

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Predictive Risk Model for School Readiness at age 3 years using the UK Millennium Cohort Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024851
Article Type:	Research
Date Submitted by the Author:	17-Jun-2018
Complete List of Authors:	Camacho, Christine; University of Liverpool Department of Public Health and Policy, Straatmann, Viviane; University of Liverpool Department of Public Health and Policy Day, Jennie; University of Liverpool Department of Public Health and Policy Taylor-Robinson, David; University of Liverpool, Department of Public Health and Policy
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, SOCIAL MEDICINE

SCHOLARONE™
Manuscripts

Peer Review Only

1
2
3 **Predictive Risk Model for School Readiness at age 3 years using the UK Millennium**
4 **Cohort Study**
5

6 Miss CL Camacho*¹, Dr VS Straatmann¹, Dr JC Day¹, Prof DC Taylor-Robinson¹
7

8 *Affiliations: ¹Public Health and Policy, University of Liverpool, Liverpool, UK*
9

10 *Address correspondence to: Christine Camacho, Department of Public Health and Policy, University*
11 *of Liverpool, Liverpool, United Kingdom, L69 3GB, [c.camacho@nhs.net], +44 07973395585*
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57

For peer review only

ABSTRACT

Objectives

The aim of this study was to develop a predictive risk model (PRM) for school readiness measured at age 3 years using perinatal and early infancy data.

Design and Participants

This paper describes the development of a predictive risk model. Predictors were identified from the UK Millennium Cohort Study (MCS) wave 1 data, collected when participants were 9 months old. The outcome was school readiness at age 3 years, measured by the Bracken School Readiness Assessment. Stepwise selection and dominance analysis were used to specify 2 models. The models were compared by the area under the receiver operating characteristic curve (AUROC) and integrated discrimination improvement (IDI).

Results

Data were available for 9,487 complete cases. At age 3, 11.7% (95% CI 11.0-12.3%) of children were not school ready. The variables identified were: parents' Socio-Economic Classification, child's ethnicity, maternal education, income band, sex, household number of children, mother's age, low birth weight, mother's mental health, infant developmental milestones, breastfeeding, parents' employment, housing type. A parsimonious model included the first six listed variables (model 2). The AUROC for model 1 was 0.80 (95% CI 0.78-0.81) and 0.78 (95% CI 0.77-0.79) for model 2. Model 1 resulted in a small improvement in discrimination (IDI=1.3%, $p<0.001$).

Conclusions

Perinatal and infant risk factors predicted school readiness at age 3 with good discrimination. Social determinants were strong predictors of school readiness. This study demonstrates that school readiness can be predicted by six attributes collected around the time of birth.

Strengths and limitations of this study

- Use of a large, representative, and contemporary cohort study offered a wide range of predictor variables which minimised the likelihood of overfitting.
- Multiple imputation and bootstrapping were used to evaluate the impact of missing data and internal validity, respectively.
- The main outcome measure, the Bracken School Readiness Assessment, was developed in the US, and is not routinely used in the UK.
- This model was not externally validated, which would have given further indication of generalisability.

INTRODUCTION

Early childhood is critical time for lifelong physical, social, emotional and cognitive development. A wide range of factors are associated with early cognitive development (ECD)[1]. Interventions in the first three years of life improve the trajectory of ECD[2] and deliver the greatest return on investment[3], yet it is unclear how best to identify children at most risk of delayed ECD, to enable appropriate targeting of interventions.

Cognitive development measures in children are good indicators of later educational achievement, predict health and social care needs in adults[4,5], and are associated with long term health outcomes[6]. There has been a growing policy interest in school readiness as a measure of ECD[7], and school readiness is a key public health indicator in children in the UK. Good school readiness lays a platform for future learning, employment and health[8,9]. In 2016, 31% of children in England were deemed not school ready at the end of their reception year (aged 4-5 years)[10].

Predictive risk models (PRMs) are well-established in many clinical disciplines to identify groups or individuals at risk of poor outcomes but there have been few attempts to predict ECD from early childhood characteristics[11–15]. Using PRMs in this context could facilitate targeted early intervention as part of a proportionate universalism approach. The aim of this study was to develop a PRM for school readiness measured at age 3 years using perinatal and early infancy data from the UK Millennium Cohort Study (MCS).

METHODS**Data Source**

The PRM was developed and validated using MCS data. The MCS is a nationally representative birth cohort study which recruited 18,550 children born from September 2000 to January 2002, followed up in ongoing data collection waves[16]. The sample was clustered at the level of electoral ward and stratified to allow over representation of children living in deprived areas and areas with high concentrations of ethnic minorities[17]. Survey weightings were used to correct for attrition and non-response[18]. Data were collected from the main responder (usually mothers) by trained interviewers in participants' homes using a

combination of interviews and self-completed questions. All singleton children in the first (aged 9 months) and second (aged 3 years) waves of the MCS with completed data for the outcome and predictors were eligible for inclusion (n=9,487).

Outcome

School readiness was measured at age 3 using the Bracken School Readiness Assessment (BSRA) which consists of 6 subtests relating to colours, letters, numbers/counting, sizes, comparisons and shapes[19]. The BSRA and its predecessors have demonstrated good reliability[20] and validity against other measures and teacher assessments[21].

The BSRA raw scores were summed and adjusted for age to provide a standardised composite score[19]. Scores were grouped into 5 categories based on the mean standardised score: very advanced (131-149), advanced (116-130), average (85-115), delayed (70-84) and very delayed (56-69)[22]. BSRA scores were recoded to a binary variable of either school ready ≥ 85 very advanced/advanced/average) or not school ready (< 85 ; delayed/very delayed)[23].

Predictors

29 variables which were identified from previous research to predict cognitive development and were included in the MCS[1,2,4,6,24–31]. The selected predictor variables were grouped according to the Dahlgren and Whitehead theoretical model[32] of social determinants of health as depicted in Figure 1.

<<Figure 1 here>>

Group 1 – Demographic and Individual factors

Demographic characteristics included child sex, maternal ethnicity, child weight, pre-term birth, mother's age, home language, maternal mental health and child development categorised as shown in Box 1.

Box 1 – Coding of Group 1 demographic and individual factors

Categorisation of Demographic and Individual factors

Child sex – 'female' and 'male'

Maternal ethnicity – 'white', 'mixed', 'Indian', 'Pakistani and Bangladeshi', 'Black' and 'other'

Child weight at birth – low (< 2.5 kg) or normal/high (≥ 2.5 kg)

Preterm birth – gestation period less than 37 weeks

Mother's age in years at birth of first child – grouped into 4 categories (14-19, 20-29, 30-39, 40+ years)

Home language – 'English only', 'English and another language', 'another language only'

Mental health (1) – Sad or low for > 2 weeks since baby, coded as 'yes' or 'no'

Mental health (2) – Diagnosis of depression or serious anxiety, coded as 'yes' or 'no'

Mental health (3) – 9-item modified version of the Rutter Malaise Inventory³⁹, coded as 'low' or (0-3) 'high' (4-9) scores²⁷.

Child development – 8 items from Denver Developmental Screening Test and 5 items from MacArthur Communicative Development Inventory, coded as 'above average' (13-17), 'average' (18-19) and 'below average' (20-36).

Group 2 – Lifestyle Factors

1
2
3 Self-reported maternal smoking was coded as 'never smoked', 'smoked before pregnancy'
4 and 'smoked during pregnancy'. Maternal alcohol consumption during pregnancy were
5 categorised as 'never or very infrequent', 'occasional', 'regularly' and 'most or everyday'.
6 Breastfeeding duration was grouped as 'never', 'one week or less', '1 – 6 weeks', '6 weeks –
7 6 months' and 'over 6 months'.
8
9

10 Group 3 – Social and Community Factors

11 The number of children in household was coded as '1', '2-3' or '4+', and being the eldest or
12 only child was recorded as 'yes' or 'no'. The number of parents or carers was either '1' or
13 '2'. Mothers were asked how much time they had spent time in care before the age of 17, this
14 was recoded as 'yes' or 'no' to indicate if they had ever been in care.
15
16

17 Group 4 – Living and Working Conditions

18 Maternal education was categorised into six groups 'degree plus (higher degree and first
19 degree qualifications)', 'diploma (in higher education)', 'A-levels', 'GCSE grades A–C',
20 'GCSE grades D–G' and 'none of these qualifications'. Parent's employment status was
21 classified as either 'both', 'one' or 'neither' parents in work. Housing tenure was coded as
22 'owner occupied', 'private rented', 'social housing' and 'other'. The response to the question,
23 "How common is pollution, grime or other environmental problems?" was recorded as
24 'common', 'not common' and 'not at all'. Presentation for first antenatal visit was recorded
25 as late if after 12 weeks. Maternal attachment was measured using a 6-item Condon Maternal
26 Attachment Questionnaire[33] grouped as 'low (10-21), 'average' (22-23) and 'high (24-27)'.
27
28
29
30

31 Group 5 – Socioeconomic and Wider Factors

32 The National Statistics Socio-Economic Classification (NS-SEC) was used to categorise
33 mothers as: 'managerial & professional', 'intermediate', 'small employers & own account',
34 'lower supervisory & technical', 'semi-routine & routine', 'never worked & long-term
35 unemployed'. Net household income was reported by identification of the correct band on a
36 show card and grouped into 4 quartile bands[24]: '£0-£11,000', '£11,000-£22,000', '£22,000-
37 £33,000' and '£33,000+'. Poverty was defined as an equivalised household income 60%
38 below the median before housing costs according to the Organisation for Economic Co-
39 operation and Development Household Equivalence Scale. Families reported receipt of any
40 means-tested benefits, including Jobseekers Allowance, Income Support, Working Families
41 Tax Credit or Disabled Persons Tax Credit. Indices of Multiple Deprivation (IMD) from 2004
42 were used as an indicator of area level deprivation. IMD scores were divided into quintiles,
43 with 1 the most deprived quintile, and 5 the least deprived.
44
45
46
47

48 **Statistical analyses**

49 Analyses were conducted using Stata v14.2 (StataCorp LP, 2017). Survey weights were
50 applied to take account of clustering, stratification and oversampling in the survey design,
51 and attrition between survey waves[34]. A calculation based on the number of events per
52 variable (EPV) was used to determine sample size for the PRM. The EPV for this study is 68,
53 which exceeds the EPV of 10 suggested to minimise overfitting[35], so the sample is
54 sufficiently large to test 29 predictor variables.
55
56
57

1
2
3
4 Descriptive analysis of each predictor and school readiness was carried out to ascertain the
5 prevalence of each predictor in the sample. Univariable logistic regression analyses
6 calculating odds ratios (ORs) and 95% confidence intervals (95% CI) were carried out to
7 assess the unadjusted association of each variable with the outcome.
8
9

10 A multivariable logistic regression model including all 29 variables was reduced using
11 automated forward and backwards stepwise selection (using a cut off p-value of 0.1). The
12 predictors included in the resulting model (model 1) were checked for collinearity.
13 Dominance analysis (repeated regression analyses on subsets of variables) was used to
14 produce a ranking and weighting for each predictor in model 1[36]. These rankings were used
15 to specify a more parsimonious model (model 2) containing the top 6 predictors, selected to
16 maximise parsimony and performance. The integrated discrimination improvement (IDI) was
17 also calculated to assess difference in performance between models as the percentage change
18 in individuals being correctly assigned by the model[37].
19
20
21

22 The area under the ROC curve (AUROC) and its 95% CI was used to measure discriminatory
23 power of the models. Classification, including sensitivity and specificity, was assessed at the
24 maximised probability cut off point where the sensitivity and specificity curves intersected.
25 Calibration of the model was assessed using the Pearson Chi-squared test[38]. Bootstrapping
26 was used for internal validation of the model using 1000 iterations. An optimised AUROC,
27 which takes account of overfitting, was calculated as the difference between baseline model
28 performance and performance across the bootstrap samples[39].
29
30
31

32 A complete case approach was used for the primary analysis. As a sensitivity analysis,
33 multiple imputation by chained equation was performed to impute missing data (imputed
34 sample, n=13,650). Variables from the first sweep and the outcome variable were used to
35 shape the imputation of the missing data (maternal education, child's sex, mother's age at
36 birth of first child and school readiness at age 3). Twenty imputed datasets were generated,
37 and Rubin's rules were used to calculate results across the imputed datasets[40]. Ethical
38 approval for each wave of the MCS was granted by NHS Multicentre Research Ethics
39 Committees[41]. No further ethical approval was required for this secondary analysis of MCS
40 data.
41
42
43
44

45 **Patient and public involvement**

46 There was no direct patient or public involvement in this analysis. However the MCS has an
47 ongoing programme of participant and public engagement.
48
49

50 **RESULTS**

51 There were 15,381 singleton children surveyed in MCS2, of which 13,650 had an outcome
52 recorded for school readiness. Of these children 70% (n=9,487) had complete data for the
53 outcomes and all the predictor variables. The characteristics of the imputed sample were
54 similar to the complete case sample (Table 1); results are reported for complete cases (see
55 Supplementary file 1 for imputed sample results).
56
57

Table 1 - Description of perinatal, sociodemographic and economic characteristics by school ready of sample and imputed sample

Is Child School Ready?	Complete Cases (n=9,487)		Imputed Data (n=13,650)	
	Yes (%)	No (%)	Yes (%)	No (%)
All	88.3	11.7	85.5	14.5
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS				
Gender				
Female	91.6	8.4	89.4	10.6
Male	85.1	14.9	82.6	17.4
Ethnicity				
White	90.4	9.6	88.6	11.4
Mixed	91.1	8.9	84.7	15.3
Indian	79.3	20.7	78.1	21.9
Pakistani and Bangladeshi	55.7	44.3	56.3	43.7
Black or Black British	79.8	20.2	68.0	32.0
Other ethnic group	73.6	26.4	74.3	25.7
Mother's age at birth of first child				
14-19	78.0	22.0	76.4	23.6
20-29	87.9	12.1	86.1	13.9
30-39	95.0	5.0	94.4	5.6
40+	76.9	23.1	76.0	24.0
Birth weight (<2500grams)				
normal/high	88.8	11.2	86.1	13.9
low birthweight	80.2	19.8	77.7	22.3
Maternal Mental Health (Diagnosed depression/anxiety)				
No	89.0	11.0	86.0	14.0
Yes	86.0	14.0	84.4	15.6
Child developmental milestones				
Above average	90.0	10.0	87.5	12.5
Average	89.2	10.8	86.8	13.2
Below average	86.6	13.4	83.4	16.6
GROUP 2 - LIFESTYLE FACTORS				
Duration of breastfeeding				
6 months or more	92.5	7.5	90.5	9.5
6 weeks - 6 months	89.8	10.2	87.8	12.2
1 - 6 weeks	88.8	11.2	85.9	14.1
one week or less	88.8	11.2	86.4	13.6
Never	82.6	17.4	80.0	20.0
GROUP 3 - SOCIAL & COMMUNITY NETWORKS				
Number of children in family				
One child	92.0	8.0	89.1	10.9
Two or three children	87.7	12.3	85.0	15.0
Four or more children	71.7	28.3	70.2	29.8
Maternal education				
Degree plus	95.6	4.4	95.1	4.9

Diploma	94.6	5.4	93.9	6.1
A levels	92.7	7.3	92.0	8.0
GCSE A-C	88.5	11.5	87.4	12.6
GCSE D-G	81.0	19.0	79.1	20.9
None	71.3	28.7	69.2	30.8
GROUP 4 - LIVING & WORKING CONDITIONS				
Workforce status				
Both parents in work	92.6	7.4	91.6	8.4
One parent in work	85.8	14.2	83.4	16.6
Neither parent in work	68.5	31.5	70.1	29.9
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS				
Housing tenure				
Owner occupied	91.9	8.1	90.7	9.3
Private rented	83.8	16.2	80.5	19.5
Social housing	75.8	24.2	74.8	25.2
Other	83.4	16.6	81.0	19.0
Social class				
managerial & professional	95.5	4.5	94.6	5.4
intermediate	93.1	6.9	92.1	7.9
small employers & own account	91.3	8.7	89.1	10.9
lower supervisory & technical	87.2	12.8	84.0	16.0
semi-routine & routine	81.9	18.1	80.0	20.0
never worked & long-term unemployed	60.2	39.8	62.1	37.9
Annual income				
£33,000+	95.7	4.3	94.9	5.1
£22,000-£33,000	92.5	7.5	91.7	8.3
£11,000-£22,000	85.0	15.0	83.9	16.1
£0-£11,000	73.8	26.2	74.1	25.9

11.7% (95%CI 11.0-12.3%) of children aged 3 years were classified as not being school ready, but this varied significantly by the parents' ethnicity, maternal education and social class (Table 1). All 29 predictor variables were significantly associated with school readiness in univariable logistic regression analysis ($p < 0.1$), so none were excluded at this stage.

The stepwise method reduced the final multivariable logistic regression model to 13 predictors: child's sex and ethnicity, mother's age at birth of first child, birthweight, maternal mental health, child development milestones, duration of breastfeeding, number of children in family, maternal education, parents' workforce status, housing tenure, social class and annual family income. In the adjusted analysis, Pakistani and Bangladeshi children were 4 times more likely to not be school ready than white children (OR 4.19 95% CI 3.14-5.58). The full results are shown in Table 2. There was no evidence of collinearity.

Table 2 - Unadjusted and adjusted associations and dominance analysis for the predictor variables in model 1 (13 predictors)

Predictors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.8 (5)
Male	1.76 (1.54,2.01)	2.05 (1.73,2.41)	
Ethnicity			
White	1	1	14.7 (2)
Mixed	1.4 (0.96,2.04)	1.39 (0.77,2.53)	
Indian	1.85 (1.23,2.77)	2.54 (1.64,3.96)	
Pakistani and Bangladeshi	5.94 (4.82,7.32)	4.19 (3.14,5.58)	
Black or Black British	4.06 (2.90,5.69)	1.99 (1.09,3.63)	
Other ethnic group	2.33 (1.38,3.93)	2.92 (1.57,5.43)	
Mother's age at birth of first child			
30-39	1	1	2.9 (10)
40+	2.83 (2.29,3.49)	1.04 (0.67,1.61)	
20-29	5.57 (4.20,7.37)	1.26 (0.96,1.64)	
14-19	6.02 (4.84,7.48)	1.29 (0.93,1.79)	
Birth weight (<2500grams)			
Normal/high	1	1	1.6 (12)
Low birthweight	1.7 (1.34,2.16)	1.39 (1.02,1.90)	
Maternal Mental Health (Diagnosed depression/anxiety)			
No	1	1	0.4 (13)
Yes	1.33 (1.16,1.53)	1.29 (1.08,1.54)	
Child developmental milestones			
Above average	1	1	2.4 (11)
Average	1.04 (0.89,1.22)	1.38 (1.11,1.72)	
Below average	1.4 (1.20,1.64)	1.81 (1.46,2.23)	
GROUP 2 - LIFESTYLE FACTORS			
Duration of breastfeeding			
6 months or more	1	1	4.0 (9)
6 weeks - 6 months	1.25 (1.02,1.53)	1.04 (0.80,1.35)	
One week or less	1.67 (1.34,2.09)	1.19 (0.89,1.60)	
1 - 6 weeks	1.68 (1.36,2.07)	1.25 (0.95,1.63)	
Never	2.74 (2.29,3.27)	1.49 (1.19,1.87)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	8.1 (6)
Two or three children	1.44 (1.27,1.63)	1.4 (1.17,1.69)	
Four or more children	3.71 (3.04,4.54)	2.74 (1.99,3.76)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	13.8 (3)
Diploma	1.3 (0.93,1.81)	0.8 (0.52,1.22)	
A levels	1.66 (1.22,2.25)	1.02 (0.67,1.53)	

GCSE A-C	3.02 (2.34,3.90)	1.29 (0.88,1.87)	
GCSE D-G	5.55 (4.21,7.30)	1.54 (1.02,2.34)	
None	9.62 (7.61,12.16)	1.68 (1.15,2.45)	
Workforce status			
Both parents in work	1	1	
One parent in work	1.79 (1.49,2.14)	0.81 (0.66,1.00)	7.0 (7)
Neither parent in work	5.39 (4.36,6.67)	1.2 (0.86,1.67)	
Housing tenure			
Owner occupied	1	1	
Private rented	2.68 (2.16,3.33)	1.2 (0.87,1.66)	5.7 (8)
Social housing	3.89 (3.34,4.53)	1.46 (1.17,1.82)	
Other	2.65 (2.10,3.35)	0.89 (0.62,1.29)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	
Intermediate	1.5 (1.19,1.89)	1.05 (0.77,1.45)	
Small employers & own account	2.11 (1.44,3.08)	1.42 (0.87,2.32)	17.6 (1)
Lower supervisory & technical	3.72 (2.76,5.00)	1.67 (1.11,2.52)	
Semi-routine & routine	4.99 (4.13,6.01)	1.97 (1.46,2.67)	
Never worked & long-term unemployed	12.07 (9.48,15.37)	2.47 (1.68,3.63)	
Annual income			
£33,000+	1	1	
£22,000-£33,000	1.71 (1.31,2.25)	1.3 (0.94,1.78)	12.2 (4)
£11,000-£22,000	3.97 (3.12,5.07)	1.65 (1.22,2.24)	
£0-£11,000	7.7 (6.10,9.72)	2.26 (1.59,3.20)	

Dominance analysis showed that social class was the most important predictor (weighting=17.6), followed by ethnic group (weighting=14.7) and maternal education (weighting=13.8) (Table 2). Analysis of the predictor weightings suggests that social factors (average weighting 11.3, SD 4.9) are stronger predictors of school readiness than demographic and lifestyle factors (average weighting 5.5, SD 4.9).

The AUROC was 0.80 (95% CI 0.78-0.81) for model 1 (n=9,487), which indicates a “good” level of discrimination[42]. The AUROC for model 2 (n=11,146) was 0.78 (95% CI 0.77-0.79). Internal validation using bootstrap optimism suggests that the model would have good discriminatory power in an independent sample (adjusted AUROC 0.79). The Pearson Chi-squared tests were both non-significant indicating adequate calibration (model 1, p=0.07, model 2, p=0.13)[43]. IDI showed there was a small but significant difference in performance, with model 1 resulting in a 1.3% (p<0.001) improvement in discrimination (Figure 2). IDI was also used to test the relative performance of models with all (1-13) variables, with variables added in according to their rank from the dominance analysis. These analyses informed the choice of a top 6-predictor model (social class, child’s ethnic group, maternal education, income band, sex and number of children) (Supplementary material 2).

<<Figure 2 here>>

1
2
3 Sensitivity and specificity were plotted against probability cut-offs to select the optimal cut
4 off point to assess the PRM's classification (model 1, cut-off=0.12; model 2, cut-off=0.14)
5 (Figure 3 **Error! Reference source not found.**). For model 1, at this cut-off point sensitivity
6 was 72% (95% CI 69.0%-74.3%) and specificity was 74% (95% CI 73.5%-75.3%).
7 Sensitivity of model 2 was similar - 72% (95% CI 69.9%-74.5%). Specificity was lower -
8 71% (95% CI 69.6%-71.4%), so this model would generate more false positive results than
9 the model 1, but performance was still in the acceptable range. At a probability cut-off of
10 12%, 31% of the screened population tested would be identified as being at high risk of poor
11 school readiness using model 1.
12
13

14
15 <<Figure 3 here>>
16

17 **DISCUSSION**

18 **Findings**

19
20 This study developed a PRM for school readiness at age 3 years using perinatal and early
21 childhood data from the MCS. Model 1 with 13 variables had good discrimination
22 (AUROC=0.80) and classification (sensitivity=72%, specificity= 74% at a maximised cut
23 off). Dominance analysis found the most important variables in predicting school readiness
24 related to socioeconomic conditions (social class, maternal education, family income) and
25 ethnicity. A parsimonious model performed similarly well (AUROC=0.78), suggesting it is
26 possible to predict school readiness at age 3 using just six variables from the perinatal period
27 and early infancy.
28
29
30

31 **Comparison with previous studies**

32 The predictors of school readiness identified here corroborate previous findings. Male sex,
33 maternal education, income, family composition, parental employment, housing and
34 breastfeeding have been identified as significant risk factors of ECD in other
35 studies[4,11,12,14,15,24]. Social factors were the most important predictors, corresponding
36 with current thinking on the social determinants of cognitive development[6,44].
37
38
39

40 A few recent studies have used PRM and ROC curves to analyse the association between
41 perinatal and early childhood predictors with cognitive development, but this is the first UK
42 study to develop a PRM with a good level of predictive discrimination for early cognitive
43 development (ECD)[11,12,14,15,45]. The model reported here has good predictive strength,
44 and compares favourably to similar PRMs, which with one exception[14], achieved only fair
45 or poor discrimination[11,12,15,45]. Chittleborough et al used the ALSPAC UK birth cohort
46 to test the predictive validity of 2 models for ECD[11]. They found that maternal age alone
47 failed to predict ECD (AUROC~0.5), and a model with 6 predictors achieved only poor
48 discrimination (AUROC=0.67). Camargo-Figuera et al used IQ as a measure of ECD and
49 developed a PRM with 12 predictors using the Brazilian Pelotas birth cohort; their model had
50 good discrimination (AUROC=0.8) and calibration, with sensitivity and specificity of 72%
51 and 74% respectively[14].
52
53
54

55 **Strengths and Limitations**

1
2
3 A strength of this study was the use of representative and contemporary UK cohort study as
4 the data source, this offered a wide range of predictor variables and a large sample size which
5 minimised the likelihood of overfitting. The cohort design also ensured correct temporal
6 ordering and blinding with respect to the predictors. A theoretical model informed the PRM
7 and statistical selection was used to specify variables. Multiple imputation was used to assess
8 the impact of missing data. Bootstrapping showed good internal validity suggesting the
9 model would be generalisable to another population[39].
10
11

12 There are some limitations of this study to be considered. The main outcome, the BSRA,
13 whilst validated as a measure of school readiness, was developed in the US and is not
14 routinely used in the UK[21]. Many variables were dichotomised or grouped, which may be
15 less sensitive than continuous measures. Longitudinal studies are subject to attrition and non-
16 response which can introduce attrition bias, the use of survey weights partially adjust for this,
17 but it was not possible to use these when calculating the AUROC. Sensitivity analysis using
18 multiple imputation showed the effect of missing data was negligible, similar to other
19 PRMs[11,12]. Most of the predictor variables were based on maternal self-report which may
20 be subject to recall bias, and external validation was not conducted.
21
22
23
24

25 **Policy Implications**

26 The existing literature, and these findings, indicate that a PRM could plausibly be used to
27 identify a group of children at high risk of poor ECD who may benefit from early
28 intervention. If implemented as part of a “proportionate universalism” approach[6], PRMs
29 could mitigate socioeconomic inequalities by providing early years settings with a
30 mechanism for directing their resources to those children at highest risk of poor cognitive
31 development. With new child and maternity datasets now being collected electronically in
32 England, it may be possible to apply a PRM at population level through the use of linked
33 administrative datasets as has been done in Australia[12].
34
35
36

37 Poor cognitive development is associated with a range of negative health and social outcomes
38 and contributes to inequalities in society[3,5,6], so this is of public health importance.
39 Chittleborough et al showed that even a model with poor discrimination has benefits over just
40 using young maternal age to direct resources[11]. Similarly, McKean et al established that
41 their PRM was better than existing clinical tools used to identify higher-risk children for early
42 intervention[45].
43
44

45 The practical implications of using such a PRM as a screening tool should be considered. The
46 model reported here would identify 31% of children at high risk of not being school ready.
47 An average English Local Authority with a population of 230,000 would therefore have 900
48 ‘at risk’ children per year. This percentage equates with national data; in 2015/16, 31% of
49 children in England were not school ready when tested at age 4-5[10]. However, Nelson et al
50 (2016) comment that Early Intervention services would be overwhelmed by the level of
51 demand generated by such PRMs[15]. A criterion for screening programmes is that
52 interventions should be available, it is thus important to further consider the implications of
53 using a PRM to assess ECD in the context of available resources.
54
55
56
57

