Identifying adverse childhood experiences with electronic health records of linked mothers and children in England: a multistage development and validation study

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Summary

Background Electronic health records (EHRs) of mothers and children provide an opportunity to identify adverse childhood experiences (ACEs) during crucial periods of childhood development, yet well developed indicators of ACEs remain scarce. We aimed to develop clinically relevant indicators of ACEs for linked EHRs of mothers and children using a multistage prediction model of child maltreatment and maternal intimate partner violence (IPV).

Methods In this multistage development and validation study, we developed a representative population-based birth cohort of mothers and children in England, followed from up to 2 years before birth to up to 5 years after birth across the Clinical Practice Research Datalink (CPRD) GOLD (primary care), Hospital Episode Statistics (secondary care), and the Office for National Statistics mortality register. We included livebirths in England between July 1, 2004, and June 30, 2016, to mothers aged 16–55 years, who had registered with a general practitioner (GP) that met CPRD quality standards before 21 weeks of gestation. The primary outcome (reference standard) was any child maltreatment or maternal IPV in either the mother's or child's record from 2 years before birth (maternal IPV only) to 5 years after birth. We used seven prediction models, combined with expert ratings, to systematically develop indicators. We validated the final indicators by integrating results from machine learning models, survival analyses, and clustering analyses in the validation cohort.

Findings We included data collected between July 1, 2002, and June 27, 2018. Of 376 006 eligible births, we included 211 393 mother–child pairs (422 786 patients) from 400 practices, of whom 126 837 mother–child pairs (60·0%; 240 practices) were randomly assigned to a derivation cohort and 84 556 pairs (40·0%; 160 practices) to a validation cohort. We included 63 indicators in six ACE domains: maternal mental health problems, maternal substance misuse, adverse family environments, child maltreatment, maternal IPV, and high-risk presentations of child maltreatment. Excluding the seven indicators in the reference standard, 56 indicators showed high discriminative validity for the reference standard of any child maltreatment or maternal IPV between 2 years before and 5 years after birth (validation cohort, area under the receiver operating characteristic curve 0·85 [95% CI 0·84–0·86]). During the 2 years before birth and 5 years after birth, the overall period prevalence of maternal IPV and child maltreatment (reference standard) was 2·3% (2876 of 126 837 pairs) in the derivation cohort and 2·3% (1916 of 84 556 pairs) in the validation cohort. During the 2 years before and after birth, the period prevalence was 39·1% (95% CI 38·7–39·5; 34 773 pairs) for any of the 63 ACE indicators, 22·2% (21·8–22·5%; 20 122 pairs) for maternal mental health problems, 15·7% (15·4–16·0%; 14 549 pairs) for adverse family environments, 8·1% (7·8–8·3%; 6808 pairs) for high-risk presentations of child maltreatment, 6·9% (6·7–7·2%; 7856 pairs) for maternal substance misuse, and 3·0% (2·9–3·2%; 2540 pairs) for any child maltreatment (2·4% [2·3–5·6%; 2051 pairs]) and maternal IPV (1·0% [0·8–1·0%; 875 pairs]). 62·6% (21 785 of 34 773 pairs) of ACEs were recorded in primary care only, and 72·3% (25 140 cases) were recorded in the maternal record only.

Interpretation We developed clinically relevant indicators for identifying ACEs using the EHRs of mothers and children presenting to general practices and hospital admissions. Over 70% of ACEs were identified via maternal records and were recorded in primary care by GPs within 2 years of birth, reinforcing the importance of reviewing parental and carer records to inform clinical responses to children. ACE indicators can contribute to longitudinal surveillance informing public health policy and resource allocation. Further evaluation is required to determine how ACE indicators can be used in clinical practice.

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Introduction

Adverse childhood experiences (ACEs) are potentially traumatic or neglectful experiences that can profoundly affect the health and development of children.[1–3] ACEs often co-occur in the family, ranging from child maltreatment and neglect,[4] to growing up in a household

Research in context

Evidence before this study

Electronic health records (EHRs) are readily available and increasingly used for identifying adverse childhood experiences (ACEs), yet well developed indicators of ACEs remain scarce. We searched 18 electronic databases for articles published in English using the following search terms: TITLE or ABSTRACT ((abuse* OR maltreat* OR neglect* OR adversity* OR "adverse child*" OR violen*") AND ("electronic* OR administrative* OR routine*") AND ("record* or data") AND (specifici* OR accuracy* OR sensi* OR reliability* OR valid* OR "verified*" OR "chart$review" OR "manual$review")) between Jan 1, 1980, and May 31, 2021, for studies comparing indicators of ACEs in EHRs against an independent reference standard. Published indicators of ACEs for EHRs were scarce and limited to specific ACEs and family members in isolation. No study had systematically validated indicators for linked mothers and children that included child maltreatment and maternal intimate partner violence (IPV).

Added value of this study

Using a multistage risk prediction framework of child maltreatment and maternal IPV, we systematically developed 63 indicators clustered around six clinically recognisable domains of ACEs in mothers and children. We used a large birth cohort study of linked mothers and children across England with data from the Clinical Practice Research Datalink GOLD, Hospital Episode Statistics, and the mortality register from the Office for National Statistics. The developed ACE indicators showed high validity for discriminating between mothers and children with recorded maternal IPV and child maltreatment, relative to children who had not been exposed to these experiences.

Implications of all the available evidence

ACE indicators have the potential to support public health policy and monitoring efforts to enable better planning of resources and longitudinal surveillance. Further evaluation is required to establish the effectiveness of ACE indicators for screening or case finding to target interventions for vulnerable families in clinical practice.

with parental mental health problems, and maternal intimate partner violence (IPV).[5] Failure to identify and measure ACEs can substantially undermine opportunities to act,[6] and can place children at risk of considerable harm in the longer term.[7] Children with ACEs face increased risks of hospital admissions,[8] chronic conditions,[2] teenage pregnancies,[9] suicide,[10] and intergenerational violence.[11]

In the UK and the USA, national prevention strategies expanded their aims in 2020 to reduce ACEs as a precursor to long-term health problems.[12–15] However, to achieve this goal, data systems for identifying ACEs and vulnerable families must first be carefully developed and quantified. The absence of validated indicators for identifying ACEs in routine electronic health records (EHRs) represents an important obstacle.[1] Policy makers and services often rely on small self-report studies, local samples, and non-validated methods for identifying ACEs and vulnerable families.[15–18] The few longitudinal studies in the UK that have measured ACEs in EHRs were based on individual data sources in specific populations (eg, hospital admissions),[19] or on family members in isolation (eg, maternal mental health problems; appendix pp 45–46).[8,20] Studies to date have also differed in their approach to defining ACEs or have combined multiple risk groups that are difficult to disentangle.[21]

See Online for appendix

In the UK, first-time mothers are offered 13 antenatal appointments and between one and three postnatal primary care appointments.[22] Children routinely attend primary care for surveillance and vaccinations from 6–8 weeks to 4–6 years after birth.[23] The ability to link EHRs of mothers and children provides an opportunity to identify ACEs during crucial periods of prevention of long-term harm.[24,25] This study aimed to develop clinically relevant indicators of ACEs in linked EHRs, with the potential to aid longitudinal public health monitoring and prompt early assessment of support needs for vulnerable children and mothers before and after birth. We used a multistage prediction framework of child maltreatment and maternal IPV to develop indicators. First, we identified candidate ACE indicators using a systematic review.[1] Then, we assessed the relevance of indicators against a reference standard of child maltreatment or maternal IPV using an integrative predictive and explanatory approach,[26,27] combining risk estimates from multiple variable selection models, cluster analyses, and expert ratings.[28] We used a large representative birth cohort of mothers and children in England followed from 2 years before birth up to 5 years after birth across primary and secondary care.[29] Indicator selections and predictions of child maltreatment or maternal IPV were theoretically informed (appendix p 3).[30–32]

