Mental health and peer relationship problems in preterm born adolescents: Which factors predict absence of symptoms?

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Abstract

Background and aim: Preterm birth is associated with difficulties in mental health and peer relationships in adolescence; however, most preterm adolescents do not experience these difficulties.

Objective: To apply machine learning models to identify key early predictors of better mental health and peer relationships in preterm adolescents.

Methods: The participants of the current study included 1472 preterm and 16,389 full-term individuals from the UK Millennium Cohort Study (2000-02). Early factors included a range of measurements across the following broad categories in infancy and early childhood: sociodemographic, family structure and environment, child-related birth and infancy factors, and early childhood factors. Mental health and peer relationships were assessed at 11, 14, and 17 years using the Strengths and Difficulties Questionnaire.

Results: The prediction model in preterm born adolescents had the highest accuracy for 17 years of age and in hyperactivity/inattention disorders (75%, 82.7%, 92%, at 11, 14 and 17 years respectively) and conduct/oppositional disorders (80%, 78%, 87.1%, respectively). A similar pattern was found in full-term born adolescents. Family structure and environment related factors in early childhood contributed to better mental health and peer relationships problems in both preterm and full-term adolescents. In preterm born adolescents, motor skills in infancy and better cognitive development and emotional regulation in early childhood predicted better mental health and peer relationships.

Conclusions: This study suggests that machine learning can help paediatricians differentiate preterm children who will not develop mental health symptoms and peer relationship problems from those at risk for developing these problems in adolescence.

Keywords: preterm birth, positive outcomes, Millennium Cohort Study

Approximately one in ten babies are born preterm (<37 weeks of gestation) worldwide, which has increased significantly in the recent decades [1]. Improvements in neonatal care, such as the use of assisted ventilation, the introduction of advanced technology [2] and changing attitudes towards intensive care [3] have resulted in marked increases in the survival rate of preterm infants. However, preterm birth has been linked to adverse outcomes across the life course such as reduced brain volume, abnormalities in the brain structures such as cerebral white matter and the prefrontal cortex, abnormalities in brain connectivity [4, 5], as well as cognitive deficits[6-8] and lower academic achievement [9, 10] in comparison to those born full-term. Moreover, it has been associated with a behavioural and personality phenotype which includes being socially withdrawn and timid [11, 12]. These difficulties are likely to predispose preterm born children to be at risk for increased rate of emotional and behavioural problems [13-16], and difficulties in peer relationships [17, 18].

The impacts of preterm birth might be particularly evident in adolescence [17, 19, 20] due to physical, biological, and social transitions during adolescence with peer relationships becoming increasingly more important during this stage of life [21] as the time spent with peers increases dramatically during this period [22]. It is also a crucial period for the onset of psychiatric disorders [23] with 34.6% of disorders starting before 14 years of age with a peak age of 14.5 years [24]. However, it is important to note that, despite these risks, the outcomes of preterm birth have considerable variability across individuals. To illustrate, it was shown that 84% of preterm children had optimal outcomes on social, emotional, and behavioural domains at 2 years of age [25]. Another study found that approximately 45% of preterm children showed no difficulties on a range of developmental domains such as psychosocial functioning and behavioural development at 5.5 years of age [26].

Although there is increasing evidence for the negative impact of preterm birth on adolescence mental health and peer relationships, less is known about the factors that can promote the absence of these outcomes in adolescence after preterm birth [17]. Evidence from

previous studies suggests that a large range of factors including sociodemographic characteristics, family structure and environment, birth and infancy factors, and early childhood factors could promote adaptive outcomes in terms of mental health and peer relationships after preterm birth [27-31]. However, it is unclear which of these factors are the most important ones for absence of mental health symptoms and peer relationship problems at different stages of adolescence after preterm birth.

To this end, the large number of factors that might influence the absence of mental health symptoms and peer relationship problems after preterm birth in adolescence requires analytical techniques with the ability to handle large and heterogeneous data sets. Machine learning techniques have this capacity as well as other advantages such as fewer assumptions about distributions of the data, numerous options of non-parametric models and dimensionality reduction techniques, and most notable their strong predictive capabilities.[32] This approach could help gain a better understanding of a population and increase predictive power, as features that are shown to be important across mathematically unique algorithms likely represent fundamental characteristics of that population and are therefore important in predicting the outcome [32]. Thus, the current study aimed to determine which early factors are most important for adolescence optimal outcomes in mental health and peer relationships after preterm birth focusing on 4 broad headings: sociodemographic, family structure and environment, birth and infancy factors, and early childhood factors, and whether the important factors differ for preterm and full-term born adolescents.

Methods

Participants

The current study used data from the Millennium Cohort Study (MCS), which is a nationally representative longitudinal study of 18,522 infants born in the United Kingdom [33]. A random two stage sample of all infants born in England and Wales between September 2000 and August 2001, and in Scotland and Northern Ireland between November 2000 and January 2022, who

were alive and living in the UK at age 9 months was drawn from Child Benefit registers that cover virtually all children in the UK. The sample is geographically clustered with over-sampling of ethnic minority and disadvantaged areas. The first sweep of interviews with cohort members' mothers took place when the infants were 9 months old and follow up interviews were conducted when the children were 3, 5, 7, 11, 14, 17 and 22 years of age. The current study focused on the assessments made at 9 months, 3, 5, 11 ,14 and 17 years of age. The interviews included questions on a wide variety of topics, including health, education, social, family, and economic status of the cohort members' households. Detailed information on the sampling and scope of MCS is available at: http://www.cls.ioe.ac.uk/. Ethical approval and written informed consent for all participants were obtained (London - Hampstead Research Ethics Committee, REC reference 14/LO/0868). Participants of the current study included N=1472 preterm and N=16,389 full-term participants.

Measures

Preterm birth. Gestational age in full weeks plus days was extracted from medical records as a continuous variable, which was recoded into a categorical variable according to the following birth groups: preterm (<37 completed weeks of gestation); and full-term (37-41 completed weeks of gestation).

Mental health symptoms and peer relationship problems in adolescence. Strengths and Difficulties Questionnaire (SDQ) was used to measure mental health symptoms and peer relationships in adolescence, which was completed by parents at three assessment points when children were 11, 14, and 17 years old. The SDQ is a widely used and psychometrically valid behavioral screening tool suitable for community samples [34]. In addition to focusing on common areas of emotional and behavioral difficulties (i.e., emotional symptoms, hyperactivity/inattention, and conduct problems), SDQ also measures peer relationship problems.

Each subscale includes 5 items with scores ranging from 0 to 10. The following clinical cut-offs[35] are applied to reflect risk of disorders or problems: anxiety-depressive disorders ≥ 5, hyperactivity-inattention disorders ≥ 7, conduct-oppositional disorders ≥ 4, peer relationship problems ≥ 4, and total difficulties ≥ 17.[36] The absence of clinical symptoms were defined by scores below these cut-offs: anxiety-depressive disorders < 5, hyperactivity-inattention disorders < 7, conduct-oppositional disorders < 4, peer relationship problems < 4, and total difficulties < 17.

Early factors. Early factors were considered under 4 broad headings: sociodemographic, family structure and environment, birth and infancy factors, and early childhood factors. Measurement details and sweep for each variable are presented in Table 1.

Data Analyses. The analyses were conducted in two steps. First, analysis of variance and χ^2 tests were performed to compare the preterm group with full-term group on the predictors and outcomes. Next, the data preparation and the machine learning approaches were implemented as describe in the following section.

Data cleaning and preparation

Missing values were imputed, using the sklearn IterativeImputer function and random forest algorithm as the base estimator in line with a previous study [37]. The commonly used 80:20 training were applied to test dataset split, with the training set further divided into training and validation sets. An over-sampling (i.e., Synthetic Minority Oversampling Technique: SMOTE) technique was applied to balance the two classes (clinical symptoms vs absence of clinical symptoms) and avoid potential issues of overfitting.

To match the proportion of the outcome variable as in the overall dataset, StratifiedKFold cross-validation was used, repeated 5 times with 3 different splits. SMOTE was applied to the training data before fitting the models, to avoid data leakage within a cross-validation fold, i.e., overestimated model performance. Finally, the models were evaluated on the original test data.

