89 (3.47-4.32)	5.23 (3.47-6.99)	3.74 (3.49-3.99)
Any ACE	9.94 (8.27-11.6)	6.84 (5.75-7.92)	5.77 (4.35-7.19)	8.64 (7.52-9.77)
AFEs	8.16 (7.23-9.09)	6.09 (5.16-7.03)	5.2 (3.49-6.9)	7.27 (6.65-7.9)
Maternal MHPs	9.67 (7.13-12.22)	7.54 (6.49-8.6)	5.88 (4.27-7.49)	8.72 (7.25-10.2)
Maternal SM	15.28 (2.58-27.98)	5.19 (4-6.37)	4.33 (1.89-6.77)	11.15 (3.67-18.63)
HRP-CM	22.18 (14.79-29.57)	9.05 (5.22-12.87)	7.02 (3.89-10.15)	16.82 (11.72-21.93)
CM	15.72 (4.95-26.49)	7.25 (4.97-9.52)	7.33 (2.73-11.93)	12.28 (5.74-18.82)
IPV	7.39 (5.74-9.04)	6.68 (4.47-8.89)	4.16 (0.91-7.41)	6.97 (5.69-8.25)
Number of ACEs in firstborn				
0	3.51 (3.17-3.84)	3.91 (3.49-4.33)	5.4 (3.6-7.21)	3.74 (3.49-3.99)
1	8.23 (6.95-9.51)	6.36 (5.07-7.66)	5.56 (4.06-7.06)	7.45 (6.32-8.58)
2	11.02 (9.45-12.6)	8.28 (6.7-9.86)	7.15 (4.06-10.24)	9.88 (8.76-11)
≥*3*	25.63 (5.23-46.03)	8.57 (6.17-10.97)	6.35 (3.12-9.59)	18.76 (6.59-30.94)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	2.81 (2.33-3.4)	1.94 (1.57-2.39)	1.63 (1.23-2.17)	2.81 (2.33-3.4)
AFEs	1.5 (1.27-1.77)	1.12 (0.9-1.39)	0.96 (0.67-1.36)	1.5 (1.27-1.77)
Maternal MHPs	1.99 (1.52-2.62)	1.56 (1.31-1.85)	1.21 (0.92-1.61)	1.99 (1.52-2.62)
Maternal SM	2.8 (1.23-6.39)	0.95 (0.75-1.21)	0.79 (0.45-1.39)	2.8 (1.23-6.39)
HRP-CM	4.89 (3.47-6.89)	2 (1.26-3.15)	1.55 (0.98-2.46)	4.89 (3.47-6.89)
CM	2.78 (1.38-5.59)	1.28 (0.91-1.8)	1.3 (0.68-2.46)	2.78 (1.38-5.59)
IPV	1.27 (0.99-1.63)	1.15 (0.8-1.65)	0.72 (0.33-1.58)	1.27 (0.99-1.63)
Number of ACEs in firstborn				
1	2.35 (1.92-2.86)	1.81 (1.42-2.32)	1.59 (1.17-2.15)	2.35 (1.92-2.86)
2	3.14 (2.67-3.7)	2.36 (1.89-2.95)	2.04 (1.3-3.21)	3.14 (2.67-3.7)
≥*3*	7.31 (3.32-16.1)	2.44 (1.8-3.31)	1.81 (1.07-3.07)	7.31 (3.32-16.1)

Data are adjusted and inverse-probability-weighted incidence rate ratios and mean number of children with mental health problems (MHPs) per 100 mothers by ACEs in firstborn. Adjusted for birth year, practice region, firstborn sex, and number of children per mother. AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 10. Adjusted weighted IRRs and mean number of all-cause emergency admissions among children by age groups born to mothers with firstborns exposed to ACEs (sibling sub-cohort, n=355,898 children)