Methods

Study design and participants

This study followed the guidelines for accurate and transparent health estimates reporting,[33] and the reporting guidelines for prediction model and development (appendix pp 47–54).[34] We derived a population-based birth cohort using the mother–baby link in the Clinical Practice Research Datalink (CPRD) GOLD database via the CALIBER platform (appendix p 4).[35] The CPRD GOLD database contains anonymised primary care data from

approximately 6·9% of UK general practices, with recorded symptoms, diagnoses, prescriptions, and referrals to secondary care. CPRD GOLD is broadly representative of the general population.[36] Mothers and children are linked in the CPRD via unique household identifiers and maternity records, matched with high validity.[37] In 2004, the mother–baby link contained data from 676 practices, with 400 practices (59%) consenting for linkage to other data sources. Most practices (329 [82%] of 400 general practices) contributed data for at least 10 years or until 2014.[36]

Mothers and children were linked to the Hospital Episodes Statistics Admitted Patient Care database (HES-APC), the mortality register from the Office for National Statistics, and the Index of Multiple Deprivation 2015. The HES-APC provides data on hospital admissions, including birth or delivery records, from all hospitals in England funded by the National Health Service (NHS).[38] The Office for National Statistics includes data on cause-specific mortality from registered death certificates. The Index of Multiple Deprivation 2015 is the official national metric for relative deprivation in England and comprises a composite score across seven domains based on a patient's postcode (eg, average income, employment status, or crime levels).[39] This index can be classified into five quantiles, from the least deprived to the most deprived. Detailed study procedures and information on data sources are provided in the appendix (pp 4–5).

We included livebirths in England between July 1, 2004, and June 30, 2016, to mothers aged 16–55 years, who had registered with a general practitioner (GP) that met CPRD GOLD quality standards before 21 weeks of gestation. We selected a random child per mother to avoid clustering effects due to multiple children, given that several variable selection models could not computationally handle clustering on the secure analytical server (random-effects forest >168 h; appendix pp 21–22). Children had to be registered with the practice within 6 months after birth, with follow-up data collected until the child's first birthday (figure 1). We calculated conception dates using validated algorithms.[37] The 20-week minimum cutoff before birth avoided exclusion of extreme preterm births and captured pre-birth data for the full cohort.[40] This study was approved by the UK Medicines and Healthcare products Regulatory Agency Independent Scientific Advisory Committee (19_162R), under Section 251 (NHS Social Care Act 2006), for the use of anonymised records in research without individual participant written consent.

Data selection

We included data collected between July 1, 2002, and June 27, 2018, with births starting from July 1, 2004, to June 30, 2016. This period allowed for 2 years of follow-up before and after birth. Follow-up for the primary analyses ranged from a minimum of 20 weeks of gestation and 1 year following birth, to a maximum of 2 years before birth to 5 years after birth, and included practice deregistration, the last data collection date of the practice, and death or the study end date, whichever came first (appendix p 4). We restricted the period for ACEs to the first 5 years after birth to minimise attrition (eg, practice deregistration) and to avoid ACEs related to events outside the immediate family (eg, teenage peer relationships). This period is consistent with prioritised care interventions for mothers and children.[12,41,42]

Indicators and domains of ACEs

We developed two measures of ACEs for EHRs: indicators (ie, grouped codes or measures) and domains (ie, grouped indicators; table 1). Definitions, selection procedures, and excluded candidate indicators are provided in the appendix (pp 6–31). Briefly, we identified 408 candidate indicators for ACEs using systematic reviews of code lists and previous studies.[1] We used predefined criteria from Public Health England,[41,47] WHO,[25] and previous reviews to classify indicators of ACEs (appendix pp 6–9).[48,49] We manually grouped candidate indicators into six broader ACE domains consistent with the original ACE study.[5,29] We added the domain, high-risk presentations of child maltreatment. This domain encompassed indicators based on guidance from the National Institute for Health and Care Excellence and the Royal College of General Practitioners, which addressed presentations that should raise concerns for child maltreatment.[50,51]

We defined candidate indicators by combining information from the EHRs of both mothers and children across all sources (eg, Read codes, International Classification of Diseases 9th or 10th edition, prescriptions, or self-report measures). We treated mothers and children with no indicator as unexposed. We used multiple rule-based algorithms to prevent misclassification of specific indicators as due to other causes (eg, accidents; appendix pp 16–17). The complete code lists are available on the ACEs in EHRs website.

For the **ACEs in EHRs website** see https://acesinehrs.com/

We assessed the relevance of candidate indicators on the basis of their association with a clinically defined reference standard in a multistage prediction model. We expected the selected indicators to reflect a continuum of clinical relevance, ranging from high relevance to low relevance.

To add covariates to the prediction models, we included variables on demographics, deprivation quantiles, and clinical characteristics recorded during pregnancy or up to 2 years before birth.[40,52] We ascertained birthweight, gestational age, maternal age, and congenital anomalies (European Registry of Congenital Anomalies and Twins guidelines) from both the mothers' and children's records in the CPRD and the Hospital Episodes Statistics database.[53]

Outcomes

The primary outcome (ie, reference standard) was any recorded child maltreatment or maternal IPV in the

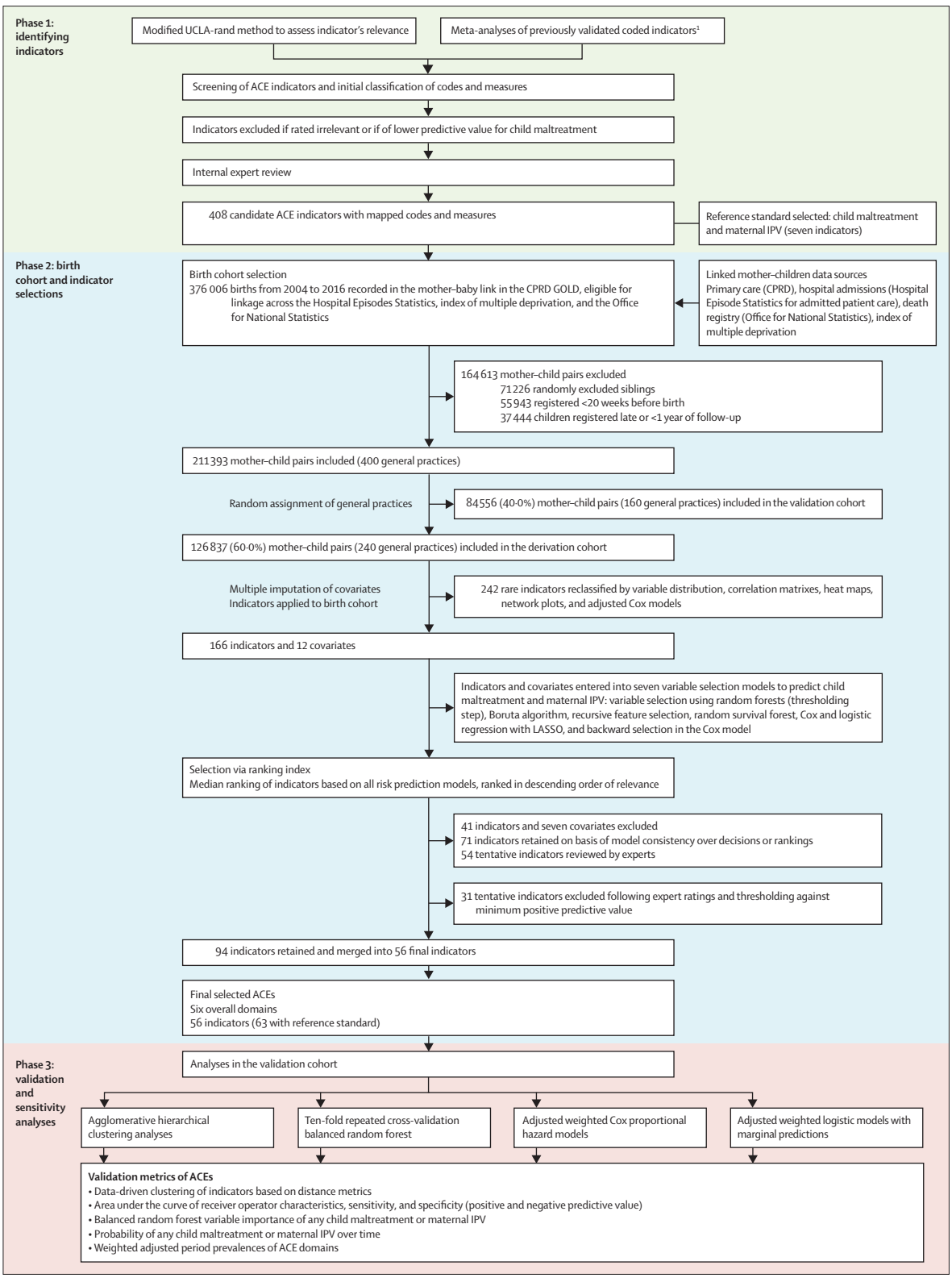

Figure 1: **Overview of the development and validation of ACE indicators**
ACE=adverse childhood experience. CPRD=Clinical Practice Research Datalink. GP=general practitioner. IPV=intimate partner violence. LASSO=Least absolute shrinkage and selection operator. UCLA=University of California at Los Angeles.