Machine learning methods

In line with previous studies [37, 38], four models: logistic regression, XGBoost (Extreme gradient boosting), random forest, and kNN (K-Nearest Neighbors), and the following evaluation metrics: AUC (Area under the curve), accuracy, sensitivity (i.e., recall), specificity, precision, and F-score (i.e., F1) were selected.

The training time for all models was approximately 10 minutes for the preterm and 20 minutes for the full-term group. Models' hyperparameters were optimised with GridSearch from sklearn, and F1 as a scoring metric due to its account for both positive and negative class cases.

Feature importance was determined with sklearn's attribute "feature_importances_". The higher the feature's score, the more important it is for a model's performance.

Results

Appendix Table A1 shows the characteristics of the sample according to preterm and full-term birth. Comparisons between preterm and full-term adolescents on the prevalence of absence and presence clinical symptoms are shown in Table 2.

Machine learning: Model performance evaluation and feature importance

The performance of the four models (XGBoost, random forest, kNN, and logistic regression) were compared as the baseline model, on the *total difficulties* outcome (Figure 1), using prediction accuracy and feature importance. In the pre-term group, random forest demonstrated better performance, particularly at age 14 across all metrics, and at age 17 (falling slightly behind XGBoost only in specificity). At age 11, random forest was the most accurate model. In the full-term group, this model achieved the highest accuracy, precision and specificity across all age groups (apart from the latter for age 14). Therefore, given its superior performance in the majority of cases that were tested, *random forest* was selected and applied for the purposes of this study.

The results in Figure 2 (and Table A2) show that random forest had high accuracy rate ranging from 72.2% to 92% for the preterm adolescents, and from 76.4% to 91.8% for the full-

term adolescents in predicting absence of clinical symptoms. In preterm adolescents, the model was more accurate in predicting absence of clinical symptoms at 17 years of age and in hyperactivity/inattention disorders (75%, 82.7%, 92%) and conduct/oppositional disorders (80%, 78%, 87.1%) in comparison to anxiety/depressive disorders (76.2%, 75.7%, 78.7%) and peer relationship problems (72.2%, 75.2%, 75.5%) at 11, 14 and 17 years respectively. A similar pattern was found in full-term born adolescents.

The AUC (i.e., balanced accuracy) results were higher for the older age groups (i.e., 17 years) than 11 years. Moreover, the model had the best performance in specificity, ranging from 82% to 94.4% in the preterm group and 90% to 97% in the full-term group, implying that it is highly accurate in predicting cases where an adolescent born preterm or full-term do not have clinical symptoms. Nevertheless, the model showed poorer performance in sensitivity (i.e., ability to predict cases with a disorder/difficulty), precision and F1.

Feature importances in predicting absence of clinical symptoms

Figure 3 shows the 5 most important features in predicting absence of clinical symptoms for preterm and full-term born individuals. At 14 and 17 years, previous assessments of the same disorder or problem were the most significant predictors for all outcomes.

Low maternal psychological distress (at 9 months and 3 years) and female sex emerged as the strongest predictors of absence of clinical symptoms across varying outcomes and stages in adolescence in both the preterm and full-term groups. Additional key factors are summarized below.

In preterm adolescents, predictors of absence of clinical symptoms in anxiety-depressive disorders included parent-child closeness at 3 years, fine motor skills at 9 months, and birthweight, respectively for different stages in adolescence (i.e., 11, 14, and 17 years). For absence of clinical symptoms in hyperactivity/inattention disorders, other key predictors included independence and self-regulation at 3 years, parental education at tertiary level, and verbal knowledge at 3 years, respectively for different stages in adolescence (i.e., 11, 14, and 17

years). For absence of clinical symptoms in conduct/oppositional disorders, other key predictors included being breast fed, parental education at tertiary level, and verbal knowledge at 3 years, respectively for different stages in adolescence (i.e., 11, 14, and 17 years). For absence of clinical symptoms in peer relationship problems, parent-child closeness at 3 years, social support at 3 years, and communication skills at 3 years were key predictors respectively for different stages in adolescence (i.e., 11, 14, and 17 years).

In full-term adolescents, the highest ranked features for predicting absence of clinical symptoms in anxiety-depressive disorders were parenting competence and breast feeding. For absence of clinical symptoms in hyperactivity/inattention disorders and conduct/oppositional disorders, other important predictors included the frequency parents read books at 3 years and maternal non-smoking during pregnancy. For absence of clinical symptoms in peer relationships, independence and self-regulation at 3 years, and parent-child closeness at 3 years were other key predictors.

The key predictor for absence of clinical symptoms in total difficulties at 11 years in both groups was low maternal psychological distress at 3 years. In the preterm group, fine motor skills at 9 months were another top predictor of absence of clinical symptoms in total difficulties at 14 years.

Discussion

This study applied machine learning algorithms to establish the key factors predicting the absence of clinical-level symptoms in mental health and peer relationships among adolescents born preterm and full-term. The random forest model performed the best, showing high accuracy and specificity rates for both the preterm and full-term adolescents, although sensitivity, precision and F1 were lower. Family structure and environment related factors emerged as strong predictors of the absence of clinical symptoms in both preterm and full-term adolescents. In preterm adolescents, however, infancy and early childhood developmental factors were also important.

The model's high accuracy indicates that it reliably distinguishes adolescents with and without clinical symptoms, although average F1 value suggests that the model is not optimal and requires improvement. One possible approach to enhance the performance of the model is to apply the same technique to a larger sample size by combining multiple cohorts. However, this finding may also be because of the imbalanced nature between the two groups: a small clinical symptoms group and a large group without the clinical symptoms [32].

For both preterm and full-term born adolescents, family and environment related factors in early childhood (i.e., low maternal psychological distress, parent-child closeness, parenting competency) were key predictors of low anxiety-depressive symptoms at 11 years. In line with the findings of previous research [39], these findings highlight the importance of good quality family structure and environment during early years for both preterm and full-term adolescents. In preterm adolescents, birth and child-related factors such as birthweight and motor skills also played a role in predicting absence of clinical symptoms at ages 14 and 17 years. Good motor skills might potentially influence the ability of preterm children to participate in peer activities, which might increase their opportunities for making social connections and peer social learning leading to a decreased susceptibility to anxiety-depressive disorders in adolescence [11].

Female sex and low maternal psychological distress were important predictors of absence of clinical symptoms for both preterm and full-term born adolescents. However, for the preterm group, factors such as independence and self-regulation at 3 years were more important than female sex in predicting better outcomes at 11 years, while verbal knowledge at 3 years played a more significant role in predicting lower symptom levels at 17 years. This is in line with previous studies that suggest better self-regulation and verbal knowledge in early childhood are associated with fewer hyperactivity symptoms among preterm born children [40].

Regarding conduct-oppositional disorders, parental education was an important predictor in both preterm and full-term born adolescents. For preterm adolescents, breast feeding was the strongest predictor of absence of clinical symptoms in early adolescence, while for full-term

adolescents, the frequency of parents reading to their child at 3 years was the strongest predictor. In middle adolescence, parent-related factors continued to be associated with better outcomes in both groups. By late adolescence, parent-related factors (such as low maternal psychological distress, parent-child closeness, and parental education) remained key factors for full-term adolescents, whereas for preterm adolescents, child-related factors (such as verbal knowledge and low peer problems at age 3) played a more prominent role. In line with previous research, the findings highlight the importance of parent-related factors in predicting better mental health and peer relationships in both preterm and full-term adolescents. It was shown that preterm born children have lower verbal knowledge and fewer friends and feel less accepted by peers in early childhood than full-term children [41, 42]. Better verbal knowledge and peer relationships in early childhood could promote preterm children's integration at school with peers which might be associated with less conduct problems symptoms.

Parent-related factors in early childhood were key predictors of better peer relationships for both preterm and full-term adolescents. For preterm adolescents, factors such as fine-motor skills at 9 months, communication skills and verbal knowledge at 3 years were additional predictors. This finding further highlights the importance of motor skills and cognitive skills in better peer relationships of preterm adolescents [43].