1
2
3 Further research is needed to test the external validity of predictive risk models for ECD for
4 example in another cohort or with linked administrative datasets. PRMs raise ethical issues,
5 labelling very young children as being high risk of poor development could be stigmatising
6 for families. PRMs would generate false positives (and false negatives), which could cause
7 unnecessary distress. Use of PRMs to identify children at risk of developmental delay should
8 include support and counselling for families, as well as timely access to appropriate
9 interventions. Investment in early intervention would be required, which would have
10 opportunity costs for services locally.
11
12

13 14 **CONCLUSION**

15 This study has identified a set of predictive risk factors from the perinatal period and early
16 infancy that can predict school readiness at age 3 with a good level of accuracy. Poor
17 cognitive development is socially patterned, evident from a very young age and leads to
18 persistent disadvantage throughout life. It is possible that PRMs could be used to identify
19 high risk children and target appropriate interventions and resources to improve their
20 developmental trajectories, and to reduce social inequalities early in the life course.
21
22
23
24

25 26 **STATEMENTS**

27 **Funding**

28 This research received no specific grant from any funding agency in the public, commercial
29 or not for profit sectors. DTR is funded by the MRC on a Clinician Scientist Fellowship
30 (MR/P008577/1).
31
32

33 **Competing Interests**

34 We confirm that authors have no conflicts of interest to disclose.
35
36

37 **Contributors**

38 CLC, JCD and DTR planned the study. CLC and VSS conducted the analysis under the
39 supervision of DTR. CLC led the drafting of the manuscript. All authors contributed to data
40 interpretation, manuscript drafting and revisions and agreed the submitted version of the
41 manuscript.
42
43

44 **Data Sharing**

45 The Millennium Cohort Study dataset is available from the UK Data Service.
46
47

48 **ACKNOWLEDGEMENTS**

49 We would like to acknowledge all the families and researchers who are part of the UK
50 Millennium Cohort Study, without whom this research would not have been possible.
51
52
53
54
55
56
57

REFERENCES

- 1 National Research Council (US) and Institute of Medicine (US) Committee on Integrating the Science of Early Childhood Development. *From Neurons to Neighborhoods: The Science of Early Childhood Development*. Washington (DC) : National Academies Press (US) 2000. <http://www.ncbi.nlm.nih.gov/books/NBK225557/>
- 2 Black MM, Walker SP, Fernald LC, *et al*. Early childhood development coming of age: science through the life course. *The Lancet* 2016.
- 3 Heckman JJ. Skill formation and the economics of investing in disadvantaged children. *Science* 2006;**312**:1900–2. doi:312/5782/1900 [pii]
- 4 Hobcraft JN, Kiernan KE. Predictive factors from age 3 and infancy for poor child outcomes at age 5 relating to children’s development, behaviour and health: evidence from the Millennium Cohort Study. York : University of York 2010. <http://www.york.ac.uk/media/spsw/documents/research-and-publications/HobcraftKiernan2010PredictiveFactorsChildrensDevelopmentMillenniumCohort.pdf> (accessed 28 May 2017).
- 5 Caspi A, Houts RM, Belsky DW, *et al*. Childhood forecasting of a small segment of the population with large economic burden. *Nat Hum Behav* 2016;**1**:0005.
- 6 Marmot M, Allen J, Goldblatt P, *et al*. Fair society, healthy lives: strategic review of health inequalities in England post 2010. Marmot Review Team 2010.
- 7 Public Health England. Improving school readiness: creating a better start for London. London: 2015.
- 8 Pia Rebello Britto. School Readiness - A conceptual framework. New York, NY: : UNICEF 2012.
- 9 Marmot M, Friel S, Bell R, *et al*. Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet* 2008;**372**:1661–9. doi:10.1016/S0140-6736(08)61690-6
- 10 Public Health England. Public Health Profiles. 2017.<https://fingertips.phe.org.uk/profile-group/child-health> (accessed 13 Jun 2017).
- 11 Chittleborough CR, Lawlor DA, Lynch JW. Young Maternal Age and Poor Child Development: Predictive Validity From a Birth Cohort. *Pediatrics* 2011;**127**:e1436–44. doi:10.1542/peds.2010-3222
- 12 Chittleborough CR, Searle AK, Smithers LG, *et al*. How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study. *Early Child Res Q* 2016;**35**:19–30.
- 13 Brownell MD, Ekuma O, Nickel NC, *et al*. A population-based analysis of factors that predict early language and cognitive development. *Early Child Res Q* 2016;**35**:6–18.
- 14 Camargo-Figuera FA, Barros AJ, Santos IS, *et al*. Early life determinants of low IQ at age 6 in children from the 2004 Pelotas Birth Cohort: a predictive approach. *BMC Pediatr* 2014;**14**:308. doi:10.1186/s12887-014-0308-1

- 1
2
3 15 Nelson BB, Dudovitz RN, Coker TR, *et al.* Predictors of Poor School Readiness in Children
4 Without Developmental Delay at Age 2. *Pediatrics* 2016;**138**:e20154477. doi:10.1542/peds.2015-
5 4477
- 6
7 16 Connelly R, Platt L. Cohort Profile: UK Millennium Cohort Study (MCS). *Int J Epidemiol*
8 2014;**43**:1719–25. doi:10.1093/ije/dyu001
- 9
10 17 Kirstine Hansen. Millennium Cohort Study First, Second, Third and Fourth Surveys. A Guide to
11 the Datasets (Seventh Edition). London: : Centre for Longitudinal Studies 2012.
- 12
13 18 Ian Plewis. The Millennium Cohort Study: Technical Report on Sampling. London: : Institute of
14 Education 2007.
- 15
16 19 Kirstine Henson. Millennium Cohort Study. First, Second, Third and Fourth Surveys. A Guide to
17 the Datasets. Centre for Longitudinal Studies 2012. [http://www.cls.ioe.ac.uk/shared/get-](http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=598&itemtype=document)
18 [file.ashx?id=598&itemtype=document](http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=598&itemtype=document)
- 19
20 20 Bracken B. Bracken Basic Concept Scale–Revised. San Antonio, TX: : The Psychological
21 Corporation 1998.
- 22
23 21 Panter JE, Bracken BA. Validity of the Bracken School Readiness Assessment for predicting first
24 grade readiness. *Psychol Sch* 2009;**46**:397–409.
- 25
26 22 Connelly R. Millennium Cohort Study Data Note 2013/1: Interpreting Test Scores. London: :
27 Centre for Longitudinal Studies, Institute of Education 2013. <http://www.cls.ioe.ac.uk/> (accessed
28 4 Mar 2018).
- 29
30 23 Steyerberg E. *Clinical prediction models: a practical approach to development, validation, and*
31 *updating*. Springer Science & Business Media 2008.
32 [https://books.google.co.uk/books?hl=en&lr=&id=kHGK58cLsMIC&oi=fnd&pg=PR2&dq=Clinical+](https://books.google.co.uk/books?hl=en&lr=&id=kHGK58cLsMIC&oi=fnd&pg=PR2&dq=Clinical+Prediction+Models+A+Practical+Approach+to+Development,+Validation,+and+Updating&ots=TNSaD1dEhk&sig=YhVMJY6Pfllylv_T1qMJYLMvLiI)
33 [Prediction+Models+A+Practical+Approach+to+Development,+Validation,+and+Updating&](https://books.google.co.uk/books?hl=en&lr=&id=kHGK58cLsMIC&oi=fnd&pg=PR2&dq=Clinical+Prediction+Models+A+Practical+Approach+to+Development,+Validation,+and+Updating&ots=TNSaD1dEhk&sig=YhVMJY6Pfllylv_T1qMJYLMvLiI)
34 [ots=TNSaD1dEhk&sig=YhVMJY6Pfllylv_T1qMJYLMvLiI](https://books.google.co.uk/books?hl=en&lr=&id=kHGK58cLsMIC&oi=fnd&pg=PR2&dq=Clinical+Prediction+Models+A+Practical+Approach+to+Development,+Validation,+and+Updating&ots=TNSaD1dEhk&sig=YhVMJY6Pfllylv_T1qMJYLMvLiI)
- 35
36 24 Kiernan KE, Mensah FK. Maternal indicators in pregnancy and children’s infancy that signal
37 future outcomes for children’s development, behaviour and health: evidence from the Millennium
38 Cohort Study. York: : University of York 2010.
- 39
40 25 Kiernan KE, Huerta MC. Economic deprivation, maternal depression, parenting and children’s
41 cognitive and emotional development in early childhood. *Br J Sociol* 2008;**59**:783–806.
- 42
43 26 Shenkin SD, Starr JM, Deary IJ. Birth weight and cognitive ability in childhood: a systematic
44 review. *Psychol Bull* 2004;**130**:989.
- 45
46 27 Jefferis BJMH, Power C, Hertzman C. Birth weight, childhood socioeconomic environment, and
47 cognitive development in the 1958 British birth cohort study. *BMJ* 2002;**325**:305.
48 doi:10.1136/bmj.325.7359.305
- 49
50 28 Kramer MS, Aboud F, Mironova E, *et al.* Breastfeeding and Child Cognitive Development: New
51 Evidence From a Large Randomized Trial. *Arch Gen Psychiatry* 2008;**65**:578–84.
52 doi:10.1001/archpsyc.65.5.578
- 53
54 29 Walker SP, Wachs TD, Grantham-McGregor S, *et al.* Inequality in early childhood: risk and
55 protective factors for early child development. *The Lancet* 2011;**378**:1325–38.
- 56
57
58
59
60

- 1
2
3 30 Murray GK, Jones PB, Kuh D, *et al.* Infant developmental milestones and subsequent cognitive
4 function. *Ann Neurol* 2007;**62**:128–36. doi:10.1002/ana.21120
- 5
6 31 Kelly Y, Sacker A, Gray R, *et al.* Light drinking in pregnancy, a risk for behavioural problems
7 and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;**38**:129–40. doi:10.1093/ije/dyn230
- 8
9 32 Dahlgren G, Whitehead M. Policies and strategies to promote social equity in health. *Stockh Inst
10 Future Stud* 1991.
- 11
12 33 Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development of a self-
13 report questionnaire instrument. *J Reprod Infant Psychol* 1998;**16**:57–76.
- 14
15 34 Sosthenes C. Ketende, Elizabeth M. Jones. User Guide to Analysing MCS Data Using STATA.
16 Centre for Longitudinal Studies, Institute of Education 2011.
- 17
18 35 Peduzzi P, Concato J, Feinstein AR, *et al.* Importance of events per independent variable in
19 proportional hazards regression analysis II. Accuracy and precision of regression estimates. *J Clin
20 Epidemiol* 1995;**48**:1503–1510.
- 21
22 36 Azen R, Traxel N. Using Dominance Analysis to Determine Predictor Importance in Logistic
23 Regression. *J Educ Behav Stat* 2009;**34**:319–47. doi:10.3102/1076998609332754
- 24
25 37 Pencina MJ, D'Agostino RB, Pencina KM, *et al.* Interpreting Incremental Value of Markers
26 Added to Risk Prediction Models. *Am J Epidemiol* 2012;**176**:473–81. doi:10.1093/aje/kws207
- 27
28 38 Windmeijer FAG. The asymptotic distribution of the sum of weighted squared residuals in binary
29 choice models. *Stat Neerlandica* 1990;**44**:69–78.
- 30
31 39 Steyerberg EW, Harrell FE, Borsboom GJJM, *et al.* Internal validation of predictive models. *J
32 Clin Epidemiol* 2001;**54**:774–81. doi:10.1016/S0895-4356(01)00341-9
- 33
34 40 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and
35 guidance for practice. *Stat Med* 2011;**30**:377–99. doi:10.1002/sim.4067
- 36
37 41 Centre for Longitudinal Studies. MCS Ethical Review and Consent. London: : Institute of
38 Education 2014. <http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=1601&itemtype=document>
- 39
40 42 Pepe MS, Janes H, Longton G, *et al.* Limitations of the Odds Ratio in Gauging the Performance
41 of a Diagnostic, Prognostic, or Screening Marker. *Am J Epidemiol* 2004;**159**:882–90.
42 doi:10.1093/aje/kwh101
- 43
44 43 Hosmer DW, Hjort NL. Goodness-of-fit processes for logistic regression: simulation results. *Stat
45 Med* 2002;**21**:2723–2738.
- 46
47 44 Wilkinson RG, Marmot M. *Social Determinants of Health: The Solid Facts*. World Health
48 Organization 2003.
- 49
50 45 McKean C, Law J, Mensah F, *et al.* Predicting Meaningful Differences in School-Entry Language
51 Skills from Child and Family Factors Measured at 12 months of Age. *Int J Early Child
52 2016*;**48**:329–51. doi:10.1007/s13158-016-0174-0
- 53
54
55
56
57
58
59
60

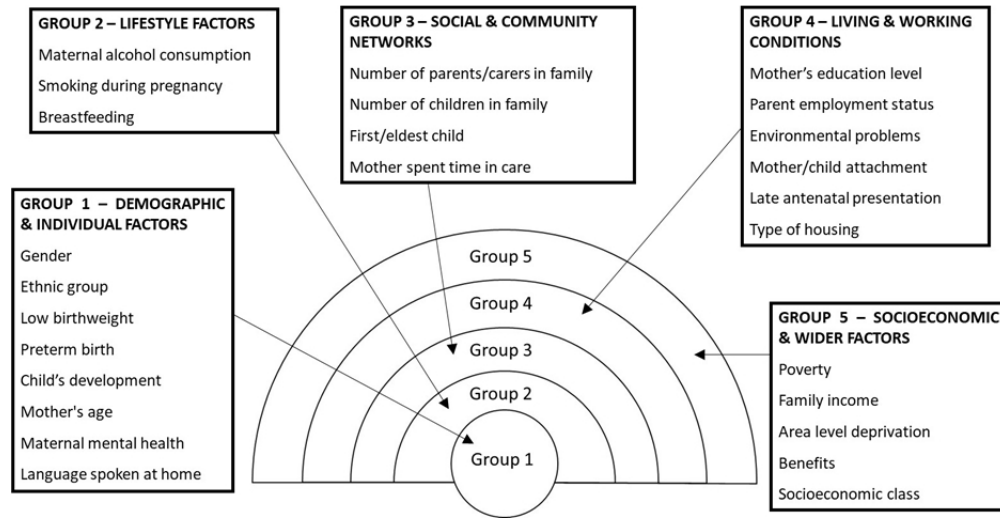
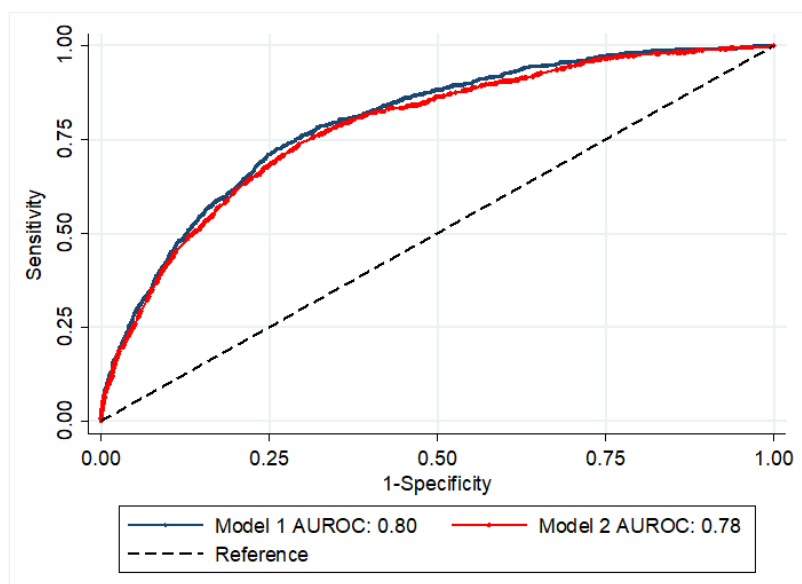


Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and Whitehead, 1991)

99x50mm (240 x 240 DPI)



AUROC cut off points are: 0.9-1 = excellent, 0.8-<0.9 = good, 0.7-<0.8 = fair, 0.6-<0.7 = poor, 0.5-<0.6 = fail

Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

92x59mm (240 x 240 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

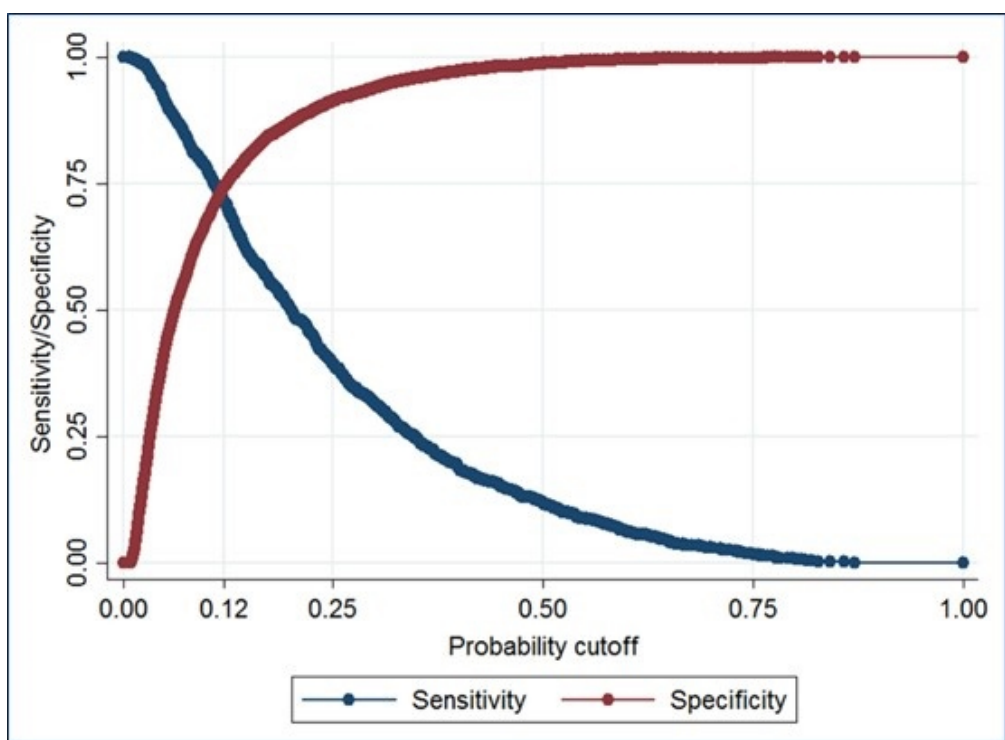


Figure 3 - Maximised probability cut off of sensitivity and specificity of model 1

58x43mm (240 x 240 DPI)

1
2
3 **SUPPLEMENTARY FILE 1**
4

5 Table 1 - Adjusted associations for the predictor variables in model 1 (13 predictors) using
6 multiple imputed data (n=11,879)
7

Predictor	Adjusted OR (95% CI)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS	
Gender	
Male	1
Female	0.47 (0.41-0.54)
Ethnicity	
White	1
Mixed	1.04 (0.62-1.75)
Indian	2.68 (1.85-3.89)
Pakistani and Bangladeshi	3.85 (2.94-5.04)
Black or Black British	2.31 (1.43-3.72)
Other ethnic group	3.95 (2.30-6.77)
Mother's age at birth of first child	
30-39	1
40+	1.05 (0.67-1.64)
20-29	1.22 (0.99-1.51)
14-19	1.22 (0.93-1.59)
Birth weight (<2500grams)	
Normal/high	1
Low birthweight	1.52 (1.18-1.97)
Maternal Mental Health (Diagnosed depression/anxiety)	
No	1
Yes	1.15 (0.98-1.34)
Child developmental milestones	
Above average	1
Average	1.29 (1.07-1.57)
Below average	1.60 (1.33-1.92)
GROUP 2 - LIFESTYLE FACTORS	
Duration of breastfeeding	
6 months or more	1
6 weeks - 6 months	1.17 (0.92-1.48)
One week or less	1.15 (0.90-1.48)
1 - 6 weeks	1.22 (0.96-1.57)
Never	1.58 (1.29-1.95)
GROUP 3 - SOCIAL & COMMUNITY NETWORKS	
Number of children in family	
One child	1
Two or three children	1.40 (1.19-1.63)
Four or more children	2.48 (1.94-3.16)
GROUP 4 - LIVING & WORKING CONDITIONS	

Maternal education	
Degree plus	1
Diploma	0.88 (0.61-1.26)
A-levels	1.13 (0.80-1.59)
GCSE A-C	1.34 (1.01-1.78)
GCSE D-G	1.72 (1.23-2.39)
None	1.74 (1.28-2.38)
Workforce status	
Both parents in work	1
One parent in work	0.94 (0.78-1.12)
Neither parent in work	1.21 (0.93-1.57)
Housing tenure	
Owner occupied	1
Private rented	1.18 (0.90-1.54)
Social housing	1.43 (1.18-1.72)
Other	0.96 (0.69-1.35)
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS	
Social class	
Managerial & professional	1
Intermediate	0.98 (0.75-1.29)
Small employers & own account	1.32 (0.87-2.00)
Lower supervisory & technical	1.50 (1.06-2.13)
Semi-routine & routine	1.77 (1.38-2.27)
Never worked & long-term unemployed	2.19 (1.53-3.15)
Annual income	
£33,000+	1
£22,000-£33,000	1.33 (1.02-1.72)
£11,000-£22,000	1.67 (1.30-2.14)
£0-£11,000	2.14 (1.60-2.87)
ROC Analysis	
AUROC = 0.79 (95% CI 0.78 - 0.80)	

SUPPLEMENTARY FILE 2

Results of integrated discrimination improvement (IDI) analysis, variables added according to their rank from the dominance analysis.

Variables included	IDI (%)	p	1-IDI
1	7.3%	<0.00001	92.7%
2	5.3%	<0.00001	94.7%
3	3.8%	<0.00001	96.2%
4	3.5%	<0.00001	96.5%
5	2.3%	<0.00001	97.7%
6	1.3%	<0.00001	98.7%
7	1.0%	<0.00001	99.0%
8	0.9%	<0.00001	99.1%
9	0.6%	0.00001	99.4%
10	0.6%	0.00001	99.4%
11	0.2%	0.01402	99.8%
12	0.0%	0.52356	100.0%

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	3
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	3
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	3-4
	5b	Describe eligibility criteria for participants.	4
	5c	Give details of treatments received, if relevant.	
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4
	6b	Report any actions to blind assessment of the outcome to be predicted.	
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors. <small>temporal ordering in cohort</small>	
Sample size	8	Explain how the study size was arrived at.	5
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	5-6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	6
Risk groups	11	Provide details on how risk groups were created, if done.	
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6-7
Model development	14a	Specify the number of participants and outcome events in each analysis.	10
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	8-10
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	
	15b	Explain how to use the prediction model.	
Model performance	16	Report performance measures (with CIs) for the prediction model.	10
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11-12
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11-13
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	
Funding	22	Give the source of funding and the role of the funders for the present study.	

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development of a Predictive Risk Model for School Readiness at age 3 years using the UK Millennium Cohort Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024851.R1
Article Type:	Research
Date Submitted by the Author:	01-Feb-2019
Complete List of Authors:	Camacho, Christine; University of Liverpool Department of Public Health and Policy, Straatmann, Viviane; University of Liverpool Department of Public Health and Policy; Karolinska Institutet, Ageing Research Day, Jennie; University of Liverpool Department of Public Health and Policy Taylor-Robinson, David; University of Liverpool, Department of Public Health and Policy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Epidemiology, Health policy
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, SOCIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 **Development of a Predictive Risk Model for School Readiness at age 3 years using the**
4 **UK Millennium Cohort Study**
5

6
7 Miss CL Camacho*¹, Dr VS Straatmann^{1,2}, Dr JC Day¹, Prof DC Taylor-Robinson¹
8

9 *Affiliations: ¹Public Health and Policy, University of Liverpool, Liverpool, UK; ²Aging*
10 *Research, Karolinska Institute, Stockholm, Sweden*
11

12
13 *Address correspondence to: Christine Camacho, Department of Public Health and Policy, University*
14 *of Liverpool, Liverpool, United Kingdom, L69 3GB, [c.camacho@nhs.net], +44 07973395585*
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

ABSTRACT

Objectives

The aim of this study was to develop a predictive risk model (PRM) for school readiness measured at age 3 years using perinatal and early infancy data.

Design and Participants

This paper describes the development of a predictive risk model. Predictors were identified from the UK Millennium Cohort Study (MCS) wave 1 data, collected when participants were 9 months old. The outcome was school readiness at age 3 years, measured by the Bracken School Readiness Assessment. Stepwise selection and dominance analysis were used to specify 2 models. The models were compared by the area under the receiver operating characteristic curve (AUROC) and integrated discrimination improvement (IDI).

Results

Data were available for 9,487 complete cases. At age 3, 11.7% (95% CI 11.0-12.3%) of children were not school ready. The variables identified were: parents' Socio-Economic Classification, child's ethnicity, maternal education, income band, sex, household number of children, mother's age, low birth weight, mother's mental health, infant developmental milestones, breastfeeding, parents' employment, housing type. A parsimonious model included the first six listed variables (model 2). The AUROC for model 1 was 0.80 (95% CI 0.78-0.81) and 0.78 (95% CI 0.77-0.79) for model 2. Model 1 resulted in a small improvement in discrimination (IDI=1.3%, $p<0.001$).

Conclusions

Perinatal and infant risk factors predicted school readiness at age 3 with good discrimination. Social determinants were strong predictors of school readiness. This study demonstrates that school readiness can be predicted by six attributes collected around the time of birth.

Strengths and limitations of this study

- Use of a large, representative, and contemporary cohort study to demonstrate the feasibility of predicting school readiness from data collected in infancy.
- Multiple imputation and bootstrapping were used to evaluate the impact of missing data and internal validity, respectively.
- The main outcome measure, the Bracken School Readiness Assessment, was developed in the US, and is not routinely used in the UK.
- This model was not externally validated, which would have given an indication of generalisability.

INTRODUCTION

Early childhood is a critical time for lifelong physical, social, emotional and cognitive development. A wide range of factors are associated with early cognitive development (ECD)[1]. Interventions in the first three years of life can improve the trajectory of ECD[2] and deliver the greatest return on investment[3], yet it is unclear how best to identify children at most risk of delayed ECD, to enable appropriate targeting of interventions.

Cognitive development measures in children are good indicators of later educational achievement, predict health and social care needs in adults[4,5], and are associated with long term health outcomes[6]. There has been a growing policy interest in school readiness as a measure of ECD[7], and school readiness is a key public health indicator in children in the UK. Good school readiness lays a platform for future learning, employment and health[8,9].

School readiness is currently a major focus in England [10] and national metrics are collected to capture changes over time. In 2017, 29% of children in England were deemed not school ready at the end of their reception year (aged 4-5 years)[11]. There was nearly a 20% point gap in performance between the most (62% school ready) and the least (80%) deprived deciles of Index of Multiple Deprivation [12]. In UK policy there has been a focus on demographic factors e.g. maternal age, in targeting early interventions for children[13]. This study will explore the importance of different variables in predicting school readiness.

Previous research has identified a wide range of variables associated with early cognitive development. Predictive risk models (PRMs) are well-established in many clinical disciplines and have more recently been applied to child development. Using PRMs in this context could facilitate targeted early intervention as part of a proportionate universalism approach, which requires universal action with the scale and intensity of interventions proportionate to the level of need[6]. Most models thus far have shown fair or poor discrimination and there have been very few studies in the UK [14–18]. The aim of this study was to develop, for the first time, a PRM for school readiness measured at age 3 years using perinatal and early infancy data from the UK Millennium Cohort Study (MCS).