child's or the mother's record from 2 years before birth (maternal IPV only) to 5 years after birth. Child maltreatment included neglect,[4] harm caused during pregnancy (eg, neonatal abstinence syndrome),[1,45] deaths related to child maltreatment, and social service referrals for children (appendix pp 8–9, 24–25).[54,55] In the absence of a consensus reference standard for ACEs, child maltreatment and maternal IPV provide a clinically important outcome measured in childhood,[56,57] and represent a probable cumulation of underlying adversity (appendix p 3).[2,58–60] Because GPs do not record ACEs at every presentation that raises concern,[61,62] indicators were not required to occur before the outcome (excluded in sensitivity analyses; appendix p 42). The seven indicators of child maltreatment or maternal IPV in the reference standard were excluded from the risk prediction models, but were included for estimating prevalences and for clustering analyses.

Statistical analysis

Detailed statistical methods are provided in the appendix (pp 21–22, 26–27). Briefly, we randomly assigned 60% of general practices to a derivation cohort for model development (appendix p 4). The remaining 40% of general practices were assigned to a validation cohort. Some indicators were used in their existing form, whereas indicators with less than 100 unique records were reclassified into neighbouring indicators for statistical power. Continuous variables (eg, alcohol units) were dichotomised on the basis of validated higher risk cutoff scores (appendix pp 16–17). We used pairwise correlation matrices, network plots, and adjusted Cox proportional hazard models with inverse probability weighting to reclassify indicators (appendix pp 21–22).[63–65]

Having preprocessed 166 candidate indicators, we established the relevance of each indicator by combining results from multiple variable selection models of child maltreatment and maternal IPV into a ranking index (appendix pp 26–27). We followed the procedures of Haq and colleagues[66] to rank indicators in descending order of risk association for each model (ie, greatest risk association was ranked first for highest relevance).[67] The median (IQR) ranking of each indicator acted as a summary measure of relevance. Given the aims of this study to identify indicators that reflected a continuum of clinically meaningful risk groups consistent with previous ACE definitions (appendix pp 6–7), traditional metrics used to compare performance (eg, Brier score or smallest subset)[68] were not appropriate for these aims.[26] The ranking index ensured that we selected indicators on the basis of multiple relevance metrics, incorporating the strength of each model.[69–71] We used results from seven variable selection algorithms,[72–74] with a wide range of thresholds and output metrics including:[66,75] four supervised machine learning models (ie, variable selection using random forests [thresholding step], random survival forest, recursive feature selection, and random forest Boruta

	ACE domains and final indicators	Number of codes
CM (reference standard)[1,4,43]		
CM1*	Child protection or safeguarding*	50
CM2*	CM not otherwise specified, including physical or sexual abuse (merged)*	154
CM3*	Neglect (including neonatal abstinence syndrome or fetal alcohol spectrum disorders), and emotional or psychological abuse*	76
CM4*	Social service involved (including parental imprisonment or criminal activity)*	80
CM5*	Child in care*	107
Suspected CM†		
CM6	Suspected CM, not otherwise specified (including neglect and social service involvements)	244
CM7	Child assaulted, not otherwise specified (including physical or sexual abuse [≤10], rib fractures [≤3]‡)	545
Maternal IPV (reference standard)*		
Maternal IPV1*	Maternal IPV, not otherwise specified (including physical or sexual abuse)*	67
Maternal IPV2*	Mother assaulted plus child protection recording or incident during pregnancy*‡	554
Suspected maternal IPV†		
Maternal IPV3	Suspected maternal IPV, not otherwise specified	33
Maternal IPV4	Suspected maternal IPV, physical or sexual abuse	45
Maternal IPV5	Mother assaulted, not otherwise specified (hospital admission only)	119
Maternal IPV6	Mother assaulted plus high-risk presentations (algorithm)‡	236
HRP-CM		
Child injuries		
HRP-CM1	Bruising and contusions (≤3)‡	114
HRP-CM2	Superficial injuries of head, neck, or multiple body parts (≤3)‡	37
HRP-CM3	Thermal injuries: head, face, or neck (≤3)‡	161
HRP-CM4	Thermal injuries: trunk, back, or trachea (≤3)‡	53
HRP-CM5	Skull fractures or intracranial crush injury (≤3)‡	16
Harm by undetermined intent		
HRP-CM6	Child harm by undetermined intent: rare injuries and life-threatening events (eg, retinal haemorrhages, drownings, sudden unexpected death in infancy, or firearm injuries [≤10])‡	239
HRP-CM7	Child harm by undetermined intent: exposure to unspecified factor (≤10)‡	4
Potential failure to provide		
HRP-CM8	Failure to thrive (eg, excessive thirst or suspected malnutrition [≤10])‡	48
HRP-CM9	Non-attendance of child appointments (≥3 appointments within 2 years [≤10])‡	16
MSM		
MSM1	Severe drug misuse (dependence)	564
MSM2	Moderate drug misuse (all other)	213
MSM3	Maternal drug prescription for opioid dependence (multipurpose usage)	21
MSM4	Family substance misuse (ie, unspecified family member)	19
MSM5	Severe alcohol misuse (including self-report measures of ≥35 alcohol units per week[44])‡	273
AFEs		
Antenatal care and health visit concerns		
AFE1	High-risk antenatal presentation: specific to social risk	2
AFE2	High-risk antenatal presentation: psychosocial risk, not otherwise specified	38
AFE3	Unwanted or concealed pregnancy (including attempted abortion of current child)	46
AFE4	Psychosocial health problem with lower-level intervention	20
AFE5	Increasing concern of health visitor	11

(Table 1 continues on next page)

	ACE domains and final indicators	Number of codes
(Continued from previous page)		
Parental conflicts, disruptions, and causes for concerns		
AFE6	Family disruptions and parental conflicts, not otherwise specified	108
AFE7	Parental separations	27
AFE8	Mother with legal problems	32
AFE9	Family is cause for concern[45]	182
AFE10	Problems related to negative childhood events	26
AFE11	Mother assaulted, not otherwise specified (GP record only)	1
Vulnerable families		
AFE12	Housing problems, effects of deprivation, and refugees (excluding homelessness)	57
AFE13	Homelessness (child or mother)	22
AFE14	Vulnerable family, not otherwise specified (including care programme approach)	31
AFE15	Family or parental support referral	12
AFE16	Problems related to psychosocial circumstances	24
AFE17	Maternal learning or intellectual disability	276
AFE18	Increased concerns of maternal incapacity	10
AFE19	Maternal problems with daily living or limited capacity to work (including financial concerns)	41
Maternal MHPs		
Common MHPs		
Maternal MHP1	Depression (including use of antidepressants)†	818
Maternal MHP2	Self-harm or suicide attempts	744
Maternal MHP3	Anxiety disorder, not otherwise specified (including use of anxiolytics)†	549
Maternal MHP4	Panic disorder (including agoraphobia or health anxiety)	24
Maternal MHP5	Obsessive-compulsive disorders	27
Maternal MHP6	Post-traumatic stress disorder (including acute stress disorder)	72
Maternal MHP7	Sleep-wake disorders	33
Maternal MHP8	MHPs not otherwise specified	17
Maternal MHP9	Referred to or seen by a mental health professional (tier 3 service or above)	180
Maternal MHP10	Puerperal MHPs, not otherwise specified	5
Eating disorders		
Maternal MHP11	Anorexia nervosa	13
Maternal MHP12	Eating disorders, not otherwise specified (including bulimia)	49
Psychosis and personality disorders		
Maternal MHP13	Psychosis (including mental health sections not otherwise specified)	339
Maternal MHP14	Use of antipsychotics	324
Maternal MHP15	Bipolar disorders	66
Maternal MHP16	Personality disorders (eg, borderline personality disorder)	177
Neurodevelopmental disorders§		
Maternal MHP17	Neurodevelopmental conditions and conduct disorders	245