All-cause emergency admissions among children aged 0-18 years				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACE	123.15 (122.46-123.83)	126.98 (126.26-127.7)	136.13 (134.23-138.03)	125.81 (125.35-126.28)
Any ACE	188.28 (187.18-189.39)	162.64 (161.53-163.75)	170.11 (167.45-172.77)	175.95 (175.22-176.68)
AFEs	162.02 (160.3-163.75)	163.16 (159.37-166.94)	123.09 (122.19-123.99)	171.29 (170.15-172.43)
Maternal MHPs	182.07 (180.64-183.5)	171.14 (169.64-172.64)	180.3 (176.79-183.82)	177.28 (176.31-178.26)
Maternal SM	186.43 (183.24-189.61)	161.17 (157.91-164.43)	159.85 (152.73-166.97)	173.54 (171.37-175.71)
HRP-CM	313.23 (310.15-316.31)	182.32 (179.75-184.89)	196.21 (190.6-201.82)	247.93 (246.01-249.85)
CM	251.13 (245.55-256.72)	174.49 (169.39-179.59)	180.25 (169.87-190.63)	212.38 (208.79-215.98)
IPV	184.49 (179.34-189.65)	188.49 (182.75-194.23)	170.64 (160.14-181.14)	184.41 (180.81-188.01)
Number of ACEs in firstborn				
0	122.69 (122.01-123.37)	127.11 (126.39-127.83)	137.71 (135.78-139.63)	125.75 (125.29-126.21)
1	171.29 (170.05-172.52)	153.15 (151.89-154.41)	159.34 (156.32-162.37)	162.67 (161.84-163.5)
2	208.71 (206.28-211.14)	181.42 (178.93-183.91)	196.13 (190.49-201.77)	196.21 (194.55-197.86)
≥*3*	295.84 (290.68-301)	211.38 (206.53-216.23)	213.31 (203.73-222.89)	252.91 (249.55-256.27)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	1.53 (1.52-1.54)	1.32 (1.31-1.33)	1.38 (1.36-1.41)	1.53 (1.52-1.54)
AFEs	1.28 (1.26-1.29)	1.14 (1.13-1.16)	1.15 (1.12-1.18)	1.28 (1.26-1.29)
Maternal MHPs	1.31 (1.3-1.33)	1.24 (1.22-1.25)	1.3 (1.28-1.33)	1.31 (1.3-1.33)
Maternal SM	1.28 (1.26-1.3)	1.11 (1.08-1.13)	1.1 (1.05-1.15)	1.28 (1.26-1.3)
HRP-CM	2.35 (2.32-2.37)	1.37 (1.34-1.39)	1.47 (1.43-1.51)	2.35 (2.32-2.37)
CM	1.72 (1.69-1.76)	1.2 (1.16-1.23)	1.24 (1.17-1.31)	1.72 (1.69-1.76)
IPV	1.25 (1.22-1.29)	1.28 (1.24-1.32)	1.16 (1.09-1.23)	1.25 (1.22-1.29)
Number of ACEs in firstborn				
1	1.4 (1.38-1.41)	1.25 (1.24-1.26)	1.3 (1.27-1.33)	1.4 (1.38-1.41)
2	1.7 (1.68-1.72)	1.48 (1.46-1.5)	1.6 (1.55-1.65)	1.7 (1.68-1.72)
≥*3*	2.41 (2.37-2.46)	1.72 (1.68-1.76)	1.74 (1.66-1.82)	2.41 (2.37-2.46)
All-cause emergency admissions among children aged 0-4 years				
Firstborn exposure	**Weighted and adjusted means(95% CI) per 100 children**			
No ACE	77.33 (76.75-77.92)	82.51 (81.95-83.07)	86.33 (84.93-87.72)	80.58 (80.21-80.95)
Any ACE	121.51 (120.57-122.45)	106.85 (105.99-107.7)	108.45 (106.53-110.37)	113.46 (112.87-114.04)
AFEs	118.3 (116.86-119.74)	106.9 (105.57-108.24)	102.8 (100.1-105.49)	111.38 (110.47-112.28)
Maternal MHPs	116.23 (115.01-117.44)	112.34 (111.18-113.49)	114.81 (112.29-117.33)	114.3 (113.52-115.07)
Maternal SM	114.2 (111.65-116.75)	106.92 (104.47-109.36)	103.98 (98.98-108.98)	109.79 (108.13-111.46)
HRP-CM	212.03 (209.38-214.69)	118.92 (116.96-120.87)	127.6 (123.58-131.61)	160.35 (158.84-161.86)
CM	165.74 (161.03-170.46)	116.14 (112.24-120.03)	110.18 (103.06-117.3)	136.68 (133.87-139.49)
IPV	116.2 (111.93-120.47)	121.75 (117.45-126.05)	108.12 (100.85-115.38)	117.51 (114.72-120.31)
Number of ACEs in firstborn				
0	76.98 (76.4-77.56)	82.56 (82-83.13)	87.34 (85.93-88.76)	80.54 (80.17-80.91)
1	109.24 (108.2-110.28)	100.87 (99.89-101.84)	101.63 (99.45-103.82)	104.65 (103.99-105.31)
2	137.88 (135.82-139.95)	116.86 (114.98-118.74)	124.35 (120.36-128.33)	126.9 (125.6-128.21)
≥*3*	189.46 (185.19-193.73)	140.41 (136.75-144.08)	135.48 (128.83-142.13)	160.84 (158.24-163.43)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	1.57 (1.56-1.59)	1.38 (1.37-1.4)	1.40 (1.37-1.43)	1.57 (1.56-1.59)
AFEs	1.31 (1.3-1.33)	1.19 (1.17-1.2)	1.14 (1.11-1.17)	1.31 (1.3-1.33)
Maternal MHPs	1.32 (1.3-1.33)	1.27 (1.26-1.29)	1.30 (1.27-1.33)	1.32 (1.3-1.33)
Maternal SM	1.22 (1.2-1.25)	1.15 (1.12-1.17)	1.11 (1.06-1.17)	1.22 (1.2-1.25)
HRP-CM	2.53 (2.49-2.56)	1.42 (1.39-1.44)	1.52 (1.47-1.57)	2.53 (2.49-2.56)
CM	1.78 (1.73-1.84)	1.25 (1.21-1.29)	1.19 (1.11-1.27)	1.78 (1.73-1.84)
IPV	1.24 (1.19-1.28)	1.30 (1.25-1.34)	1.15 (1.07-1.23)	1.24 (1.19-1.28)
Number of ACEs in firstborn				
1	1.42 (1.4-1.44)	1.31 (1.29-1.33)	1.32 (1.29-1.35)	1.42 (1.4-1.44)
2	1.79 (1.76-1.82)	1.52 (1.49-1.55)	1.62 (1.56-1.67)	1.79 (1.76-1.82)
≥*3*	2.46 (2.4-2.52)	1.82 (1.77-1.87)	1.76 (1.67-1.85)	2.46 (2.4-2.52)

Data are adjusted and inverse-probability-weighted incidence rate ratios and mean number of children with all-cause emergency admissions per 100 mothers by ACEs in firstborn. Adjusted for birth year, practice region, firstborn sex, and number of children per mother. AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 11. Adjusted weighted IRRs and mean number of all-cause emergency admissions among children by age groups born to mothers with firstborns exposed to ACEs (sibling sub-cohort, n=355,898 children)