Regarding total difficulties, better outcomes in full-term adolescents were by family structure and environment (e.g., low maternal psychological distress). For the preterm group, in addition to these factors, fine-motor skills in infancy and peer relationships problems at 3 years of age also played a role.

Clinical Implications

These findings have both theoretical and clinical significance. They help clarify the mechanisms of resilience after preterm birth by identifying which early parental, environmental and child related factors might buffer against adolescence difficulties [44]. Given that the outcomes were defined as the absence of clinical symptoms, an important question is whether

the identified protective factors can be strengthened through interventions. Evidence from randomized control trials indicates that strengthening parental sensitive parenting, decreasing parental psychological distress, and supporting preterm children's early motor development and self-regulation skills can have long-term benefits [45, 46]. Beyond interventions, these findings have practical relevance for communication with parents. When protective factors are present, they can provide parents of preterm children with a balanced reassurance of a more positive outlook, whereas their absence can guide counselling towards the importance of early support. Importantly, these predictors should be regarded as probabilistic rather than deterministic markers as they increase the likelihood of adaptive trajectories but do not guarantee them. Thus, these findings suggest that the predictors identified here may not only be valuable for advancing theoretical understanding but also could play a role in shaping preventative strategies, informing clinical decision-making, and supporting families in navigating their child's developmental trajectory.

Strengths and Limitations

This study extends the previous research which identified several factors for better mental health and peer relationship outcomes in adolescence after preterm birth by examining the interacting effects of these factors and using a combined model that focused on prediction and explanation using a prospective design. Although the use of machine learning in this study is innovative, it has limitations. First, the dataset size was modest for machine learning purposes. However, for psychological research, it is considered a large population-based sample. Moreover, decision tree models were applied to the dataset before [47]. Second, although the study used cross-validation to increase generalizability of results, there is a risk of identifying predictors in the test and validation sets that may not be as important in a new sample. Third, the current study focused on the whole spectrum of preterm birth which makes it difficult to evaluate the findings based on the different sub-categories of preterm birth.

To conclude

For the purposes of developing a tool for identifying adolescents with better outcomes in adolescence, the results suggest that motor skills in infancy, early childhood verbal knowledge, and self-regulation skills have better utility for preterm adolescents, while low maternal psychological distress, and parent-child closeness in early childhood have utility for both preterm and full-term adolescents.

References

[1] S. Chawanpaiboon *et al.*, "Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis," (in eng), *Lancet Glob Health,* vol. 7, no. 1, pp. e37-e46, Jan 2019, doi: 10.1016/s2214-109x(18)30451-0.

[2] S. Saigal and L. W. Doyle, "An overview of mortality and sequelae of preterm birth from infancy to adulthood," *The Lancet,* vol. 371, no. 9608, pp. 261-269, 2008, doi: 10.1016/S0140-6736(08)60136-1.

[3] R. A. Polin *et al.*, "Surfactant Replacement Therapy for Preterm and Term Neonates With Respiratory Distress," *Pediatrics,* vol. 133, no. 1, pp. 156-163, 2014, doi: 10.1542/peds.2013-3443.

[4] A. Menegaux *et al.*, "Aberrant cortico-thalamic structural connectivity in premature-born adults," (in eng), *Cortex,* vol. 141, pp. 347-362, Aug 2021, doi: 10.1016/j.cortex.2021.04.009.

[5] J. J. Volpe, "Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances," (in eng), *Lancet Neurol,* vol. 8, no. 1, pp. 110-24, Jan 2009, doi: 10.1016/s1474-4422(08)70294-1.

[6] A. T. Bhutta, M. A. Cleves, P. H. Casey, M. M. Cradock, and K. J. S. Anand, "Cognitive and Behavioral Outcomes of School-Aged Children Who Were Born PretermA Meta-analysis," *JAMA,* vol. 288, no. 6, pp. 728-737, 2002, doi: 10.1001/jama.288.6.728.

[7] E. S. Twilhaar, R. M. Wade, J. F. de Kieviet, J. B. van Goudoever, R. M. van Elburg, and J. Oosterlaan, "Cognitive Outcomes of Children Born Extremely or Very Preterm Since the 1990s and Associated Risk Factors: A Meta-analysis and Meta-regression," (in eng), *JAMA Pediatr,* vol. 172, no. 4, pp. 361-367, Apr 1 2018, doi: 10.1001/jamapediatrics.2017.5323.

[8] L. D. Breeman, J. Jaekel, N. Baumann, P. Bartmann, and D. Wolke, "Preterm Cognitive Function Into Adulthood," (in eng), *Pediatrics,* vol. 136, no. 3, pp. 415-23, Sep 2015, doi: 10.1542/peds.2015-0608.

[9] A. Bilgin, M. Mendonca, and D. Wolke, "Preterm Birth/Low Birth Weight and Markers Reflective of Wealth in Adulthood: A Meta-analysis," *Pediatrics,* vol. 142, no. 1, 2018, doi: 10.1542/peds.2017-3625.

[10] C. S. Aarnoudse-Moens, N. Weisglas-Kuperus, J. B. van Goudoever, and J. Oosterlaan, "Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children," (in eng), *Pediatrics,* vol. 124, no. 2, pp. 717-28, Aug 2009, doi: 10.1542/peds.2008-2816.

[11] A. Montagna and C. Nosarti, "Socio-Emotional Development Following Very Preterm Birth: Pathways to Psychopathology," (in eng), *Front Psychol,* vol. 7, p. 80, 2016, doi: 10.3389/fpsyg.2016.00080.

[12] S. Johnson and N. Marlow, "Preterm Birth and Childhood Psychiatric Disorders," *Pediatric Research,* vol. 69, no. 8, pp. 11-18, 2011/05/01 2011, doi: 10.1203/PDR.0b013e318212faa0.

[13] C. Nosarti *et al.*, "Preterm birth and psychiatric disorders in young adult life," (in eng), *Arch Gen Psychiatry,* vol. 69, no. 6, pp. E1-8, Jun 2012, doi: 10.1001/archgenpsychiatry.2011.1374.

[14] A. Bilgin *et al.*, "Changes in emotional problems, hyperactivity and conduct problems in moderate to late preterm children and adolescents born between 1958 and 2002 in the United Kingdom," *JCPP Advances,* vol. 1, no. 2, p. e12018, 2021, doi: https://doi.org/10.1111/jcv2.12018.

[15] P. J. Anderson *et al.*, "Psychiatric disorders in individuals born very preterm / very low-birth weight: An individual participant data (IPD) meta-analysis," *eClinicalMedicine,* vol. 42, 2021, doi: 10.1016/j.eclinm.2021.101216.

[16] A. C. Burnett, P. J. Anderson, J. Cheong, L. W. Doyle, C. G. Davey, and S. J. Wood, "Prevalence of psychiatric diagnoses in preterm and full-term children, adolescents and young adults: a meta-analysis," (in eng), *Psychol Med,* vol. 41, no. 12, pp. 2463-74, Dec 2011, doi: 10.1017/s003329171100081x.

[17] A. Bilgin *et al.*, "Emotional problems and peer victimization in adolescents born very preterm and full-term: Role of self-control skills in childhood," *Development and Psychopathology,* pp. 1-10, 2022, doi: 10.1017/S0954579422001201.

[18] K. L. Day, R. J. Van Lieshout, T. Vaillancourt, and L. A. Schmidt, "Peer victimization in survivors of premature birth and low birth weight: Review and recommendations," *Aggression and Violent Behavior,* vol. 25, pp. 259-265, 2015/11/01/ 2015, doi: https://doi.org/10.1016/j.avb.2015.09.010.

[19] K. L. Day, R. J. Van Lieshout, T. Vaillancourt, S. Saigal, M. H. Boyle, and L. A. Schmidt, "Peer Victimization in Extremely Low Birth Weight Survivors," (in eng), *Clin Pediatr (Phila),* vol. 54, no. 14, pp. 1339-45, Dec 2015, doi: 10.1177/0009922815580770.