Details regarding ascertainment of indicators are provided in the appendix (pp 10–31). ACE=adverse childhood experience. CM=child maltreatment. IPV=intimate partner violence. HRP=high-risk presentation. MSM=maternal substance misuse. AFEs=adverse family environments. MHP=mental health problem. *Indicators were combined into the primary outcome (reference standard) and excluded from the development and validation phase. †Suspected CM and suspected maternal IPV were subdomains containing less specific maltreatment-related indicators used in the development process to expand the final CM and maternal IPV domains, respectively. ‡Indicators are defined by multiple rule-based algorithms, including age restrictions in years (upper age cutoff 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 cutoff score on a validated self-report instrument. Medications, interventions, and psychiatric symptoms were combined into appropriate disorder clusters using validated algorithms.[46] §Neurodevelopmental disorders are included as a diagnostic cluster in the Diagnostic and Statistical Manual of Mental Disorders (5th edn) and International Classification of Diseases (10th or 11th edn).

Table 1: **Final six ACE domains and 63 indicators included in validation analyses**

algorithm), logistic and Cox regression models with least absolute shrinkage and selection operator (Harrell C index), and a Cox model with stepwise backward variable selection (Akaike's information criterion). We included indicators consistently retained across models and excluded consistently omitted indicators (Fleiss' kappa agreement statistic ≥0·6).[76]

We used a ten-fold repeated cross-validation for variable selection models (appendix pp 21–22, 26–27). All machine learning models were balanced by randomly downsampling the derivation cohort to minimise overfitting by the imbalanced number of reference standard cases compared with non-cases.[63]

This process left tentative indicators with a median ranking in between the two thresholds. Four experts on family violence (RG, LL, GF, and JA) independently rated tentative indicators (plus 50% already included or excluded) on the basis of clinical credibility and relevance criteria on a scale of 1–10 (appendix pp 33–37).[28,77] The expert panel were masked to the decisions of the variable selection model. We retained indicators that were consistently rated by experts to be at least five on the relevance and credibility scale (Fleiss' kappa statistic ≥0·6). As we retained a large amount of indicators in the final stage, we combined indicators with less than 150 observations into neighbouring indicators by repeating the initial reclassification step, before applying them to the validation cohort (original indicators shown in the appendix pp 11–16).

We validated indicators in four ways in the validation cohort. First, we confirmed the manually grouped indicators of ACE domains by entering them into an agglomerative hierarchical clustering model based on Jaccard's similarity index.[78] This bottom-up approach systematically clustered indicator pairs into larger domains without pre-specification. Second, we assessed the accuracy and predictive value of ACEs for identifying the reference standard without covariates. We used a weighted-balanced random-forest model,[79,80] trained in the derivation cohort with ten-fold repeated cross-validation to model predictions in the validation cohort. The random-forest model was built with a minimum of 1000 trees and 30 observations to attempt splits.[81] To gauge predictive performance, we computed receiver operating characteristic (ROC) curves and the area under the ROC curve (AUC). We used Delong's method to compute 95% CIs for the AUC.[82] We examined agreement between predicted and observed probabilities over risk deciles of any child maltreatment or maternal IPV by plotting calibration curves and calculating the Brier score (appendix p 39).

Third, as expected by the cumulative stress model, we established if there was a dose–response relationship between the number of ACE domains and the reference standard.[30–32] We used inverse probability-weighted and adjusted Cox proportional hazard models and Kaplan-Meier curves to estimate differences in overall

probability of child maltreatment or maternal IPV by ACE domain and by number of ACEs over time,[83] compared with non-exposed mother–child pairs. We checked model assumptions of Kaplan-Meier estimates using log–log plots and the link test.[84] We also provided the cross-validated random-forest model permutation importance values. These values are defined as the mean decrease in the model's overall predictive ability when data for an indicator is randomly shuffled—ie, how much the model depends on the indicator. The scaled permutation importance values scores range from 0% (not important) to 100% (important). Finally, to aid with the comparison of external estimates,[20] we used inverse probability-weighted logistic regression models (adjusted for birth year) to compute the period prevalence of ACEs between 2 years before and after birth. This time interval is consistent with period prevalences from previous studies,[20] and ensured that most mother–child pairs at baseline could be included in the denominator.

We did sensitivity analyses in the validation cohort to test the robustness of the final indicators, including extending the exposure period, cohort inclusion criteria (eg, siblings or birth years), excluding patients with outcomes recorded after the indicator, comparing birth years (2004 *vs* 2014), and comparing general practices' years of data contribution (ending before 2014 *vs* ending after 2014).

There were no missing data for ACE indicators because we assumed that children with no event were unexposed. Data were missing for birth characteristics of covariates on parity, gestational age, birthweight, and social deprivation obtained during pregnancy or up to 2 years before birth (table 1). We imputed missing values separately for each cohort under the missing-at-random assumption. Predictors in the model included all maternal and birth characteristics listed in table 1, any suspected child maltreatment or maternal IPV, maternal ACEs (maternal substance misuse and maternal mental health problems) based on validated indicators, and the reference standard of child maltreatment or maternal IPV (appendix pp 21–22). We used the multivariate imputation by chained equations package in R to create 25 imputed datasets (25 iterations for each imputation) and the sjmisc::merge_imputations function to combine estimates from imputed datasets.

We did all analyses on University College London's secure analytical server (the Data Safe Haven; certified to ISO27001 information security standards), using Stata (version 16) and R (version 4.1) with the caret,[85] ranger, hmisc, rms, mice, glmnet, pROC, recipes, meta, rmda, and tidyverse packages (complete list available online).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