All-cause emergency admissions among children aged 5-11 years				
Firstborn exposure	**Firstborn**	**Second born child**	**Third born child**	**Any child**
	Weighted and adjusted means (95% CI) per 100 children			
No ACEs	36.31 (35.97-36.66)	39.95 (38.79-41.11)	54.66 (54.1-55.22)	37.23 (36.98-37.48)
Any ACE	45.63 (45-46.26)	44.13 (42.57-45.69)	135.93 (134.53-137.35)	50.61 (50.21-51)
AFEs	52.15 (51.3-53.01)	45.45 (44.47-46.42)	45.37 (43.04-47.71)	49.18 (48.56-49.79)
Maternal MHPs	53.57 (52.83-54.3)	48.79 (47.94-49.65)	46.82 (44.72-48.93)	51.34 (50.8-51.87)
Maternal SM	61.8 (60.01-63.59)	39.98 (38.19-41.78)	31.64 (27.75-35.52)	51.87 (50.62-53.11)
HRP-CM	85.74 (84.21-87.28)	50.4 (48.94-51.86)	45.64 (42.42-48.87)	69.93 (68.89-70.98)
CM	73.12 (70.23-76.01)	45.37 (42.53-48.21)	52.5 (45.7-59.3)	61.48 (59.49-63.47)
IPV	53.92 (51.25-56.59)	55.62 (52.18-59.06)	41.93 (35.45-48.41)	53.57 (51.56-55.58)
Number of ACEs in firstborn				
0	36.2 (35.86-36.55)	38.18 (37.77-38.6)	40.42 (39.24-41.59)	37.21 (36.96-37.46)
1	50.16 (49.54-50.79)	42.89 (42.18-43.6)	41.74 (39.95-43.53)	46.91 (46.46-47.36)
2	57.14 (55.92-58.35)	52.91 (51.45-54.36)	51.93 (48.48-55.39)	55.22 (54.33-56.12)
≥3	94.82 (91.99-97.65)	55.47 (52.71-58.22)	50.51 (44.74-56.27)	77.53 (75.59-79.47)
	Weighted and adjusted IRRs (95% CI)			
Any ACE	1.51 (1.49-1.53)	1.26 (1.24-1.28)	1.22 (1.17-1.26)	1.51 (1.49-1.53)
AFEs	1.26 (1.24-1.28)	1.1 (1.07-1.12)	1.09 (1.04-1.15)	1.26 (1.24-1.28)
Maternal MHPs	1.33 (1.31-1.35)	1.21 (1.19-1.24)	1.16 (1.11-1.22)	1.33 (1.31-1.35)
Maternal SM	1.46 (1.42-1.51)	0.95 (0.9-0.99)	0.75 (0.66-0.85)	1.46 (1.42-1.51)
HRP-CM	2.17 (2.13-2.21)	1.28 (1.24-1.31)	1.15 (1.08-1.24)	2.17 (2.13-2.21)
CM	1.72 (1.65-1.79)	1.07 (1-1.14)	1.24 (1.09-1.41)	1.72 (1.65-1.79)
IPV	1.26 (1.2-1.32)	1.3 (1.22-1.38)	0.98 (0.84-1.14)	1.26 (1.2-1.32)
Number of ACEs in firstborn				
1	1.39 (1.36-1.41)	1.18 (1.16-1.21)	1.15 (1.1-1.21)	1.39 (1.36-1.41)
2	1.58 (1.54-1.62)	1.46 (1.42-1.51)	1.43 (1.34-1.53)	1.58 (1.54-1.62)
≥3	2.62 (2.54-2.7)	1.53 (1.46-1.61)	1.4 (1.24-1.56)	2.62 (2.54-2.7)
All-cause emergency admissions among children aged 12-18 years				
Firstborn exposure		**Weighted and adjusted means (95% CI) per 100 children**		
No ACEs	9 (8.88-9.12)	9.58 (9.31-9.85)	5.76 (5.02-6.51)	9.07 (8.96-9.17)
Any ACE	10.76 (10.42-11.09)	9.79 (9.1-10.47)	5.32 (3.58-7.06)	10.51 (10.21-10.81)
AFEs	10.76 (10.42-11.09)	9.79 (9.1-10.47)	5.32 (3.58-7.06)	11.71 (11.51-11.9)
Maternal MHPs	11.49 (11.21-11.78)	10.75 (10.16-11.33)	10.57 (8.44-12.69)	11.35 (11.09-11.6)
Maternal SM	11.53 (10.78-12.28)	9.27 (7.84-10.7)	6 (2.08-9.92)	11.06 (10.4-11.71)
HRP-CM	18.37 (17.74-19.01)	14.12 (12.93-15.32)	5.63 (3.09-8.17)	17.44 (16.88-17.99)
CM	15.79 (14.48-17.1)	10.83 (8.59-13.07)	9.72 (2.98-16.46)	14.78 (13.64-15.91)
IPV	14.93 (13.63-16.23)	8.37 (6.23-10.5)	0 (0.01-0.01)	13.61 (12.49-14.74)
Number of ACEs in firstborn				
0	7.89 (7.76-8.02)	9.08 (8.79-9.37)	4.31 (3.57-5.05)	8.07 (7.95-8.18)
1	11.13 (10.88-11.38)	10.77 (10.24-11.29)	10.55 (8.66-12.45)	11.06 (10.84-11.28)
2	14.19 (13.66-14.73)	12.08 (11.01-13.14)	3.28 (1.34-5.22)	13.68 (13.21-14.15)
≥3	14.12 (13.1-15.14)	8.65 (6.9-10.41)	7.58 (2.32-12.85)	13.11 (12.22-14)
Firstborn exposure		**Weighted and adjusted IRRs (95% CI)**		
Any ACE	1.51 (1.47-1.55)	1.38 (1.32-1.45)	1.11 (0.94-1.32)	1.51 (1.47-1.55)
AFEs	1.19 (1.16-1.24)	1.09 (1.01-1.17)	0.59 (0.43-0.82)	1.19 (1.16-1.24)
Maternal MHPs	1.32 (1.29-1.36)	1.24 (1.17-1.31)	1.22 (0.99-1.49)	1.32 (1.29-1.36)
Maternal SM	1.26 (1.18-1.34)	1.01 (0.87-1.18)	0.65 (0.34-1.26)	1.26 (1.18-1.34)
HRP-CM	2.13 (2.06-2.21)	1.64 (1.5-1.79)	0.65 (0.42-1.03)	2.13 (2.06-2.21)
CM	1.73 (1.59-1.88)	1.18 (0.96-1.46)	1.06 (0.53-2.13)	1.73 (1.59-1.88)
IPV	1.63 (1.49-1.78)	0.91 (0.71-1.18)	0 (0-0)	1.63 (1.49-1.78)
Number of ACEs in firstborn				
1	1.41 (1.37-1.45)	1.36 (1.29-1.44)	1.34 (1.12-1.6)	1.41 (1.37-1.45)
2	1.8 (1.73-1.87)	1.53 (1.4-1.67)	0.42 (0.23-0.75)	1.8 (1.73-1.87)
≥3	1.79 (1.66-1.93)	1.1 (0.89-1.34)	0.96 (0.48-1.92)	1.79 (1.66-1.93)

Data are adjusted and inverse-probability-weighted incidence rate ratios and mean number of children with all-cause emergency admissions per 100 mothers by ACEs in firstborn. Adjusted for birth year, practice region, firstborn sex, and number of children per mother. AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 12. Cohort characteristics of subgroups used in three sensitivity analyses by the number of children with MHPs per mother