[20] A. Bilgin, A. Brylka, D. Wolke, H. Trower, N. Baumann, and S. Lemola, "Subjective Well-Being and Self-Esteem in Preterm Born Adolescents: An Individual Participant Data Meta-Analysis," (in eng), *J Dev Behav Pediatr,* vol. 42, no. 8, pp. 613-620, Oct-Nov 01 2021, doi: 10.1097/dbp.0000000000000947.

[21] K. Rubin, W. Bukowski, and J. Parker, "Peer interactions, relationships, and groups.," in *Handbook of Child Psychology: Social, emotional, and personality development*, Eisenberg N Ed. New York: Wiley, 2006, pp. 571-645.

[22] P. Lam, H. Hiscock, and M. Wake, "Outcomes of infant sleep problems: a longitudinal study of sleep, behavior, and maternal well-being," (in eng), *Pediatrics,* vol. 111, no. 3, pp. e203-7, Mar 2003, doi: 10.1542/peds.111.3.e203.

[23] P. J. Uhlhaas *et al.*, "Towards a youth mental health paradigm: a perspective and roadmap," *Molecular Psychiatry,* vol. 28, no. 8, pp. 3171-3181, 2023/08/01 2023, doi: 10.1038/s41380-023-02202-z.

[24] M. Solmi *et al.*, "Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies," *Molecular Psychiatry,* vol. 27, no. 1, pp. 281-295, 2022/01/01 2022, doi: 10.1038/s41380-021-01161-7.

[25] S. Johnson *et al.*, "Differentiating the Preterm Phenotype: Distinct Profiles of Cognitive and Behavioral Development Following Late and Moderately Preterm Birth," (in eng), *J Pediatr,* vol. 193, pp. 85-92.e1, Feb 2018, doi: 10.1016/j.jpeds.2017.10.002.

[26] E. S. Twilhaar, V. Pierrat, L. Marchand-Martin, V. Benhammou, M. Kaminski, and P. Y. Ancel, "Profiles of Functioning in 5.5-Year-Old Very Preterm Born Children in France: The EPIPAGE-2 Study," (in eng), *J Am Acad Child Adolesc Psychiatry,* vol. 61, no. 7, pp. 881-891, Jul 2022, doi: 10.1016/j.jaac.2021.09.001.

[27] L. M. Reyes, J. Jaekel, P. Bartmann, and D. Wolke, "Peer Relationship Trajectories in Very Preterm and Term Individuals from Childhood to Early Adulthood," *Journal of Developmental & Behavioral Pediatrics,* vol. 42, no. 8, pp. 621-630, 2021, doi: 10.1097/dbp.0000000000000949.

[28] K. Treyvaud *et al.*, "Psychiatric outcomes at age seven for very preterm children: rates and predictors," (in eng), *J Child Psychol Psychiatry,* vol. 54, no. 7, pp. 772-9, Jul 2013, doi: 10.1111/jcpp.12040.

[29] S. Johnson and N. Marlow, "Growing up after extremely preterm birth: lifespan mental health outcomes," (in eng), *Semin Fetal Neonatal Med,* vol. 19, no. 2, pp. 97-104, Apr 2014, doi: 10.1016/j.siny.2013.11.004.

[30] A. Bilgin and D. Wolke, "Maternal Sensitivity in Parenting Preterm Children: A Meta-analysis," (in eng), *Pediatrics,* vol. 136, no. 1, pp. e177-93, Jul 2015, doi: 10.1542/peds.2014-3570.

[31] J. Jaekel *et al.*, "The association between gestation at birth and maternal sensitivity: An individual participant data (IPD) meta-analysis," *Early Human Development,* vol. 203, p. 106227, 2025/04/01/ 2025, doi: https://doi.org/10.1016/j.earlhumdev.2025.106227.
[32] D. B. Dwyer, P. Falkai, and N. Koutsouleris, "Machine Learning Approaches for Clinical Psychology and Psychiatry," *Annual Review of Clinical Psychology,* vol. 14, no. 1, pp. 91-118, 2018, doi: 10.1146/annurev-clinpsy-032816-045037.
[33] R. Connelly and L. Platt, "Cohort profile: UK Millennium Cohort Study (MCS)," (in eng), *International journal of epidemiology,* vol. 43, no. 6, pp. 1719-25, Dec 2014, doi: 10.1093/ije/dyu001.
[34] E. Flouri, E. Papachristou, E. Midouhas, G. B. Ploubidis, G. Lewis, and H. Joshi, "Developmental cascades of internalising symptoms, externalising problems and cognitive ability from early childhood to middle adolescence," (in eng), *Eur Psychiatry,* vol. 57, pp. 61-69, Apr 2019, doi: 10.1016/j.eurpsy.2018.12.005.
[35] A. Bryant, J. Guy, and J. Holmes, "The Strengths and Difficulties Questionnaire Predicts Concurrent Mental Health Difficulties in a Transdiagnostic Sample of Struggling Learners," (in eng), *Front Psychol,* vol. 11, p. 587821, 2020, doi: 10.3389/fpsyg.2020.587821.
[36] M. Wolpert, A. Görzig, J. Deighton, A. J. B. Fugard, R. Newman, and T. Ford, "Comparison of indices of clinically meaningful change in child and adolescent mental health services: difference scores, reliable change, crossing clinical thresholds and 'added value' – an exploration using parent rated scores on the SDQ," *Child and Adolescent Mental Health,* vol. 20, no. 2, pp. 94-101, 2015, doi: https://doi.org/10.1111/camh.12080.
[37] A. Sheetal, Z. Jiang, and L. Di Milia, "Using machine learning to analyze longitudinal data: A tutorial guide and best-practice recommendations for social science researchers," *Applied Psychology,* vol. 72, no. 3, pp. 1339-1364, 2023, doi: https://doi.org/10.1111/apps.12435.
[38] A. E. Tate, R. C. McCabe, H. Larsson, S. Lundström, P. Lichtenstein, and R. Kuja-Halkola, "Predicting mental health problems in adolescence using machine learning techniques," (in eng), *PLoS One,* vol. 15, no. 4, p. e0230389, 2020, doi: 10.1371/journal.pone.0230389.
[39] A. Bilgin *et al.*, "Problems in peer relationships and low engagement in romantic relationships in preterm born adolescents: effects of maternal warmth in early childhood," *European Child & Adolescent Psychiatry,* 2024/03/16 2024, doi: 10.1007/s00787-024-02399-6.
[40] L. J. Woodward, Z. Lu, A. R. Morris, and D. M. Healey, "Preschool self regulation predicts later mental health and educational achievement in very preterm and typically developing children," (in eng), *Clin Neuropsychol,* vol. 31, no. 2, pp. 404-422, Feb 2017, doi: 10.1080/13854046.2016.1251614.
[41] K. M. Heuser, J. Jaekel, and D. Wolke, "Origins and Predictors of Friendships in 6- to 8-Year-Old Children Born at Neonatal Risk," *The Journal of Pediatrics,* vol. 193, pp. 93-101.e5, 2018/02/01/ 2018, doi: https://doi.org/10.1016/j.jpeds.2017.09.072.
[42] K. Sanchez *et al.*, "Communication in children born very preterm: a prospective cohort study," *Developmental Medicine & Child Neurology,* vol. 62, no. 4, pp. 506-512, 2020, doi: https://doi.org/10.1111/dmcn.14360.
[43] A. Brylka *et al.*, "Physical Activity, Mental Health, and Well-Being in Very Pre-Term and Term Born Adolescents: An Individual Participant Data Meta-Analysis of Two Accelerometry Studies," *International Journal of Environmental Research and Public Health,* vol. 18, no. 4, p. 1735, 2021. [Online]. Available: https://www.mdpi.com/1660-4601/18/4/1735.
[44] D. Wolke, Y. Zhou, Y. Liu, R. Eves, M. Mendonça, and E. S. Twilhaar, "A systematic review of conceptualizations and statistical methods in longitudinal studies of resilience,"

Nature Mental Health, vol. 3, no. 9, pp. 1088-1099, 2025/09/01 2025, doi: 10.1038/s44220-025-00479-3.

[45] R. C. Silveira *et al.*, "Parent-Guided Developmental Intervention for Infants With Very Low Birth Weight: A Randomized Clinical Trial," (in eng), *JAMA Netw Open,* vol. 7, no. 7, p. e2421896, Jul 1 2024, doi: 10.1001/jamanetworkopen.2024.21896.