	Overall cohort (n=211 393)	Derivation cohort (n=126 837)	Validation cohort (n=84 556)
Maternal characteristics			
Follow-up time before birth, years	2·0 (2·0–2·0)	2·0 (2·0–2·0)	2·0 (2·0–2·0)
Available follow-up time after birth, years	4·5 (2·5–5·0)	4·5 (2·5–5·0)	4·5 (2·5–5·0)
Age at birth, years*			
≤19	7054 (3·3%)	4243 (3·3%)	2811 (3·3%)
20–39	147 234 (69·6%)	88 489 (69·8%)	58 745 (69·5%)
≥40	57 105 (27·0%)	34 105 (26·9%)	23 000 (27·2%)
Maternal parity*			
0	65 214 (30·8%)	39 167 (30·9%)	26 047 (30·8%)
1–3	83 175 (39·3%)	49 891 (39·3%)	33 284 (39·4%)
≥4*	8259 (3·9%)	4935 (3·9%)	3324 (3·9%)
Missing data	54 745 (25·9%)	32 844 (25·9%)	21 901 (25·9%)
Socioeconomic status quintile*			
1 (least deprived)	46 539 (22·0%)	27 873 (22·0%)	18 666 (22·1%)
2	42 695 (20·2%)	25 415 (20·0%)	17 280 (20·4%)
3	41 306 (19·5%)	24 873 (19·6%)	16 433 (19·4%)
4	41 634 (19·7%)	24 986 (19·7%)	16 648 (19·7%)
5 (most deprived)	39 066 (18·5%)	23 593 (18·6%)	15 473 (18·3%)
Missing data	153 (0·1%)	97 (0·1%)	56 (0·1%)
Ethnicity			
White	178 388 (84·4%)	107 006 (84·4%)	71 382 (84·4%)
Asian	14 706 (7·0%)	8793 (6·9%)	5913 (7·0%)
Black	7656 (3·6%)	4631 (3·7%)	3025 (3·6%)
Other	2662 (1·3%)	1591 (1·3%)	1071 (1·3%)
Mixed	3248 (1·5%)	2003 (1·6%)	1245 (1·5%)
Missing data	4733 (2·2%)	2813 (2·2%)	1920 (2·3%)
Location of general practice (region of England, UK)			
London	37 999 (18·0%)	22 780 (18·0%)	15 219 (18·0%)
Northeast, northwest, and Yorkshire	39 387 (18·6%)	23 681 (18·7%)	15 706 (18·6%)
East and west Midlands	27 418 (13·0%)	16 473 (13·0%)	10 945 (12·9%)
East	24 173 (11·4%)	14 522 (11·4%)	9651 (11·4%)
Southeast, southwest, and south central	82 416 (39·0%)	49 381 (38·9%)	33 035 (39·1%)
Health comorbidities (Global Burden of Disease classification scheme)*			
Cardiovascular and circulatory diseases	25 874 (12·2%)	15 612 (12·3%)	10 262 (12·1%)
Chronic respiratory diseases	24 101 (11·4%)	14 551 (11·5%)	9550 (11·3%)
Diabetes and endocrine diseases	22 352 (10·6%)	13 499 (10·6%)	8853 (10·5%)
Musculoskeletal disorders	10 514 (5·0%)	6331 (5·0%)	4183 (4·9%)
Neurological disorders†	1377 (0·7%)	855 (0·7%)	522 (0·6%)
Lower respiratory infections and other infections‡	22 261 (10·5%)	13 481 (10·6%)	8780 (10·4%)
Maternal disorders§	24 101 (11·4%)	14 551 (11·5%)	9550 (11·3%)

(Table 2 continues on next page)

Results

Of 376 006 eligible births between July 1, 2004, and June 30, 2016, we included 211 393 mother–child pairs (422 786 patients), with mothers followed up from up to 2 years before birth (median follow-up 2·0 years [IQR 2·0–2·0]) and mother–child pairs followed up to 5 years after birth (median 4·5 years [2·5–5·0]; figure 1). We

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	Overall cohort (n=211 393)	Derivation cohort (n=126 837)	Validation cohort (n=84 556)
(Continued from previous page)			
Delivery characteristics			
Time to GP registration after birth, months			
<2 months	197 555 (93·5%)	118 549 (93·5%)	79 006 (93·4%)
≥2–3 months	9405 (4·4%)	5622 (4·4%)	3783 (4·5%)
≥3–6 months	4433 (2·1%)	2666 (2·1%)	1767 (2·1%)
Sex of child			
Male	108 221 (51·2%)	64 962 (51·2%)	43 259 (51·2%)
Female	103 172 (48·8%)	61 875 (48·8%)	41 297 (48·8%)
Multiple pregnancy*			
Singleton	201 261 (95·2%)	120 766 (95·2%)	80 495 (95·2%)
Multiple (eg, twins)*	3244 (1·5%)	1960 (1·5%)	1284 (1·5%)
Missing data	6829 (3·2%)	4071 (3·2%)	2758 (3·3%)
Gestational age at birth, weeks*			
≥37	165 535 (78·3%)	99 338 (78·3%)	66 197 (78·3%)
<37	13 232 (6·3%)	7900 (6·2%)	5332 (6·3%)
Missing data	32 626 (15·4%)	19 599 (15·5%)	13 027 (15·4%)
Birthweight, g*			
≥3500	80 992 (38·3%)	48 604 (38·3%)	32 388 (38·3%)
2500–3499	95 749 (45·3%)	57 477 (45·3%)	38 272 (45·3%)
<2500*	10 565 (5·0%)	6312 (5·0%)	4253 (5·0%)
Missing data	24 087 (11·4%)	14 444 (11·4%)	9643 (11·4%)
Congenital anomaly*	9559 (4·5%)	5677 (4·5%)	3882 (4·6%)
Birth year*			
2004–10	137 216 (64·9%)	82 208 (64·8%)	55 008 (65·1%)
2011–18	74 177 (35·1%)	44 629 (35·2%)	29 548 (34·9%)

Data are median (IQR) or n (%). GP=general practitioner. *Denotes covariates included across risk prediction models for the selection of indicators. †Neurological disorders included epilepsy, multiple sclerosis, and motor neuron disease. ‡Other infections included diarrhoeal diseases, malaria, meningitis, and sexually transmitted infections. §Maternal disorders included maternal sepsis, maternal hypertensive disorders, pre-eclampsia, and gestational diabetes.

Table 2: **Cohort characteristics**

included 400 general practices (median 500 pairs per practice [IQR 247–720]). We randomly assigned 240 general practices (126 837 [60·0%] mother–child pairs) to the derivation cohort and 160 practices (84 556 [40·0%] pairs) to the validation cohort (figure 1). The derivation and validation cohorts were similar across key child and maternal characteristics (table 2). For the main follow-up period (from 2 years before birth to 5 years after birth), the overall period prevalence of the reference standard of maternal IPV and child maltreatment was 2·3% (2876 of 126 837 pairs) in the derivation cohort and 2·3% in the validation cohort (1916 of 84 556 pairs).

We initially identified 408 ACE indicators, which were condensed into 166 indicators (178 with covariates) following redistribution of rare indicators (figure 1). We entered all 166 indicators and 12 covariates of birth characteristics and maternal comorbidities into seven variable selection models of child maltreatment and maternal IPV (table 2; figure 2). There was large variation in selected indicators between different models (appendix p 31). Overall, we identified 71 consistently retained and 41 consistently excluded indicators across at least five models, leaving 54 tentative indicators for expert relevance ratings (appendix pp 10–15). The largest proportion (28 [68%]) of exclusions were indicators relating to high-risk presentations of child maltreatment (eg, fractures, intracranial injuries, contusions, or ano-genital symptoms). Models consistently retained any suspected child maltreatment or maternal IPV and covariates related to ACEs (eg, younger maternal age or social deprivation). After the expert panel resolved disagreements over inclusions (Fleiss kappa interrater agreement >0·64), 94 indicators were combined into 56 final indicators (63 including the seven indicators making up the reference standard; table 1). This step ensured a minimum of 100 observations per indicator when applied to the smaller validation cohort. Covariates were excluded from the final selection.

The final 63 indicators clustered into six ACE domains, broadly confirming the manual groupings based on clinical relevance and existing ACE concepts. These domains were maternal mental health problems, maternal substance misuse, adverse family environments, child maltreatment, maternal IPV, and high-risk presentations of child maltreatment. In the dendrogram of hierarchically clustered indicators, including indicators as part of the reference standard, a few individual indicators clustered outside their originally grouped clusters (appendix p 33). We made no changes to the original domains, given that underlying coding descriptions of outlying indicators matched originally grouped domains better conceptually. For instance, compared with other maternal mental health problems, post-traumatic stress disorder clustered closer to violence-related indicators but was retained under maternal mental health problems.

Table 3 shows validation estimates of the grouped final indicators (domains) in the validation cohort (calibration curves and ROC curves are shown in the appendix [pp 39–40]). The full model involving all 56 ACE indicators showed a good balance between sensitivity (72%) and specificity (84%) for identifying the reference standard of any child maltreatment or maternal IPV (AUC 0·85 [95% CI 0·84–0·86]; table 3). The model also showed good agreement between predicted and observed probabilities of any child maltreatment or maternal IPV over the range of risk deciles (calibration intercept 0, slope 1, Brier score 0·137).