	Excluding experimental HES-A&E (2012-2020)				ACEs in CPRD (primary care only) and MHPs in HES/ONS only				Excluding single households (i.e. siblings only)			
	Overall (n=176335)	**No child with MHP (n=149490)**	**1 child with MHP (n=25355)**	**≥2 children with MHPs (n=1490)**	**Overall (n=333048)**	**No child with MHP (n=304505)**	**1 child with MHP (n=.27071)**	**≥2 children with MHPs (n=1472)**	**Overall (n=161151)**	**No child with MHP (n=123554)**	**1 child with MHP (n=32058)**	**≥2 children with MHPs (n=5539)**
Maternal age at first birth, years*	30.0 (26.0-34.0)	31.0 (26.0-35.0)	29.0 (24.0-34.0)	27.0 (23.0-32.0)	30.0 (26.0-34.0)	31.0 (26.0-35.0)	30.0 (25.0-34.0)	27.0 (22.0-31.0)	29.0 (24.0-32.0)	29.0 (25.0-32.0)	28.0 (23.0-32.0)	27.0 (22.0-32.0)
≤19	6900 (3.9)	5250 (3.5)	1530 (6.0)	120 (8.1)	13878 (4.2)	11997 (3.9)	1718 (6.3)	163 (11.1)	9300 (5.8)	6129 (5.0)	2643 (8.2)	528 (9.5)
20-29	71855 (40.7)	59751 (40.0)	11305 (44.6)	799 (53.6)	131784 (39.6)	119304 (39.2)	11684 (43.2)	796 (54.1)	79423 (49.3)	60114 (48.7)	16335 (51.0)	2974 (53.7)
30-39	87829 (49.8)	76129 (50.9)	11162 (44.0)	538 (36.1)	170007 (51.0)	157166 (51.6)	12346 (45.6)	495 (33.6)	70371 (43.7)	55743 (45.1)	12672 (39.5)	1956 (35.3)
≥40	9751 (5.5)	8360 (5.6)	1358 (5.4)	33 (2.2)	17379 (5.2)	16038 (5.3)	1323 (4.9)	18 (1.2)	2057 (1.3)	1568 (1.3)	408 (1.3)	81 (1.5)
Median follow-up, any child	12.5 (10.0-18.1)	12.3 (9.91-17.6)	13.2 (10.8-19.8)	21.7 (19.2-24.8)	15.7 (11.7-22.0)	15.5 (11.5-21.5)	17.3 (13.5-25.9)	28.2 (22.3-34.3)	22.3 (17.6-27.9)	21.4 (17.1-26.9)	24.7 (19.7-29.8)	29.0 (24.0-34.0)
Index of multiple deprivation quintile*												
1 (least deprived)	39487 (22.4)	34099 (22.8)	5106 (20.1)	282 (18.9)	77411 (23.2)	71782 (23.6)	5379 (19.9)	250 (17.0)	38734 (24.0)	30471 (24.7)	7199 (22.5)	1064 (19.2)
2	34492 (19.6)	29674 (19.9)	4572 (18.0)	246 (16.5)	66303 (19.9)	61330 (20.1)	4749 (17.5)	224 (15.2)	32585 (20.2)	25475 (20.6)	6137 (19.1)	973 (17.6)
3	32727 (18.6)	27869 (18.6)	4610 (18.2)	248 (16.6)	61467 (18.5)	56354 (18.5)	4851 (17.9)	262 (17.8)	29267 (18.2)	22663 (18.3)	5661 (17.7°/4)	943 (17.0)
4	33997 (19.3)	28694 (19.2)	5011 (19.8)	292 (19.6)	62433 (18.7)	56754 (18.6)	5376 (19.9)	303 (20.6)	29116 (18.1)	22172 (17.9)	5847 (18.2)	1097 (19.8)
5 (most deprived)	35508 (20.1)	29038 (19.4)	6048 (23.9)	422 (28.3)	64600 (19.4)	57461 (18.9)	6707 (24.8)	432 (29.3)	31008 (19.2)	22384 (18.1)	7166 (22.4)	1458 (26.3)
Missing data	124 (0.1)	116 (0.1)	8 (0.0)	0 (0)	834 (0.3)	824 (0.3)	9 (0.0)	1 (0.1)	441 (0.3)	389 (0.3)	48 (0.1)	4 (0.1)
Maternal ethnicity												
White	144766 (82.1)	121541 (81.3)	21900 (86.4)	1325 (88.9)	276841 (83.1)	252304 (82.9)	23234 (85.8)	1303 (88.5)	135439 (84.0)	102127 (82.7)	28278 (88.2)	5034 (90.9)
Asian	18134 (10.3)	16299 (10.9)	1757 (6.9)	78 (5.2)	30518 (9.2)	28530 (9.4)	1897 (7.0)	91 (6.2)	15225 (9.4)	12881 (10.4)	2087 (6.5)	257 (4.6)
Black	8235 (4.7)	7210 (4.8)	974 (3.8)	51 (3.4)	14243 (4.3)	13027 (4.3)	1164 (4.3)	52 (3.5)	5842 (3.6)	4810 (3.9)	893 (2.8)	139 (2.5)
Mixed	2474 (1.4)	2064 (1.4)	388 (1.5)	22 (1.5)	4120 (1.2)	3727 (1.2)	372 (1.4)	21 (1.4)	1801 (1.1)	1385 (1.1)	357 (1.1)	59 (1.1)
Other	944 (0.5)	829 (0.6)	110 (0.4)	5 (0.3)	1928 (0.6)	1775 (0.6)	149 (0.6)	4 (0.3)	805 (0.5)	686 (0.6)	107 (0.3)	12 (0.2)
Missing data	1782 (1.0)	1547 (1.0)	226 (0.9)	9 (0.6)	5398 (1.6)	5142 (1.7)	255 (0.9)	1 (0.1)	2039 (1.3)	1665 (1.3)	336 (1.0)	38 (0.7)
Birthweight, g												
≥3500	61566 (34.9)	52516 (35.1)	8569 (33.8)	481 (32.3)	110489 (33.2)	101691 (33.4)	8376 (30.9)	422 (28.7)	51633 (32.0)	39860 (32.3)	10103 (31.5)	1670 (30.1)
2500-3499	79863 (45.3)	67997 (45.5)	11235 (44.3)	631 (42.3)	143341 (43.0)	131335 (43.1)	11417 (42.2)	589 (40.0)	70708 (43.9)	54709 (44.3)	13724 (42.8)	2275 (41.1)
<2500	6839 (3.9)	5553 (3.7)	1193 (4.7)	93 (6.2)	12753 (3.8)	11360 (3.7)	1293 (4.8)	100 (6.8)	6674 (4.1)	4962 (4.0)	1415 (4.4)	297 (5.4)
Missing data	28067 (15.9)	23424 (15.7)	4358 (17.2)	285 (19.1)	66465 (20.0)	60119 (19.7)	5985 (22.1)	361 (24.5)	32136 (19.9)	24023 (19.4)	6816 (21.3)	1297 (23.4)
Gestational age at birth, weeks												
≥37	136950 (77.7)	116855 (78.2)	19048 (75.1)	1047 (70.3)	234624 (70.4)	215711 (70.8)	18024 (66.6)	889 (60.4)	112717 (69.9)	87578 (70.9)	21640 (67.5)	3499 (63.2)
<37	10767 (6.1)	8681 (5.8)	1948 (7.7°/4)	138 (9.3)	19387 (5.8)	17258 (5.7)	1970 (7.3)	159 (10.8)	9750 (6.1)	7216 (5.8)	2092 (6.5)	442 (8.0)
Missing data	28618 (16.2)	23954 (16.0)	4359 (17.2)	305 (20.5)	79037 (23.7)	71536 (23.5)	7077 (26.1)	424 (28.8)	38684 (24.0)	28760 (23.3)	8326 (26.0)	1598 (28.8)
Location of general practice (region of England, UK)												
London	30229 (17.1)	25997 (17.4)	4023 (15.9)	209 (14.0)	52057 (15.6)	47198 (15.5)	4608 (17.0)	251 (17.1)	22527 (14.0)	17987 (14.6)	3914 (12.2)	626 (11.3)
East and West Midlands	30913 (17.5)	26418 (17.7)	4268 (16.8)	227 (15.2)	58469 (17.6)	54074 (17.8)	4211 (15.6)	184 (12.5)	28272 (17.5)	21718 (17.6)	5658 (17.6)	896 (16.2)
East of England	8157 (4.6)	6845 (4.6)	1224 (4.8)	88 (5.9)	17373 (5.2)	16350 (5.4)	982 (3.6)	41 (2.8)	9031 (5.6)	6977 (5.6)	1743 (5.4)	311 (5.6)