METHODS

Overview

Data from the MCS were used to explore the relationship between the outcome, school readiness, and 29 predictor variables using logistic regression analysis. Following univariable analysis to test for unadjusted associations, automated stepwise regression analyses were used to select variables for inclusion in the PRM. Dominance analysis was used to rank and weight included predictors, and integrated discrimination improvement (IDI) was calculated to assess the difference in performance between models. A receiver operator characteristic (ROC) curve was used to evaluate how well the model discriminated school readiness. The area under an ROC curve (AUROC) gives a measure of how well the regression model predicts school readiness at age 3. Traditionally accepted AUROC cut off points are: 0.9-1 = excellent, 0.8- $<$ 0.9 = good, 0.7- $<$ 0.8 = fair, 0.6- $<$ 0.7 = poor, 0.5- $<$ 0.6 = fail[19]. Multiple imputation was used to assess the impact of missing data in the sample.

Data Source

The PRM was developed and validated using MCS data. The MCS is a nationally representative birth cohort study which recruited 18,550 children born from September 2000 to January 2002, followed up in ongoing data collection waves. The sampling frame was government child benefit records, which had almost universal coverage at the time of sampling. The sample was clustered at the level of electoral ward and stratified to allow over representation of children living in deprived areas and areas with high concentrations of ethnic minorities[20]. Further information about the MCS sample is available in the cohort profile[21]. Data were collected from the main responder (usually mothers) by trained interviewers in participants' homes using a combination of interviews and self-completed questions. All singleton children in the first (aged 9 months) and second (aged 3 years) waves of the MCS with completed data for the outcome and predictors were eligible for inclusion (n=9,487).

Outcome

School readiness was measured using the Bracken School Readiness Assessment (BSRA) which consists of 6 subtests relating to colours, letters, numbers/counting, sizes, comparisons and shapes[22]. The assessment was carried out by interviewers during the second data collection wave when children were aged approximately 3 years old. The BSRA and its predecessors have demonstrated good reliability[23] and validity against other measures and teacher assessments[24].

The BSRA raw scores were summed and adjusted for age to provide a standardised composite score[22]. Scores were grouped according to cut-offs recommended by Bracken which reflected a 'normative classification' whereby children were categorised as very delayed, delayed, average, advanced or very advanced [25]. We used the same cut off score as Bracken (mean standardised composite score $<$ 85, 1 standard deviation below mean) but collapsed the categories of delayed or very delayed into a single category equivalent to not being school ready. We have dichotomised the outcome 'school readiness' in line with UK policy, and to allow the testing of a PRM using ROC analysis which requires a binary outcome [26].

Predictors

29 predictor variables were used, which were collected at age 9 months in the first wave of MCS data collection during which data relevant to pregnancy, birth and the perinatal period was captured retrospectively. These were identified from previous research to predict cognitive development and were included in the MCS[1,2,4,6,27–34]. The selected predictor variables were grouped according to the Dahlgren and Whitehead theoretical model[35] of social determinants of health as depicted in Figure 1. This model was chosen to provide a framework for categorising predictors to allow analysis of the determinants of early cognitive development.

<<Figure 1 here>>

Group 1 – Demographic and Individual factors

Demographic characteristics included child sex, maternal ethnicity, child weight, pre-term birth, mother's age, home language, maternal mental health and child development categorised as shown in Box 1.

Box 1 – Coding of Group 1 demographic and individual factors

Categorisation of Demographic and Individual factors

Child sex – 'female' and 'male'

Maternal ethnicity – 'white', 'mixed', 'Indian', 'Pakistani and Bangladeshi', 'Black' and 'other'

Child weight at birth – low (<2.5kg) or normal/high (≥2.5kg)

Preterm birth – gestation period less than 37 weeks

Mother's age in years at birth of first child – grouped into 4 categories (14-19, 20-29, 30-39, 40+ years)

Home language – 'English only', 'English and another language', 'another language only'

Mental health (1) – Sad or low for >2 weeks since baby, coded as 'yes' or 'no'

Mental health (2) – Diagnosis of depression or serious anxiety, coded as 'yes' or 'no'

Mental health (3) – 9-item modified version of the Rutter Malaise Inventory³⁹, coded as 'low' or (0-3) 'high' (4-9) scores²⁷.

Child development – 8 items from Denver Developmental Screening Test and 5 items from MacArthur Communicative Development Inventory, scored on a continuous scale from 13 (above average) to 36 (below average)

Group 2 – Lifestyle Factors

Self-reported maternal smoking was coded as 'never smoked', 'smoked before pregnancy' and 'smoked during pregnancy'. Maternal alcohol consumption during pregnancy were categorised as 'never or very infrequent', 'occasional', 'regularly' and 'most or everyday'. Breastfeeding duration was grouped as 'never', 'one week or less', '1 – 6 weeks', '6 weeks – 6 months' and 'over 6 months'.

Group 3 – Social and Community Factors

The number of children in household was coded as '1', '2-3' or '4+', and being the eldest or only child was recoded as 'yes' or 'no'. The number of parents or carers was either '1' or '2'. Mothers were asked how much time they had spent time in care before the age of 17, this was recoded as 'yes' or 'no' to indicate if they had ever been in care.

Group 4 – Living and Working Conditions

1
2
3 Maternal education was categorised into six groups ‘degree plus (higher degree and first degree
4 qualifications)’, ‘diploma (in higher education)’, ‘A-levels’, ‘GCSE grades A–C’, ‘GCSE
5 grades D–G’ and ‘none of these qualifications’. Parent’s employment status was classified as
6 either ‘both’, ‘one’ or ‘neither’ parents in work¹. Housing tenure was coded as ‘owner
7 occupied’, ‘private rented’, ‘social housing’ and ‘other’. The response to the question, “How
8 common is pollution, grime or other environmental problems?” was recoded as ‘common’, ‘not
9 common’ and ‘not at all’. Presentation for first antenatal visit was recoded as late if after 12
10 weeks. Maternal attachment was measured using a 6-item Condon Maternal Attachment
11 Questionnaire[36] grouped as ‘low (10-21), ‘average’ (22-23) and ‘high (24-27) .
12
13
14
15

16 Group 5 – Socioeconomic and Wider Factors

17 The National Statistics Socio-Economic Classification (NS-SEC) was used to code job details
18 for main respondents (the majority of which were mothers) as: ‘managerial & professional’,
19 ‘intermediate’, ‘small employers & own account’, ‘lower supervisory & technical’, ‘semi-
20 routine & routine’, ‘never worked & long-term unemployed’. Net household income was
21 reported by identification of the correct band on a show card and grouped into 4 quartile
22 bands[27]: ‘£0-£11,000’, ‘£11,000-£22,000’, ‘£22,000-£33,000’ and ‘£33,000+’. Poverty was
23 defined as an equivalised household income 60% below the median before housing costs
24 according to the Organisation for Economic Co-operation and Development Household
25 Equivalence Scale. Families reported receipt of any means-tested benefits, including
26 Jobseekers Allowance, Income Support, Working Families Tax Credit or Disabled Persons Tax
27 Credit. Indices of Multiple Deprivation (IMD) from 2004 were linked retrospectively to wave
28 1 data to give small area level deprivation measure. IMD scores were divided into quintiles,
29 with 1 the most deprived quintile, and 5 the least deprived.
30
31
32
33
34
35

36 Statistical analyses

37 Analyses were conducted using Stata v14.2 (StataCorp LP, 2017). Survey weights were applied
38 to take account of clustering, stratification and oversampling in the survey design, and attrition
39 between survey waves, using the svyset command (pweight=BOVWT2) and svy prefix for
40 regression modelling[37]. The number of events per variable (EPV) exceeds 35, the predictors
41 were checked for collinearity, a large number of predictors were used and all were significantly
42 associated with the outcome suggesting a robust logistic regression model with sufficient
43 sample size [38,39].
44
45
46

47 Descriptive analysis of each predictor and school readiness was carried out to ascertain the
48 prevalence of each predictor in the sample. Univariable logistic regression analyses calculating
49 odds ratios (ORs) and 95% confidence intervals (95% CI) were carried out to assess the
50 unadjusted association of each variable with the outcome.
51
52
53

54 A multivariable logistic regression model including all 29 variables was reduced using
55 automated forward and backwards stepwise selection (using a cut off p-value of 0.1)..
56 Dominance analysis (repeated regression analyses on subsets of variables) was used to produce
57
58

59 ¹ Being on leave from work is classed as being in employment
60

1
2
3 a ranking and weighting for each predictor in model 1[40]. These rankings were used to specify
4 a more parsimonious model (model 2) containing the top 6 predictors, selected to maximise
5 parsimony and performance. The integrated discrimination improvement (IDI) using the
6 complete case sample from model 1 was calculated to assess difference in performance
7 between models as the percentage change in individuals being correctly assigned by the
8 model[41].
9
10

11
12 The area under the ROC curve (AUROC) and its 95% CI was used to measure discriminatory
13 power of the models. Classification, including sensitivity and specificity, was assessed at the
14 maximised probability cut off point where the sensitivity and specificity curves intersected.
15 Calibration of the model was assessed using the Pearson Chi-squared test[42]. Bootstrapping
16 was used for internal validation; model performance was assessed using 1000 bootstrap
17 samples, model optimism was averaged across all iterations to obtain an optimism estimate.
18 An optimism-corrected AUROC, which takes account of overfitting, was calculated as the
19 difference between unadjusted performance and the optimism estimate [43].
20
21
22

23
24 A complete case approach was used for the primary analysis. As a sensitivity analysis, multiple
25 imputation by chained equation was performed to impute missing data (imputed sample,
26 n=13,650). Variables from the first sweep and the outcome variable were used to shape the
27 imputation of the missing data (maternal education, child's sex, mother's age at birth of first
28 child and school readiness at age 3). Twenty imputed datasets were generated, and Rubin's
29 rules were used to calculate results across the imputed datasets[44].
30
31
32

33
34 Robustness tests were carried out in which the final model was tested with an alternative
35 outcome measure for early cognitive development (the British Ability Scales, also tested at age
36 3 in the MCS); different coding of outcome and predictor variables (e.g. maternal age as a
37 continuous variable); and with the addition of another predictor variable (child care type at age
38 9 months). See supplementary file 1 for further details.
39
40

41 **Ethics and Patient and public involvement**

42
43 Ethical approval for each wave of the MCS was granted by NHS Multicentre Research Ethics
44 Committees[45]. No further ethical approval was required for this secondary analysis of MCS
45 data. There was no direct patient or public involvement in this analysis. However, the MCS has
46 an ongoing programme of participant and public engagement.
47
48

49 **RESULTS**

50
51 There were 15,381 singleton children surveyed in MCS2, of which 13,650 had an outcome
52 recorded for school readiness. Of these children 70% (n=9,487) had complete data for the
53 outcomes and all the predictor variables. There were no significant differences in the
54 characteristics of the imputed sample and the complete case sample (p value >0.05 for all chi-
55 squared tests) (Table 1); results are reported for complete cases (see Supplementary file 2 for
56 imputed sample results).
57
58
59
60

Table 1 - Description of perinatal, sociodemographic and economic characteristics by school ready of sample and imputed sample

Is Child School Ready?	Complete Cases (n=9,487)		Imputed Data (n=13,650)	
	Yes (%)	No (%)	Yes (%)	No (%)
All	88.3	11.7	85.5	14.5
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS				
Gender				
Female	91.6	8.4	89.4	10.6
Male	85.1	14.9	82.6	17.4
Ethnicity				
White	90.4	9.6	88.6	11.4
Mixed	91.1	8.9	84.7	15.3
Indian	79.3	20.7	78.1	21.9
Pakistani and Bangladeshi	55.7	44.3	56.3	43.7
Black or Black British	79.8	20.2	68	32
Other ethnic group	73.6	26.4	74.3	25.7
Mother's age at birth of first child				
14-19	78	22	76.4	23.6
20-29	87.9	12.1	86.1	13.9
30-39	95	5	94.4	5.6
40+	76.9	23.1	76	24
Birth weight (<2500grams)				
normal/high	88.8	11.2	86.1	13.9
low birthweight	80.2	19.8	77.7	22.3
Maternal Mental Health (Diagnosed depression/anxiety)				
No	89	11	86	14
Yes	86	14	84.4	15.6
Child developmental milestones				
Child development score (mean, 95%CI)	19.3 (19.2,19.3)	19.9 (19.7,20.1)	19.1 (19.0,19.1)	19.6 (19.4,19.7)
GROUP 2 - LIFESTYLE FACTORS				
Duration of breastfeeding				
6 months or more	92.5	7.5	90.5	9.5
6 weeks - 6 months	89.8	10.2	87.8	12.2
1 - 6 weeks	88.8	11.2	85.9	14.1
one week or less	88.8	11.2	86.4	13.6
Never	82.6	17.4	80	20
GROUP 3 - SOCIAL & COMMUNITY NETWORKS				
Number of children in family				
One child	92	8	89.1	10.9
Two or three children	87.7	12.3	85	15
Four or more children	71.7	28.3	70.2	29.8
Maternal education				
Degree plus	95.6	4.4	95.1	4.9
Diploma	94.6	5.4	93.9	6.1
A levels	92.7	7.3	92	8

GCSE A-C	88.5	11.5	87.4	12.6
GCSE D-G	81	19	79.1	20.9
None	71.3	28.7	69.2	30.8
GROUP 4 - LIVING & WORKING CONDITIONS				
Workforce status				
Both parents in work	92.6	7.4	91.6	8.4
One parent in work	85.8	14.2	83.4	16.6
Neither parent in work	68.5	31.5	70.1	29.9
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS				
Housing tenure				
Owner occupied	91.9	8.1	90.7	9.3
Private rented	83.8	16.2	80.5	19.5
Social housing	75.8	24.2	74.8	25.2
Other	83.4	16.6	81	19
Social class				
managerial & professional	95.5	4.5	94.6	5.4
intermediate	93.1	6.9	92.1	7.9
small employers & own account	91.3	8.7	89.1	10.9
lower supervisory & technical	87.2	12.8	84	16
semi-routine & routine	81.9	18.1	80	20
never worked & long-term unemployed	60.2	39.8	62.1	37.9
Annual income				
£33,000+	95.7	4.3	94.9	5.1
£22,000-£33,000	92.5	7.5	91.7	8.3
£11,000-£22,000	85	15	83.9	16.1
£0-£11,000	73.8	26.2	74.1	25.9

11.7% (95%CI 11.0-12.3%) of children aged 3 years were classified as not being school ready, but this varied significantly by the parents' ethnicity, maternal education and social class (Table 1). All 29 predictor variables were significantly associated with school readiness in univariable logistic regression analysis ($p < 0.1$), so none were excluded at this stage.

The stepwise method reduced the final multivariable logistic regression model to 13 predictors: child's sex and ethnicity, mother's age at birth of first child, birthweight, maternal mental health, child development milestones, duration of breastfeeding, number of children in family, maternal education, parents' workforce status, housing tenure, social class and annual family income. In the adjusted analysis, Pakistani and Bangladeshi children were 4 times more likely to not be school ready than white children (OR 4.19 95% CI 3.14-5.58). The full results are shown in Table 2. There was no evidence of collinearity.

Table 2 - Unadjusted and adjusted associations and dominance analysis for the predictor variables in model 1 (13 predictors)

Predictors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			

Gender			
Female	1	1	9.5 (5)
Male	1.76 (1.54,2.01)	2.03 (1.72,2.39)	
Ethnicity			
White	1	1	
Mixed	1.4 (0.96,2.04)	1.42 (0.78,2.58)	
Indian	1.85 (1.23,2.77)	2.58 (1.65,4.03)	14.7 (2)
Pakistani and Bangladeshi	5.94 (4.82,7.32)	4.27 (3.20,5.69)	
Black or Black British	4.06 (2.90,5.69)	2.1 (1.13,3.88)	
Other ethnic group	2.33 (1.38,3.93)	2.92 (1.55,5.48)	
Mother's age at birth of first child			
30-39	1	1	
40+	2.83 (2.29,3.49)	1.05 (0.68,1.63)	2.9 (11)
20-29	5.57 (4.20,7.37)	1.28 (0.98,1.66)	
14-19	6.02 (4.84,7.48)	1.32 (0.95,1.83)	
Birth weight (<2500grams)			
Normal/high	1	1	1.4 (12)
Low birthweight	1.7 (1.34,2.16)	1.26 (0.92,1.72)	
Maternal Mental Health (Diagnosed depression/anxiety)			
No	1	1	0.4 (13)
Yes	1.33 (1.16,1.53)	1.28 (1.07,1.53)	
Child developmental milestones			
Developmental score	1.07 (1.05,1.10)	1.1 (1.07,1.14)	3.9 (11)
GROUP 2 - LIFESTYLE FACTORS			
Duration of breastfeeding			
6 months or more	1	1	
6 weeks - 6 months	1.25 (1.02,1.53)	1.05 (0.81,1.36)	
One week or less	1.67 (1.34,2.09)	1.19 (0.89,1.59)	3.9 (10)
1 - 6 weeks	1.68 (1.36,2.07)	1.25 (0.96,1.65)	
Never	2.74 (2.29,3.27)	1.49 (1.19,1.87)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	
Two or three children	1.44 (1.27,1.63)	1.38 (1.15,1.66)	7.8 (6)
Four or more children	3.71 (3.04,4.54)	2.67 (1.94,3.68)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	
Diploma	1.3 (0.93,1.81)	0.81 (0.53,1.24)	
A levels	1.66 (1.22,2.25)	1.02 (0.68,1.55)	13.6 (3)
GCSE A-C	3.02 (2.34,3.90)	1.3 (0.89,1.88)	
GCSE D-G	5.55 (4.21,7.30)	1.54 (1.02,2.34)	
None	9.62 (7.61,12.16)	1.68 (1.15,2.43)	
Workforce status			
Both parents in work	1	1	
One parent in work	1.79 (1.49,2.14)	0.82 (0.67,1.00)	6.9 (7)
Neither parent in work	5.39 (4.36,6.67)	1.21 (0.87,1.68)	

Housing tenure			
Owner occupied	1	1	
Private rented	2.68 (2.16,3.33)	1.21 (0.87,1.67)	5.7 (8)
Social housing	3.89 (3.34,4.53)	1.45 (1.16,1.81)	
Other	2.65 (2.10,3.35)	0.9 (0.62,1.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	
Intermediate	1.5 (1.19,1.89)	1.06 (0.77,1.45)	
Small employers & own account	2.11 (1.44,3.08)	1.41 (0.87,2.28)	17.4 (1)
Lower supervisory & technical	3.72 (2.76,5.00)	1.65 (1.09,2.50)	
Semi-routine & routine	4.99 (4.13,6.01)	1.97 (1.46,2.66)	
Never worked & long-term unemployed	12.07 (9.48,15.37)	2.49 (1.69,3.66)	
Annual income			
£33,000+	1	1	
£22,000-£33,000	1.71 (1.31,2.25)	1.31 (0.96,1.79)	12.0 (4)
£11,000-£22,000	3.97 (3.12,5.07)	1.64 (1.22,2.22)	
£0-£11,000	7.7 (6.10,9.72)	2.26 (1.60,3.19)	

Dominance analysis showed that social class was the most important predictor (weighting=17.6), followed by ethnic group (weighting=14.7) and maternal education (weighting=13.8) (Table 2). Analysis of the predictor weightings suggests that social factors (average weighting 11.3, SD 4.9) are stronger predictors of school readiness than demographic and lifestyle factors (average weighting 5.5, SD 4.9). IDI was used to test the relative performance of models with all (1-13) variables, with variables added in according to their rank from the dominance analysis (Supplementary File 3). These analyses informed the specification of model 2, which was comprised of the top 6 predictors: social class, child's ethnic group, maternal education, income band, sex and number of children (see Supplementary File 4 for Model 2 results).

The AUROC was 0.80 (95% CI 0.78-0.81) for model 1 (n=9,487), which indicates a "good" level of discrimination[19]. The AUROC for model 2 (n=11,146) was 0.78 (95% CI 0.77-0.79). Internal validation using bootstrap optimism correction suggests that the model would have good discriminatory power in an independent sample (adjusted AUROC model 1 = 0.79, model 2=0.76). The Pearson Chi-squared tests were both non-significant indicating adequate calibration (model 1, p=0.07, model 2, p=0.13)[46]. IDI showed there was a small but significant difference in performance, with model 1 resulting in a 1.3% (p=<0.001) improvement in discrimination (Figure 2).

<<Figure 2 here>>

Sensitivity and specificity were plotted against probability cut-offs to select the optimal cut off point to assess the PRM's classification (model 1, cut-off=0.12; model 2, cut-off=0.14) (Figure 3 **Error! Reference source not found.**). For model 1, at this cut-off point sensitivity was 72% (95% CI 69.0%-74.3%) and specificity was 74% (95% CI 73.5%-75.3%). Sensitivity of model 2 was similar - 72% (95% CI 69.9%-74.5%). Specificity was lower - 71% (95% CI 69.6%-

1
2
3 71.4%), so this model would generate more false positive results than the model 1, but
4 performance was still in the acceptable range. At a probability cut-off of 12%, 31% of the
5 screened population tested would be identified as being at high risk of poor school readiness
6 using model 1.
7
8

9
10 <<Figure 3 here>>
11

12 A sensitivity analysis using an alternative outcome measure (British Ability Scales, BAS),
13 showed that the BSRA measure led to improved discrimination (AUROC = 0.79 (95% CI 0.78-
14 0.81) for BAS; AUROC = 0.80 (95% CI 0.78-0.81) for BSRA, $p=0.002$). See supplementary
15 file 1 for further details.
16
17

18 19 **DISCUSSION**

20 **Findings**

21 This study developed a PRM for school readiness at age 3 years using perinatal and early
22 childhood data from the MCS. Model 1 with 13 variables had good discrimination
23 (AUROC=0.80) and classification (sensitivity=72%, specificity= 74% at a maximised cut off).
24 Dominance analysis found the most important variables in predicting school readiness related
25 to socioeconomic conditions (social class, maternal education, family income) and ethnicity.
26 A parsimonious model performed similarly well (AUROC=0.78), suggesting it is possible to
27 predict school readiness at age 3 using just six variables from the perinatal period and early
28 infancy.
29
30
31
32

33 **Comparison with previous studies**

34 The value added of this study is that it is the first UK study to show that school readiness can
35 be predicted with good discrimination with a small number of variables collected in infancy.
36 The predictors of school readiness identified here corroborate previous findings. Male sex,
37 maternal education, income, family composition, parental employment, housing and
38 breastfeeding have been identified as significant risk factors of delayed ECD in other
39 studies[4,14,15,17,18,27]. Social factors were the most important predictors, corresponding
40 with current thinking on the social determinants of cognitive development[6,47].
41
42
43
44

45 The model reported here has good predictive strength, and compares favourably to similar
46 PRMs, which with one exception[17], achieved only fair or poor discrimination[14,15,18,48].
47 Chittleborough et al used the ALSPAC UK birth cohort to test the predictive validity of 2
48 models for ECD[14]. They used a different outcome measure (School entry assessment aged
49 4-5) and used 6 predictors in their model, which appear to be chosen a priori, rather than by a
50 statistical routine. They found that maternal age alone failed to predict ECD (AUROC~0.5),
51 and a model with 6 predictors achieved only poor discrimination (AUROC=0.67). Camargo-
52 Figuera et al used IQ as a measure of ECD and developed a PRM with 12 predictors using the
53 Brazilian Pelotas birth cohort; their model had good discrimination (AUROC=0.8) and
54 calibration, with sensitivity and specificity of 72% and 74% respectively[17]. We believe the
55 use of a representative cohort for model development, stepwise regression to select predictor
56
57
58
59
60

1
2
3 variables and dominance analysis to specify a simplified model contributed to the good
4 performance of this PRM.
5
6

7 **Strengths and Limitations**

8 A strength of this study was the use of a representative and contemporary UK cohort study as
9 the data source. This offered a wide range of predictor variables and a large sample size which
10 minimised the likelihood of overfitting. The cohort design also ensured correct temporal
11 ordering and blinding with respect to the predictors. A theoretical model informed the PRM
12 and statistical selection was used to specify variables. Multiple imputation was used to assess
13 the impact of missing data. Bootstrapping showed good internal validity[49].
14
15
16

17 There are some limitations of this study to be considered. The main outcome, the BSRA, whilst
18 validated as a measure of school readiness, was developed in the US and is not routinely used
19 in the UK[24]. The BSRA measures a small set of pre-academic skills, but an analysis of MCS
20 data linked to teacher reports showed that Bracken scores are strongly associated with the
21 EYFS measure of school readiness used in English schools [4]. Many variables were
22 dichotomised or grouped, which may be less sensitive than continuous measures. Longitudinal
23 studies are subject to attrition and non-response which can introduce attrition bias, the use of
24 survey weights partially adjust for this, but it was not possible to use these when calculating
25 the AUROC. Sensitivity analysis using multiple imputation showed the effect of missing data
26 was negligible, similar to other PRMs[14,15]. Most of the predictor variables were based on
27 maternal self-report which may be subject to recall bias, and external validation was not
28 conducted. The predictor variables identified may not be causally associated with school
29 readiness and there are other predictors which may be associated with the outcome which were
30 not included in this model e.g. childcare in infancy[50].
31
32
33
34
35
36

37 **Policy Implications**

38 The existing literature, and these findings, indicate that a PRM could plausibly be used to
39 identify a group of children at high risk of poor ECD who may benefit from early intervention.
40 If implemented as part of a “proportionate universalism” approach[6], PRMs could mitigate
41 socioeconomic inequalities by providing early years settings with a mechanism for directing
42 their resources to those children at highest risk of poor cognitive development. With new child
43 and maternity datasets now being collected electronically in England, it may be possible to
44 apply a PRM at population level through the use of linked administrative datasets as has been
45 done in Australia[15].
46
47
48
49

50 Poor cognitive development is associated with a range of negative health and social outcomes
51 and contributes to inequalities in society[3,5,6], so this is of public health importance.
52 Chittleborough et al showed that even a model with poor discrimination has benefits over just
53 using young maternal age to direct resources[14]. Similarly, McKean et al established that their
54 PRM was better than existing clinical tools used to identify higher-risk children for early
55 intervention[48].
56
57

58 The practical implications of using such a PRM as a screening tool should be considered. The
59 model reported here would identify 31% of children screened as being ‘at risk’ of delayed
60

1
2
3 school readiness. An exemplar English Local Authority with a total population of 230,000, and
4 3000 children aged under 1 year would identify 900 'at risk' children per year if the PRM was
5 applied to this cohort. This percentage equates with national data; in 2015/16, 31% of children
6 in England were not school ready when tested at age 4-5[11]. However, the overall accuracy
7 of the model is 74%, so over 200 children would be incorrectly classified; this could lead to
8 stigmatisation of families and unnecessary use of resources. Nelson et al (2016) comment that
9 Early Intervention services would be overwhelmed by the level of demand generated by such
10 PRMs[18]. A criterion for screening programmes is that interventions should be available, it is
11 thus important to further consider the implications of using a PRM to assess ECD in the context
12 of available resources.
13
14
15
16

17
18 Further research is needed to test the external validity of predictive risk models for ECD for
19 example in another cohort or with linked administrative datasets. PRMs raise ethical issues;
20 labelling very young children as being at risk of poor development could be stigmatising for
21 families, particularly when social factors are the strongest predictors as in this analysis. PRMs
22 would generate false positives (and false negatives), which could cause unnecessary distress.
23 Use of PRMs to identify children at risk of developmental delay should include support and
24 counselling for families, as well as timely access to appropriate interventions. Investment in
25 early intervention would be required, which would have opportunity costs for services locally.
26
27
28

29 **CONCLUSION**

30
31 This study has identified a set of predictive risk factors from the perinatal period and early
32 infancy that can predict school readiness at age 3 with a good level of accuracy. Poor cognitive
33 development is socially patterned, evident from a very young age and leads to persistent
34 disadvantage throughout life. It is possible that PRMs could be used to identify high risk
35 children and target appropriate interventions and resources to improve their developmental
36 trajectories, and to reduce social inequalities early in the life course.
37
38
39

40 **STATEMENTS**

41 **Funding**

42
43 This research received no specific grant from any funding agency in the public,
44 commercial or not for profit sectors. DTR is funded by the MRC on a Clinician
45 Scientist Fellowship (MR/P008577/1).
46
47
48
49

50 **Competing Interests**

51
52 We confirm that authors have no conflicts of interest to disclose.
53
54
55

56 **Contributors**

1
2
3
4 CLC, JCD and DTR planned the study. CLC and VSS conducted the analysis under
5 the supervision of DTR. CLC led the drafting of the manuscript. All authors contributed
6 to data interpretation, manuscript drafting and revisions and agreed the submitted
7 version of the manuscript.
8
9
10

11 12 13 **Data Sharing**

14
15 The Millennium Cohort Study dataset is available from the UK Data Service.
16
17

18 **ACKNOWLEDGEMENTS**

19 We would like to acknowledge all the families and researchers who are part of the UK
20 Millennium Cohort Study, without whom this research would not have been possible.
21
22

23 **FIGURE CAPTIONS**

24 Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and
25 Whitehead, 1991)

26 Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

27
28 Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

REFERENCES

- 1 National Research Council (US) and Institute of Medicine (US) Committee on Integrating the Science of Early Childhood Development. *From Neurons to Neighborhoods: The Science of Early Childhood Development*. Washington (DC): : National Academies Press (US) 2000. <http://www.ncbi.nlm.nih.gov/books/NBK225557/>
- 2 Black MM, Walker SP, Fernald LC, *et al*. Early childhood development coming of age: science through the life course. *The Lancet* 2016.
- 3 Heckman JJ. Skill formation and the economics of investing in disadvantaged children. *Science* 2006;**312**:1900–2. doi:312/5782/1900 [pii]
- 4 Hobcraft JN, Kiernan KE. Predictive factors from age 3 and infancy for poor child outcomes at age 5 relating to children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010. <http://www.york.ac.uk/media/spsw/documents/research-and-publications/HobcraftKiernan2010PredictiveFactorsChildrensDevelopmentMillenniumCohort.pdf> (accessed 28 May 2017).
- 5 Caspi A, Houts RM, Belsky DW, *et al*. Childhood forecasting of a small segment of the population with large economic burden. *Nat Hum Behav* 2016;**1**:0005.
- 6 Marmot M, Allen J, Goldblatt P, *et al*. Fair society, healthy lives: strategic review of health inequalities in England post 2010. Marmot Review Team 2010.
- 7 Public Health England. Improving school readiness: creating a better start for London. London: 2015.
- 8 Pia Rebello Britto. School Readiness - A conceptual framework. New York, NY: : UNICEF 2012.
- 9 Marmot M, Friel S, Bell R, *et al*. Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet* 2008;**372**:1661–9. doi:10.1016/S0140-6736(08)61690-6
- 10 Abreu L, Roberts N. Children’s early years development and school readiness. 2016. <https://researchbriefings.parliament.uk/ResearchBriefing/Summary/CDP-2016-0141> (accessed 30 Jan 2019).
- 11 Public Health England. Public Health Profiles. 2017.<https://fingertips.phe.org.uk/profile-group/child-health> (accessed 13 Jun 2017).
- 12 Early years foundation stage profile results: 2017 to 2018. GOV.UK. <https://www.gov.uk/government/statistics/early-years-foundation-stage-profile-results-2017-to-2018> (accessed 22 Jan 2019).
- 13 FPH, FNP. Family Nurse Partnership. Faculty of Public Health 20102015.