[46] V. Dell'Aversana, M. Tofani, and D. Valente, "Emotional Regulation Interventions on Developmental Course for Preterm Children: A Systematic Review of Randomized Control Trials," (in eng), *Children (Basel),* vol. 10, no. 3, Mar 22 2023, doi: 10.3390/children10030603.

[47] D. Waynforth, "Identifying Risk Factors for Premature Birth in the UK Millennium Cohort Using a Random Forest Decision-Tree Approach," *Reproductive Medicine,* vol. 3, no. 4, pp. 320-333, 2022. [Online]. Available: https://www.mdpi.com/2673-3897/3/4/25.

Table 1. Description of included factors, measurement, and age of assessment.

Factors/variables	Measurement	Age at Assessment (Wave of the Study)
Sociodemographic Characteristics		
Sex	Male/female	9 mo (1)
Ethnicity	White Majority/Non-White Minority	9 mo (1)
Income	OECD UK equivalized quartiles	3 y (2)
Parental Highest Education Level	Highest NVQ level in the household	9 mo (1)
Maternal age at birth	in years	9 mo (1)
Family Structure and Environment		
Marital status	Cohabitating/married vs single	9 mo (1)
First or later child	Yes/no	
Low maternal psychological distress	Malaise Inventory & Kessler (K6) Scale recoded to indicate low distress	9 mo (1) & 3y (3); 5y (3)
Social support	Level of emotional, financial and instrumental support received	9 mo (1)
Parent Relationship Quality	Golombok-Rust Inventory for Marital State	9 mo (1)
Physical violence in relationship	No grabbing, pushing, shaking, hitting, kicking	9 mo (1)
Parent-child closeness	Pianta Child-Parent Relationship Scale	3 y (2)
Parent-child conflict	Pianta Child-Parent Relationship Scale	3 y (2)
Emotional & verbal responsivity	Home Observation for Measurement of the Environment scale	3 y (2)
Stimulating home environment (reading to child)	Frequency of reading to child (every day, several times a week, once or twice a week, once or twice a month, less often)	3 y (2)
Parenting beliefs	Attitudes towards child rearing	9 mo (1)
Parenting style	Firm rules and discipline; Lots of fun Have not really thought about it; Firm discipline plus lots of fun; Doing my best for the children	3 y (2)
Immediate responding to crying	Parent responds to baby immediately when crying	9 mo (1)
Bed-sharing	Parental bed-sharing with the baby	9 mo (1)
Discipline practices	Straus's Conflict Tactics Scale	3 y (2)
Parenting competence	Parent feels that they are a good parent	3 y (2)
Parental self-esteem	Rosenberg Self Esteem Inventory	9 mo (1)
Bonding	Condon Maternal Attachment Questionnaire	9 mo (1)
Birth and Infancy Factors		
Smoking during pregnancy	Yes/no	9 mo (1)
Breast feeding	Yes/no	9 mo (1)
Gross-motor development	Denver Developmental Screening Test	9 mo (1)
Fine-motor development	Denver Developmental Screening Test	9 mo (1)
Communication skills	MacArthur Communicative Development Inventories	9 mo (1)

Temperament		
Mood	Carey Infant Temperament Scale	9 mo (1)
Apprehension-withdrawal	Carey Infant Temperament Scale	9 mo (1)
Adaptiveness	Carey Infant Temperament Scale	9 mo (1)
Regularity	Carey Infant Temperament Scale	9 mo (1)
Night waking frequency	Frequency of night-waking	9 mo (1)
Crying is problematic	Parent thinks infant crying is problematic	9 mo (1)
Early Childhood Factors		
Neurosensory Impairments		
Cognitive Ability		
School Readiness	Bracken School Readiness Questionnaire	3 y (2)
Verbal Knowledge	Naming Vocabulary measure from the British Ability Scales II	3 y (2)
Self-regulation: Independence	Child Social Behavior Questionnaire	3 y (2)
Emotional dysregulation	Child Social Behavior Questionnaire	3 y (2)
Screen media exposure	Hours a day child watches TV or videos	3 y (2)
Mental Health in Early Childhood		
Emotional symptoms	Strengths and Difficulties Questionnaire	3 y (2)
Hyperactivity/inattention	Strengths and Difficulties Questionnaire	3 y (2)
Conduct problems	Strengths and Difficulties Questionnaire	3 y (2)
Peer relationship problems	Strengths and Difficulties Questionnaire	3 y (2)
Total Problems	Strengths and Difficulties Questionnaire	3 y (2)

mo: months; y: years

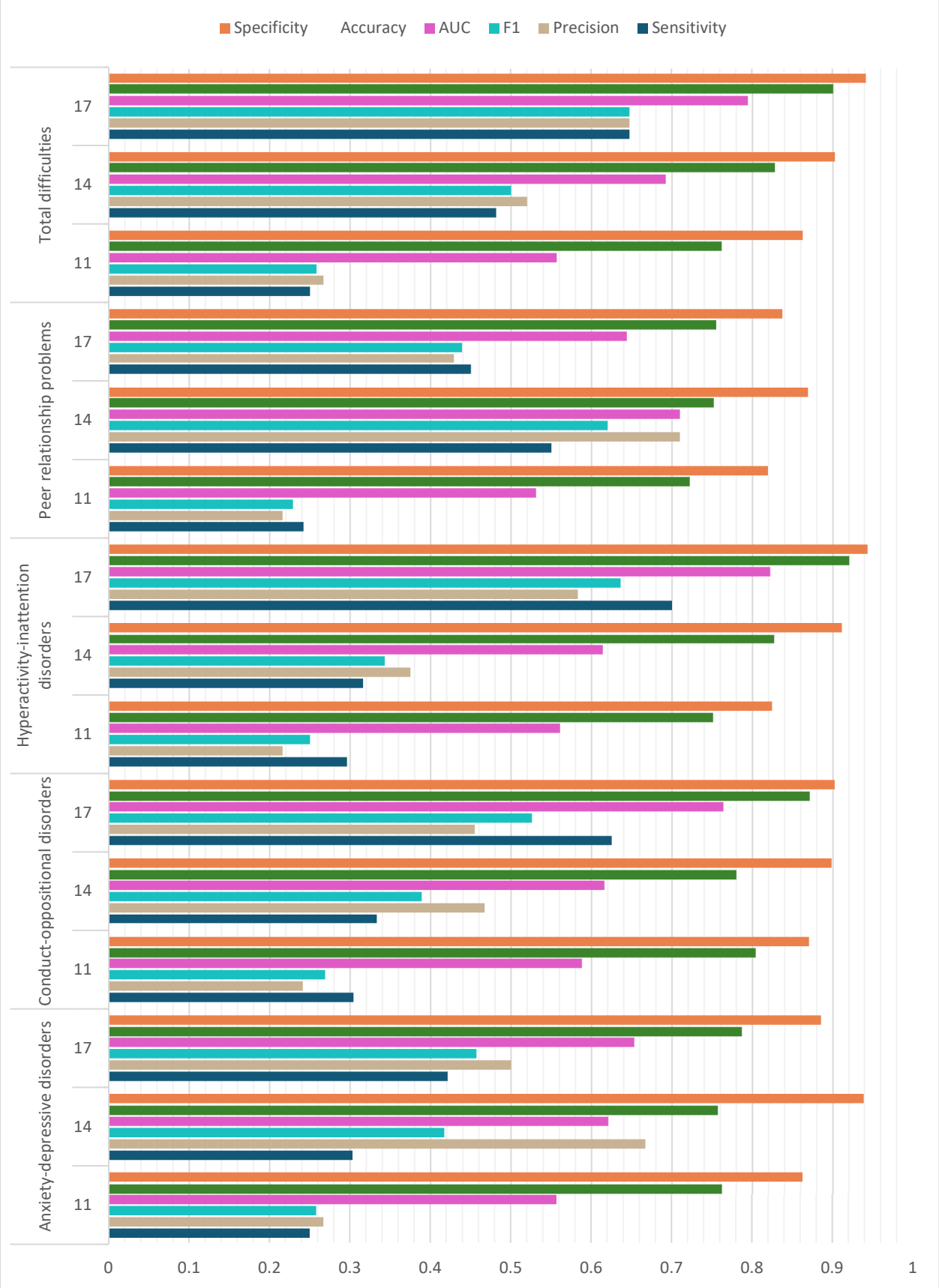
Table 2. Prevalence of adaptive outcomes in mental health and peer problems in preterm and full-term adolescents