Northeast, northwest, & Yorkshire	47551 (27.0)	39940 (26.7°/4)	7190 (28.4)	421 (28.3)	91603 (27.5)	83126 (27.3)	8002 (29.6)	475 (32.3)	44312 (27.5)	33368 (27.0)	9282 (29.0)	1662 (30.0)
Southeast & southwest	594&5 (33.7)	50290 (33.6)	8650 (34.1)	545 (36.6)	113546 (34.1)	103757 (34.1)	9268 (34.2)	521 (35.4)	57009 (35.4)	43504 (35.2)	11461 (35.8)	2044 (36.9)
Sex of firstborn child												
Female	85914 (48.7)	75399 (50.4)	9915 (39.1)	600 (40.3)	162261 (48.7)	149388 (49.1)	12226 (45.2)	647 (44.0)	77988 (48.4)	61163 (49.5)	14299 (44.6)	2526 (45.6)
Male	90421 (51.3)	74091 (49.6)	15440 (60.9)	890 (59.7)	170787 (51.3)	155117 (50.9)	14845 (54.8)	825 (56.0)	83163 (51.6)	62391 (50.5)	17759 (55.4)	3013 (54.4)
Total number of children												
1	94840 (53.8)	82797 (55.4)	12043 (47.5)	0 (0)	171897 (51.6)	159795 (52.5)	12102 (44.7)	0 (0)				
2	67332 (38.2)	55748 (37.3)	10556 (41.6)	1028 (69.0)	127277 (38.2)	115555 (37.9)	10860 (40.1)	862 (58.6)	127277 (79.0)	99604 (80.6)	24258 (75.7°/4)	3415 (61.7)
≥3	14163 (8.0)	10945 (7.3)	2756 (10.9)	462 (31.0)	33874 (10.2)	29155 (9.6)	4109 (15.2)	610 (41.4)	33874 (21.0)	23950 (19.4)	7800 (24.3)	2124 (38.3)
Year of birth												
2002-2010	133403 (75.7)	111291 (74.4)	20730 (81.8)	1382 (92.8)	290116 (87.1)	263266 (86.5)	25399 (93.8)	1451 (98.6)	144235 (89.5)	108830 (88.1)	29974 (93.5)	5431 (98.1)
2011-2018	42932 (24.3)	38199 (25.6)	4625 (18.2)	108 (7.2)	42932 (12.9)	41239 (13.5)	1672 (6.2)	21 (1.4)	16916 (10.5)	14724 (11.9)	2084 (6.5)	108 (1.9)
Any ACE	75578 (42.9)	61091 (40.9)	13589 (53.6)	898 (60.3)	110650 (33.2)	98293 (32.3)	11637 (43.0)	720 (48.9)	57706 (35.8)	40665 (32.9)	14048 (43.8)	2993 (54.0)
AFEs	27506 (15.6)	22143 (14.8)	5028 (19.8)	335 (22.5)	46079 (13.8)	40968 (13.5)	4800 (17.7)	311 (21.1)	23121 (14.3)	16441 (13.3)	5494 (17.1)	1186 (21.4)
Maternal MHPs	39671 (22.5)	30719 (20.5)	8352 (32.9)	600 (40.3)	66928 (20.1)	58791 (19.3)	7645 (28.2)	492 (33.4)	32331 (20.1)	21509 (17.4)	8752 (27.3)	2070 (37.4)
Maternal SM	18041 (10.2)	15102 (10.1)	2785 (11.0)	154 (10.3)	4797 (1.4)	4195 (1.4)	571 (2.1)	31 (2.1)	6540 (4.1)	4610 (3.7)	1595 (5.0)	335 (6.0)
HRP-CM	15148 (8.6)	11795 (7.9)	3133 (12.4)	220 (14.8)	20274 (6.1)	17891 (5.9)	2265 (8.4)	118 (8.0)	11789 (7.3)	8217 (6.7)	2950 (9.2)	622 (11.2)
CM	4399 (2.5)	3303 (2.2)	1023 (4.0)	73 (4.9)	4770 (1.4)	4074 (1.3)	651 (2.4)	45 (3.1)	2953 (1.8)	1972 (1.6)	794 (2.5)	187 (3.4)
IPV	3303 (1.9)	2422 (1.6)	826 (3.3)	55 (3.7°/4)	4228 (1.3)	3627 (1.2)	575 (2.1)	26 (1.8)	2455 (1.5)	1583 (1.3)	720 (2.2)	152 (2.7°/4)
Number of ACEs in firstborn												
0	100757 (57.1)	88399 (59.1)	11766 (46.4)	592 (39.7)	222398 (66.8)	206212 (67.7)	15434 (57.0)	752 (51.1)	103445 (64.2)	82889 (67.1)	18010 (56.2)	2546 (46.0)
1	51363 (29.1)	42571 (28.5)	8263 (32.6)	529 (35.5)	81682 (24.5)	73302 (24.1)	7900 (29.2)	480 (32.6)	41281 (25.6)	30047 (24.3)	9365 (29.2)	1869 (33.7)
2	17824 (10.1)	13893 (9.3)	3678 (14.5)	253 (17.0)	22974 (6.9)	19940 (6.5)	2846 (10.5)	188 (12.8)	12501 (7.8)	8218 (6.7)	3481 (10.9)	802 (14.5)
≥3	6391 (3.6)	4627 (3.1)	1648 (6.5)	116 (7.8)	5994 (1.8)	5051 (1.7)	891 (3.3)	52 (3.5)	3924 (2.4)	2400 (1.9)	1202 (3.7)	322 (5.8)

Data is n (%) unless specified. *Median (IQR). ACEs=adverse childhood experiences, AFE= Adverse family environment, CM=Child maltreatment-CM=High-risk presentations of child maltreatment, IMD=Index of Multiple Deprivation, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 13. Results from three sensitivity analyses: Incidence rate ratios and the mean number of children per mother associated with firstborn exposure to ACEs in sub-cohort

	Main cohort analysis		Excluding experimental HES-A&E (2012-2020)		ACEs in CPRD (primary care only) only) and MHPs in HES/ONS only		Excluding single households (i.e. siblings only)	
Firstborn exposure	**Mean n children MHP per 100 mothers (95% CI)**	**IRR (95% CI)**	**Mean n children MHP per 100 mothers (95% CI)**	**IRR (95% CI)**	**Mean n children MHP per 100 mothers (95% CI)**	**IRR (95% CI)**	**Mean n children MHP per 100 mothers (95% CI)**	**IRR (95% CI)**
No Ace	17.3 (17.2-17.5)	Ref	12.4 (12.2-12.6)	Ref	14.9 (14.7-15.1)	Ref	18.24 (18.06-18.43)	Ref
Any ACE	29.8 (29.4-30.1)	1.7 (1.7-1.7)	21.4 (21.1-21.8)	1.7 (1.7-1.8)	25.3 (24.6-26.1)	1.7 (1.6-1.8)	36.2 (35.7-36.7)	1.7 (1.6-1.7)
AFEs	28.9 (28.4-29.4)	1.4 (1.4-1.4)	21.7 (21.1-22.2)	1.4 (1.4-1.5)	24.1 (21.9-26.3)	1.5 (1.4-1.6)	35.7 (34.9-36.5)	1.4 (1.4-1.4)
Maternal MHPs	33.5 (33.1-34.0)	1.8 (1.8-1.8)	25.4 (24.9-25.9)	1.9 (1.8-1.9)	27.8 (26.7-28.8)	1.8 (1.7-1.9)	42 (41.3-42.7)	1.8 (1.8-1.8)
Maternal SM	32.6 (31.5-33.6)	1.5 (1.4-1.4)	19.4 (18.7-20.1)	1.2 (1.2-1.3)	22 (20.7-23.2)	1.4 (1.3-1.5)	35.5 (34.2-36.8)	1.3 (1.3-1.4)
HRP-CM	31.8 (31.0-32.5)	1.5 (1.5-1.6)	25 (24.2-25.8)	1.6 (1.6-1.7)	30.8 (28.9-32.7)	1.9 (1.8-2.1)	38.5 (37.3-39.7)	1.5 (1.4-1.5)
CM	38.3 (36.7-39.9)	1.8 (1.7-1.9)	28.5 (26.9-30.1)	1.8 (1.7-1.9)	25.2 (22.5-27.8)	1.6 (1.4-1.7)	46 (43.4-48.7)	1.7 (1.6-1.8)
IPV	37.8 (36.0-39.6)	1.8 (1.7-1.9)	30 (28.1-32)	1.9 (1.8-2)	29 (25.8-32.2)	1.8 (1.6-2)	46.6 (43.8-49.5)	1.8 (1.6-1.9)
Number of ACEs in firstborn								
0	17.3 (17.1-17.5)	Ref	12.4 (12.2-12.6)	Ref	14.9 (14.7-15.1)	Ref	21.8 (21.5-22)	Ref
1	26.3 (26.0-26.7)	1.5 (1.5-1.5)	18.8 (18.4-19.1)	1.5 (1.5-1.6)	24.2 (23.4-24.9)	1.6 (1.6-1.7)	32.5 (32-33.1)	1.5 (1.5-1.5)
2	35.7 (34.9-36.4)	2.0 (2.0-2.1)	25.6 (24.8-26.4)	2.1 (2-2.1)	32 (29.7-34.4)	2.1 (2-2.3)	43.5 (42.3-44.7)	2 (1.9-2.1)
≥3	45.3 (43.8-46.8)	2.6 (2.5-2.7)	33.4 (31.9-35)	2.7 (2.6-2.8)	37.5 (31.6-43.4)	2.5 (2.1-2.9)	54.9 (52.5-57.4)	2.5 (2.4-2.6)