Individual ACE domains showed a consistent dose–response relationship with any child maltreatment or maternal IPV (figure 3A). More closely related indicators of the reference standard (eg, suspected child maltreatment or maternal IPV) showed high specificity (range 99–100%), positive predictive values (41–43%), and good calibration (Brier score 0·191), but lower overall ROC AUC (range 0·55–0·64). By contrast, broader domains (eg, maternal mental health problems, adverse family environments, and maternal substance misuse) showed higher overall AUC values (range 0·67–0·72), but

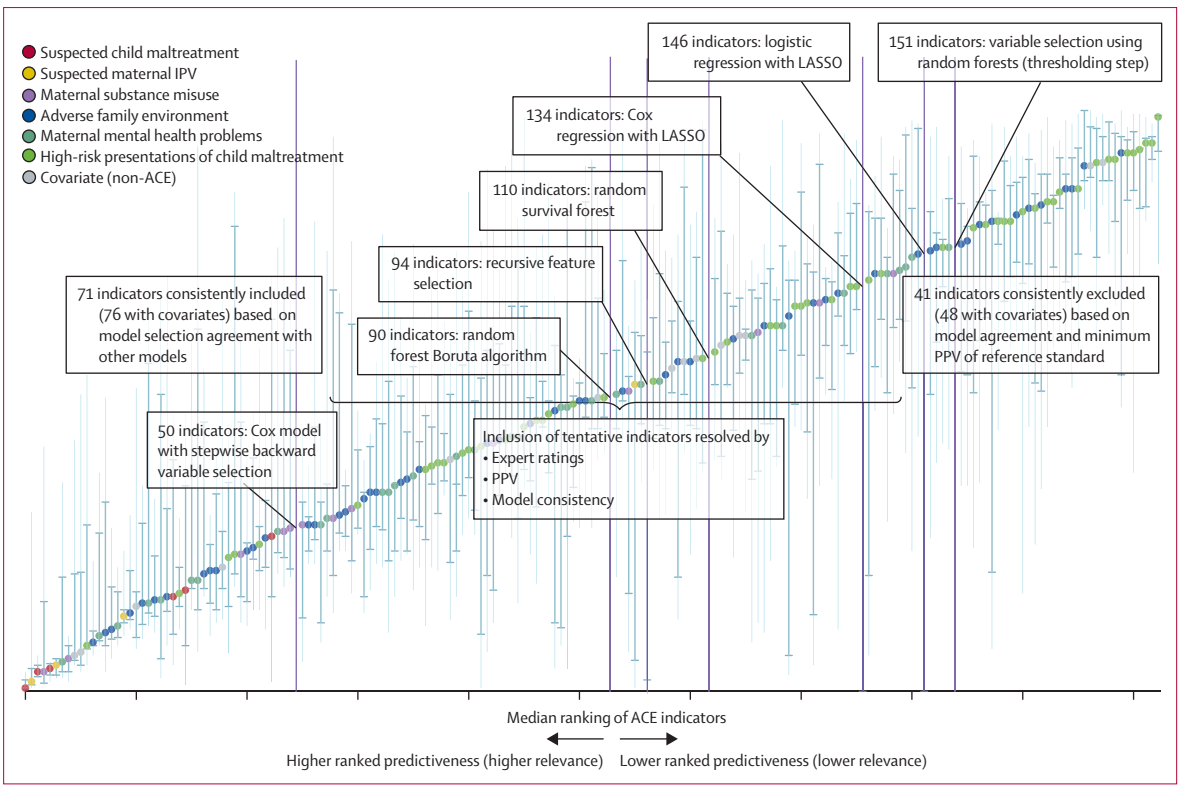

Figure 2: **Median (IQR) relevance rankings for 166 ACE indicators and 12 covariates from seven cross-validated variable selection models of child maltreatment and maternal IPV in the derivation cohort**

Rankings provided in descending order of risk association with any child maltreatment or maternal IPV from 2 years before birth to 5 years after birth (ie, highest value ranked first and lowest value ranked 178th). Dark blue error bars indicate IQR and light blue error bars depict the complete range for all cross-validated models. Vertical purple lines represent the model-specific cutoffs for inclusion of indicators. Indicator-specific rankings are available in the appendix (pp 10–15). ACE=adverse childhood experience. FGM=female genital mutilation. IPV=intimate partner violence. LASSO=Least absolute shrinkage and selection operator. PPV=positive predictive value.

	AUC (95% CI)	F1 score*	True positives	True negatives	False positives	False negatives	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Any ACE	0·85 (0·84–0·86)	0·17	1371	69 388	13 252	545	72%	84%	9%	99%
Maternal mental health problems	0·72 (0·70–0·73)	0·11	1149	64 736	17 904	767	60%	78%	6%	99%
Maternal substance misuse	0·68 (0·66–0·69)	0·14	870	72 626	10 014	1046	45%	88%	8%	99%
Adverse family environment	0·67 (0·66–0·69)	0·14	809	74 166	8474	1107	42%	90%	9%	99%
Suspected child maltreatment	0·64 (0·63–0·65)	0·34	551	81 906	734	1365	29%	99%	43%	98%
High-risk presentations of child maltreatment	0·59 (0·58–0·60)	0·11	487	76 049	6591	1429	25%	92%	7%	98%
Suspected maternal IPV	0·55 (0·55–0·56)	0·17	207	82 344	296	1709	11%	100%	41%	98%

Arranged in descending order of AUC estimates. ACE=adverse childhood experience. AUC=area under the curve. IPV=intimate partner violence. *F1 scores portray a measure of precision and recall.

Table 3: **Performance metrics of each ACE domain's predictive ability of any child maltreatment or maternal IPV using repeated cross-validated weighted-balanced random forests in the validation cohort from up to 2 years before birth to 5 years after birth (n=84 556)**

lower specificity (78–90%) and underpredictions of any child maltreatment or maternal IPV (table 3; appendix p 39). This pattern remained consistent in survival analyses of the probability of child maltreatment or maternal IPV within 5 years after birth. Compared with no ACEs, the adjusted and weighted hazard ratio (HR) ranged from 10·0 (95% CI 8·1–12·2) for any ACE and 32·97 (26·63–40·83) for any suspected child maltreatment or maternal IPV, to 7·05 (5·74–8·67) for maternal substance misuse and 3·42 (2·86–4·10) for high-risk presentations of child maltreatment (figure 3A). The probability of any child maltreatment or maternal IPV also increased for each increase in the number of ACEs (adjusted weighted HR range 3·1–100·0; figure 3B). Random forest importance values for individual ACE indicators are shown in figure 4A.

When applying all six ACE domains (63 indicators) to the validation cohort (84 556 mother–child pairs), the adjusted and weighted period prevalence during the 2 years before and after birth was 39·1% (95% CI 38·7–39·5; 34 773 pairs) for any ACE, 22·2% (21·8–22·5%; 20 122 pairs) for maternal mental health problems, 15·7% (15·4–16·0%; 14 549 pairs) for adverse family environments, 6·9% (6·7–7·2%; 7856 pairs) for