	Preterm	Full-term	p
11y			
Anxiety-depressive disorders			
Clinical symptoms	83 (8.6%)	676 (6.2%)	.003
Adaptive outcomes	885 (91.4%)	10277 (93.8%)	
Hyperactivity-inattention disorders			
Clinical symptoms	85 (8.8%)	712 (6.5%)	.007
Adaptive outcomes	882 (91.2%)	10224 (93.5%)	
Conduct-oppositional disorders			
Clinical symptoms	56 (5.8%)	510 (4.7%)	.119
Adaptive outcomes	915 (94.2%)	10443 (95.3%)	
Peer relationship problems			
Clinical symptoms	79 (8.2%)	645 (5.9%)	.005
Adaptive outcomes	890 (91.8%)	10316 (94.1%)	
Total difficulties			
Clinical symptoms	99 (10.3%)	788 (7.2%)	.001
Adaptive outcomes	866 (89.7%)	10133 (92.8%)	
14y			
Anxiety-depressive disorders			
Clinical symptoms	82 (10.1%)	714 (7.5%)	.007
Adaptive outcomes	729 (89.9%)	8810 (92.5%)	
Hyperactivity-inattention disorders			
Clinical symptoms	59 (7.3%)	525 (5.5%)	.037
Adaptive outcomes	752 (92.7%)	8999 (94.5%)	
Conduct-oppositional disorders			
Clinical symptoms	52 (6.4%)	478 (5%)	.084
Adaptive outcomes	759 (93.6%)	9046 (92.3%)	
Peer relationship problems			
Clinical symptoms	81 (10%)	761 (8%)	.046
Adaptive outcomes	730 (90%)	8763 (92%)	
Total difficulties			
Clinical symptoms	83 (10.2%)	712 (7.5%)	.005
Adaptive outcomes	728 (89.8%)	8812 (92.5%)	
17y			
Anxiety-depressive disorders			
Clinical symptoms	80 (10.7%)	680 (7.8%)	.006
Adaptive outcomes	671 (89.3%)	8021 (92.2%)	
Hyperactivity-inattention disorders			
Clinical symptoms	22 (2.9%)	267 (3.1%)	.832
Adaptive outcomes	729 (97.1%)	8434 (96.9%)	
Conduct-oppositional disorders			
Clinical symptoms	27 (3.6%)	275 (3.2%)	.516
Adaptive outcomes	724 (96.4%)	8426 (96.8%)	
Peer relationship problems			
Clinical symptoms	76 (10.1%)	638 (7.3%)	.006
Adaptive outcomes	675 (89.9%)	8063 (92.7%)	
Total difficulties			
Clinical symptoms	56 (7.5%)	525 (6.1%)	.155
Adaptive outcomes	695 (92.5%)	8166 (93.9%)	

Figure 1. Performance metrics for four models XGBoost (xgb), random forest (rf), kNN (knn) and logistic regression (base) in predicting the absence of *total difficulties* at age 11, 14 and 17 for preterm and full-term born adolescents

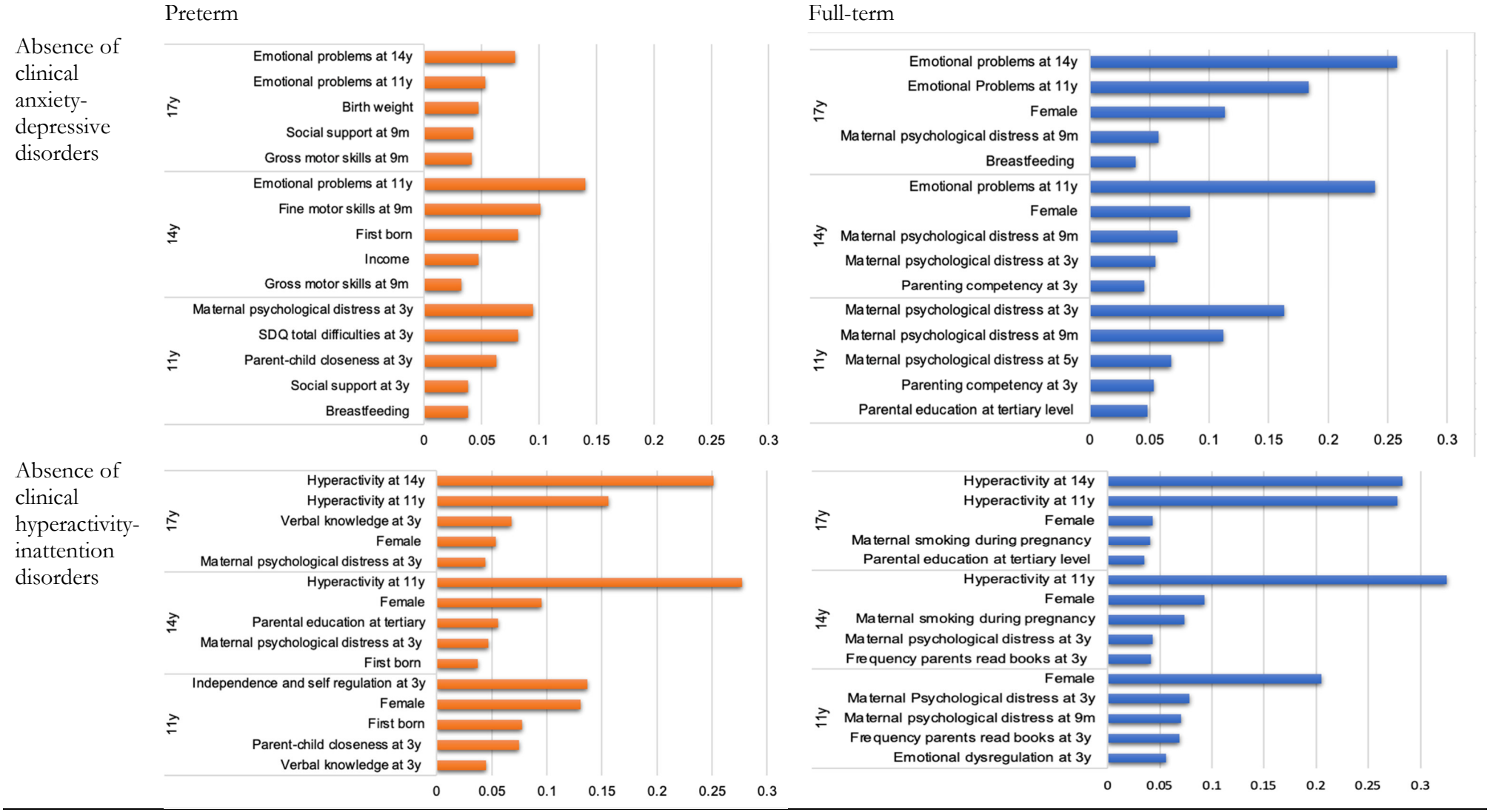
XGBoost: Extreme gradient boosting; kNN: K-Nearest Neighbors.