Data are adjusted and inverse probability weighted incidence rate ratios and mean number of children with MHPs by ACEs in firstborn and step of adjustment. Means are expressed as the number of children per 100 mothers. All estimates were adjusted for birth year, practice region, birth year, firstborn sex and number of children per mother. ACEs=adverse childhood experiences, AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IMD=Index of Multiple Deprivation, IRR=incidence rate ratio, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 14. Cohort characteristics of sensitivity analysis comparing single vs. multiple child families stratified by number of children with MHPs

	Overall		No child with MHP		1 child with MHP		≥2 children with MHPs (n=5539)
	Single child (N=171897)	**Multiple child (N=161151)**	**Single child (N=143553)**	**Multiple child (N=123554)**	**Single child (N=28344)**	**Multiple child (N=32058)**	**Multiple child (N=5539)**
Maternal age at first birth, years*	32.0 (28.0·36.0)	29.0 (24.0·32.0)	32.0 (28.0·36.0)	29.0 (25.0·32.0)	32.0 (27.0·36.0)	28.0 (23.0-32.0)	27.0 (22.0-32.0)
≤19	4578 (2.7%)	9300 (5.8%)	3562 (2.5%)	6129 (5.0%)	1016 (3.6%)	2643 (8.2%)	528 (9.5%)
20-29	52361 (30.5%)	79423 (49.3%)	43398 (30.2%)	60114 (48.7%)	8963 (31.6%)	16335 (51.0%)	2974 (53.7%)
30-39	99636 (58.0%)	70371 (43.7%)	83870 (58.4%)	55743 (45.1%)	15766 (55.6%)	12672 (39.5%)	1956 (35.3%)
≥40	15322 (8.9%)	2057 (1.3%)	12723 (8.9%)	1568 (1.3%)	2599 (9.2%)	408 (1.3%)	81 (1.5%)
Median follow-up, any child*	13.3 (10.8-15.9)	13.8 (11.4-16.1)	13.0 (10.6-15.7)	13.4 (11.1-15.9)	14.5 (11.9-16.7)	14.6 (12.2-16.6)	15.7 (13.6-17.3)
Index of multiple deprivation quintile							
1 (least deprived)	38677 (22.5%)	38734 (24.0%)	32901 (22.9%)	30471 (24.7%)	5776 (20.4%)	7199 (22.5%)	1064 (19.2%)
2	33718 (19.6%)	32585 (20.2%)	28522 (19.9%)	25475 (20.6%)	5196 (18.3%)	6137 (19.1%)	973 (17.6%)
3	32200 (18.7%)	29267 (18.2%)	26980 (18.8%)	22663 (18.3%)	5220 (18.4%)	5661 (17.7%)	943 (17.0%)
4	33317 (19.4%)	29116 (18.1%)	27623 (19.2%)	22172 (17.9%)	5694 (20.1%)	5847 (18.2%)	1097 (19.8%)
5 (most deprived)	33592 (19.5%)	31008 (19.2%)	27168 (18.9%)	22384 (18.1%)	6424 (22.7%)	7166 (22.4%)	1458 (26.3%)
Missing data	393 (0.2%)	441 (0.3%)	359 (0.3%)	389 (0.3%)	34 (0.1%)	48 (0.1%)	4 (0.1%)
Maternal ethnicity							
White	141402 (82.3%)	135439 (84.0%)	116692 (81.3%)	102127 (82.7%)	24710 (87.2%)	28278 (88.2%)	5034 (90.9%)
Asian	15293 (8.9%)	15225 (9.4%)	13729 (9.6%)	12881 (10.4%)	1564 (5.5%)	2087 (6.5%)	257 (4.6%)
Black	8401 (4.9%)	5842 (3.6%)	7271 (5.1%)	4810 (3.9%)	1130 (4.0%)	893 (2.8%)	139 (2.5%)
Mixed	2319 (1.3%)	1801 (1.1%)	1937 (1.3%)	1385 (1.1%)	382 (1.3%)	357 (1.1%)	59 (1.1%)
Other	1123 (0.7%)	805 (0.5%)	983 (0.7%)	686 (0.6%)	140 (0.5%)	107 (0.3%)	12 (0.2%)
Missing data	3359 (2.0%)	2039 (1.3%)	2941 (2.0%)	1665 (1.3%)	418 (1.5%)	336 (1.0%)	38 (0.7%)
Birthweight, g							
≥3500	58856 (34.2%)	51633 (32.0%)	49500 (34.5%)	39860 (32.3%)	9356 (33.0%)	10103 (31.5%)	1670 (30.1%)
2500-3499	72633 (42.3%)	70708 (43.9%)	60908i42.4%)	54709 (44.3%)	11725 (41.4%)	13724 (42.8%)	2275 (41.1%)
<2500	6079 (3.5%)	6674 (4.1%)	4832 (3.4%)	4962 (4.0%)	1247 (4.4%)	1415 (4.4%)	297 (5.4%)
Missing data	34329 (20.0%)	32136 (19.9%)	28313 (19.7%)	24023 (19.4%)	6016 (21.2%)	6816 (21.3%)	1297 (23.4%)
Gestational age at birth, weeks							
≥37	121907 (70.9%)	112717 (69.9%)	102725 (71.6%)	87578 (70.9%)	19182 (67.7%)	21640 (67.5%)	3499 (63.2%)
<37	9637 (5.6%)	9750 (6.1%)	7693 (5.4%)	7216 (5.8%)	1944 (6.9%)	2092 (6.5%)	442 (8.0%)
Missing data	40353 (23.5%)	38684 (24.0%)	33135 (23.1%)	28760 (23.3%)	7218 (25.5%)	8326 (26.0%)	1598 (28.8%)
Location of general practice (region of England, UK)							
East and west Midlands	30197 (17.6%)	28272 (17.5%)	25186 (17.5%)	21718 (17.6%)	5011 (17.7%)	5658 (17.6%)	896 (16.2%)
East of England	8342 (4.9%)	9031 (5.6%)	7001 (4.9%)	69TT (5.6%)	1341 (4.7%)	1743 (5.4%)	311 (5.6%)
London	29530 (17.2%)	22527 (14.0%)	25061 (17.5%)	17987 (14.6%)	4469 (15.8%)	3914 (12.2%)	626 (11.3%)
Northeast, northwest, and	47291 (27.5%)	44312 (27.5%)	39111 (27.2%)	33368 (27.0%)	8180 (28.9%)	9282 (29.0%)	1662 (30.0%)
Southeast and southwest	56537 (32.9%)	57009 (35.4%)	47194 (32.9%)	43504 (35.2%)	9343 (33.0%)	11461 (35.8%)	2044 (36.9%)
Sex of firstborn child							
Female	84273 (49.0%)	77988 (48.4%)	71834 (50.0%)	61163 (49.5%)	12439 (43.9%)	14299 (44.6%)	2526 (45.6%)
Male	87624 (51.0%)	83163 (51.6%)	71719 (50.0%)	62391 (50.5%)	15905 (56.1%)	17759 (55.4%)	3013 (54.4%)
Total number of children							
1	171897 (100%)	0 (0%)	143553 (100%)	0 (0%)	28344 (100%)	0 (0%)	0 (0%)