- 14 Chittleborough CR, Lawlor DA, Lynch JW. Young Maternal Age and Poor Child Development: Predictive Validity From a Birth Cohort. *Pediatrics* 2011;**127**:e1436–44. doi:10.1542/peds.2010-3222
- 15 Chittleborough CR, Searle AK, Smithers LG, *et al.* How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study. *Early Child Res Q* 2016;**35**:19–30.
- 16 Brownell MD, Ekuma O, Nickel NC, *et al.* A population-based analysis of factors that predict early language and cognitive development. *Early Child Res Q* 2016;**35**:6–18.
- 17 Camargo-Figuera FA, Barros AJ, Santos IS, *et al.* Early life determinants of low IQ at age 6 in children from the 2004 Pelotas Birth Cohort: a predictive approach. *BMC Pediatr* 2014;**14**:308. doi:10.1186/s12887-014-0308-1
- 18 Nelson BB, Dudovitz RN, Coker TR, *et al.* Predictors of Poor School Readiness in Children Without Developmental Delay at Age 2. *Pediatrics* 2016;**138**:e20154477. doi:10.1542/peds.2015-4477
- 19 Pepe MS, Janes H, Longton G, *et al.* Limitations of the Odds Ratio in Gauging the Performance of a Diagnostic, Prognostic, or Screening Marker. *Am J Epidemiol* 2004;**159**:882–90. doi:10.1093/aje/kwh101
- 20 Kirstine Hansen. Millennium Cohort Study First, Second, Third and Fourth Surveys. A Guide to the Datasets (Seventh Edition). London: : Centre for Longitudinal Studies 2012.
- 21 Connelly R, Platt L. Cohort Profile: UK Millennium Cohort Study (MCS). *Int J Epidemiol* 2014;**43**:1719–25. doi:10.1093/ije/dyu001
- 22 Kirstine Hansen. Millennium Cohort Study. First, Second, Third and Fourth Surveys. A Guide to the Datasets. Centre for Longitudinal Studies 2012.
<http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=598&itemtype=document>
- 23 Bracken B. Bracken Basic Concept Scale–Revised. San Antonio, TX: : The Psychological Corporation 1998.
- 24 Panter JE, Bracken BA. Validity of the Bracken School Readiness Assessment for predicting first grade readiness. *Psychol Sch* 2009;**46**:397–409.
- 25 Connelly R. Millennium Cohort Study Data Note 2013/1: Interpreting Test Scores. London: : Centre for Longitudinal Studies, Institute of Education 2013.
- 26 Steyerberg E. *Clinical prediction models: a practical approach to development, validation, and updating.* Springer Science & Business Media 2008.
- 27 Kiernan KE, Mensah FK. Maternal indicators in pregnancy and children’s infancy that signal future outcomes for children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010.
- 28 Kiernan KE, Huerta MC. Economic deprivation, maternal depression, parenting and children’s cognitive and emotional development in early childhood. *Br J Sociol* 2008;**59**:783–806.

- 1
2
3 29 Shenkin SD, Starr JM, Deary IJ. Birth weight and cognitive ability in childhood: a
4 systematic review. *Psychol Bull* 2004;**130**:989.
5
6
7 30 Jefferis BJMH, Power C, Hertzman C. Birth weight, childhood socioeconomic
8 environment, and cognitive development in the 1958 British birth cohort study. *BMJ*
9 2002;**325**:305. doi:10.1136/bmj.325.7359.305
10
11 31 Kramer MS, Aboud F, Mironova E, *et al*. Breastfeeding and Child Cognitive
12 Development: New Evidence From a Large Randomized Trial. *Arch Gen Psychiatry*
13 2008;**65**:578–84. doi:10.1001/archpsyc.65.5.578
14
15 32 Walker SP, Wachs TD, Grantham-McGregor S, *et al*. Inequality in early childhood: risk
16 and protective factors for early child development. *The Lancet* 2011;**378**:1325–38.
17
18 33 Murray GK, Jones PB, Kuh D, *et al*. Infant developmental milestones and subsequent
19 cognitive function. *Ann Neurol* 2007;**62**:128–36. doi:10.1002/ana.21120
20
21 34 Kelly Y, Sacker A, Gray R, *et al*. Light drinking in pregnancy, a risk for behavioural
22 problems and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;**38**:129–40.
23 doi:10.1093/ije/dyn230
24
25 35 Dahlgren G, Whitehead M. Policies and strategies to promote social equity in health.
26 *Stockh Inst Future Stud* 1991.
27
28 36 Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development
29 of a self-report questionnaire instrument. *J Reprod Infant Psychol* 1998;**16**:57–76.
30
31 37 Sosthenes C. Ketende, Elizabeth M. Jones. User Guide to Analysing MCS Data Using
32 STATA. Centre for Longitudinal Studies, Institute of Education 2011.
33
34 38 Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per
35 variable in logistic regression analysis. *J Clin Epidemiol* 1996;**49**:1373–9.
36 doi:10.1016/S0895-4356(96)00236-3
37
38 39 Courvoisier DS, Combescure C, Agoritsas T, *et al*. Performance of logistic regression
39 modeling: beyond the number of events per variable, the role of data structure. *J Clin*
40 *Epidemiol* 2011;**64**:993–1000.
41
42 40 Azen R, Traxel N. Using Dominance Analysis to Determine Predictor Importance in
43 Logistic Regression. *J Educ Behav Stat* 2009;**34**:319–47.
44 doi:10.3102/1076998609332754
45
46 41 Pencina MJ, D'Agostino RB, Pencina KM, *et al*. Interpreting Incremental Value of
47 Markers Added to Risk Prediction Models. *Am J Epidemiol* 2012;**176**:473–81.
48 doi:10.1093/aje/kws207
49
50 42 Windmeijer FAG. The asymptotic distribution of the sum of weighted squared residuals
51 in binary choice models. *Stat Neerlandica* 1990;**44**:69–78.
52
53 43 Austin PC, Steyerberg EW. Events per variable (EPV) and the relative performance of
54 different strategies for estimating the out-of-sample validity of logistic regression models.
55 *Stat Methods Med Res* 2017;**26**:796–808.
56
57
58
59
60

- 1
2
3 44 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues
4 and guidance for practice. *Stat Med* 2011;**30**:377–99. doi:10.1002/sim.4067
5
6
7 45 Centre for Longitudinal Studies. MCS Ethical Review and Consent. London: : Institute of
8 Education 2014. [http://www.cls.ioe.ac.uk/shared/get-](http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=1601&itemtype=document)
9 [file.ashx?id=1601&itemtype=document](http://www.cls.ioe.ac.uk/shared/get-file.ashx?id=1601&itemtype=document)
10
11 46 Hosmer DW, Hjort NL. Goodness-of-fit processes for logistic regression: simulation
12 results. *Stat Med* 2002;**21**:2723–2738.
13
14 47 Wilkinson RG, Marmot M. *Social Determinants of Health: The Solid Facts*. World
15 Health Organization 2003.
16
17 48 McKean C, Law J, Mensah F, *et al*. Predicting Meaningful Differences in School-Entry
18 Language Skills from Child and Family Factors Measured at 12 months of Age. *Int J*
19 *Early Child* 2016;**48**:329–51. doi:10.1007/s13158-016-0174-0
20
21 49 Steyerberg EW, Harrell FE, Borsboom GJJM, *et al*. Internal validation of predictive
22 models. *J Clin Epidemiol* 2001;**54**:774–81. doi:10.1016/S0895-4356(01)00341-9
23
24 50 Côté SM, Doyle O, Petitcherc A, *et al*. Child Care in Infancy and Cognitive Performance
25 Until Middle Childhood in the Millennium Cohort Study. *Child Dev* 2013;**84**:1191–208.
26 doi:10.1111/cdev.12049
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

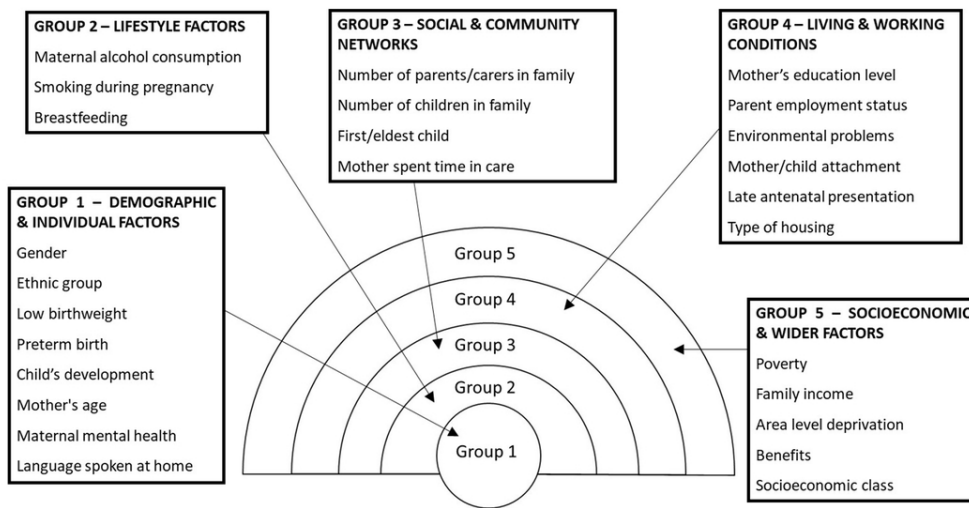
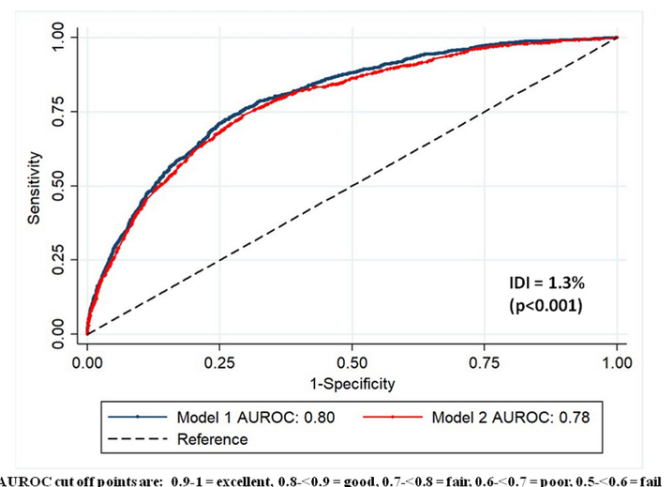


Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and Whitehead, 1991)

90x50mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



AUROC cut off points are: 0.9-1 = excellent, 0.8-0.9 = good, 0.7-0.8 = fair, 0.6-0.7 = poor, 0.5-0.6 = fail

Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI
90x50mm (300 x 300 DPI)

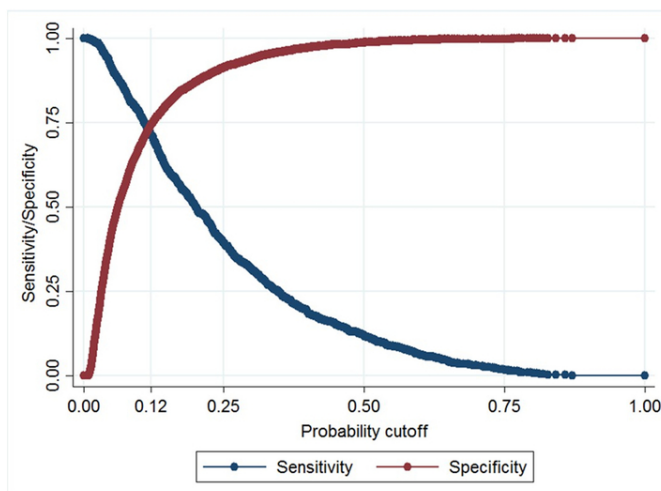


Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1

90x50mm (300 x 300 DPI)

SUPPLEMENTARY FILE 1

Robustness tests were carried out in which the final model was tested with an alternative outcome measure for early cognitive development (British Ability Scales), different coding of variables and the addition of another predictor variable (child care type at age 9 months).

1. Using BAS as an alternative outcome variable

An alternative measure of early cognitive development contained in the MSC are the British Ability Scales (BAS), measured at age 3. BAS scores were dichotomised to 1 SD below the mean as cut off for 'fail'. There is a moderate positive correlation between BAS and BSRA scores ($r=0.5722$, $p<0.0001$). The table below compares performance of the models; there is a small but statistically significant improvement in discrimination using BSRA as an outcome measure compared to BAS.

Outcome variable	N	AUROC (95% CI)
BSRA	9487	0.80 (0.78,0.81)
BAS	9487	0.79 (0.77,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb6)$; $\text{chi}2(1) = 9.20$, $\text{Prob}>\text{chi}2 = 0.002$

2. Robustness tests of the BSRA outcome measure

The BSRA cut off used in the main analysis was a mean standardised composite score <85 , which is 1 standard deviation below the mean. The standardisation sample was from a US population. As the BSRA has not been validated in the UK, we tested the model using dichotomised percentile ranks instead of MSCS as the outcome variable (cut off point 1 SD below mean).

There was no significant difference in model performance (AUROC=0.80 for both models, $p=0.43$). There is evidence to suggest that within the Millennium Cohort Study percentile scores can be misleading in indicating the difference between the performance of cohort members because they are on an ordinal, rather than interval, scale. An outcome based on MSCS was therefore retained.

3. Coding of predictor variables

As a sensitivity analysis the coding of 4 predictor variables was altered: maternal age (from categorical to continuous), developmental scores (from categorical to continuous) and ethnicity (from categorical to binary). The impact of this on final model performance is shown below:

Description	n	AUROC	Comparative AUROC (n=9310)
Final model	9487	0.80	0.79 (0.77,0.81)
Developmental score (continuous)	9487	0.80	0.80 (0.78,0.81)
Maternal age (continuous)	9310	0.79	0.79 (0.78,0.81)
Ethnicity (binary)	9487	0.79	0.79 (0.78,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb2) = \text{area}(xb3) = \text{area}(xb4)$; $\text{chi}2(3) = 9.98$; $\text{Prob}>\text{chi}2 = 0.02$

In summary, there were small but statistically significant differences between the models. The only change which improved model discrimination was using continuous development

1
2
3 scores, so this was incorporated into the final model. There is a U-shaped relationship
4 between school readiness and maternal age, so there was a clear rationale for including this
5 as a categorical predictor.
6
7

8
9 4. Testing the impact of an additional predictor

10 There are other measures in the MCS which could have been used as predictors in this
11 analysis. We have done a sensitivity analysis adding childcare type at 9 months to the final
12 model. This reduces the overall discrimination of the model (AUROC = 0.77 vs 0.80),
13 however this could be due to missing data as the child care variable is less complete. There
14 is a statistically significant association with school readiness and child care type in the
15 multivariable model, with children in formal child care settings more likely to be school
16 ready than those being looked after by parents (OR = 1.76, p=0.02)
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33

34 The Stata Do file for all analyses is available at:
35 <https://www.dropbox.com/s/zxsl4cl87imyp0/SchoolreadinessPRM.do?dl=0>
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9

SUPPLEMENTARY FILE 2

Table 1 - Adjusted associations for the predictor variables in model 1 (13 predictors) using multiple imputed data (n=11,879)

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Predictor	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS		
Gender		
Female	1	8.5 (5)
Male	1.86 (1.62,2.14)	
Ethnicity		
White	1	15.7 (3)
Mixed	1.04 (0.62,1.75)	
Indian	2.68 (1.85,3.89)	
Pakistani and Bangladeshi	3.85 (2.94,5.04)	
Black or Black British	2.31 (1.43,3.72)	
Other ethnic group	3.95 (2.30,6.77)	
Mother's age at birth of first child		
30-39	1	1.5 (12)
40+	1.05 (0.67,1.64)	
20-29	1.22 (0.99,1.51)	
14-19	1.22 (0.93,1.59)	
Birth weight (<2500grams)		
Normal/high	1	1.2 (13)
Low birthweight	1.52 (1.18,1.97)	
Maternal Mental Health (Diagnosed depression/anxiety)		
No	1	1.5 (11)
Yes	1.15 (0.98,1.34)	
Child developmental milestones		
Developmental score	1.10 (1.07,1.13)	2.8 (10)
GROUP 2 - LIFESTYLE FACTORS		
Duration of breastfeeding		
6 months or more	1	3.6 (9)
6 weeks - 6 months	1.17 (0.92,1.48)	
One week or less	1.15 (0.90,1.48)	
1 - 6 weeks	1.22 (0.96,1.57)	
Never	1.58 (1.29,1.95)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS		
Number of children in family		
One child	1	7.1 (6)
Two or three children	1.40 (1.19,1.63)	
Four or more children	2.48 (1.94,3.16)	
GROUP 4 - LIVING & WORKING CONDITIONS		
Maternal education		
Degree plus	1	16.7 (2)

Diploma	0.88 (0.61,1.26)	
A levels	1.13 (0.80,1.59)	
GCSE A-C	1.34 (1.01,1.78)	
GCSE D-G	1.72 (1.23,2.39)	
None	1.74 (1.28,2.38)	
Workforce status		
Both parents in work	1	
One parent in work	0.94 (0.78,1.12)	6.5 (7)
Neither parent in work	1.21 (0.93,1.57)	
Housing tenure		
Owner occupied	1	
Private rented	1.18 (0.90,1.54)	5.5 (8)
Social housing	1.43 (1.18,1.72)	
Other	0.96 (0.69,1.35)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS		
Social class		
Managerial & professional	1	
Intermediate	0.98 (0.75,1.29)	
Small employers & own account	1.32 (0.87,2.00)	17.6 (1)
Lower supervisory & technical	1.50 (1.06,2.13)	
Semi-routine & routine	1.77 (1.38,2.27)	
Never worked & long-term unemployed	2.19 (1.53,3.15)	
Annual income		
£33,000+	1	
£22,000-£33,000	1.33 (1.02,1.72)	11.9 (4)
£11,000-£22,000	1.67 (1.30,2.14)	
£0-£11,000	2.14 (1.60,2.87)	
ROC Analysis	AUROC = 0.79 (95% CI 0.78,0.80)	

SUPPLEMENTARY FILE 3

Integrated discrimination improvement (IDI) analysis was run using Stata function 'idi', which compares the discrimination ability between two logistic regression prediction models. In the first stage of this analysis, the IDI of a PRM with just the strongest predictor variable (social class) was compared to a model with all 13 predictors. Adding the additional 12 predictors lead to a 7.3% increase in IDI. In each subsequent analysis, an additional predictor variable was added according to the ranking of variables from the dominance analysis (Table 1).

Predictor	Weighting	Rank
Social Class	17.38	1
Ethnic group	14.66	2
Maternal education	13.55	3
Income band	12	4
Gender	9.54	5
Number of children	7.84	6
Parent's employment	6.9	7
Housing type	5.65	8
Child development	3.9	9
Breastfeeding	3.9	10
Mother's age at birth of first child	2.87	11
Low birth weight	1.42	12
Mental health	0.38	13

Table 1 - Results of the dominance analysis for model 1

The full results of integrated discrimination improvement (IDI) analysis are shown in Table 2.

Variables included	IDI (%)	p	1-IDI
1	7.3%	<0.00001	92.7%
2	5.3%	<0.00001	94.7%
3	3.8%	<0.00001	96.2%
4	3.5%	<0.00001	96.5%
5	2.3%	<0.00001	97.7%
6	1.3%	<0.00001	98.7%
7	1.0%	<0.00001	99.0%
8	0.9%	<0.00001	99.1%
9	0.6%	0.00001	99.4%
10	0.6%	0.00001	99.4%
11	0.2%	0.01402	99.8%
12	0.0%	0.52356	100.0%

Table 2 - Results of integrated discrimination improvement analysis for 12 models

A 6-predictor model was chosen as this offered the optimal balance between parsimony and discrimination.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SUPPLEMENTARY FILE 4

Table 1 - Adjusted associations for the predictor variables in model 2 (6 predictors) using complete cases (n=11,146) and multiple imputed data (n=11,879). The weightings and rank are from dominance analysis of the complete case sample.

Predictors	Adjusted OR (95% CI) - complete case	Adjusted OR (95% CI) - multiple imputation	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.9 (5)
Male	1.99 (1.72,2.31)	1.93 (1.68,2.22)	
Ethnicity			
White	1	1	13.7 (4)
Mixed	1.2 (0.77,1.88)	1.26 (0.83,1.90)	
Indian	1.64 (1.09,2.47)	1.72 (1.14,2.59)	
Pakistani and Bangladeshi	2.67 (2.10,3.41)	2.71 (2.11,3.47)	
Black or Black British	2.32 (1.52,3.54)	2.69 (1.80,4.02)	
Other ethnic group	1.98 (1.10,3.58)	2.06 (1.27,3.32)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	9.5 (6)
Two or three children	1.48 (1.27,1.73)	1.45 (1.25,1.69)	
Four or more children	2.89 (2.23,3.75)	2.62 (2.03,3.38)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	20.5 (3)
Diploma	0.87 (0.58,1.29)	0.88 (0.60,1.28)	
A levels	1.05 (0.72,1.53)	1.06 (0.74,1.52)	
GCSE A-C	1.43 (1.02,1.99)	1.55 (1.14,2.12)	
GCSE D-G	1.78 (1.23,2.58)	2.14 (1.51,3.03)	
None	2.01 (1.44,2.81)	2.42 (1.77,3.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	26.0 (1)
Intermediate	1.17 (0.88,1.55)	1.14 (0.86,1.51)	
Small employers & own account	1.44 (0.91,2.28)	1.52 (0.99,2.33)	
Lower supervisory & technical	2.01 (1.42,2.86)	1.92 (1.37,2.68)	
Semi-routine & routine	2.41 (1.86,3.12)	2.16 (1.68,2.78)	
Never worked & long-term unemployed	3.34 (2.41,4.63)	2.95 (2.14,4.07)	
Annual income			
£33,000+	1	1	20.6 (2)
£22,000-£33,000	1.33 (0.97,1.81)	2.65 (2.01,3.50)	
£11,000-£22,000	1.88 (1.42,2.50)	1.75 (1.32,2.31)	
£0-£11,000	2.98 (2.26,3.92)	1.29 (0.95,1.75)	

ROC Analysis	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,146	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,879
---------------------	---	---

For peer review only



TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	3
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	3
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	3-4
	5b	Describe eligibility criteria for participants.	4
	5c	Give details of treatments received, if relevant.	
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4
	6b	Report any actions to blind assessment of the outcome to be predicted.	
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors. <small>temporal ordering in cohort</small>	
Sample size	8	Explain how the study size was arrived at.	5
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	5-6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	6
Risk groups	11	Provide details on how risk groups were created, if done.	
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6-7
Model development	14a	Specify the number of participants and outcome events in each analysis.	10
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	8-10
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	
	15b	Explain how to use the prediction model.	
Model performance	16	Report performance measures (with CIs) for the prediction model.	10
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11-12
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11-13
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	
Funding	22	Give the source of funding and the role of the funders for the present study.	

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development of a Predictive Risk Model for School Readiness at age 3 years using the UK Millennium Cohort Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024851.R2
Article Type:	Research
Date Submitted by the Author:	29-Mar-2019
Complete List of Authors:	Camacho, Christine; University of Liverpool Department of Public Health and Policy, Straatmann, Viviane; University of Liverpool Department of Public Health and Policy; Karolinska Institute, Aging Research Centre Day, Jennie; University of Liverpool Department of Public Health and Policy Taylor-Robinson, David; University of Liverpool, Department of Public Health and Policy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Epidemiology, Health policy, Research methods
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, SOCIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 **Development of a Predictive Risk Model for School Readiness at age 3 years using the**
4 **UK Millennium Cohort Study**
5

6
7 Miss CL Camacho*¹, Dr VS Straatmann^{1,2}, Dr JC Day¹, Prof DC Taylor-Robinson¹
8

9 *Affiliations: ¹Public Health and Policy, University of Liverpool, Liverpool, UK; ²Aging*
10 *Research Centre, Karolinska Institute, Stockholm, Sweden*
11

12
13 *Address correspondence to: Christine Camacho, Department of Public Health and Policy, University*
14 *of Liverpool, Liverpool, United Kingdom, L69 3GB, [c.camacho@nhs.net], +44 07973395585*
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

ABSTRACT

Objectives

The aim of this study was to develop a predictive risk model (PRM) for school readiness measured at age 3 years using perinatal and early infancy data.