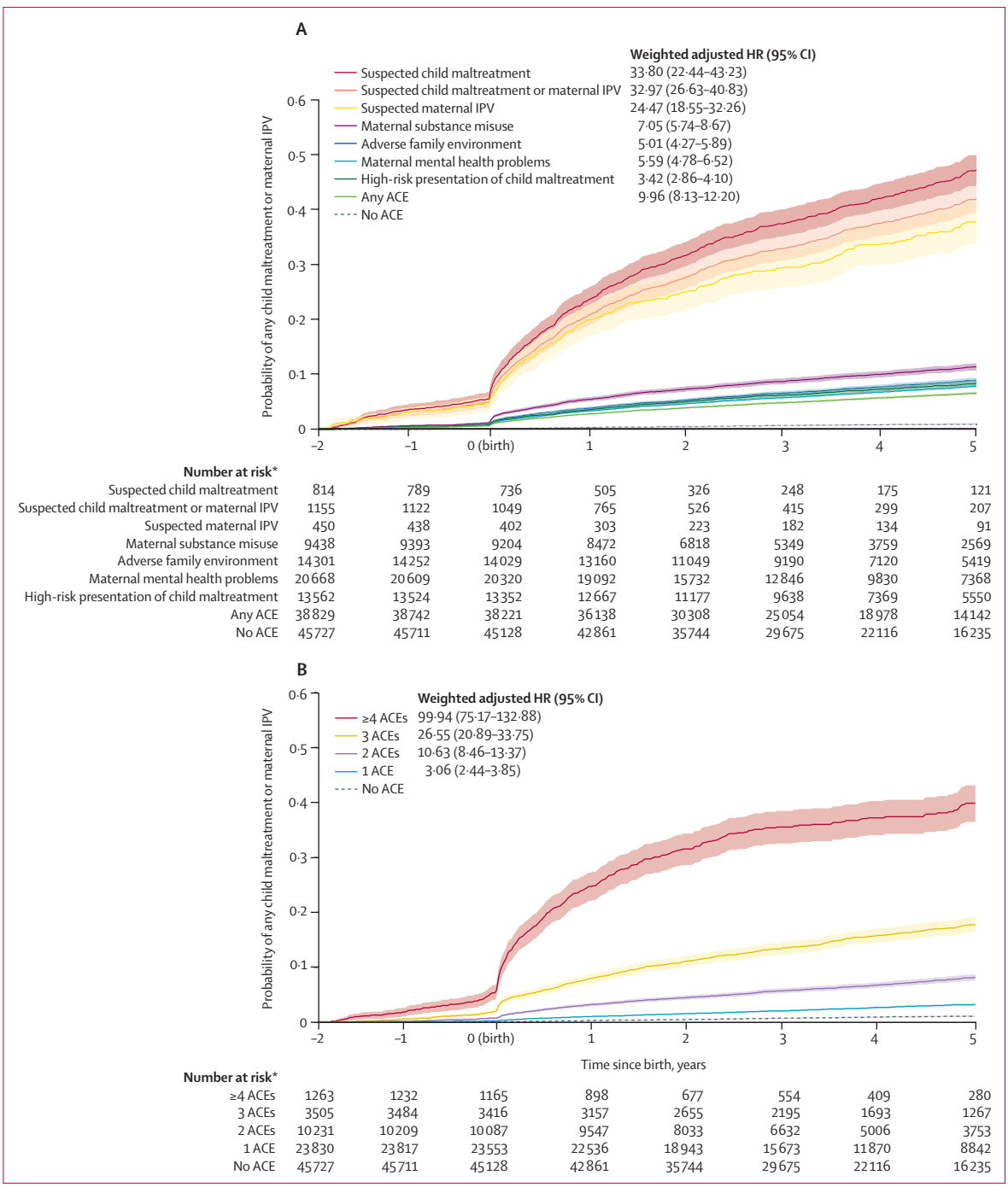

Figure 3: **Kaplan-Meier curves for the probability of any child maltreatment or maternal IPV by ACE domain and by number of ACEs in the validation cohort (n=84556)**

Kaplan-Meier curves present the probability of any child maltreatment or maternal IPV (reference standard) over time by ACE domain (A) and by the number of ACEs (B), from 2 years before birth to 5 years after birth, relative to mother–child pairs with no ACEs. ACE=adverse childhood experience. HR=hazard ratio. IPV=intimate partner violence. *At baseline, the number at risk represents the total number of exposed mother–child pairs by ACE domain who had not yet experienced the reference standard for the entire 7-year period.

maternal substance misuse, 8·1% (7·8–8·3%; 6808 pairs) for high-risk presentations of child maltreatment, 2·4% (2·3–5·6%; 2051 pairs) for child maltreatment, 1·0% (0·8–1·0%; 875 pairs) for maternal IPV, and 3·0% (2·9–3·2%; 2540 pairs) for any child maltreatment or maternal IPV (appendix p 41; figure 4B). For the same

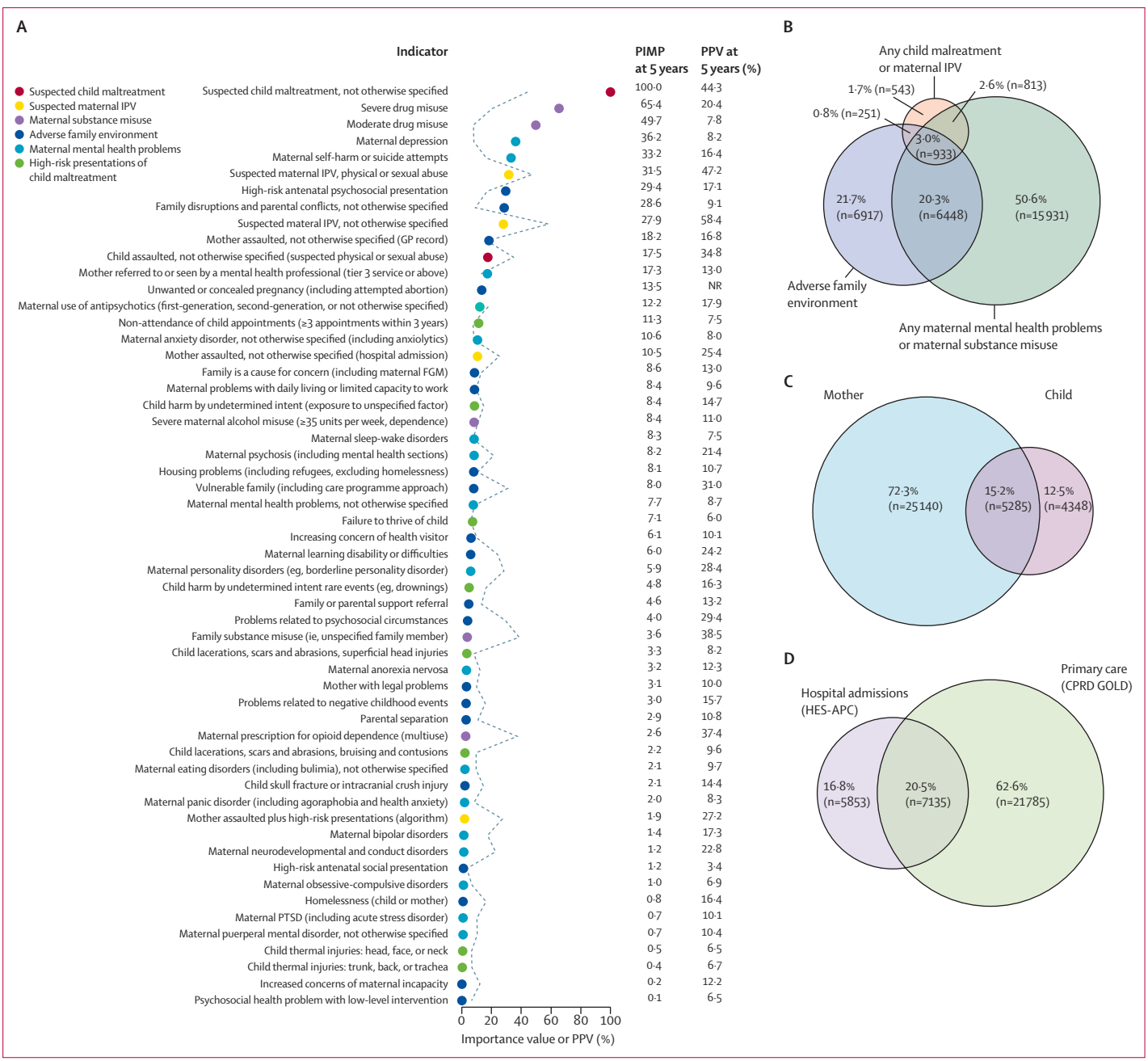

Figure 4: **Random forest variable importance values and PPVs of ACE indicators measured 2 years before to 5 years after birth, and Venn diagrams of ACE overlap measured 2 years before and after birth in the validation cohort**

(A) PIMP values (circles) and PPVs (dashed line) of ACE indicators for predicting any child maltreatment or maternal IPV (reference standard) from 2 years before birth to 5 years after birth in the validation cohort from a split sample, cross-validated, random forest model. Indicators refer to both children and mothers, unless specified. PIMP values refer to the average decrease in the model's prediction performance after randomly shuffling indicators (ie, breaking the association with the outcome). A higher PIMP value meant that the model relied more on the specific indicator for prediction performance. PPVs calculated by dividing reference standard cases by indicator positive cases. Overlap of recorded ACEs measured 2 years before birth to 2 years after birth by five different ACE domains collapsed into three domains (B), which included 31 836 exposed pairs and excluded the high-risk presentation of child maltreatment domain; by individual (C; ie, maternal *vs* child record), and by data source (D) for the final individual indicators. All estimates are from the validation cohort (n=84 556 mother–child pairs). ACE=adverse childhood experience. CPRD=Clinical Practice Research Datalink. GP=general practitioner. HES-APC=Hospital Episodes Statistics database for admitted patient care. IPV=intimate partner violence. PIMP=permutation variable importance. PPV=positive predictive value. PTSD=post-traumatic stress disorder.