2	0 (0%)	127277 (79.0%)	0 (0%)	99604 (80.6%)	0 (0%)	24258 (75.7%)	3415 (61.7%)
≥3	0 (0%)	33874 (21.0%)	0 (0%)	23950 (19.4%)	0 (0%)	7800 (24.3%)	2124 (38.3%)
Year of birth							
2002-2010	145881 (84.9%)	144235 (89.5%)	120078 (83.6%)	108830 (88.1%)	25803 (91.0%)	29974 (93.5%)	5431 (98.1%)
2011-2018	26016 (15.1%)	16916 (10.5%)	23475 (16.4%)	14724 (11.9%)	2541 (9.0%)	2084 (6.5%)	108 (1.9%)
Any ACE	68994 (40.1%)	60326 (37.4%)	54731 (38.1%)	42915 (34.7%)	14263 (50.3%)	14386 (44.9%)	3025 (54.6%)
AFEs	25303 (14.7%)	23121 (14.3%)	20017 (13.9%)	16441 (13.3%)	5286 (18.6%)	5494 (17.1%)	1186 (21.4%)
Maternal MHPs	39744 (23.1%)	32331 (20.1%)	30227 (21.1%)	21509 (17.4%)	9517 (33.6%)	8752 (27.3%)	2070 (37.4%)
Maternal SM	12378 (7.2%)	10331 (6.4%)	10335 (7.2%)	7819 (6.3%)	2043 (7.2%)	2137 (6.7%)	375 (6.8%)
HRP-CM	13005 (7.6%)	11789 (7.3%)	10047 (7.0%)	8217 (6.7%)	2958 (10.4%)	2950 (9.2%)	62 (211.2%)
CM	3465 (2.0%)	2953 (1.8%)	2566 (1.8%)	1972 (1.6%)	899 (3.2%)	794 (2.5%)	187 (3.4%)
IPV	2809 (1.6%)	2455 (1.5%)	2081 (1.4%)	1583 (1.3%)	728 (2.6%)	720 (2.2%)	152 (2.7%)
Number of ACEs in firstborn							
0	102903 (59.9%)	100825 (62.6%)	88822 (61.9%)	80639 (65.3%)	14081 (49.7%)	17672 (55.1%)	2514 (45.4%)
1	47976 (27.9%)	42976 (26.7%)	38909 (27.1%)	31519 (25.5%)	9067 (32.0%)	9558 (29.8%)	1899 (34.3%)
2	15800 (9.2%)	13227 (8.2%)	12095 (8.4%)	8838 (7.2%)	3705 (13.1%)	3589 (11.2%)	800 (14.4%)
≥3	5218 (3.0%)	4123 (2.6%)	3727 (2.6%)	2558 (2.1%)	1491 (5.3%)	1239 (3.9%)	326 (5.9%)

Data is n (%) unless specified. *Median (IQR). ACEs=adverse childhood experiences, AFE= Adverse family environment, CM=Child maltreatment, HRP-CM=High-risk presentations of child maltreatment, IMD=Index of Multiple Deprivation, IPV= Intimate partner violence, MHPs=mental health problems; SM=Substance misuse

eTable 15. Sensitivity analyses: comparing the risk of MHP in children among mothers (333,048) with a single child (n=197,894) vs mothers with multiple children (n=281,964)

Sub-group	adjusted weighted HR (95% CI)	Estimated relative aw HZ (95% CI)	p-value for comparison
Any child	1.79 (1.76-1.82)		
Single child only (ACE in firstborn)	1.81 (1.77-1.86)	0.98 (0.95-1.01)	0.155
Multiple child family (ACE in firstborn)	1.77 (1.74-1.81)		

This table presents a sensitivity analysis comparing the risk of MHPs in children from mothers with only one child vs mothers with multiple children. We did this analysis in the primary cohort by re-running the Cox proportional hazards model with a dummy coded interaction term for single vs multiple child households, followed by marginal effects analysis to compare the differences.[28] All estimates inverse probability weighted and adjusted for birth year, practice region, birth year, firstborn sex. ACEs=adverse childhood experiences, awHZ= adjusted and inverse probability weighted hazard ratios.

Interpretation: *the estimated marginal difference of 0.98 (95% CI: 0.95-1.01) with a p-value of 0.155 suggests that the difference in the effect of ACEs on MHP risk between single-child and multiple-child families is not statistically significant. This indicates that ACEs increase MHP risk in both family types.*

eTable 16. The RECORD statement (extension of the STROBE statement) – checklist of items, that should be reported in observational studies using routinely collected health data

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title and abstract	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title and abstract Title and abstract Title and abstract
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			4, 5-6
Objectives	3	State specific objectives, including any prespecified hypotheses			2, 5-6
Study Design	4	Present key elements of study design early in the paper			Abstract, 5-15, figure 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Abstract, 6-12, figure 1, Supplementary eTable1

Participants	6	*Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Abstract, 6-12, figure 1, Supplementary eTable1, etable 3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Abstract, box 1, 7-10, table 1-2, supplementary etable 5. Code lists and measures by indicators and adversity domains provided online.
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		box 1, 7-10, table 1-2, Supplementary eTables 2-5.
Bias	9	Describe any efforts to address potential sources of bias		12, Supplementary eTables 2-5
Study size	10	Explain how the study size was arrived at		5-6, fig 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why		9-12, box 1, Supplementary eTable 2-5. Frameworks, code lists and measures by grouped indicators provided online.
Statistical methods	12	Describe all statistical methods, including		10-12, Supplementary eTable 2

		those used to control for confounding Describe any methods used to examine subgroups and interactions Explain how missing data were addressed *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy Describe any sensitivity analyses		
Data access and cleaning methods		..	RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	21, Supplementary eTable 1
			RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	All algorithms provided online
Linkage		..	RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	6-7, figure 1, Supplementary eTable 1 + specific references provided
Participants	13	Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) Give reasons for non- participation at each stage.	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	figure 1 (flow diagram), 5-7, Supplementary eTable 1,