Design and Participants

This paper describes the development of a predictive risk model. Predictors were identified from the UK Millennium Cohort Study (MCS) wave 1 data, collected when participants were 9 months old. The outcome was school readiness at age 3 years, measured by the Bracken School Readiness Assessment. Stepwise selection and dominance analysis were used to specify 2 models. The models were compared by the area under the receiver operating characteristic curve (AUROC) and integrated discrimination improvement (IDI).

Results

Data were available for 9,487 complete cases. At age 3, 11.7% (95% CI 11.0-12.3%) of children were not school ready. The variables identified were: parents' Socio-Economic Classification, child's ethnicity, maternal education, income band, sex, household number of children, mother's age, low birth weight, mother's mental health, infant developmental milestones, breastfeeding, parents' employment, housing type. A parsimonious model included the first six listed variables (model 2). The AUROC for model 1 was 0.80 (95% CI 0.78-0.81) and 0.78 (95% CI 0.77-0.79) for model 2. Model 1 resulted in a small improvement in discrimination (IDI=1.3%, $p<0.001$).

Conclusions

Perinatal and infant risk factors predicted school readiness at age 3 with good discrimination. Social determinants were strong predictors of school readiness. This study demonstrates that school readiness can be predicted by six attributes collected around the time of birth.

Strengths and limitations of this study

- Use of a large, representative, and contemporary cohort study to demonstrate the feasibility of predicting school readiness from data collected in infancy.
- Multiple imputation and bootstrapping were used to evaluate the impact of missing data and internal validity, respectively.
- The main outcome measure, the Bracken School Readiness Assessment, was developed in the US, and is not routinely used in the UK.
- This model was not externally validated, which would have given an indication of generalisability.

INTRODUCTION

Early childhood is a critical time for lifelong physical, social, emotional and cognitive development. A wide range of factors are associated with early cognitive development (ECD)[1]. Interventions in the first three years of life can improve the trajectory of ECD[2] and deliver the greatest return on investment[3], yet it is unclear how best to identify children at most risk of delayed ECD, to enable appropriate targeting of interventions.

Cognitive development measures in children are good indicators of later educational achievement, predict health and social care needs in adults[4,5], and are associated with long term health outcomes[6]. There has been a growing policy interest in school readiness as a measure of ECD[7], and school readiness is a key public health indicator in children in the UK. Good school readiness lays a platform for future learning, employment and health[8,9].

School readiness is currently a major focus in England for policy makers, educators and the public health community [10] and national metrics are collected to capture changes over time. In 2017, 29% of children in England were deemed not school ready at the end of their reception year (aged 4-5 years)[11]. The percentage of children school ready was nearly 20% higher in the most affluent decile (80% school ready) compared to the most deprived decile (62% school ready) when areas were classified into deciles according to the Index for Multiple Deprivation [12]. In UK policy there has been a focus on demographic factors e.g. maternal age, in targeting early interventions for children[13]. This study will explore the importance of different variables in predicting school readiness.

Previous research has identified a wide range of variables associated with early cognitive development. Predictive risk models (PRMs) are well-established in many clinical disciplines and have more recently been applied to child development. Using PRMs in this context could facilitate targeted early intervention as part of a proportionate universalism approach, which requires universal action with the scale and intensity of interventions proportionate to the level of need[6]. Most models thus far have shown fair or poor discrimination and there have been very few studies in the UK [14–18]. The aim of this study was to develop, for the first time, a PRM for school readiness measured at age 3 years using perinatal and early infancy data from the UK Millennium Cohort Study (MCS).

METHODS

Overview

Data from the MCS were used to explore the relationship between the outcome, school readiness, and 29 predictor variables using logistic regression analysis. Following univariable analysis to test for unadjusted associations, automated stepwise regression analyses were used to select variables for inclusion in the PRM. Dominance analysis was used to rank and weight included predictors, and integrated discrimination improvement (IDI) was calculated to assess the difference in performance between models. A receiver operator characteristic (ROC) curve was used to evaluate how well the model discriminated school readiness. The area under an ROC curve (AUROC) gives a measure of how well the regression model predicts school readiness at age 3. Traditionally accepted AUROC cut off points are: 0.9-1 = excellent, 0.8- $<$ 0.9 = good, 0.7- $<$ 0.8 = fair, 0.6- $<$ 0.7 = poor, 0.5- $<$ 0.6 = fail[19]. Multiple imputation was used to assess the impact of missing data in the sample.

Data Source

The PRM was developed and validated using MCS data. The MCS is a nationally representative birth cohort study which recruited 18,550 children born from September 2000 to January 2002, followed up in ongoing data collection waves. The sampling frame was government child benefit records, which had almost universal coverage at the time of sampling. The sample was clustered at the level of electoral ward and stratified to allow over representation of children living in deprived areas and areas with high concentrations of ethnic minorities[20]. Further information about the MCS sample is available in the cohort profile[21]. Data were collected from the main responder (usually mothers) by trained interviewers in participants' homes using a combination of interviews and self-completed questions. All singleton children in the first (aged 9 months) and second (aged 3 years) waves of the MCS with completed data for the outcome and predictors were eligible for inclusion (n=9,487).

Outcome

School readiness was measured using the Bracken School Readiness Assessment (BSRA) which consists of 6 subtests relating to colours, letters, numbers/counting, sizes, comparisons and shapes[20]. The assessment was carried out by interviewers during the second data collection wave when children were aged approximately 3 years old. The BSRA and its predecessors have demonstrated good reliability[22] and validity against other measures and teacher assessments[23].

The BSRA raw scores were summed and adjusted for age to provide a standardised composite score[20]. Scores were grouped according to cut-offs recommended by Bracken which reflected a 'normative classification' whereby children were categorised as very delayed, delayed, average, advanced or very advanced [24]. We used the same cut off score as Bracken (mean standardised composite score $<$ 85, 1 standard deviation below mean) but collapsed the categories of delayed or very delayed into a single category equivalent to not being school

ready. We have dichotomised the outcome ‘school readiness’ in line with UK policy, and to allow the testing of a PRM using ROC analysis which requires a binary outcome [25].

Predictors

29 predictor variables were used, which were collected at age 9 months in the first wave of MCS data collection during which data relevant to pregnancy, birth and the perinatal period was captured retrospectively. These were identified from previous research to predict cognitive development and were included in the MCS[1,2,4,6,26–33]. The selected predictor variables were grouped according to the Dahlgren and Whitehead theoretical model[34] of social determinants of health as depicted in Figure 1. This model was chosen to provide a framework for categorising predictors to allow analysis of the determinants of early cognitive development.

<<Figure 1 here>>

Group 1 – Demographic and Individual factors

Demographic characteristics included child sex, maternal ethnicity, child weight, pre-term birth, mother’s age, home language, maternal mental health and child development categorised as shown in Box 1.

Box 1 – Coding of Group 1 demographic and individual factors

Categorisation of Demographic and Individual factors

Child sex – ‘female’ and ‘male’

Maternal ethnicity – ‘white’, ‘mixed’, ‘Indian’, ‘Pakistani and Bangladeshi’, ‘Black’ and ‘other’

Child weight at birth – low (<2.5kg) or normal/high (≥2.5kg)

Preterm birth – gestation period less than 37 weeks

Mother’s age in years at birth of first child – grouped into 4 categories (14-19, 20-29, 30-39, 40+ years)

Home language – ‘English only’, ‘English and another language’, ‘another language only’

Mental health (1) – Sad or low for >2 weeks since baby, coded as ‘yes’ or ‘no’

Mental health (2) – Diagnosis of depression or serious anxiety, coded as ‘yes’ or ‘no’

Mental health (3) – 9-item modified version of the Rutter Malaise Inventory³⁹, coded as ‘low’ or (0-3) ‘high’ (4-9) scores²⁷.

Child development – 8 items from Denver Developmental Screening Test and 5 items from MacArthur Communicative Development Inventory, scored on a continuous scale from 13 (above average) to 36 (below average)

Group 2 – Lifestyle Factors

Self-reported maternal smoking was coded as ‘never smoked’, ‘smoked before pregnancy’ and ‘smoked during pregnancy’. Maternal alcohol consumption during pregnancy were categorised as ‘never or very infrequent’, ‘occasional’, ‘regularly’ and ‘most or everyday’. Breastfeeding duration was grouped as ‘never’, ‘one week or less’, ‘1 – 6 weeks’, ‘6 weeks – 6 months’ and ‘over 6 months’.

Group 3 – Social and Community Networks

The number of children in household was coded as ‘1’, ‘2-3’ or ‘4+’, and being the eldest or only child was recoded as ‘yes’ or ‘no’. The number of parents or carers was either ‘1’ or ‘2’.

1
2
3 Mothers were asked how much time they had spent time in care before the age of 17, this was
4 recoded as 'yes' or 'no' to indicate if they had ever been in care.
5
6

7 Group 4 – Living and Working Conditions

8 Maternal education was categorised into six groups 'degree plus (higher degree and first degree
9 qualifications)', 'diploma (in higher education)', 'A-levels', 'GCSE grades A–C', 'GCSE
10 grades D–G' and 'none of these qualifications'. Parent's employment status was classified as
11 either 'both', 'one' or 'neither' parents in work¹. Housing tenure was coded as 'owner
12 occupied', 'private rented', 'social housing' and 'other'. The response to the question, "How
13 common is pollution, grime or other environmental problems?" was recoded as 'common', 'not
14 common' and 'not at all'. Presentation for first antenatal visit was recoded as late if after 12
15 weeks. Maternal attachment was measured using a 6-item Condon Maternal Attachment
16 Questionnaire[35] grouped as 'low (10-21)', 'average' (22-23) and 'high (24-27)'.
17
18
19
20
21

22 Group 5 – Socioeconomic and Wider Factors

23 The National Statistics Socio-Economic Classification (NS-SEC) was used to code job details
24 for main respondents (the majority of which were mothers) as: 'managerial & professional',
25 'intermediate', 'small employers & own account', 'lower supervisory & technical', 'semi-
26 routine & routine', 'never worked & long-term unemployed'. Net household income was
27 reported by identification of the correct band on a show card and grouped into 4 quartile
28 bands[26]: '£0-£11,000', '£11,000-£22,000', '£22,000-£33,000' and '£33,000+'. Poverty was
29 defined as an equivalised household income 60% below the median before housing costs
30 according to the Organisation for Economic Co-operation and Development Household
31 Equivalence Scale. Families reported receipt of any means-tested benefits, including
32 Jobseekers Allowance, Income Support, Working Families Tax Credit or Disabled Persons Tax
33 Credit. Indices of Multiple Deprivation (IMD) from 2004 which had been retrospectively
34 linked to wave 1 data were used to give small area level deprivation measures [20]. IMD scores
35 were divided into quintiles, with 1 the most deprived quintile, and 5 the least deprived.
36
37
38
39
40

41 Statistical analyses

42 Analyses were conducted using Stata v14.2 (StataCorp LP, 2017). Survey weights were applied
43 to take account of clustering, stratification and oversampling in the survey design, and attrition
44 between survey waves, using the svyset command (pweight=BOVWT2) and svy prefix for
45 regression modelling[36]. The number of events per variable (EPV) exceeds 35, the predictors
46 were checked for collinearity, a large number of predictors were used and all were significantly
47 associated with the outcome suggesting a robust logistic regression model with sufficient
48 sample size [37,38].
49
50
51

52 Descriptive analysis of each predictor and school readiness was carried out to ascertain the
53 prevalence of each predictor in the sample. Univariable logistic regression analyses calculating
54 odds ratios (ORs) and 95% confidence intervals (95% CI) were carried out to assess the
55 unadjusted association of each variable with the outcome.
56
57

58
59 ¹ Being on leave from work is classed as being in employment
60

1
2
3
4
5 A multivariable logistic regression model including all 29 variables was reduced using
6 automated forward and backwards stepwise selection (using a cut off p-value of 0.1).
7 Dominance analysis (repeated regression analyses on subsets of variables) was used to produce
8 a ranking and weighting for each predictor in model 1[39]. These rankings were used to specify
9 a more parsimonious model (model 2) containing the top 6 predictors, selected to maximise
10 parsimony and performance. The integrated discrimination improvement (IDI) using the
11 complete case sample from model 1 was calculated to assess difference in performance
12 between models as the percentage change in individuals being correctly assigned by the
13 model[40].
14
15
16
17

18 The area under the ROC curve (AUROC) and its 95% CI was used to measure discriminatory
19 power of the models. Classification, including sensitivity and specificity, was assessed at the
20 maximised probability cut off point where the sensitivity and specificity curves intersected.
21 Calibration of the model was assessed using the Pearson Chi-squared test[41]. Bootstrapping
22 was used for internal validation of the final model, without repeating selection of predictors in
23 each bootstrap sample. Model performance was assessed using 1000 bootstrap samples, model
24 optimism was averaged across all iterations to obtain an optimism estimate. An optimism-
25 corrected AUROC, which takes account of overfitting, was calculated by subtracting the
26 optimism estimate from the uncorrected AUROC[42].
27
28
29
30

31 A complete case approach was used for the primary analysis. As a sensitivity analysis, multiple
32 imputation by chained equation was performed to impute missing data using the ‘mi impute
33 chained’ command in Stata. Three predictor variables from the first sweep (maternal education,
34 child’s sex, mother’s age at birth of first child) and the outcome variable were to shape the
35 imputation process (imputed sample, n=11,897). Twenty imputed datasets were generated, and
36 Rubin’s rules were used to calculate results across the imputed datasets[43].
37
38
39

40 Robustness tests were carried out in which the final model was tested with an alternative
41 outcome measure for early cognitive development (the British Ability Scales, also tested at age
42 3 in the MCS); different coding of outcome and predictor variables (e.g. maternal age as a
43 continuous variable); and with the addition of another predictor variable (child care type at age
44 9 months). See supplementary file 1 for further details.
45
46
47

48 **Ethics and Patient and public involvement**

49 Ethical approval for each wave of the MCS was granted by NHS Multicentre Research Ethics
50 Committees[44]. No further ethical approval was required for this secondary analysis of MCS
51 data. There was no direct patient or public involvement in this analysis. However, the MCS has
52 an ongoing programme of participant and public engagement.
53
54
55

56 **RESULTS**

57 There were 15,381 singleton children surveyed in MCS2, of which 13,650 had an outcome
58 recorded for school readiness. Of these children 70% (n=9,487) had complete data for the
59 outcomes and all the predictor variables. There were no significant differences in the
60

characteristics of the imputed sample and the complete case sample (p value >0.05 for all chi-squared tests) (Table 1); results are reported for complete cases (see Supplementary file 2 for imputed sample results).

Table 1 - Description of perinatal, sociodemographic and economic characteristics by school ready of sample and imputed sample

Is Child School Ready?	Complete Cases (n=9,487)		Imputed Data (n=11,897)	
	Yes (%)	No (%)	Yes (%)	No (%)
All	88.3	11.7	85.5	14.5
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS				
Gender				
Female	91.6	8.4	89.4	10.6
Male	85.1	14.9	82.6	17.4
Ethnicity				
White	90.4	9.6	88.6	11.4
Mixed	91.1	8.9	84.7	15.3
Indian	79.3	20.7	78.1	21.9
Pakistani and Bangladeshi	55.7	44.3	56.3	43.7
Black or Black British	79.8	20.2	68	32
Other ethnic group	73.6	26.4	74.3	25.7
Mother's age at birth of first child				
14-19	78	22	76.4	23.6
20-29	87.9	12.1	86.1	13.9
30-39	95	5	94.4	5.6
40+	76.9	23.1	76	24
Birth weight (<2500grams)				
normal/high	88.8	11.2	86.1	13.9
low birthweight	80.2	19.8	77.7	22.3
Maternal Mental Health (Diagnosed depression/anxiety)				
No	89	11	86	14
Yes	86	14	84.4	15.6
Child developmental milestones				
Child development score (mean, 95%CI)	19.3 (19.2,19.3)	19.9 (19.7,20.1)	19.1 (19.0,19.1)	19.6 (19.4,19.7)
GROUP 2 - LIFESTYLE FACTORS				
Duration of breastfeeding				
6 months or more	92.5	7.5	90.5	9.5
6 weeks - 6 months	89.8	10.2	87.8	12.2
1 - 6 weeks	88.8	11.2	85.9	14.1
one week or less	88.8	11.2	86.4	13.6
Never	82.6	17.4	80	20
GROUP 3 - SOCIAL & COMMUNITY NETWORKS				
Number of children in family				
One child	92	8	89.1	10.9
Two or three children	87.7	12.3	85	15
Four or more children	71.7	28.3	70.2	29.8

GROUP 4 - LIVING & WORKING CONDITIONS				
Maternal education				
Degree plus	95.6	4.4	95.1	4.9
Diploma	94.6	5.4	93.9	6.1
A levels	92.7	7.3	92	8
GCSE A-C	88.5	11.5	87.4	12.6
GCSE D-G	81	19	79.1	20.9
None	71.3	28.7	69.2	30.8
Workforce status				
Both parents in work	92.6	7.4	91.6	8.4
One parent in work	85.8	14.2	83.4	16.6
Neither parent in work	68.5	31.5	70.1	29.9
Housing tenure				
Owner occupied	91.9	8.1	90.7	9.3
Private rented	83.8	16.2	80.5	19.5
Social housing	75.8	24.2	74.8	25.2
Other	83.4	16.6	81	19
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS				
Social class				
managerial & professional	95.5	4.5	94.6	5.4
intermediate	93.1	6.9	92.1	7.9
small employers & own account	91.3	8.7	89.1	10.9
lower supervisory & technical	87.2	12.8	84	16
semi-routine & routine	81.9	18.1	80	20
never worked & long-term unemployed	60.2	39.8	62.1	37.9
Annual income				
£33,000+	95.7	4.3	94.9	5.1
£22,000-£33,000	92.5	7.5	91.7	8.3
£11,000-£22,000	85	15	83.9	16.1
£0-£11,000	73.8	26.2	74.1	25.9

11.7% (95%CI 11.0-12.3%) of children aged 3 years were classified as not being school ready, but this varied significantly by the parents' ethnicity, maternal education and social class (Table 1). All 29 predictor variables were significantly associated with school readiness in univariable logistic regression analysis ($p < 0.1$), so none were excluded at this stage.

The stepwise method reduced the final multivariable logistic regression model to 13 predictors: child's sex and ethnicity, mother's age at birth of first child, birthweight, maternal mental health, child development milestones, duration of breastfeeding, number of children in family, maternal education, parents' workforce status, housing tenure, social class and annual family income. In the adjusted analysis, Pakistani and Bangladeshi children were 4 times more likely to not be school ready than white children (OR 4.19 95% CI 3.14-5.58). The full results are shown in Table 2. There was no evidence of collinearity.

Table 2 - Unadjusted and adjusted associations and dominance analysis for the predictor variables in model 1 (13 predictors)

Predictors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.5 (5)
Male	1.76 (1.54,2.01)	2.03 (1.72,2.39)	
Ethnicity			
White	1	1	14.7 (2)
Mixed	1.4 (0.96,2.04)	1.42 (0.78,2.58)	
Indian	1.85 (1.23,2.77)	2.58 (1.65,4.03)	
Pakistani and Bangladeshi	5.94 (4.82,7.32)	4.27 (3.20,5.69)	
Black or Black British	4.06 (2.90,5.69)	2.1 (1.13,3.88)	
Other ethnic group	2.33 (1.38,3.93)	2.92 (1.55,5.48)	
Mother's age at birth of first child			
30-39	1	1	2.9 (11)
40+	2.83 (2.29,3.49)	1.05 (0.68,1.63)	
20-29	5.57 (4.20,7.37)	1.28 (0.98,1.66)	
14-19	6.02 (4.84,7.48)	1.32 (0.95,1.83)	
Birth weight (<2500grams)			
Normal/high	1	1	1.4 (12)
Low birthweight	1.7 (1.34,2.16)	1.26 (0.92,1.72)	
Maternal Mental Health (Diagnosed depression/anxiety)			
No	1	1	0.4 (13)
Yes	1.33 (1.16,1.53)	1.28 (1.07,1.53)	
Child developmental milestones			
Developmental score	1.07 (1.05,1.10)	1.1 (1.07,1.14)	3.9 (11)
GROUP 2 - LIFESTYLE FACTORS			
Duration of breastfeeding			
6 months or more	1	1	3.9 (10)
6 weeks - 6 months	1.25 (1.02,1.53)	1.05 (0.81,1.36)	
One week or less	1.67 (1.34,2.09)	1.19 (0.89,1.59)	
1 - 6 weeks	1.68 (1.36,2.07)	1.25 (0.96,1.65)	
Never	2.74 (2.29,3.27)	1.49 (1.19,1.87)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	7.8 (6)
Two or three children	1.44 (1.27,1.63)	1.38 (1.15,1.66)	
Four or more children	3.71 (3.04,4.54)	2.67 (1.94,3.68)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	13.6 (3)
Diploma	1.3 (0.93,1.81)	0.81 (0.53,1.24)	
A levels	1.66 (1.22,2.25)	1.02 (0.68,1.55)	
GCSE A-C	3.02 (2.34,3.90)	1.3 (0.89,1.88)	
GCSE D-G	5.55 (4.21,7.30)	1.54 (1.02,2.34)	
None	9.62 (7.61,12.16)	1.68 (1.15,2.43)	
Workforce status			

Both parents in work	1	1	
One parent in work	1.79 (1.49,2.14)	0.82 (0.67,1.00)	6.9 (7)
Neither parent in work	5.39 (4.36,6.67)	1.21 (0.87,1.68)	
Housing tenure			
Owner occupied	1	1	
Private rented	2.68 (2.16,3.33)	1.21 (0.87,1.67)	
Social housing	3.89 (3.34,4.53)	1.45 (1.16,1.81)	5.7 (8)
Other	2.65 (2.10,3.35)	0.9 (0.62,1.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	
Intermediate	1.5 (1.19,1.89)	1.06 (0.77,1.45)	
Small employers & own account	2.11 (1.44,3.08)	1.41 (0.87,2.28)	17.4 (1)
Lower supervisory & technical	3.72 (2.76,5.00)	1.65 (1.09,2.50)	
Semi-routine & routine	4.99 (4.13,6.01)	1.97 (1.46,2.66)	
Never worked & long-term unemployed	12.07 (9.48,15.37)	2.49 (1.69,3.66)	
Annual income			
£33,000+	1	1	
£22,000-£33,000	1.71 (1.31,2.25)	1.31 (0.96,1.79)	
£11,000-£22,000	3.97 (3.12,5.07)	1.64 (1.22,2.22)	12.0 (4)
£0-£11,000	7.7 (6.10,9.72)	2.26 (1.60,3.19)	

Dominance analysis showed that social class was the most important predictor (weighting=17.6), followed by ethnic group (weighting=14.7) and maternal education (weighting=13.8) (Table 2). Analysis of the predictor weightings suggests that social factors (average weighting 11.3, SD 4.9) are stronger predictors of school readiness than demographic and lifestyle factors (average weighting 5.5, SD 4.9). IDI was used to test the relative performance of models with all (1-13) variables, with variables added in according to their rank from the dominance analysis (Supplementary File 3). These analyses informed the specification of model 2, which was comprised of the top 6 predictors: social class, child's ethnic group, maternal education, income band, sex and number of children (see Supplementary File 4 for Model 2 results).

The AUROC was 0.80 (95% CI 0.78-0.81) for model 1 (n=9,487), which indicates a "good" level of discrimination[19]. The AUROC for model 2 (n=11,146) was 0.78 (95% CI 0.77-0.79). Internal validation using bootstrap optimism correction suggests that the model would have good discriminatory power in an independent sample (adjusted AUROC model 1 = 0.79, model 2=0.76). The Pearson Chi-squared tests were both non-significant indicating adequate calibration (model 1, p=0.07, model 2, p=0.13)[45]. IDI showed there was a small but significant difference in performance, with model 1 resulting in a 1.3% (p=<0.001) improvement in discrimination (Figure 2).