Figure 2. Random forest model performance metrics in predicting better outcomes in preterm born individuals at ages 11, 14 and 17

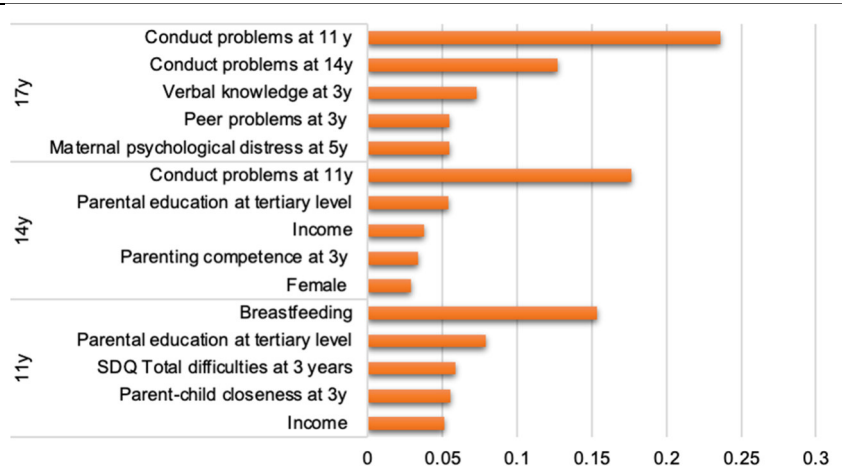


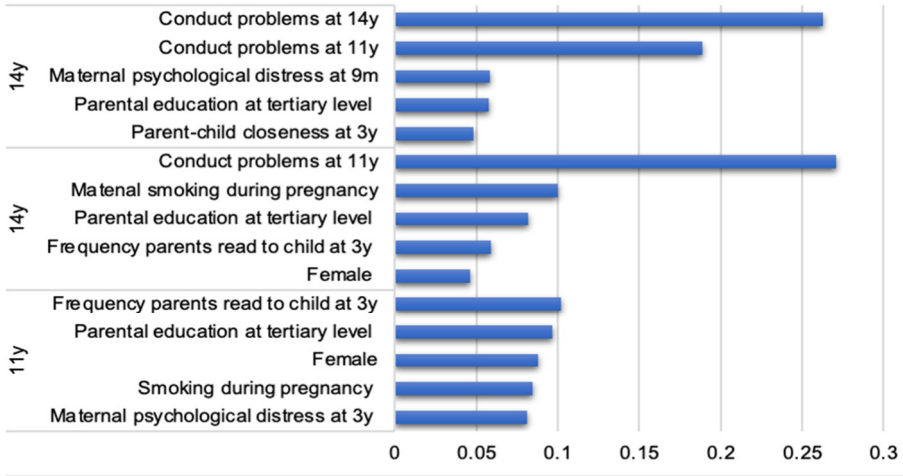
Please note that above values are for the absence of clinical symptoms in the respective disorders. AUC: Area under the curve; F1: F score.

Figure 3. Feature importances in predicting absence of clinical outcomes in preterm and full-term born adolescents

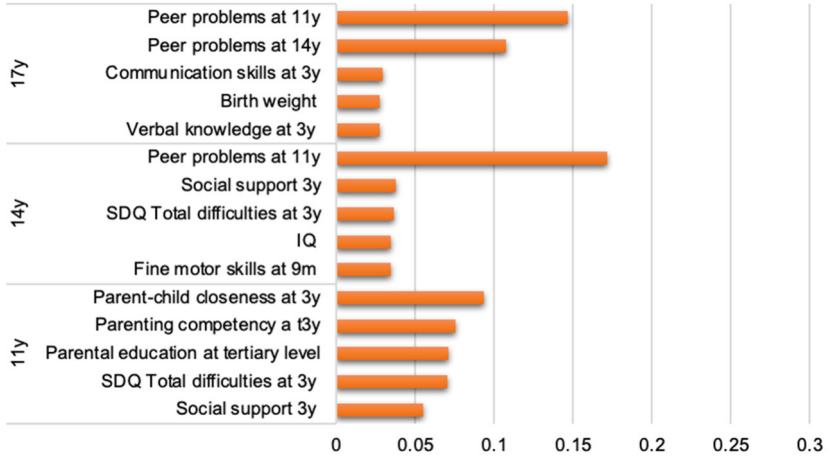


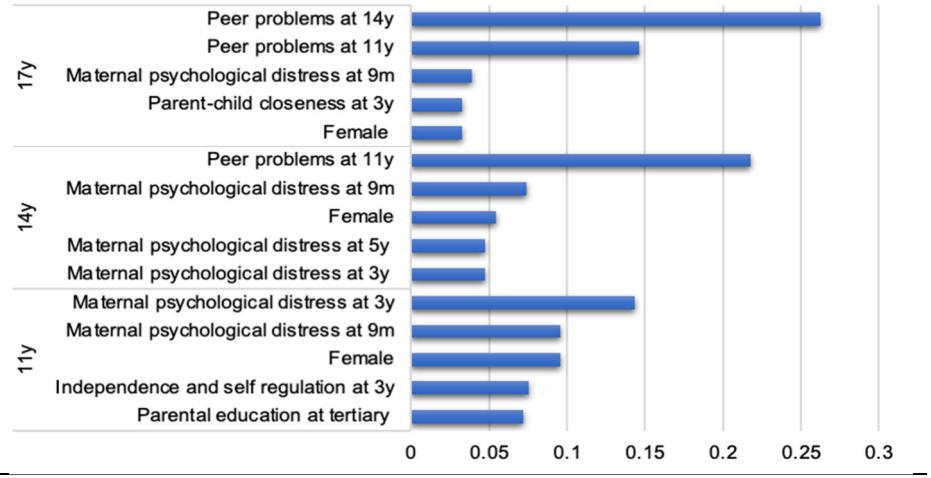
Absence of clinical conduct-oppositional disorders

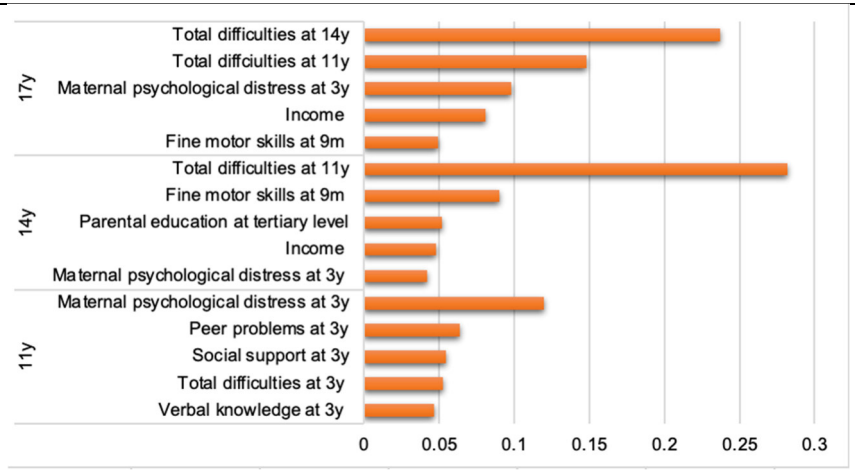
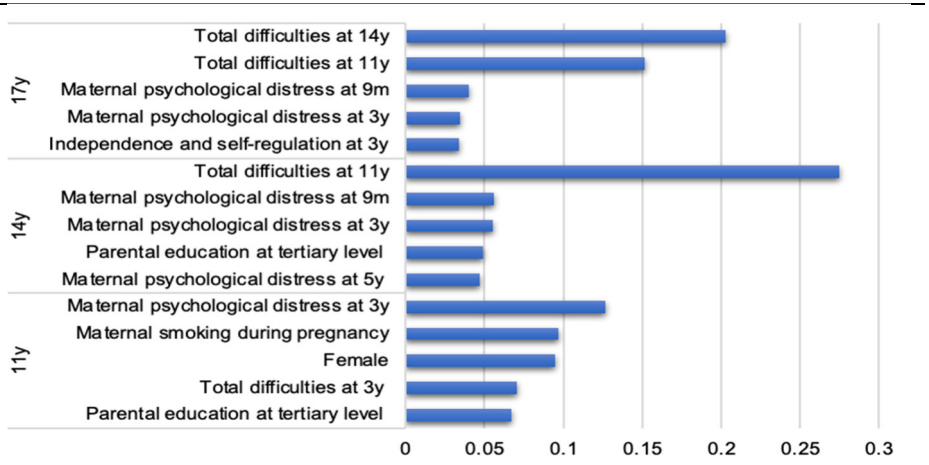




Absence of clinical peer relationship problems





Absence of clinical total difficulties		

*Please note that maternal psychological distress and smoking during pregnancy reflect the following: low maternal psychological distress; not smoking during pregnancy