		Consider use of a flow diagram		
Descriptive data	14	Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders Indicate the number of participants with missing data for each variable of interest *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)		Table 1
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures		14-16, Supplementary eTables 2-4
Main results	16	Give unadjusted estimates and, if applicable, confounder- adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included Report category boundaries when continuous variables were categorised If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		14-16, figs 2-4, Table 2, Supplementary eTables 2-4
Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses		12, 16, Supplementary eTables 2-4
Key results	18	Summarise key results with reference to study objectives		17-18
Limitations	19	Discuss limitations of the study, taking	RECORD 19.1: Discuss the implications of using	19

		into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		17-19
Generalisability	21	Discuss the generalisability (external validity) of the study results		17-19, 20
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		12, 22
Accessibility of protocol, raw data, and programming code		..	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Methods for implementations are referenced in-text where relevant: www.ACEsinEHRs.com + github. CPRD ISAC Protocol is available on request.

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015;n press.*Checklist is protected under Creative Commons Attribution (CC BY) license.

References supplement

1. Herrett E, Gallagher AM, Bhaskaran K, et al. Data resource profile: clinical practice research datalink (CPRD). *International journal of epidemiology*. 2015;44(3):827-836.
2. Wolf A, Dedman D, Campbell J, et al. Data resource profile: clinical practice research Datalink (CPRD) aurum. *International journal of epidemiology*. 2019;48(6):1740-1740g.
3. Minassian C, Williams R, Meeraus WH, Smeeth L, Campbell OM, Thomas SL. Methods to generate and validate a Pregnancy Register in the UK Clinical Practice Research Datalink primary care database. *Pharmacoepidemiology and drug safety*. 2019;28(7):923-933.
4. CPRD. CPRD Aurum Mother Baby Link Documentation. Accessed 29 October, 2024. https://www.cprd.com/sites/default/files/2023-02/CPRD_Aurum_MotherBabyLink_Documentation_v0.3.pdf
5. CPRD. CPRD Mother Baby Link Documentation. Accessed 29 October, 2024. https://www.cprd.com/sites/default/files/2022-02/MotherBabyLink_Documentation_v1.2.pdf
6. NHS Digital. Patients Registered at a GP Practice - August 2021. 2021;
7. CPRD Mother Baby Link Documentation (2017).
8. Herbert A, Wijlaars L, Zylbersztejn A, Cromwell D, Hardelid P. Data resource profile: hospital episode statistics admitted patient care (HES APC). *International journal of epidemiology*. 2017;46(4):1093-1093i.
9. NHS England Digital. Hospital Episode Statistics Data Dictionary. Accessed October 29, 2024. https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics/hospital-episode-statistics-data-dictionary
10. Hospital Episode Statistics (HES) Admitted Patient Care and CPRD primary care data Documentation (set 22/January 2022) (2021).
11. ONS. Ethnic group classifications: Census 2021. https://www.ons.gov.uk/census/census2021dictionary/variablesbytopic/ethnicgroupnationalidentitylanguageandreligionvariablescensus2021/ethnicgroup/classifications
12. CPRD. Hospital Episode Statistics (HES) Accident & Emergency and CPRD primary care data Documentation (set 21). Accessed 29 October, 2024. https://www.cprd.com/sites/default/files/2022-02/Documentation_HES_AE_set21.pdf
13. CPRD. Hospital Episode Statistics (HES) Outpatient Care and CPRD primary care data Documentation (set 21). Accessed October 29, 2024. https://www.cprd.com/sites/default/files/2022-02/Documentation_HES_OP_set21.pdf
14. Office for National Statistics. The English Indices of Deprivation 2019 Statistical Release. Accessed 29 October, 2024. https://assets.publishing.service.gov.uk/media/5d8e26f6ed915d5570c6cc55/IoD2019_Statistical_Release.pdf
15. ONS. User guide to mortality statistics. Accessed 29 October, 2024. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/methodologies/userguidetomortalitystatisticsjuly2017#information-collected-at-death-registration
16. CPRD. ONS death registration data and CPRD primary care data Documentation (set 22/January 2022). Accessed 29 October, 2024. https://www.cprd.com/sites/default/files/2022-02/Documentation_Death_set22_v2.6.pdf
17. Denaxas S, Gonzalez-Izquierdo A, Direk K, et al. UK phenomics platform for developing and validating electronic health record phenotypes: CALIBER. *Journal of the American Medical Informatics Association*. 2019;26(12):1545-1559.
18. Denaxas SC, George J, Herrett E, et al. Data resource profile: cardiovascular disease research using linked bespoke studies and electronic health records (CALIBER). *International journal of epidemiology*. 2012;41(6):1625-1638.

19. Syed S, Gonzalez-Izquierdo A, Allister J, Feder G, Li L, Gilbert R. Identifying adverse childhood experiences with electronic health records of linked mothers and children in England: a multistage development and validation study. *The Lancet Digital Health*. 2022;4(7):e482-e496.
20. Howe CJ, Cole SR, Lau B, Napravnik S, Eron Jr JJ. Selection bias due to loss to follow up in cohort studies. *Epidemiology (Cambridge, Mass)*. 2016;27(1):91.
21. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. *Statistical methods in medical research*. 2013;22(3):278-295.
22. De Stavola BL, Herle M, Pickles A. Framing causal questions in life course epidemiology. *Annual Review of Statistics and Its Application*. 2022;9(1):223-248.
23. Feder G, Davies RA, Baird K, et al. Identification and Referral to Improve Safety (IRIS) of women experiencing domestic violence with a primary care training and support programme: a cluster randomised controlled trial. *The Lancet*. 2011;378(9805):1788-1795.
24. Woodman J, Freemantle N, Allister J, de Lusignan S, Gilbert R, Petersen I. Variation in recorded child maltreatment concerns in UK primary care records: a cohort study using The Health Improvement Network (THIN) database. *PLoS One*. 2012;7(11):e49808.
25. Walker SP, Wachs TD, Grantham-McGregor S, et al. Inequality in early childhood: risk and protective factors for early child development. *The lancet*. 2011;378(9799):1325-1338.
26. Harron K, Gilbert R, Fagg J, Guttmann A, van der Meulen J. Associations between pre-pregnancy psychosocial risk factors and infant outcomes: a population-based cohort study in England. *The Lancet Public Health*. 2021;6(2):e97-e105.
27. Syed S, Gilbert R, Feder G, et al. Family adversity and health characteristics associated with intimate partner violence in children and parents presenting to health care: a population-based birth cohort study in England. *The Lancet Public Health*. 2023;8(7):e520-e534.
28. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ*. 2003;326(7382):219.