<<Figure 2 here>>

Sensitivity and specificity were plotted against probability cut-offs to select the optimal cut off point to assess the PRM's classification (model 1, cut-off=0.12; model 2, cut-off=0.14) (Figure

1
2
3 **Error! Reference source not found.**) For model 1, at this cut-off point sensitivity was 72%
4 (95% CI 69.0%-74.3%) and specificity was 74% (95% CI 73.5%-75.3%). Sensitivity of model
5 2 was similar - 72% (95% CI 69.9%-74.5%). Specificity was lower - 71% (95% CI 69.6%-
6 71.4%), so this model would generate more false positive results than the model 1, but
7 performance was still in the acceptable range. At a probability cut-off of 12%, 31% of the
8 screened population tested would be identified as being 'at risk' of poor school readiness using
9 model 1.
10
11
12

13
14 <<Figure 3 here>>
15

16 A sensitivity analysis using an alternative outcome measure (British Ability Scales, BAS),
17 showed that the BSRA measure led to improved discrimination (AUROC = 0.79 (95% CI 0.78-
18 0.81) for BAS; AUROC = 0.80 (95% CI 0.78-0.81) for BSRA, p=0.002). See supplementary
19 file 1 for further details.
20
21
22

23 DISCUSSION

24 Findings

25 This study developed a PRM for school readiness at age 3 years using perinatal and early
26 childhood data from the MCS. Model 1 with 13 variables had good discrimination
27 (AUROC=0.80) and classification (sensitivity=72%, specificity= 74% at a maximised cut off).
28 Dominance analysis found the most important variables in predicting school readiness related
29 to socioeconomic conditions (social class, maternal education, family income) and ethnicity.
30 A parsimonious model performed similarly well (AUROC=0.78), suggesting it is possible to
31 predict school readiness at age 3 fairly well using just six variables from the perinatal period
32 and early infancy.
33
34
35
36
37

38 Comparison with previous studies

39 The value added of this study is that it is the first UK study to show that school readiness can
40 be predicted with good discrimination with a small number of variables collected in infancy.
41 The predictors of school readiness identified here corroborate previous findings. Male sex,
42 maternal education, income, family composition, parental employment, housing and
43 breastfeeding have been identified as significant risk factors of delayed ECD in other
44 studies[4,14,15,17,18,26]. Social factors were the most important predictors, corresponding
45 with current thinking on the social determinants of cognitive development[6,46].
46
47
48

49 The model reported here has good predictive strength, and compares favourably to similar
50 PRMs, which with one exception[17], achieved only fair or poor discrimination[14,15,18,47].
51 Chittleborough et al used the ALSPAC UK birth cohort to test the predictive validity of 2
52 models for ECD[14]. They used a different outcome measure (School entry assessment aged
53 4-5) and used 6 predictors in their model, which appear to be chosen a priori, rather than by a
54 statistical routine. They found that maternal age alone failed to predict ECD (AUROC~0.5),
55 and a model with 6 predictors achieved only poor discrimination (AUROC=0.67). Camargo-
56 Figuera et al used IQ as a measure of ECD and developed a PRM with 12 predictors using the
57 Brazilian Pelotas birth cohort; their model had good discrimination (AUROC=0.8) and
58
59
60

1
2
3 calibration, with sensitivity and specificity of 72% and 74% respectively[17]. We believe the
4 use of a representative cohort for model development, stepwise regression to select predictor
5 variables and dominance analysis to specify a simplified model contributed to the good
6 performance of this PRM.
7
8

9 **Strengths and Limitations**

11 A strength of this study was the use of a representative and contemporary UK cohort study as
12 the data source. This offered a wide range of predictor variables and a large sample size which
13 minimised the likelihood of overfitting. The cohort design also ensured correct temporal
14 ordering and blinding with respect to the predictors. A theoretical model informed the PRM
15 and statistical selection was used to specify variables. Multiple imputation was used to assess
16 the impact of missing data. Bootstrapping showed good internal validity[48].
17
18

19
20 There are some limitations of this study to be considered. The main outcome, the BSRA, whilst
21 validated as a measure of school readiness, was developed in the US and is not routinely used
22 in the UK[23]. The BSRA measures a small set of pre-academic skills and as such is a limited
23 measure of child development, which can be defined as including broader behavioural and
24 social skills. However, an analysis of MCS data linked to teacher reports showed that Bracken
25 scores are strongly associated with the broader EYFS measure of school readiness used in
26 English schools[4]. The outcome variable was dichotomised to allow ROC curve analysis. We
27 acknowledge the limitations of dichotomising school readiness ethically, conceptually (e.g.
28 children develop at different rates) and statistically (i.e. loss of information) [49,50].
29 Longitudinal studies are subject to attrition and non-response which can introduce attrition bias,
30 the use of survey weights partially adjust for this, but it was not possible to use these when
31 calculating the AUROC. Sensitivity analysis using multiple imputation showed the effect of
32 missing data was negligible, similar to other PRMs[14,15]. Most of the predictor variables
33 were based on maternal self-report which may be subject to recall bias, and external validation
34 was not conducted. The predictor variables identified may not be causally associated with
35 school readiness and there are other predictors which may be associated with the outcome
36 which were not included in this model e.g. the home learning environment (which was not
37 assessed at 9 months in the MCS) and childcare in infancy[51].
38
39
40
41
42
43
44

45 **Policy Implications**

46 The existing literature, and these findings, indicate that a PRM could plausibly be used to
47 identify a group of children at high risk of poor ECD who may benefit from early intervention.
48 If implemented as part of a “proportionate universalism” approach[6], PRMs could mitigate
49 socioeconomic inequalities by providing early years settings with a mechanism for directing
50 their resources to those children at highest risk of poor cognitive development. With new child
51 and maternity datasets now being collected electronically in England, it may be possible to
52 apply a PRM at population level through the use of linked administrative datasets as has been
53 done in Australia[15].
54
55
56

57
58 Poor cognitive development is associated with a range of negative health and social outcomes
59 and contributes to inequalities in society[3,5,6], so this is of public health importance.
60

1
2
3 Chittleborough et al showed that even a model with poor discrimination has benefits over just
4 using young maternal age to direct resources[14]. Similarly, McKean et al established that their
5 PRM was better than existing clinical tools used to identify higher-risk children for early
6 intervention[47].
7
8

9
10 The practical implications of using such a PRM as a screening tool should be considered. The
11 model reported here would identify 31% of children screened as being ‘at risk’ of delayed
12 school readiness. An exemplar English Local Authority with a total population of 230,000, and
13 3000 children aged under 1 year would identify 900 ‘at risk’ children per year if the PRM was
14 applied to this cohort. This percentage equates with national data; in 2015/16, 31% of children
15 in England were not school ready when tested at age 4-5[11]. However, the overall accuracy
16 of the model is 74%, so over 200 children would be incorrectly classified. PRMs raise ethical
17 issues; labelling very young children as being at risk of poor development could be stigmatising
18 for families, particularly when social factors are the strongest predictors as in this analysis.
19 PRMs would generate false positives (and false negatives), which could cause unnecessary
20 distress and use of resources.
21
22
23
24

25
26 Use of PRMs to identify children at risk of developmental delay should include support and
27 counselling for families, as well as timely access to appropriate interventions. Nelson et al
28 (2016) comment that Early Intervention services would be overwhelmed by the level of
29 demand generated by such PRMs[18]. A criterion for screening programmes is that
30 interventions should be available, it is thus important to further consider the implications of
31 using a PRM to assess ECD in the context of available resources. Investment in early
32 intervention would be required, which would have opportunity costs for services locally.
33 Further research is needed to test the external validity of this PRM for example in another
34 cohort or with linked administrative datasets such as the EYFS data from English schools.
35 Alternative modelling approaches which do not require a dichotomous outcome could also be
36 tested. Findings from such models could offer more nuanced predictions on school readiness.
37
38
39
40

41 **CONCLUSION**

42 This study has identified a set of predictive risk factors from the perinatal period and early
43 infancy that can predict school readiness at age 3 with a good level of accuracy. Poor cognitive
44 development is socially patterned, evident from a very young age and leads to persistent
45 disadvantage throughout life. It is possible that PRMs could be used to identify high risk
46 children and target appropriate interventions and resources to improve their developmental
47 trajectories, and to reduce social inequalities early in the life course.
48
49
50
51

52 **STATEMENTS**

53 **Funding**

54
55 This work was supported by the UK Public Health Research Consortium (PHRC). The PHRC is funded
56 by the Department of Health and Social Care Policy Research Programme. The views expressed in this
57 paper are those of the authors and do not necessarily reflect those of the Department of Health and
58
59
60

1
2
3 Social Care. Information about the wider programme of the PHRC is available from [http://phrc.](http://phrc.lshtm.ac.uk/)
4 [lshtm.ac.uk/](http://phrc.lshtm.ac.uk/). DTR is funded by the MRC on a Clinician Scientist Fellowship
5 (MR/P008577/1).
6
7
8
9

10 **Competing Interests**

11 We confirm that authors have no conflicts of interest to disclose.
12
13
14
15

16 **Contributors**

17 CLC, JCD and DTR planned the study. CLC and VSS conducted the analysis under
18 the supervision of DTR. CLC led the drafting of the manuscript. All authors contributed
19 to data interpretation, manuscript drafting and revisions and agreed the submitted
20 version of the manuscript.
21
22
23
24
25
26
27
28

29 **Data Sharing**

30 The Millennium Cohort Study dataset is available from the UK Data Service.
31
32
33

34 **ACKNOWLEDGEMENTS**

35 We would like to acknowledge all the families and researchers who are part of the UK
36 Millennium Cohort Study, without whom this research would not have been possible.
37
38
39

40 **FIGURE CAPTIONS**

41 Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and
42 Whitehead, 1991)

43 Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

44 Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

REFERENCES

- 1 National Research Council (US) and Institute of Medicine (US) Committee on Integrating the Science of Early Childhood Development. *From Neurons to Neighborhoods: The Science of Early Childhood Development*. Washington (DC): : National Academies Press (US) 2000. <http://www.ncbi.nlm.nih.gov/books/NBK225557/>
- 2 Black MM, Walker SP, Fernald LC, *et al*. Early childhood development coming of age: science through the life course. *The Lancet* 2016.
- 3 Heckman JJ. Skill formation and the economics of investing in disadvantaged children. *Science* 2006;**312**:1900–2. doi:312/5782/1900 [pii]
- 4 Hobcraft JN, Kiernan KE. Predictive factors from age 3 and infancy for poor child outcomes at age 5 relating to children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010.
- 5 Caspi A, Houts RM, Belsky DW, *et al*. Childhood forecasting of a small segment of the population with large economic burden. *Nat Hum Behav* 2016;**1**:0005.
- 6 Marmot M, Allen J, Goldblatt P, *et al*. Fair society, healthy lives: strategic review of health inequalities in England post 2010. Marmot Review Team 2010.
- 7 Public Health England. Improving school readiness: creating a better start for London. London: 2015.
- 8 Pia Rebello Britto. School Readiness - A conceptual framework. New York, NY: UNICEF 2012.
- 9 Marmot M, Friel S, Bell R, *et al*. Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet* 2008;**372**:1661–9. doi:10.1016/S0140-6736(08)61690-6
- 10 Abreu L, Roberts N. Children’s early years development and school readiness. 2016. <https://researchbriefings.parliament.uk/ResearchBriefing/Summary/CDP-2016-0141> (accessed 30 Jan 2019).
- 11 Public Health England. Public Health Profiles. 2017.<https://fingertips.phe.org.uk/profile-group/child-health> (accessed 13 Jun 2017).
- 12 Early years foundation stage profile results: 2017 to 2018. GOV.UK. <https://www.gov.uk/government/statistics/early-years-foundation-stage-profile-results-2017-to-2018> (accessed 22 Jan 2019).
- 13 FPH, FNP. Family Nurse Partnership. Faculty of Public Health 20102015.
- 14 Chittleborough CR, Lawlor DA, Lynch JW. Young Maternal Age and Poor Child Development: Predictive Validity From a Birth Cohort. *Pediatrics* 2011;**127**:e1436–44. doi:10.1542/peds.2010-3222

- 15 Chittleborough CR, Searle AK, Smithers LG, *et al.* How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study. *Early Child Res Q* 2016;**35**:19–30.
- 16 Brownell MD, Ekuma O, Nickel NC, *et al.* A population-based analysis of factors that predict early language and cognitive development. *Early Child Res Q* 2016;**35**:6–18.
- 17 Camargo-Figuera FA, Barros AJ, Santos IS, *et al.* Early life determinants of low IQ at age 6 in children from the 2004 Pelotas Birth Cohort: a predictive approach. *BMC Pediatr* 2014;**14**:308. doi:10.1186/s12887-014-0308-1
- 18 Nelson BB, Dudovitz RN, Coker TR, *et al.* Predictors of Poor School Readiness in Children Without Developmental Delay at Age 2. *Pediatrics* 2016;**138**:e20154477. doi:10.1542/peds.2015-4477
- 19 Pepe MS, Janes H, Longton G, *et al.* Limitations of the Odds Ratio in Gauging the Performance of a Diagnostic, Prognostic, or Screening Marker. *Am J Epidemiol* 2004;**159**:882–90. doi:10.1093/aje/kwh101
- 20 Kirstine Hansen. Millennium Cohort Study First, Second, Third and Fourth Surveys. A Guide to the Datasets (Seventh Edition). London: : Centre for Longitudinal Studies 2012.
- 21 Connelly R, Platt L. Cohort Profile: UK Millennium Cohort Study (MCS). *Int J Epidemiol* 2014;**43**:1719–25. doi:10.1093/ije/dyu001
- 22 Bracken B. Bracken Basic Concept Scale–Revised. San Antonio, TX: : The Psychological Corporation 1998.
- 23 Panter JE, Bracken BA. Validity of the Bracken School Readiness Assessment for predicting first grade readiness. *Psychol Sch* 2009;**46**:397–409.
- 24 Connelly R. Millennium Cohort Study Data Note 2013/1: Interpreting Test Scores. London: : Centre for Longitudinal Studies, Institute of Education 2013.
- 25 Steyerberg E. *Clinical prediction models: a practical approach to development, validation, and updating.* Springer Science & Business Media 2008.
- 26 Kiernan KE, Mensah FK. Maternal indicators in pregnancy and children’s infancy that signal future outcomes for children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010.
- 27 Kiernan KE, Huerta MC. Economic deprivation, maternal depression, parenting and children’s cognitive and emotional development in early childhood. *Br J Sociol* 2008;**59**:783–806.
- 28 Shenkin SD, Starr JM, Deary IJ. Birth weight and cognitive ability in childhood: a systematic review. *Psychol Bull* 2004;**130**:989.
- 29 Jefferis BJMH, Power C, Hertzman C. Birth weight, childhood socioeconomic environment, and cognitive development in the 1958 British birth cohort study. *BMJ* 2002;**325**:305. doi:10.1136/bmj.325.7359.305

- 1
2
3 30 Kramer MS, Aboud F, Mironova E, *et al*. Breastfeeding and Child Cognitive
4 Development: New Evidence From a Large Randomized Trial. *Arch Gen Psychiatry*
5 2008;**65**:578–84. doi:10.1001/archpsyc.65.5.578
6
7
8 31 Walker SP, Wachs TD, Grantham-McGregor S, *et al*. Inequality in early childhood: risk
9 and protective factors for early child development. *The Lancet* 2011;**378**:1325–38.
10
11 32 Murray GK, Jones PB, Kuh D, *et al*. Infant developmental milestones and subsequent
12 cognitive function. *Ann Neurol* 2007;**62**:128–36. doi:10.1002/ana.21120
13
14 33 Kelly Y, Sacker A, Gray R, *et al*. Light drinking in pregnancy, a risk for behavioural
15 problems and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;**38**:129–40.
16 doi:10.1093/ije/dyn230
17
18 34 Dahlgren G, Whitehead M. Policies and strategies to promote social equity in health.
19 *Stockh Inst Future Stud* 1991.
20
21 35 Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development
22 of a self-report questionnaire instrument. *J Reprod Infant Psychol* 1998;**16**:57–76.
23
24 36 Sosthenes C. Ketende, Elizabeth M. Jones. User Guide to Analysing MCS Data Using
25 STATA. Centre for Longitudinal Studies, Institute of Education 2011.
26
27 37 Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per
28 variable in logistic regression analysis. *J Clin Epidemiol* 1996;**49**:1373–9.
29 doi:10.1016/S0895-4356(96)00236-3
30
31 38 Courvoisier DS, Combescure C, Agoritsas T, *et al*. Performance of logistic regression
32 modeling: beyond the number of events per variable, the role of data structure. *J Clin*
33 *Epidemiol* 2011;**64**:993–1000.
34
35 39 Azen R, Traxel N. Using Dominance Analysis to Determine Predictor Importance in
36 Logistic Regression. *J Educ Behav Stat* 2009;**34**:319–47.
37 doi:10.3102/1076998609332754
38
39 40 Pencina MJ, D'Agostino RB, Pencina KM, *et al*. Interpreting Incremental Value of
40 Markers Added to Risk Prediction Models. *Am J Epidemiol* 2012;**176**:473–81.
41 doi:10.1093/aje/kws207
42
43 41 Windmeijer FAG. The asymptotic distribution of the sum of weighted squared residuals
44 in binary choice models. *Stat Neerlandica* 1990;**44**:69–78.
45
46 42 Austin PC, Steyerberg EW. Events per variable (EPV) and the relative performance of
47 different strategies for estimating the out-of-sample validity of logistic regression models.
48 *Stat Methods Med Res* 2017;**26**:796–808.
49
50 43 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues
51 and guidance for practice. *Stat Med* 2011;**30**:377–99. doi:10.1002/sim.4067
52
53 44 Centre for Longitudinal Studies. MCS Ethical Review and Consent. London: Institute of
54 Education 2014.
55
56
57
58
59
60

- 1
2
3 45 Hosmer DW, Hjort NL. Goodness-of-fit processes for logistic regression: simulation
4 results. *Stat Med* 2002;**21**:2723–2738.
5
6
7 46 Wilkinson RG, Marmot M. *Social Determinants of Health: The Solid Facts*. World
8 Health Organization 2003.
9
10 47 McKean C, Law J, Mensah F, *et al*. Predicting Meaningful Differences in School-Entry
11 Language Skills from Child and Family Factors Measured at 12 months of Age. *Int J*
12 *Early Child* 2016;**48**:329–51. doi:10.1007/s13158-016-0174-0
13
14 48 Steyerberg EW, Harrell FE, Borsboom GJJM, *et al*. Internal validation of predictive
15 models. *J Clin Epidemiol* 2001;**54**:774–81. doi:10.1016/S0895-4356(01)00341-9
16
17 49 Senn S. Disappointing dichotomies. *Pharm Stat J Appl Stat Pharm Ind* 2003;**2**:239–240.
18
19 50 Altman DG, Royston P. The cost of dichotomising continuous variables. *BMJ*
20 2006;**332**:1080. doi:10.1136/bmj.332.7549.1080
21
22
23 51 Côté SM, Doyle O, Petitclerc A, *et al*. Child Care in Infancy and Cognitive Performance
24 Until Middle Childhood in the Millennium Cohort Study. *Child Dev* 2013;**84**:1191–208.
25 doi:10.1111/cdev.12049
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

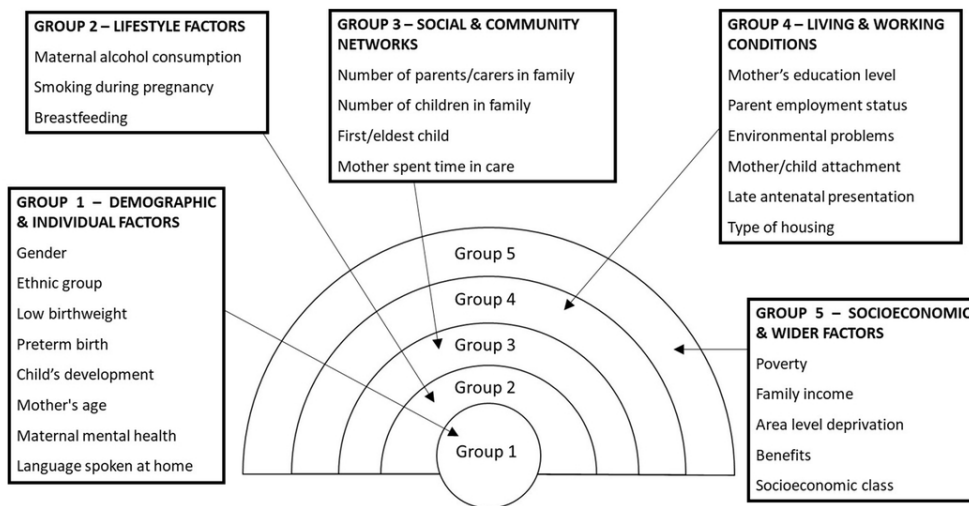
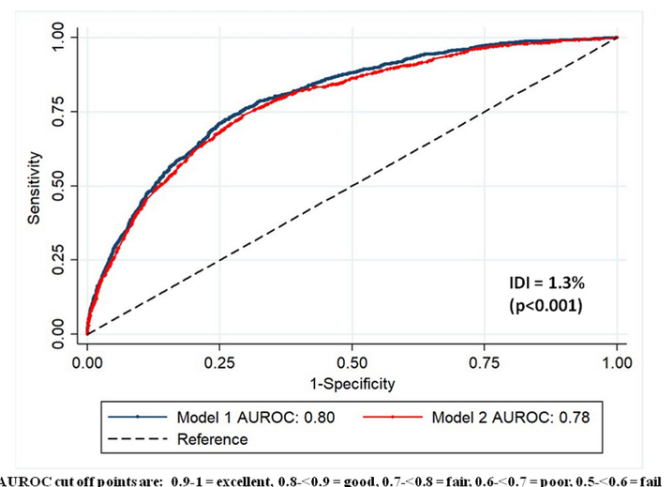


Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and Whitehead, 1991)

90x50mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



AUROC cut off points are: 0.9-1 = excellent, 0.8-0.9 = good, 0.7-0.8 = fair, 0.6-0.7 = poor, 0.5-0.6 = fail

Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI
90x50mm (300 x 300 DPI)

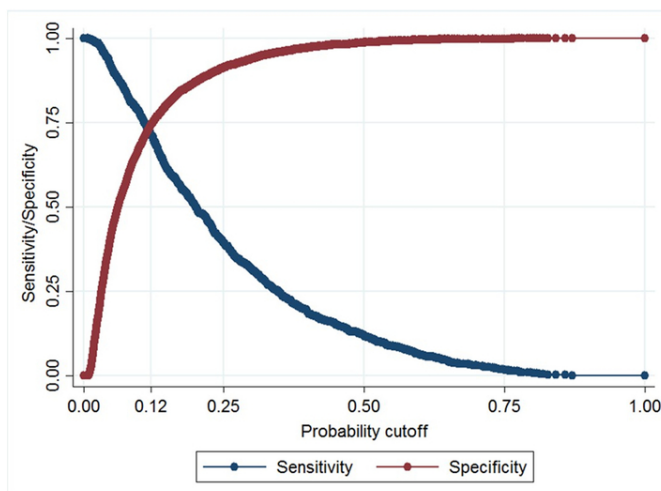


Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1

90x50mm (300 x 300 DPI)

SUPPLEMENTARY FILE 1

Robustness tests were carried out in which the final model was tested with an alternative outcome measure for early cognitive development (British Ability Scales), different coding of variables and the addition of another predictor variable (child care type at age 9 months).

1. Using BAS as an alternative outcome variable

An alternative measure of early cognitive development contained in the MSC are the British Ability Scales (BAS), measured at age 3. BAS scores were dichotomised to 1 SD below the mean as cut off for 'fail'. There is a moderate positive correlation between BAS and BSRA scores ($r=0.5722$, $p<0.0001$). The table below compares performance of the models; there is a small but statistically significant improvement in discrimination using BSRA as an outcome measure compared to BAS.

Outcome variable	N	AUROC (95% CI)
BSRA	9487	0.80 (0.78,0.81)
BAS	9487	0.79 (0.77,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb6)$; $\text{chi}2(1) = 9.20$, $\text{Prob}>\text{chi}2 = 0.002$

2. Robustness tests of the BSRA outcome measure

The BSRA cut off used in the main analysis was a mean standardised composite score <85 , which is 1 standard deviation below the mean. The standardisation sample was from a US population. As the BSRA has not been validated in the UK, we tested the model using dichotomised percentile ranks instead of MSCS as the outcome variable (cut off point 1 SD below mean).

There was no significant difference in model performance (AUROC=0.80 for both models, $p=0.43$). There is evidence to suggest that within the Millennium Cohort Study percentile scores can be misleading in indicating the difference between the performance of cohort members because they are on an ordinal, rather than interval, scale. An outcome based on MSCS was therefore retained.

3. Coding of predictor variables

As a sensitivity analysis the coding of 4 predictor variables was altered: maternal age (from categorical to continuous), developmental scores (from categorical to continuous) and ethnicity (from categorical to binary). The impact of this on final model performance is shown below:

Description	n	AUROC	Comparative AUROC (n=9310)
Final model	9487	0.80	0.79 (0.77,0.81)
Developmental score (continuous)	9487	0.80	0.80 (0.78,0.81)
Maternal age (continuous)	9310	0.79	0.79 (0.78,0.81)
Ethnicity (binary)	9487	0.79	0.79 (0.78,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb2) = \text{area}(xb3) = \text{area}(xb4)$; $\text{chi}2(3) = 9.98$; $\text{Prob}>\text{chi}2 = 0.02$

In summary, there were small but statistically significant differences between the models. The only change which improved model discrimination was using continuous development

1
2
3 scores, so this was incorporated into the final model. There is a U-shaped relationship
4 between school readiness and maternal age, so there was a clear rationale for including this
5 as a categorical predictor.
6
7

8
9 4. Testing the impact of an additional predictor

10 There are other measures in the MCS which could have been used as predictors in this
11 analysis. We have done a sensitivity analysis adding childcare type at 9 months to the final
12 model. This reduces the overall discrimination of the model (AUROC = 0.77 vs 0.80),
13 however this could be due to missing data as the child care variable is less complete. There
14 is a statistically significant association with school readiness and child care type in the
15 multivariable model, with children in formal child care settings more likely to be school
16 ready than those being looked after by parents (OR = 1.76, p=0.02)
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33

34 The Stata Do file for all analyses is available at:
35 <https://www.dropbox.com/s/zxsl4cl87imyp0/SchoolreadinessPRM.do?dl=0>
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SUPPLEMENTARY FILE 2

Table 1 - Adjusted associations for the predictor variables in model 1 (13 predictors) using multiple imputed data (n=11,879)

Predictor	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS		
Gender		
Female	1	8.5 (5)
Male	1.86 (1.62,2.14)	
Ethnicity		
White	1	15.7 (3)
Mixed	1.04 (0.62,1.75)	
Indian	2.68 (1.85,3.89)	
Pakistani and Bangladeshi	3.85 (2.94,5.04)	
Black or Black British	2.31 (1.43,3.72)	
Other ethnic group	3.95 (2.30,6.77)	
Mother's age at birth of first child		
30-39	1	1.5 (12)
40+	1.05 (0.67,1.64)	
20-29	1.22 (0.99,1.51)	
14-19	1.22 (0.93,1.59)	
Birth weight (<2500grams)		
Normal/high	1	1.2 (13)
Low birthweight	1.52 (1.18,1.97)	
Maternal Mental Health (Diagnosed depression/anxiety)		
No	1	1.5 (11)
Yes	1.15 (0.98,1.34)	
Child developmental milestones		
Developmental score	1.10 (1.07,1.13)	2.8 (10)
GROUP 2 - LIFESTYLE FACTORS		
Duration of breastfeeding		
6 months or more	1	3.6 (9)
6 weeks - 6 months	1.17 (0.92,1.48)	
One week or less	1.15 (0.90,1.48)	
1 - 6 weeks	1.22 (0.96,1.57)	
Never	1.58 (1.29,1.95)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS		
Number of children in family		
One child	1	7.1 (6)
Two or three children	1.40 (1.19,1.63)	
Four or more children	2.48 (1.94,3.16)	
GROUP 4 - LIVING & WORKING CONDITIONS		
Maternal education		
Degree plus	1	16.7 (2)

Diploma	0.88 (0.61,1.26)	
A levels	1.13 (0.80,1.59)	
GCSE A-C	1.34 (1.01,1.78)	
GCSE D-G	1.72 (1.23,2.39)	
None	1.74 (1.28,2.38)	
Workforce status		
Both parents in work	1	
One parent in work	0.94 (0.78,1.12)	6.5 (7)
Neither parent in work	1.21 (0.93,1.57)	
Housing tenure		
Owner occupied	1	
Private rented	1.18 (0.90,1.54)	5.5 (8)
Social housing	1.43 (1.18,1.72)	
Other	0.96 (0.69,1.35)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS		
Social class		
Managerial & professional	1	
Intermediate	0.98 (0.75,1.29)	
Small employers & own account	1.32 (0.87,2.00)	17.6 (1)
Lower supervisory & technical	1.50 (1.06,2.13)	
Semi-routine & routine	1.77 (1.38,2.27)	
Never worked & long-term unemployed	2.19 (1.53,3.15)	
Annual income		
£33,000+	1	
£22,000-£33,000	1.33 (1.02,1.72)	11.9 (4)
£11,000-£22,000	1.67 (1.30,2.14)	
£0-£11,000	2.14 (1.60,2.87)	
ROC Analysis	AUROC = 0.79 (95% CI 0.78,0.80)	

SUPPLEMENTARY FILE 3

Integrated discrimination improvement (IDI) analysis was run using Stata function 'idi', which compares the discrimination ability between two logistic regression prediction models. In the first stage of this analysis, the IDI of a PRM with just the strongest predictor variable (social class) was compared to a model with all 13 predictors. Adding the additional 12 predictors lead to a 7.3% increase in IDI. In each subsequent analysis, an additional predictor variable was added according to the ranking of variables from the dominance analysis (Table 1).

Predictor	Weighting	Rank
Social Class	17.38	1
Ethnic group	14.66	2
Maternal education	13.55	3
Income band	12	4
Gender	9.54	5
Number of children	7.84	6
Parent's employment	6.9	7
Housing type	5.65	8
Child development	3.9	9
Breastfeeding	3.9	10
Mother's age at birth of first child	2.87	11
Low birth weight	1.42	12
Mental health	0.38	13

Table 1 - Results of the dominance analysis for model 1

The full results of integrated discrimination improvement (IDI) analysis are shown in Table 2.

Variables included	IDI (%)	p	1-IDI
1	7.3%	<0.00001	92.7%
2	5.3%	<0.00001	94.7%
3	3.8%	<0.00001	96.2%
4	3.5%	<0.00001	96.5%
5	2.3%	<0.00001	97.7%
6	1.3%	<0.00001	98.7%
7	1.0%	<0.00001	99.0%
8	0.9%	<0.00001	99.1%
9	0.6%	0.00001	99.4%
10	0.6%	0.00001	99.4%
11	0.2%	0.01402	99.8%
12	0.0%	0.52356	100.0%

Table 2 - Results of integrated discrimination improvement analysis for 12 models

A 6-predictor model was chosen as this offered the optimal balance between parsimony and discrimination.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SUPPLEMENTARY FILE 4

Table 1 - Adjusted associations for the predictor variables in model 2 (6 predictors) using complete cases (n=11,146) and multiple imputed data (n=11,879). The weightings and rank are from dominance analysis of the complete case sample.