Appendices

Table A1. Characteristics of preterm and full-term participants

	Preterm (N= 1472; 8.4%)	Full-term (N= 16,389; 91.6%)	p
Sociodemographic Characteristics			
Sex: N (%)			.048
Female	682 (46.3%)	8002 (49%)	
Male	790 (53.7%)	8323 (51%)	
Ethnicity: N (%)			
Majority	1207 (82%)	13570 (83.1%)	.270
Minority	265 (18%)	2755 (16.9%)	
Income: M (SD)	2.54 (1.83)	2.73 (1.85)	<.001
Parental Highest Education Level: N (%)			
Below tertiary	392 (26.6%)	4063 (23.5%)	.006
Tertiary	723 (49.1%)	9078 (52.4%)	.01
Maternal age at birth: M (SD)	28.43 (6.21)	28.34 (5.88)	.58
Family Structure and Environment			
Marital status: N (%)			.06
Married/cohabitating	1165 (79.1%)	14045 (81.1%)	
Single	307 (20.9%)	3269 (18.9%)	
Birth status: N (%)			<.001
First born	704 (47.8%)	7215 (41.7%)	
Second or later born	768 (52.2%)	10,099 (58.3%)	
Parental Psychological Distress at 9m: M (SD)	1.88 (1.84)	1.67 (1.77)	<.001
Parental Psychological Distress at 3y: M (SD)	3.33 (.70)	3.26 (.67)	.001
Parental Psychological Distress at 5y: M (SD)	3.43 (.68)	3.35 (.68)	<.001
Social support at 9m: M (SD)	12.17 (2.12)	12.33 (2.11)	.009
Social support at 3y: M (SD)	8.19 (1.65)	8.44 (1.56)	<.001
Parent Relationship Quality: M (SD)	27.72 (4.84)	27.96 (4.59)	.11
Physical violence in relationship: N (%)			.71
No	1037 (96.1%)	12,054 (96.3%)	
Yes	42 (3.9%)	460 (3.7%)	
Parent-child closeness: M (SD)	25.80 (12.34)	27.15 (11.88)	<.001
Parent-child conflict: M (SD)	14.37 (7.76)	14.29 (7.63)	.69
Emotional & verbal responsivity at 3y: M (SD)	5.12 (.37)	5.11 (.37)	.49
Stimulating home environment (reading to child): M (SD)	1.90 (1.08)	1.89 (1.11)	.66
Parenting beliefs: M (SD)	21.59 (2.00)	21.63 (2.00)	.48
Parenting style: M (SD)	5.80 (6.21)	5.68 (6.34)	.50
Responding to crying: M (SD)	.69 (.53)	.69 (.53)	.85
Bed-sharing: N (%)	116 (8.4%)	1388 (9.1%)	.42
Discipline practices at 3y: M (SD)	19.53 (4.99)	20.02 (4.99)	.01
Parenting competence: M (SD)	3.86 (.92)	3.89 (.91)	.42
Parental self-esteem: M (SD)	18.59 (2.91)	18.87 (2.74)	.001
Bonding: M (SD)	19.13 (2.60)	19.22 (2.60)	.27
Birth and Infancy Factors			

Smoking during pregnancy: M (SD)	.26 (.44)	.22 (.41)	.001
Breast feeding: N (%)			.20
Yes	494 (33.6%)	5535 (32%)	
No	978 (66.4%)	11779 (68%)	
Gross-motor development: M (SD)	8.79 (1.51)	9.62 (1.18)	<.001
Fine-motor development: M (SD)	11.18 (1.23)	11.59 (.82)	<.001
Communication skills: M (SD)	10.79 (1.88)	11.69 (1.67)	<.001
Temperament: M (SD)			
Mood	19.25 (3.38)	19.18 (3.42)	.55
Apprehension-withdrawal	5.47 (2.53)	5.45 (2.39)	.83
Adaptiveness	5.92 (3.43)	5.73 (3.24)	.04
Regularity	12.89 (2.37)	12.96 (2.33)	.29
Night waking frequency: M (SD)	2.53 (1.42)	2.68 (1.45)	<.001
Crying is problematic: M (SD)	1.91 (.38)	1.93 (.25)	.004
Early Childhood Factors			
Neurosensory Impairments: M (SD)	-.23 (1.71)	.04 (.164)	<.001
Cognitive Ability: M (SD)			
School Readiness	67.64 (22.85)	69.66 (23.44)	.002
Verbal Knowledge	45.32 (15.37)	46.66 (15.79)	.002
Self-regulation: Independence: M (SD)	2.26 (.66)	2.31 (.71)	.03
Emotional dysregulation: M (SD)	1.76 (.63)	1.75 (.66)	.44
Screen media exposure (hrs per day): M (SD)	2.78 (.91)	2.77 (.94)	.76
Mental Health in Early Childhood: M (SD)			
Emotional symptoms	2.24 (1.48)	2.07 (1.39)	.002
Hyperactivity/inattention	4.40 (2.24)	4.11 (2.21)	<.001
Conduct problems	3.14 (1.83)	3.22 (1.88)	.20
Peer relationship problems	2.45 (1.47)	2.31 (1.40)	.01
Total Problems	10.20 (5.34)	9.61 (5.22)	<.001

N=Number; M=Mean; SD=Standard Deviation; m=months; y=years; hrs=hours.

Table A2. Testing: Random forest performance in accuracy, AUC (Area under the curve), sensitivity, precision, F1 (F score) and specificity in predicting the absence of mental health and peer relationship problems for preterm and full-term born adolescents at ages 11, 14 and 17

Outcome	Birth/age	Accuracy	AUC	Sensitivity	Precision	F1	Specificity
Absence of clinical anxiety-depressive disorders	preterm11	0.762	0.557	0.250	0.267	0.258	0.863
	Full-term11	0.802	0.588	0.315	0.214	0.254	0.861
	preterm14	0.757	0.621	0.303	**0.667**	0.417	**0.939**
	full-term14	**0.807**	0.638	0.371	0.469	0.414	0.906
	preterm17	0.787	**0.653**	0.421	0.500	**0.457**	0.886
	full-term17	0.764	0.650	**0.449**	0.449	0.449	0.850
Absence of clinical conduct-oppositional disorders	preterm11	0.804	0.588	0.304	0.241	0.269	0.871
	full-term11	0.850	0.631	0.356	0.296	0.324	**0.905**
	preterm14	0.780	0.616	0.333	**0.467**	0.389	0.899
	full-term14	0.819	0.670	0.456	0.409	0.431	0.883
	preterm17	**0.871**	**0.764**	**0.625**	0.455	**0.526**	0.903
	full-term17	0.847	0.681	0.459	0.402	0.429	0.903
Absence of clinical hyperactivity-inattention disorders	preterm11	0.751	0.561	0.296	0.216	0.250	0.825
	full-term11	0.823	0.628	0.376	0.283	0.323	0.880
	preterm14	0.827	0.614	0.316	0.375	0.343	0.912
	full-term14	0.894	0.718	0.497	0.480	0.488	0.939
	preterm17	**0.920**	**0.822**	**0.700**	**0.583**	**0.636**	0.944
	full-term17	0.918	0.708	0.456	0.511	0.482	**0.960**
Absence of clinical peer relationship problems	preterm11	0.722	0.531	0.242	0.216	0.229	0.820
	full-term11	0.790	0.588	0.325	0.225	0.266	0.851
	preterm14	0.752	**0.710**	**0.550**	**0.710**	**0.620**	0.870
	full-term14	0.787	0.628	0.345	0.526	0.416	**0.912**
	preterm17	0.755	0.644	0.450	0.429	0.439	0.838
	full-term17	**0.791**	0.636	0.359	0.537	0.430	**0.912**
Absence of clinical total difficulties	preterm11	0.762	0.557	0.250	0.267	0.258	0.863
	full-term11	0.847	0.624	0.347	0.268	0.302	0.900
	preterm14	0.828	0.692	0.481	0.520	0.500	0.903
	full-term14	0.900	0.689	0.426	0.503	0.461	0.953
	preterm17	0.900	**0.794**	**0.647**	**0.647**	**0.647**	0.942
	full-term17	**0.922**	0.689	0.408	0.564	0.473	**0.970**