4-year period, 62·6% of ACEs were recorded in primary care only (21785 of 34773 pairs), and 16·8% were from hospital admissions or death records only (5853 of 34773 pairs; figure 4C, D). For any of the ACEs, 72·3% (25140 cases) were recorded in the maternal record only. For any of the child maltreatment or maternal IPV, 90·6% (2302 of 2540 cases) were identified in primary care only (overall crude prevalence 2·7%).

The results of the sensitivity analyses are provided in the appendix (pp 40–44). The results remained relatively robust across all sensitivity analyses (any ACE, range AUC 0·73–0·84). However, stratification by data source showed that the ACEs recorded in the HES-APC and the Office for National Statistics mortality register only reduced the overall AUC to 0·73, relative to CPRD only, or all sources.

Discussion

We developed and evaluated 63 indicators of ACEs, which represent six distinct and clinically meaningful domains, using data from a large representative English birth cohort of 211393 mothers and children. ACE indicators were derived by combining evidence from national guidance, systematic reviews, multistage risk prediction models of child maltreatment or maternal IPV, and clinical review. Validation estimates remained robust in different subgroups analyses, and manually grouped indicator domains were broadly confirmed in clustering analyses. Overall, we found that 39·1% of linked mothers and children had ACEs recorded in primary and secondary care 2 years before and after birth. The findings underscore the potential utility of linked data systems and so-called think-family approaches to identify and measure ACEs among families most in need.

The six ACE domains broadly align with the original ACE domains[29] and map onto clinically recognisable presentations of vulnerable families who might present to health care. Our indicators are comprehensive and extend previous studies in several ways. We use data from both children and mothers to identify ACEs, and integrate theoretically informed variable selections with data-driven approaches to capture clinically relevant ACEs. Therefore, our findings complement population-level reports from the Danish Life Course Cohort Study, which used data-driven approaches (eg, trajectory analyses) to group individuals into higher and lower adversity groups.[86,87] Our prevalence estimate for any child maltreatment or maternal IPV (3%) is over ten times higher than previous estimates in nationwide studies of hospital admissions (eg, <0·1%),[19] and higher than previous studies using primary care data (eg, 1·8% for child maltreatment).[88] Estimates for the more prevalent ACEs, such as maternal substance misuse and maternal mental health problems, were also higher than previous primary care studies assessing mothers or children in isolation.[20,89]

Previous studies have differed in their approach to developing ACEs, with definitions and reference standards varying across studies. We used child maltreatment and maternal IPV as a reference standard indicative of underlying adversity and presentations requiring action.[31,58] Most previous studies determined the relevance of retrospectively reported ACEs on the basis of associations with poor health in adulthood (ie, with the assumption that ACEs predicted longer-term harm to health).[2] The longitudinal mechanisms underlying these associations are unclear and produce modest effect sizes compared with other contextual factors. A multisite birth cohort study of 3269 children found that ACEs reported in childhood showed relatively low accuracy in predicting poor health outcomes in adulthood (aged 18–45 years) when adjusting for socioeconomic factors.[90] We used a reference standard that separated the adverse experience from the adverse stress response of the child, overcoming previous measurement limitations of recall bias and influences by other life factors as children grow up.

This study has several limitations. First, the absence of an independent reference standard meant that indicators could have overestimated risk for families, in whom ACEs are more likely to be noticed and recorded (eg, families with more complex needs).[62] Second, structured data on child maltreatment and maternal IPV reflect only a small proportion of affected women and children presenting to services,[91] and many children might have concerns recorded only in free-text data that is not captured in coded data. However, linkage to self-report data of children is practically challenging and susceptible to self-report biases. Future linkage of EHRs to children's social care data offers an alternative way forward for external validation.[92] Third, CPRD GOLD contains EHRs from the Vision data system, one of the three main primary care data systems in the UK (ie, Egton Medical Information Systems, SystmOne, and Vision); however, it has the least data coverage.[93] Ever-changing policies and coding practices mean that the recording of ACEs might be influenced by different EHR systems, time-specific trends, and changes in NHS reporting demands. However, CPRD GOLD is the most widely used primary care data source for epidemiological research in the UK,[36] and the only primary care data source with validated mother–baby linkage. Further research to validate mother–baby linkages and ACEs in larger GP databases are needed to generalise findings (eg, the CPRD Aurum). Finally, we could not link children with their fathers, a long-standing issue of anonymised secondary and primary care data. Therefore, indicators would have provided an underestimation of ACEs in the family. Nevertheless, a Swedish registry study showed that maternal mental health problems (ie, the largest form of ACE) were associated with a small increased risk of child injuries, but had a significantly larger effect relative to paternal mental health problems.[94]

Our study is unique in developing ACE indicators based on the EHRs of mothers and children in primary

and secondary care. Over 70% of ACEs were identified from maternal records, with most ACEs recorded in primary care in the first years of the child's life course. ACEs are preventable and are a clinically important target for early primary care responses, including prompting additional questions, arranging home visits and referrals, and increasing monitoring opportunities.[12,95–97] Therefore, our findings emphasise the importance of using a think-family approach and linked EHR systems (eg, GP family tab) to scrutinise the primary care records of family members for ACEs. Additionally, our findings represent an important first step towards future evaluations of integrating ACE indicators into workflows for prioritising resources.[97] Care staff work under immense pressure, with recurrent staffing shortages, waiting lists, and time limits (eg, 10 mins per GP consultation).[98] In many cases, staff do not have the time to process both the child's and mother's records to examine the need for potential support to inform early responses.[99,100] At a broader level, ACE domains have the potential to help organisations better understand trends and relationships between ACEs, other risk factors (eg, obesity or smoking), and chronic conditions to commission trauma-informed care aimed at reducing risk factors.[3,13,42]

Nevertheless, the potential use of digitally curated ACE indicators in the future requires additional research before service implementation. Current ACE indicators draw on maternal records to trigger actions for the child and the mother. This method potentially exposes the mother's confidential information to the individuals involved in the child's care without her consent, including to a perpetrator of abuse (eg, potential child maltreatment triggered by maternal IPV perpetrated by the child's father). Hence, routine use of ACE indicators needs careful piloting for potential harms and benefits, potential stigma, ethics, and public acceptability, followed by randomised trials to test their efficacy in improving outcomes for children exposed to ACEs.[101] We openly provide all excluded and included ACE indicators, cross-mapped across different systems, to aid further evaluation.

Contributors

SS and RG conceived the study. SS, RG, and LL designed the study. SS and LL completed the statistical analyses. RG and LL provided study supervision. AG-I had full access to the CPRD database to extract the study population. SS, LL, AG-I, and RG accessed and verified all the data in the study. All authors contributed to the interpretation of the data, drafting of the manuscript revisions, and had final responsibility for the decision to submit for publication.

Declaration of interests

All authors declare no competing interests.

Data sharing

This study uses data from the CPRD, a research service that provides primary care and linked data for public health research. CPRD data governance does not allow distribution or access to data to other parties outside of the approved study protocol. Researchers can apply for data access with a study protocol at the CPRD website and would need approval by the Research Data Governance Secretariat. We provide all relevant code lists and coding scripts on the ACEs in EHRs library of indicators. All code is shared without investigator support.

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