Predictors	Adjusted OR (95% CI) - complete case	Adjusted OR (95% CI) - multiple imputation	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.9 (5)
Male	1.99 (1.72,2.31)	1.93 (1.68,2.22)	
Ethnicity			
White	1	1	13.7 (4)
Mixed	1.2 (0.77,1.88)	1.26 (0.83,1.90)	
Indian	1.64 (1.09,2.47)	1.72 (1.14,2.59)	
Pakistani and Bangladeshi	2.67 (2.10,3.41)	2.71 (2.11,3.47)	
Black or Black British	2.32 (1.52,3.54)	2.69 (1.80,4.02)	
Other ethnic group	1.98 (1.10,3.58)	2.06 (1.27,3.32)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	9.5 (6)
Two or three children	1.48 (1.27,1.73)	1.45 (1.25,1.69)	
Four or more children	2.89 (2.23,3.75)	2.62 (2.03,3.38)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	20.5 (3)
Diploma	0.87 (0.58,1.29)	0.88 (0.60,1.28)	
A levels	1.05 (0.72,1.53)	1.06 (0.74,1.52)	
GCSE A-C	1.43 (1.02,1.99)	1.55 (1.14,2.12)	
GCSE D-G	1.78 (1.23,2.58)	2.14 (1.51,3.03)	
None	2.01 (1.44,2.81)	2.42 (1.77,3.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	26.0 (1)
Intermediate	1.17 (0.88,1.55)	1.14 (0.86,1.51)	
Small employers & own account	1.44 (0.91,2.28)	1.52 (0.99,2.33)	
Lower supervisory & technical	2.01 (1.42,2.86)	1.92 (1.37,2.68)	
Semi-routine & routine	2.41 (1.86,3.12)	2.16 (1.68,2.78)	
Never worked & long-term unemployed	3.34 (2.41,4.63)	2.95 (2.14,4.07)	
Annual income			
£33,000+	1	1	20.6 (2)
£22,000-£33,000	1.33 (0.97,1.81)	2.65 (2.01,3.50)	
£11,000-£22,000	1.88 (1.42,2.50)	1.75 (1.32,2.31)	
£0-£11,000	2.98 (2.26,3.92)	1.29 (0.95,1.75)	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ROC Analysis	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,146	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,879
---------------------	---	---

For peer review only

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	3
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	3
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	3-4
	5b	Describe eligibility criteria for participants.	4
	5c	Give details of treatments received, if relevant.	
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4
	6b	Report any actions to blind assessment of the outcome to be predicted.	
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors. <small>temporal ordering in cohort</small>	
Sample size	8	Explain how the study size was arrived at.	5
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	5-6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	6
Risk groups	11	Provide details on how risk groups were created, if done.	
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6-7
Model development	14a	Specify the number of participants and outcome events in each analysis.	10
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	8-10
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	
	15b	Explain how to use the prediction model.	
Model performance	16	Report performance measures (with CIs) for the prediction model.	10
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11-12
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11-13
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	
Funding	22	Give the source of funding and the role of the funders for the present study.	

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development of a Predictive Risk Model for School Readiness at age 3 years using the UK Millennium Cohort Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024851.R3
Article Type:	Research
Date Submitted by the Author:	07-May-2019
Complete List of Authors:	Camacho, Christine; University of Liverpool Department of Public Health and Policy, Straatmann, Viviane; University of Liverpool Department of Public Health and Policy; Karolinska Institute, Aging Research Centre Day, Jennie; University of Liverpool Department of Public Health and Policy Taylor-Robinson, David; University of Liverpool, Department of Public Health and Policy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Epidemiology, Health policy, Research methods
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, SOCIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 **Development of a Predictive Risk Model for School Readiness at age 3 years using the**
4 **UK Millennium Cohort Study**
5

6
7 Miss CL Camacho*¹, Dr VS Straatmann^{1,2}, Dr JC Day¹, Prof DC Taylor-Robinson¹
8

9
10 *Affiliations: ¹Public Health and Policy, University of Liverpool, Liverpool, UK; ²Aging*
11 *Research Centre, Karolinska Institute, Stockholm, Sweden*
12

13 *Address correspondence to: Christine Camacho, Department of Public Health and Policy, University*
14 *of Liverpool, Liverpool, United Kingdom, L69 3GB, [c.camacho@nhs.net], +44 07973395585*
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

ABSTRACT

Objectives

The aim of this study was to develop a predictive risk model (PRM) for school readiness measured at age 3 years using perinatal and early infancy data.

Design and Participants

This paper describes the development of a predictive risk model. Predictors were identified from the UK Millennium Cohort Study (MCS) wave 1 data, collected when participants were 9 months old. The outcome was school readiness at age 3 years, measured by the Bracken School Readiness Assessment. Stepwise selection and dominance analysis were used to specify 2 models. The models were compared by the area under the receiver operating characteristic curve (AUROC) and integrated discrimination improvement (IDI).

Results

Data were available for 9,487 complete cases. At age 3, 11.7% (95% CI 11.0-12.3%) of children were not school ready. The variables identified were: parents' Socio-Economic Classification, child's ethnicity, maternal education, income band, sex, household number of children, mother's age, low birth weight, mother's mental health, infant developmental milestones, breastfeeding, parents' employment, housing type. A parsimonious model included the first six listed variables (model 2). The AUROC for model 1 was 0.80 (95% CI 0.78-0.81) and 0.78 (95% CI 0.77-0.79) for model 2. Model 1 resulted in a small improvement in discrimination (IDI=1.3%, $p<0.001$).

Conclusions

Perinatal and infant risk factors predicted school readiness at age 3 with good discrimination. Social determinants were strong predictors of school readiness. This study demonstrates that school readiness can be predicted by six attributes collected around the time of birth.

Strengths and limitations of this study

- Use of a large, representative, and contemporary cohort study to demonstrate the feasibility of predicting school readiness from data collected in infancy.
- Multiple imputation and bootstrapping were used to evaluate the impact of missing data and internal validity, respectively.
- The main outcome measure, the Bracken School Readiness Assessment, was developed in the US, and is not routinely used in the UK.
- This model was not externally validated, which would have given an indication of generalisability.

INTRODUCTION

Early childhood is a critical time for lifelong physical, social, emotional and cognitive development. A wide range of factors are associated with early cognitive development (ECD)[1]. Interventions in the first three years of life can improve the trajectory of ECD[2] and deliver the greatest return on investment[3], yet it is unclear how best to identify children at most risk of delayed ECD, to enable appropriate targeting of interventions.

Cognitive development measures in children are good indicators of later educational achievement, predict health and social care needs in adults[4,5], and are associated with long term health outcomes[6]. There has been a growing policy interest in school readiness as a measure of ECD[7], and school readiness is a key public health indicator in children in the UK. Good school readiness lays a platform for future learning, employment and health[8,9].

School readiness is currently a major focus in England for policy makers, educators and the public health community [10] and national metrics are collected to capture changes over time. In 2017, 29% of children in England were deemed not school ready at the end of their reception year (aged 4-5 years)[11]. The percentage of children school ready was nearly 20% higher in the most affluent decile (80% school ready) compared to the most deprived decile (62% school ready) when areas were classified into deciles according to the Index for Multiple Deprivation [12]. In UK policy there has been a focus on demographic factors e.g. maternal age, in targeting early interventions for children[13]. This study will explore the importance of different variables in predicting school readiness.

Previous research has identified a wide range of variables associated with early cognitive development. Predictive risk models (PRMs) are well-established in many clinical disciplines and have more recently been applied to child development. Using PRMs in this context could facilitate targeted early intervention as part of a proportionate universalism approach, which requires universal action with the scale and intensity of interventions proportionate to the level of need[6]. Most models thus far have shown fair or poor discrimination and there have been very few studies in the UK [14–18]. The aim of this study was to develop, for the first time, a PRM for school readiness measured at age 3 years using perinatal and early infancy data from the UK Millennium Cohort Study (MCS).

METHODS

Overview

Data from the MCS were used to explore the relationship between the outcome, school readiness, and 29 predictor variables using logistic regression analysis. Following univariable analysis to test for unadjusted associations, automated stepwise regression analyses were used to select variables for inclusion in the PRM. Dominance analysis was used to rank and weight included predictors, and integrated discrimination improvement (IDI) was calculated to assess the difference in performance between models. A receiver operator characteristic (ROC) curve was used to evaluate how well the model discriminated school readiness. The area under an ROC curve (AUROC) gives a measure of how well the regression model predicts school readiness at age 3. Traditionally accepted AUROC cut off points are: 0.9-1 = excellent, 0.8- $<$ 0.9 = good, 0.7- $<$ 0.8 = fair, 0.6- $<$ 0.7 = poor, 0.5- $<$ 0.6 = fail[19]. Multiple imputation was used to assess the impact of missing data in the sample.

Data Source

The PRM was developed and validated using MCS data. The MCS is a nationally representative birth cohort study which recruited 18,550 children born from September 2000 to January 2002, followed up in ongoing data collection waves. The sampling frame was government child benefit records, which had almost universal coverage at the time of sampling. The sample was clustered at the level of electoral ward and stratified to allow over representation of children living in deprived areas and areas with high concentrations of ethnic minorities[20]. Further information about the MCS sample is available in the cohort profile[21]. Data were collected from the main responder (usually mothers) by trained interviewers in participants' homes using a combination of interviews and self-completed questions. All singleton children in the first (aged 9 months) and second (aged 3 years) waves of the MCS with completed data for the outcome and predictors were eligible for inclusion (n=9,487).

Outcome

School readiness was measured using the Bracken School Readiness Assessment (BSRA) which consists of 6 subtests relating to colours, letters, numbers/counting, sizes, comparisons and shapes[20]. The assessment was carried out by interviewers during the second data collection wave when children were aged approximately 3 years old. The BSRA and its predecessors have demonstrated good reliability[22] and validity against other measures and teacher assessments[23].

The BSRA raw scores were summed and adjusted for age to provide a standardised composite score[20]. Scores were grouped according to cut-offs recommended by Bracken which reflected a 'normative classification' whereby children were categorised as very delayed, delayed, average, advanced or very advanced [24]. We used the same cut off score as Bracken (mean standardised composite score $<$ 85, 1 standard deviation below mean) but collapsed the categories of delayed or very delayed into a single category equivalent to not being school

ready. We have dichotomised the outcome ‘school readiness’ in line with UK policy, and to allow the testing of a PRM using ROC analysis which requires a binary outcome [25].

Predictors

29 predictor variables were used, which were collected at age 9 months in the first wave of MCS data collection during which data relevant to pregnancy, birth and the perinatal period was captured retrospectively. These were identified from previous research to predict cognitive development and were included in the MCS[1,2,4,6,26–33]. The selected predictor variables were grouped according to the Dahlgren and Whitehead theoretical model[34] of social determinants of health as depicted in Figure 1. This model was chosen to provide a framework for categorising predictors to allow analysis of the determinants of early cognitive development.

<<Figure 1 here>>

Group 1 – Demographic and Individual factors

Demographic characteristics included child sex, maternal ethnicity, child weight, pre-term birth, mother’s age, home language, maternal mental health and child development categorised as shown in Box 1.

Box 1 – Coding of Group 1 demographic and individual factors

Categorisation of Demographic and Individual factors

Child sex – ‘female’ and ‘male’

Maternal ethnicity – ‘white’, ‘mixed’, ‘Indian’, ‘Pakistani and Bangladeshi’, ‘Black’ and ‘other’

Child weight at birth – low (<2.5kg) or normal/high (≥2.5kg)

Preterm birth – gestation period less than 37 weeks

Mother’s age in years at birth of first child – grouped into 4 categories (14-19, 20-29, 30-39, 40+ years)

Home language – ‘English only’, ‘English and another language’, ‘another language only’

Mental health (1) – Sad or low for >2 weeks since baby, coded as ‘yes’ or ‘no’

Mental health (2) – Diagnosis of depression or serious anxiety, coded as ‘yes’ or ‘no’

Mental health (3) – 9-item modified version of the Rutter Malaise Inventory³⁹, coded as ‘low’ or (0-3) ‘high’ (4-9) scores²⁷.

Child development – 8 items from Denver Developmental Screening Test and 5 items from MacArthur Communicative Development Inventory, scored on a continuous scale from 13 (above average) to 36 (below average)

Group 2 – Lifestyle Factors

Self-reported maternal smoking was coded as ‘never smoked’, ‘smoked before pregnancy’ and ‘smoked during pregnancy’. Maternal alcohol consumption during pregnancy were categorised as ‘never or very infrequent’, ‘occasional’, ‘regularly’ and ‘most or everyday’. Breastfeeding duration was grouped as ‘never’, ‘one week or less’, ‘1 – 6 weeks’, ‘6 weeks – 6 months’ and ‘over 6 months’.

Group 3 – Social and Community Networks

The number of children in household was coded as ‘1’, ‘2-3’ or ‘4+’, and being the eldest or only child was recoded as ‘yes’ or ‘no’. The number of parents or carers was either ‘1’ or ‘2’.

1
2
3 Mothers were asked how much time they had spent time in care before the age of 17, this was
4 recoded as 'yes' or 'no' to indicate if they had ever been in care.
5
6

7 Group 4 – Living and Working Conditions

8 Maternal education was categorised into six groups 'degree plus (higher degree and first degree
9 qualifications)', 'diploma (in higher education)', 'A-levels', 'GCSE grades A–C', 'GCSE
10 grades D–G' and 'none of these qualifications'. Parent's employment status was classified as
11 either 'both', 'one' or 'neither' parents in work¹. Housing tenure was coded as 'owner
12 occupied', 'private rented', 'social housing' and 'other'. The response to the question, "How
13 common is pollution, grime or other environmental problems?" was recoded as 'common', 'not
14 common' and 'not at all'. Presentation for first antenatal visit was recoded as late if after 12
15 weeks. Maternal attachment was measured using a 6-item Condon Maternal Attachment
16 Questionnaire[35] grouped as 'low (10-21)', 'average' (22-23) and 'high (24-27)'.
17
18
19
20
21

22 Group 5 – Socioeconomic and Wider Factors

23 The National Statistics Socio-Economic Classification (NS-SEC) was used to code job details
24 for main respondents (the majority of which were mothers) as: 'managerial & professional',
25 'intermediate', 'small employers & own account', 'lower supervisory & technical', 'semi-
26 routine & routine', 'never worked & long-term unemployed'. Net household income was
27 reported by identification of the correct band on a show card and grouped into 4 quartile
28 bands[26]: '£0-£11,000', '£11,000-£22,000', '£22,000-£33,000' and '£33,000+'. Poverty was
29 defined as an equivalised household income 60% below the median before housing costs
30 according to the Organisation for Economic Co-operation and Development Household
31 Equivalence Scale. Families reported receipt of any means-tested benefits, including
32 Jobseekers Allowance, Income Support, Working Families Tax Credit or Disabled Persons Tax
33 Credit. Indices of Multiple Deprivation (IMD) from 2004 which had been retrospectively
34 linked to wave 1 data were used to give small area level deprivation measures [20]. IMD scores
35 were divided into quintiles, with 1 the most deprived quintile, and 5 the least deprived.
36
37
38
39
40

41 **Statistical analyses**

42 Analyses were conducted using Stata v14.2 (StataCorp LP, 2017). Survey weights were applied
43 to take account of clustering, stratification and oversampling in the survey design, and attrition
44 between survey waves, using the svyset command (pweight=BOVWT2) and svy prefix for
45 regression modelling[36]. The number of events per variable (EPV) exceeds 35, the predictors
46 were checked for collinearity, a large number of predictors were used and all were significantly
47 associated with the outcome suggesting a robust logistic regression model with sufficient
48 sample size [37,38].
49
50
51

52 Descriptive analysis of each predictor and school readiness was carried out to ascertain the
53 prevalence of each predictor in the sample. Univariable logistic regression analyses calculating
54 odds ratios (ORs) and 95% confidence intervals (95% CI) were carried out to assess the
55 unadjusted association of each variable with the outcome.
56
57

58
59 ¹ Being on leave from work is classed as being in employment
60

1
2
3
4
5 A multivariable logistic regression model including all 29 variables was reduced using
6 automated forward and backwards stepwise selection (using a cut off p-value of 0.1).
7 Dominance analysis (repeated regression analyses on subsets of variables) was used to produce
8 a ranking and weighting for each predictor in model 1[39]. These rankings were used to specify
9 a more parsimonious model (model 2) containing the top 6 predictors, selected to maximise
10 parsimony and performance. The integrated discrimination improvement (IDI) using the
11 complete case sample from model 1 was calculated to assess difference in performance
12 between models as the percentage change in individuals being correctly assigned by the
13 model[40].
14
15
16

17
18 The area under the ROC curve (AUROC) and its 95% CI was used to measure discriminatory
19 power of the models. Classification, including sensitivity and specificity, was assessed at the
20 maximised probability cut off point where the sensitivity and specificity curves intersected.
21 Calibration of the model was assessed using the Pearson Chi-squared test[41]. Bootstrapping
22 was used for internal validation of the final model, without repeating selection of predictors in
23 each bootstrap sample. Model performance was assessed using 1000 bootstrap samples, model
24 optimism was averaged across all iterations to obtain an optimism estimate. An optimism-
25 corrected AUROC, which takes account of overfitting, was calculated by subtracting the
26 optimism estimate from the uncorrected AUROC[42].
27
28
29
30

31 A complete case approach was used for the primary analysis. As a sensitivity analysis, multiple
32 imputation by chained equation was performed to impute missing data using the ‘mi impute
33 chained’ command in Stata. We used predictor variables with relatively little missing data
34 (maternal education, child’s sex, mother’s age at birth of first child) and the outcome as regular
35 variables in the imputation model. As such individuals with missing data for these 4 items were
36 not included in the final imputed sample (n=11,897). Twenty imputed datasets were generated,
37 and Rubin’s rules were used to calculate results across the imputed datasets[43].
38
39
40

41 Robustness tests were carried out in which the final model was tested with an alternative
42 outcome measure for early cognitive development (the British Ability Scales, also tested at age
43 3 in the MCS); different coding of outcome and predictor variables (e.g. maternal age as a
44 continuous variable); and with the addition of another predictor variable (child care type at age
45 9 months). See supplementary file 1 for further details.
46
47
48

49 **Ethics and Patient and public involvement**

50 Ethical approval for each wave of the MCS was granted by NHS Multicentre Research Ethics
51 Committees[44]. No further ethical approval was required for this secondary analysis of MCS
52 data. There was no direct patient or public involvement in this analysis. However, the MCS has
53 an ongoing programme of participant and public engagement.
54
55
56

57 **RESULTS**

58 There were 15,381 singleton children surveyed in MCS2, of which 13,650 had an outcome
59 recorded for school readiness. Of these children 70% (n=9,487) had complete data for the
60

outcomes and all the predictor variables. There were no significant differences in the characteristics of the imputed sample and the complete case sample (p value >0.05 for all chi-squared tests) (Table 1); results are reported for complete cases (see Supplementary file 2 for imputed sample results).

Table 1 - Description of perinatal, sociodemographic and economic characteristics by school ready of sample and imputed sample

Is Child School Ready?	Complete Cases (n=9,487)		Imputed Data (n=11,897)	
	Yes (%)	No (%)	Yes (%)	No (%)
All	88.3	11.7	85.5	14.5
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS				
Gender				
Female	91.6	8.4	89.4	10.6
Male	85.1	14.9	82.6	17.4
Ethnicity				
White	90.4	9.6	88.6	11.4
Mixed	91.1	8.9	84.7	15.3
Indian	79.3	20.7	78.1	21.9
Pakistani and Bangladeshi	55.7	44.3	56.3	43.7
Black or Black British	79.8	20.2	68	32
Other ethnic group	73.6	26.4	74.3	25.7
Mother's age at birth of first child				
14-19	78	22	76.4	23.6
20-29	87.9	12.1	86.1	13.9
30-39	95	5	94.4	5.6
40+	76.9	23.1	76	24
Birth weight (<2500grams)				
normal/high	88.8	11.2	86.1	13.9
low birthweight	80.2	19.8	77.7	22.3
Maternal Mental Health (Diagnosed depression/anxiety)				
No	89	11	86	14
Yes	86	14	84.4	15.6
Child developmental milestones				
Child development score (mean, 95%CI)	19.3 (19.2,19.3)	19.9 (19.7,20.1)	19.1 (19.0,19.1)	19.6 (19.4,19.7)
GROUP 2 - LIFESTYLE FACTORS				
Duration of breastfeeding				
6 months or more	92.5	7.5	90.5	9.5
6 weeks - 6 months	89.8	10.2	87.8	12.2
1 - 6 weeks	88.8	11.2	85.9	14.1
one week or less	88.8	11.2	86.4	13.6
Never	82.6	17.4	80	20
GROUP 3 - SOCIAL & COMMUNITY NETWORKS				
Number of children in family				
One child	92	8	89.1	10.9
Two or three children	87.7	12.3	85	15

Four or more children	71.7	28.3	70.2	29.8
GROUP 4 - LIVING & WORKING CONDITIONS				
Maternal education				
Degree plus	95.6	4.4	95.1	4.9
Diploma	94.6	5.4	93.9	6.1
A levels	92.7	7.3	92	8
GCSE A-C	88.5	11.5	87.4	12.6
GCSE D-G	81	19	79.1	20.9
None	71.3	28.7	69.2	30.8
Workforce status				
Both parents in work	92.6	7.4	91.6	8.4
One parent in work	85.8	14.2	83.4	16.6
Neither parent in work	68.5	31.5	70.1	29.9
Housing tenure				
Owner occupied	91.9	8.1	90.7	9.3
Private rented	83.8	16.2	80.5	19.5
Social housing	75.8	24.2	74.8	25.2
Other	83.4	16.6	81	19
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS				
Social class				
managerial & professional	95.5	4.5	94.6	5.4
intermediate	93.1	6.9	92.1	7.9
small employers & own account	91.3	8.7	89.1	10.9
lower supervisory & technical	87.2	12.8	84	16
semi-routine & routine	81.9	18.1	80	20
never worked & long-term unemployed	60.2	39.8	62.1	37.9
Annual income				
£33,000+	95.7	4.3	94.9	5.1
£22,000-£33,000	92.5	7.5	91.7	8.3
£11,000-£22,000	85	15	83.9	16.1
£0-£11,000	73.8	26.2	74.1	25.9

11.7% (95%CI 11.0-12.3%) of children aged 3 years were classified as not being school ready, but this varied significantly by the parents' ethnicity, maternal education and social class (Table 1). All 29 predictor variables were significantly associated with school readiness in univariable logistic regression analysis ($p < 0.1$), so none were excluded at this stage.

The stepwise method reduced the final multivariable logistic regression model to 13 predictors: child's sex and ethnicity, mother's age at birth of first child, birthweight, maternal mental health, child development milestones, duration of breastfeeding, number of children in family, maternal education, parents' workforce status, housing tenure, social class and annual family income. In the adjusted analysis, Pakistani and Bangladeshi children were 4 times more likely to not be school ready than white children (OR 4.19 95% CI 3.14-5.58). The full results are shown in Table 2. There was no evidence of collinearity.

Table 2 - Unadjusted and adjusted associations and dominance analysis for the predictor variables in model 1 (13 predictors)

Predictors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.5 (5)
Male	1.76 (1.54,2.01)	2.03 (1.72,2.39)	
Ethnicity			
White	1	1	14.7 (2)
Mixed	1.4 (0.96,2.04)	1.42 (0.78,2.58)	
Indian	1.85 (1.23,2.77)	2.58 (1.65,4.03)	
Pakistani and Bangladeshi	5.94 (4.82,7.32)	4.27 (3.20,5.69)	
Black or Black British	4.06 (2.90,5.69)	2.1 (1.13,3.88)	
Other ethnic group	2.33 (1.38,3.93)	2.92 (1.55,5.48)	
Mother's age at birth of first child			
30-39	1	1	2.9 (11)
40+	2.83 (2.29,3.49)	1.05 (0.68,1.63)	
20-29	5.57 (4.20,7.37)	1.28 (0.98,1.66)	
14-19	6.02 (4.84,7.48)	1.32 (0.95,1.83)	
Birth weight (<2500grams)			
Normal/high	1	1	1.4 (12)
Low birthweight	1.7 (1.34,2.16)	1.26 (0.92,1.72)	
Maternal Mental Health (Diagnosed depression/anxiety)			
No	1	1	0.4 (13)
Yes	1.33 (1.16,1.53)	1.28 (1.07,1.53)	
Child developmental milestones			
Developmental score	1.07 (1.05,1.10)	1.1 (1.07,1.14)	3.9 (11)
GROUP 2 - LIFESTYLE FACTORS			
Duration of breastfeeding			
6 months or more	1	1	3.9 (10)
6 weeks - 6 months	1.25 (1.02,1.53)	1.05 (0.81,1.36)	
One week or less	1.67 (1.34,2.09)	1.19 (0.89,1.59)	
1 - 6 weeks	1.68 (1.36,2.07)	1.25 (0.96,1.65)	
Never	2.74 (2.29,3.27)	1.49 (1.19,1.87)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	7.8 (6)
Two or three children	1.44 (1.27,1.63)	1.38 (1.15,1.66)	
Four or more children	3.71 (3.04,4.54)	2.67 (1.94,3.68)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	13.6 (3)
Diploma	1.3 (0.93,1.81)	0.81 (0.53,1.24)	
A levels	1.66 (1.22,2.25)	1.02 (0.68,1.55)	
GCSE A-C	3.02 (2.34,3.90)	1.3 (0.89,1.88)	
GCSE D-G	5.55 (4.21,7.30)	1.54 (1.02,2.34)	

None	9.62 (7.61,12.16)	1.68 (1.15,2.43)	
Workforce status			
Both parents in work	1	1	
One parent in work	1.79 (1.49,2.14)	0.82 (0.67,1.00)	6.9 (7)
Neither parent in work	5.39 (4.36,6.67)	1.21 (0.87,1.68)	
Housing tenure			
Owner occupied	1	1	
Private rented	2.68 (2.16,3.33)	1.21 (0.87,1.67)	5.7 (8)
Social housing	3.89 (3.34,4.53)	1.45 (1.16,1.81)	
Other	2.65 (2.10,3.35)	0.9 (0.62,1.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	
Intermediate	1.5 (1.19,1.89)	1.06 (0.77,1.45)	
Small employers & own account	2.11 (1.44,3.08)	1.41 (0.87,2.28)	17.4 (1)
Lower supervisory & technical	3.72 (2.76,5.00)	1.65 (1.09,2.50)	
Semi-routine & routine	4.99 (4.13,6.01)	1.97 (1.46,2.66)	
Never worked & long-term unemployed	12.07 (9.48,15.37)	2.49 (1.69,3.66)	
Annual income			
£33,000+	1	1	
£22,000-£33,000	1.71 (1.31,2.25)	1.31 (0.96,1.79)	12.0 (4)
£11,000-£22,000	3.97 (3.12,5.07)	1.64 (1.22,2.22)	
£0-£11,000	7.7 (6.10,9.72)	2.26 (1.60,3.19)	

Dominance analysis showed that social class was the most important predictor (weighting=17.6), followed by ethnic group (weighting=14.7) and maternal education (weighting=13.8) (Table 2). Analysis of the predictor weightings suggests that social factors (average weighting 11.3, SD 4.9) are stronger predictors of school readiness than demographic and lifestyle factors (average weighting 5.5, SD 4.9). IDI was used to test the relative performance of models with all (1-13) variables, with variables added in according to their rank from the dominance analysis (Supplementary File 3). These analyses informed the specification of model 2, which was comprised of the top 6 predictors: social class, child's ethnic group, maternal education, income band, sex and number of children (see Supplementary File 4 for Model 2 results).

The AUROC was 0.80 (95% CI 0.78-0.81) for model 1 (n=9,487), which indicates a "good" level of discrimination[19]. The AUROC for model 2 (n=11,146) was 0.78 (95% CI 0.77-0.79). Internal validation using bootstrap optimism correction suggests that the model would have good discriminatory power in an independent sample (adjusted AUROC model 1 = 0.79, model 2=0.76). The Pearson Chi-squared tests were both non-significant indicating adequate calibration (model 1, p=0.07, model 2, p=0.13)[45]. IDI showed there was a small but significant difference in performance, with model 1 resulting in a 1.3% (p=<0.001) improvement in discrimination (Figure 2).

<<Figure 2 here>>

1
2
3 Sensitivity and specificity were plotted against probability cut-offs to select the optimal cut off
4 point to assess the PRM's classification (model 1, cut-off=0.12; model 2, cut-off=0.14) (Figure
5 **3Error! Reference source not found.**). For model 1, at this cut-off point sensitivity was 72%
6 (95% CI 69.0%-74.3%) and specificity was 74% (95% CI 73.5%-75.3%). Sensitivity of model
7 2 was similar - 72% (95% CI 69.9%-74.5%). Specificity was lower - 71% (95% CI 69.6%-
8 71.4%), so this model would generate more false positive results than the model 1, but
9 performance was still in the acceptable range. At a probability cut-off of 12%, 31% of the
10 screened population tested would be identified as being 'at risk' of poor school readiness using
11 model 1.
12
13
14
15

16 <<Figure 3 here>>
17
18

19 A sensitivity analysis using an alternative outcome measure (British Ability Scales, BAS),
20 showed that the BSRA measure led to improved discrimination (AUROC = 0.79 (95% CI 0.78-
21 0.81) for BAS; AUROC = 0.80 (95% CI 0.78-0.81) for BSRA, p=0.002). See supplementary
22 file 1 for further details.
23
24
25

26 DISCUSSION

27 Findings

28 This study developed a PRM for school readiness at age 3 years using perinatal and early
29 childhood data from the MCS. Model 1 with 13 variables had good discrimination
30 (AUROC=0.80) and classification (sensitivity=72%, specificity= 74% at a maximised cut off).
31 Dominance analysis found the most important variables in predicting school readiness related
32 to socioeconomic conditions (social class, maternal education, family income) and ethnicity.
33 A parsimonious model performed similarly well (AUROC=0.78), suggesting it is possible to
34 predict school readiness at age 3 fairly well using just six variables from the perinatal period
35 and early infancy.
36
37
38
39

40 Comparison with previous studies

41 The value added of this study is that it is the first UK study to show that school readiness can
42 be predicted with good discrimination with a small number of variables collected in infancy.
43 The predictors of school readiness identified here corroborate previous findings. Male sex,
44 maternal education, income, family composition, parental employment, housing and
45 breastfeeding have been identified as significant risk factors of delayed ECD in other
46 studies[4,14,15,17,18,26]. Social factors were the most important predictors, corresponding
47 with current thinking on the social determinants of cognitive development[6,46].
48
49
50

51
52 The model reported here has good predictive strength, and compares favourably to similar
53 PRMs, which with one exception[17], achieved only fair or poor discrimination[14,15,18,47].
54 Chittleborough et al used the ALSPAC UK birth cohort to test the predictive validity of 2
55 models for ECD[14]. They used a different outcome measure (School entry assessment aged
56 4-5) and used 6 predictors in their model, which appear to be chosen a priori, rather than by a
57 statistical routine. They found that maternal age alone failed to predict ECD (AUROC~0.5),
58 and a model with 6 predictors achieved only poor discrimination (AUROC=0.67). Camargo-
59
60

1
2
3 Figuera et al used IQ as a measure of ECD and developed a PRM with 12 predictors using the
4 Brazilian Pelotas birth cohort; their model had good discrimination (AUROC=0.8) and
5 calibration, with sensitivity and specificity of 72% and 74% respectively[17]. We believe the
6 use of a representative cohort for model development, stepwise regression to select predictor
7 variables and dominance analysis to specify a simplified model contributed to the good
8 performance of this PRM.
9
10

11 12 **Strengths and Limitations**

13 A strength of this study was the use of a representative and contemporary UK cohort study as
14 the data source. This offered a wide range of predictor variables and a large sample size which
15 minimised the likelihood of overfitting. The cohort design also ensured correct temporal
16 ordering and blinding with respect to the predictors. A theoretical model informed the PRM
17 and statistical selection was used to specify variables. Multiple imputation was used to assess
18 the impact of missing data. Bootstrapping showed good internal validity[48].
19
20
21
22

23 There are some limitations of this study to be considered. The main outcome, the BSRA, whilst
24 validated as a measure of school readiness, was developed in the US and is not routinely used
25 in the UK[23]. The BSRA measures a small set of pre-academic skills and as such is a limited
26 measure of child development, which can be defined as including broader behavioural and
27 social skills. However, an analysis of MCS data linked to teacher reports showed that Bracken
28 scores are strongly associated with the broader EYFS measure of school readiness used in
29 English schools[4]. The outcome variable was dichotomised to allow ROC curve analysis. We
30 acknowledge the limitations of dichotomising school readiness ethically, conceptually (e.g.
31 children develop at different rates) and statistically (i.e. loss of information) [49,50].
32 Longitudinal studies are subject to attrition and non-response which can introduce attrition bias,
33 the use of survey weights partially adjust for this, but it was not possible to use these when
34 calculating the AUROC. Sensitivity analysis using multiple imputation showed the effect of
35 missing data was negligible, similar to other PRMs[14,15]. Most of the predictor variables
36 were based on maternal self-report which may be subject to recall bias, and external validation
37 was not conducted. The predictor variables identified may not be causally associated with
38 school readiness and there are other predictors which may be associated with the outcome
39 which were not included in this model e.g. the home learning environment (which was not
40 assessed at 9 months in the MCS) and childcare in infancy[51].
41
42
43
44
45
46
47

48 **Policy Implications**

49 The existing literature, and these findings, indicate that a PRM could plausibly be used to
50 identify a group of children at high risk of poor ECD who may benefit from early intervention.
51 If implemented as part of a “proportionate universalism” approach[6], PRMs could mitigate
52 socioeconomic inequalities by providing early years settings with a mechanism for directing
53 their resources to those children at highest risk of poor cognitive development. With new child
54 and maternity datasets now being collected electronically in England, it may be possible to
55 apply a PRM at population level through the use of linked administrative datasets as has been
56 done in Australia[15].
57
58
59
60

Poor cognitive development is associated with a range of negative health and social outcomes and contributes to inequalities in society[3,5,6], so this is of public health importance. Chittleborough et al showed that even a model with poor discrimination has benefits over just using young maternal age to direct resources[14]. Similarly, McKean et al established that their PRM was better than existing clinical tools used to identify higher-risk children for early intervention[47].

The practical implications of using such a PRM as a screening tool should be considered. The model reported here would identify 31% of children screened as being ‘at risk’ of delayed school readiness. An exemplar English Local Authority with a total population of 230,000, and 3000 children aged under 1 year would identify 900 ‘at risk’ children per year if the PRM was applied to this cohort. This percentage equates with national data; in 2015/16, 31% of children in England were not school ready when tested at age 4-5[11]. However, the overall accuracy of the model is 74%, so over 200 children would be incorrectly classified. PRMs raise ethical issues; labelling very young children as being at risk of poor development could be stigmatising for families, particularly when social factors are the strongest predictors as in this analysis. PRMs would generate false positives (and false negatives), which could cause unnecessary distress and use of resources.

Use of PRMs to identify children at risk of developmental delay should include support and counselling for families, as well as timely access to appropriate interventions. Nelson et al (2016) comment that Early Intervention services would be overwhelmed by the level of demand generated by such PRMs[18]. A criterion for screening programmes is that interventions should be available, it is thus important to further consider the implications of using a PRM to assess ECD in the context of available resources. Investment in early intervention would be required, which would have opportunity costs for services locally. Further research is needed to test the external validity of this PRM for example in another cohort or with linked administrative datasets such as the EYFS data from English schools. Alternative modelling approaches which do not require a dichotomous outcome could also be tested. Findings from such models could offer more nuanced predictions on school readiness.

CONCLUSION

This study has identified a set of predictive risk factors from the perinatal period and early infancy that can predict school readiness at age 3 with a good level of accuracy. Poor cognitive development is socially patterned, evident from a very young age and leads to persistent disadvantage throughout life. It is possible that PRMs could be used to identify high risk children and target appropriate interventions and resources to improve their developmental trajectories, and to reduce social inequalities early in the life course.

STATEMENTS

Funding

1
2
3 This work was supported by the UK Public Health Research Consortium (PHRC). The PHRC is funded
4 by the Department of Health and Social Care Policy Research Programme. The views expressed in this
5 paper are those of the authors and do not necessarily reflect those of the Department of Health and
6 Social Care. Information about the wider programme of the PHRC is available from [http://phrc.
8 lshtm.ac.uk/](http://phrc.
7 lshtm.ac.uk/). DTR is funded by the MRC on a Clinician Scientist Fellowship
9 (MR/P008577/1).
10
11
12
13

14 **Competing Interests**

15
16 We confirm that authors have no conflicts of interest to disclose.
17
18
19

20 **Contributors**

21
22 CLC, JCD and DTR planned the study. CLC and VSS conducted the analysis under
23 the supervision of DTR. CLC led the drafting of the manuscript. All authors contributed
24 to data interpretation, manuscript drafting and revisions and agreed the submitted
25 version of the manuscript.
26
27
28
29
30
31

32 **Data Sharing**

33
34 The Millennium Cohort Study dataset is available from the UK Data Service.
35
36
37

38 Millennium Cohort Study: First Survey, 2001-2003: [http://doi.org/10.5255/UKDA-SN-
39 4683-4](http://doi.org/10.5255/UKDA-SN-4683-4)

40
41 Millennium Cohort Study: Second Survey, 2003-2005: [http://doi.org/10.5255/UKDA-
42 SN-5350-4](http://doi.org/10.5255/UKDA-SN-5350-4)
43
44
45

46 The Data Collection is available to Registered or Authorised Users.
47
48

49 **ACKNOWLEDGEMENTS**

50 We would like to acknowledge all the families and researchers who are part of the UK
51 Millennium Cohort Study, without whom this research would not have been possible.
52
53
54

55 **FIGURE CAPTIONS**

56 Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and
57 Whitehead, 1991)

58 Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

59 Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

REFERENCES

- 1 National Research Council (US) and Institute of Medicine (US) Committee on Integrating the Science of Early Childhood Development. *From Neurons to Neighborhoods: The Science of Early Childhood Development*. Washington (DC): : National Academies Press (US) 2000. <http://www.ncbi.nlm.nih.gov/books/NBK225557/>
- 2 Black MM, Walker SP, Fernald LC, *et al*. Early childhood development coming of age: science through the life course. *The Lancet* 2016.
- 3 Heckman JJ. Skill formation and the economics of investing in disadvantaged children. *Science* 2006;**312**:1900–2. doi:312/5782/1900 [pii]
- 4 Hobcraft JN, Kiernan KE. Predictive factors from age 3 and infancy for poor child outcomes at age 5 relating to children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010.
- 5 Caspi A, Houts RM, Belsky DW, *et al*. Childhood forecasting of a small segment of the population with large economic burden. *Nat Hum Behav* 2016;**1**:0005.
- 6 Marmot M, Allen J, Goldblatt P, *et al*. Fair society, healthy lives: strategic review of health inequalities in England post 2010. Marmot Review Team 2010.
- 7 Public Health England. Improving school readiness: creating a better start for London. London: 2015.
- 8 Pia Rebello Britto. School Readiness - A conceptual framework. New York, NY: UNICEF 2012.
- 9 Marmot M, Friel S, Bell R, *et al*. Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet* 2008;**372**:1661–9. doi:10.1016/S0140-6736(08)61690-6
- 10 Abreu L, Roberts N. Children’s early years development and school readiness. 2016. <https://researchbriefings.parliament.uk/ResearchBriefing/Summary/CDP-2016-0141> (accessed 30 Jan 2019).
- 11 Public Health England. Public Health Profiles. 2017.<https://fingertips.phe.org.uk/profile-group/child-health> (accessed 13 Jun 2017).
- 12 Early years foundation stage profile results: 2017 to 2018. GOV.UK. <https://www.gov.uk/government/statistics/early-years-foundation-stage-profile-results-2017-to-2018> (accessed 22 Jan 2019).
- 13 FPH, FNP. Family Nurse Partnership. Faculty of Public Health 20102015.
- 14 Chittleborough CR, Lawlor DA, Lynch JW. Young Maternal Age and Poor Child Development: Predictive Validity From a Birth Cohort. *Pediatrics* 2011;**127**:e1436–44. doi:10.1542/peds.2010-3222

- 15 Chittleborough CR, Searle AK, Smithers LG, *et al.* How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study. *Early Child Res Q* 2016;**35**:19–30.
- 16 Brownell MD, Ekuma O, Nickel NC, *et al.* A population-based analysis of factors that predict early language and cognitive development. *Early Child Res Q* 2016;**35**:6–18.
- 17 Camargo-Figuera FA, Barros AJ, Santos IS, *et al.* Early life determinants of low IQ at age 6 in children from the 2004 Pelotas Birth Cohort: a predictive approach. *BMC Pediatr* 2014;**14**:308. doi:10.1186/s12887-014-0308-1
- 18 Nelson BB, Dudovitz RN, Coker TR, *et al.* Predictors of Poor School Readiness in Children Without Developmental Delay at Age 2. *Pediatrics* 2016;**138**:e20154477. doi:10.1542/peds.2015-4477
- 19 Pepe MS, Janes H, Longton G, *et al.* Limitations of the Odds Ratio in Gauging the Performance of a Diagnostic, Prognostic, or Screening Marker. *Am J Epidemiol* 2004;**159**:882–90. doi:10.1093/aje/kwh101
- 20 Kirstine Hansen. Millennium Cohort Study First, Second, Third and Fourth Surveys. A Guide to the Datasets (Seventh Edition). London: : Centre for Longitudinal Studies 2012.
- 21 Connelly R, Platt L. Cohort Profile: UK Millennium Cohort Study (MCS). *Int J Epidemiol* 2014;**43**:1719–25. doi:10.1093/ije/dyu001
- 22 Bracken B. Bracken Basic Concept Scale–Revised. San Antonio, TX: : The Psychological Corporation 1998.
- 23 Panter JE, Bracken BA. Validity of the Bracken School Readiness Assessment for predicting first grade readiness. *Psychol Sch* 2009;**46**:397–409.
- 24 Connelly R. Millennium Cohort Study Data Note 2013/1: Interpreting Test Scores. London: : Centre for Longitudinal Studies, Institute of Education 2013.
- 25 Steyerberg E. *Clinical prediction models: a practical approach to development, validation, and updating.* Springer Science & Business Media 2008.
- 26 Kiernan KE, Mensah FK. Maternal indicators in pregnancy and children’s infancy that signal future outcomes for children’s development, behaviour and health: evidence from the Millennium Cohort Study. York: : University of York 2010.
- 27 Kiernan KE, Huerta MC. Economic deprivation, maternal depression, parenting and children’s cognitive and emotional development in early childhood. *Br J Sociol* 2008;**59**:783–806.
- 28 Shenkin SD, Starr JM, Deary IJ. Birth weight and cognitive ability in childhood: a systematic review. *Psychol Bull* 2004;**130**:989.
- 29 Jefferis BJMH, Power C, Hertzman C. Birth weight, childhood socioeconomic environment, and cognitive development in the 1958 British birth cohort study. *BMJ* 2002;**325**:305. doi:10.1136/bmj.325.7359.305

- 1
2
3 30 Kramer MS, Aboud F, Mironova E, *et al*. Breastfeeding and Child Cognitive
4 Development: New Evidence From a Large Randomized Trial. *Arch Gen Psychiatry*
5 2008;**65**:578–84. doi:10.1001/archpsyc.65.5.578
6
7
8 31 Walker SP, Wachs TD, Grantham-McGregor S, *et al*. Inequality in early childhood: risk
9 and protective factors for early child development. *The Lancet* 2011;**378**:1325–38.
10
11 32 Murray GK, Jones PB, Kuh D, *et al*. Infant developmental milestones and subsequent
12 cognitive function. *Ann Neurol* 2007;**62**:128–36. doi:10.1002/ana.21120
13
14 33 Kelly Y, Sacker A, Gray R, *et al*. Light drinking in pregnancy, a risk for behavioural
15 problems and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;**38**:129–40.
16 doi:10.1093/ije/dyn230
17
18 34 Dahlgren G, Whitehead M. Policies and strategies to promote social equity in health.
19 *Stockh Inst Future Stud* 1991.
20
21
22 35 Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development
23 of a self-report questionnaire instrument. *J Reprod Infant Psychol* 1998;**16**:57–76.
24
25 36 Sosthenes C. Ketende, Elizabeth M. Jones. User Guide to Analysing MCS Data Using
26 STATA. Centre for Longitudinal Studies, Institute of Education 2011.
27
28 37 Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per
29 variable in logistic regression analysis. *J Clin Epidemiol* 1996;**49**:1373–9.
30 doi:10.1016/S0895-4356(96)00236-3
31
32 38 Courvoisier DS, Combescure C, Agoritsas T, *et al*. Performance of logistic regression
33 modeling: beyond the number of events per variable, the role of data structure. *J Clin*
34 *Epidemiol* 2011;**64**:993–1000.
35
36 39 Azen R, Traxel N. Using Dominance Analysis to Determine Predictor Importance in
37 Logistic Regression. *J Educ Behav Stat* 2009;**34**:319–47.
38 doi:10.3102/1076998609332754
39
40 40 Pencina MJ, D'Agostino RB, Pencina KM, *et al*. Interpreting Incremental Value of
41 Markers Added to Risk Prediction Models. *Am J Epidemiol* 2012;**176**:473–81.
42 doi:10.1093/aje/kws207
43
44 41 Windmeijer FAG. The asymptotic distribution of the sum of weighted squared residuals
45 in binary choice models. *Stat Neerlandica* 1990;**44**:69–78.
46
47 42 Austin PC, Steyerberg EW. Events per variable (EPV) and the relative performance of
48 different strategies for estimating the out-of-sample validity of logistic regression models.
49 *Stat Methods Med Res* 2017;**26**:796–808.
50
51 43 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues
52 and guidance for practice. *Stat Med* 2011;**30**:377–99. doi:10.1002/sim.4067
53
54 44 Centre for Longitudinal Studies. MCS Ethical Review and Consent. London: Institute of
55 Education 2014.
56
57
58
59
60

- 1
2
3 45 Hosmer DW, Hjort NL. Goodness-of-fit processes for logistic regression: simulation
4 results. *Stat Med* 2002;**21**:2723–2738.
5
6
7 46 Wilkinson RG, Marmot M. *Social Determinants of Health: The Solid Facts*. World
8 Health Organization 2003.
9
10 47 McKean C, Law J, Mensah F, *et al*. Predicting Meaningful Differences in School-Entry
11 Language Skills from Child and Family Factors Measured at 12 months of Age. *Int J*
12 *Early Child* 2016;**48**:329–51. doi:10.1007/s13158-016-0174-0
13
14 48 Steyerberg EW, Harrell FE, Borsboom GJJM, *et al*. Internal validation of predictive
15 models. *J Clin Epidemiol* 2001;**54**:774–81. doi:10.1016/S0895-4356(01)00341-9
16
17 49 Senn S. Disappointing dichotomies. *Pharm Stat J Appl Stat Pharm Ind* 2003;**2**:239–240.
18
19 50 Altman DG, Royston P. The cost of dichotomising continuous variables. *BMJ*
20 2006;**332**:1080. doi:10.1136/bmj.332.7549.1080
21
22 51 Côté SM, Doyle O, Petitclerc A, *et al*. Child Care in Infancy and Cognitive Performance
23 Until Middle Childhood in the Millennium Cohort Study. *Child Dev* 2013;**84**:1191–208.
24 doi:10.1111/cdev.12049
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

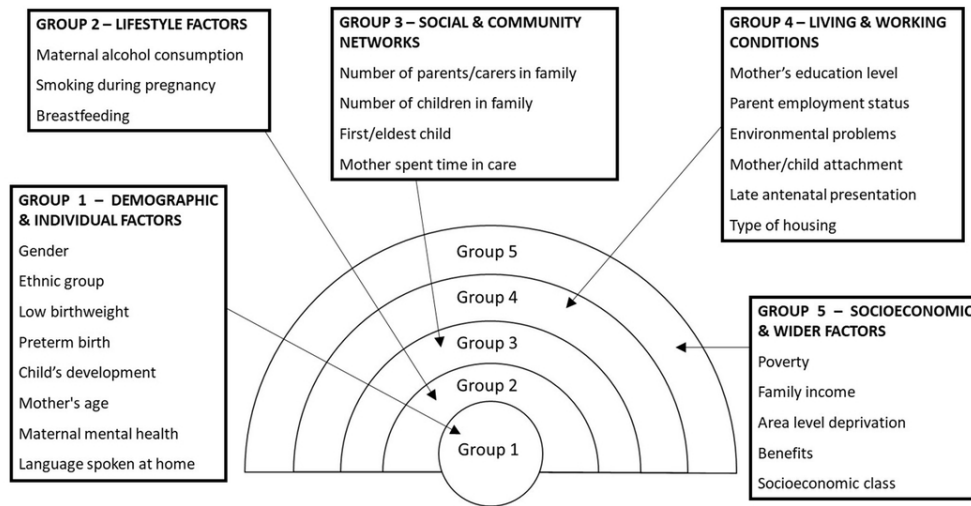
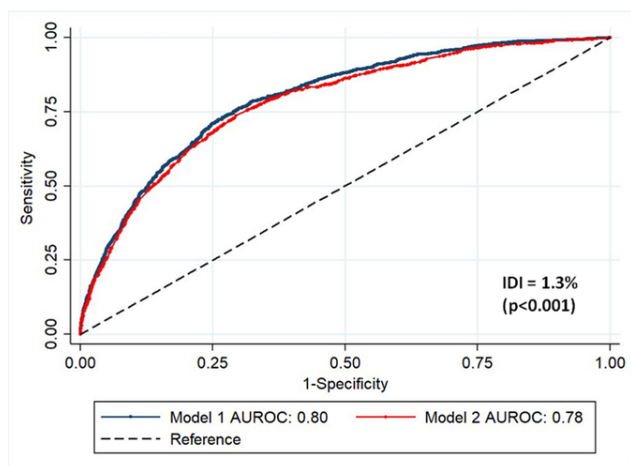


Figure 1 - Rainbow Model showing determinants of school readiness (adapted from Dahlgren and Whitehead, 1991)

90x50mm (300 x 300 DPI)



AUROC cut off points are: 0.9-1 = excellent, 0.8-0.9 = good, 0.7-0.8 = fair, 0.6-0.7 = poor, 0.5-0.6 = fail

Figure 2 - ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

90x50mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

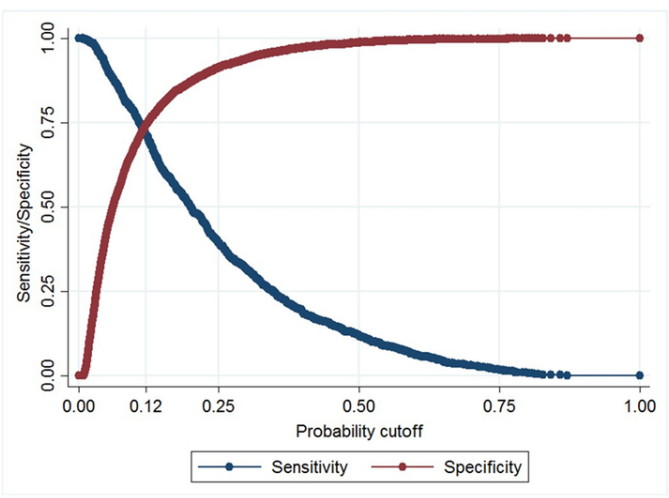


Figure 3 - Maximized probability cut off of sensitivity and specificity of model 1
90x50mm (300 x 300 DPI)

SUPPLEMENTARY FILE 1

Robustness tests were carried out in which the final model was tested with an alternative outcome measure for early cognitive development (British Ability Scales), different coding of variables and the addition of another predictor variable (child care type at age 9 months).

1. Using BAS as an alternative outcome variable

An alternative measure of early cognitive development contained in the MSC are the British Ability Scales (BAS), measured at age 3. BAS scores were dichotomised to 1 SD below the mean as cut off for 'fail'. There is a moderate positive correlation between BAS and BSRA scores ($r=0.5722$, $p<0.0001$). The table below compares performance of the models; there is a small but statistically significant improvement in discrimination using BSRA as an outcome measure compared to BAS.

Outcome variable	N	AUROC (95% CI)
BSRA	9487	0.80 (0.78,0.81)
BAS	9487	0.79 (0.77,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb6)$; $\text{chi}2(1) = 9.20$, $\text{Prob}>\text{chi}2 = 0.002$

2. Robustness tests of the BSRA outcome measure

The BSRA cut off used in the main analysis was a mean standardised composite score <85 , which is 1 standard deviation below the mean. The standardisation sample was from a US population. As the BSRA has not been validated in the UK, we tested the model using dichotomised percentile ranks instead of MSCS as the outcome variable (cut off point 1 SD below mean).

There was no significant difference in model performance (AUROC=0.80 for both models, $p=0.43$). There is evidence to suggest that within the Millennium Cohort Study percentile scores can be misleading in indicating the difference between the performance of cohort members because they are on an ordinal, rather than interval, scale. An outcome based on MSCS was therefore retained.

3. Coding of predictor variables

As a sensitivity analysis the coding of 4 predictor variables was altered: maternal age (from categorical to continuous), developmental scores (from categorical to continuous) and ethnicity (from categorical to binary). The impact of this on final model performance is shown below:

Description	n	AUROC	Comparative AUROC (n=9310)
Final model	9487	0.80	0.79 (0.77,0.81)
Developmental score (continuous)	9487	0.80	0.80 (0.78,0.81)
Maternal age (continuous)	9310	0.79	0.79 (0.78,0.81)
Ethnicity (binary)	9487	0.79	0.79 (0.78,0.80)

Ho: $\text{area}(xb1) = \text{area}(xb2) = \text{area}(xb3) = \text{area}(xb4)$; $\text{chi}2(3) = 9.98$; $\text{Prob}>\text{chi}2 = 0.02$

In summary, there were small but statistically significant differences between the models. The only change which improved model discrimination was using continuous development

1
2
3 scores, so this was incorporated into the final model. There is a U-shaped relationship
4 between school readiness and maternal age, so there was a clear rationale for including this
5 as a categorical predictor.
6
7

8
9 4. Testing the impact of an additional predictor

10 There are other measures in the MCS which could have been used as predictors in this
11 analysis. We have done a sensitivity analysis adding childcare type at 9 months to the final
12 model. This reduces the overall discrimination of the model (AUROC = 0.77 vs 0.80),
13 however this could be due to missing data as the child care variable is less complete. There
14 is a statistically significant association with school readiness and child care type in the
15 multivariable model, with children in formal child care settings more likely to be school
16 ready than those being looked after by parents (OR = 1.76, p=0.02)
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33

34 The Stata Do file for all analyses is available at:
35 <https://www.dropbox.com/s/zxsl4cl87imyp0/SchoolreadinessPRM.do?dl=0>
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SUPPLEMENTARY FILE 2

Table 1 - Adjusted associations for the predictor variables in model 1 (13 predictors) using multiple imputed data (n=11,879)

Predictor	Adjusted OR (95% CI)	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS		
Gender		
Female	1	8.5 (5)
Male	1.86 (1.62,2.14)	
Ethnicity		
White	1	15.7 (3)
Mixed	1.04 (0.62,1.75)	
Indian	2.68 (1.85,3.89)	
Pakistani and Bangladeshi	3.85 (2.94,5.04)	
Black or Black British	2.31 (1.43,3.72)	
Other ethnic group	3.95 (2.30,6.77)	
Mother's age at birth of first child		
30-39	1	1.5 (12)
40+	1.05 (0.67,1.64)	
20-29	1.22 (0.99,1.51)	
14-19	1.22 (0.93,1.59)	
Birth weight (<2500grams)		
Normal/high	1	1.2 (13)
Low birthweight	1.52 (1.18,1.97)	
Maternal Mental Health (Diagnosed depression/anxiety)		
No	1	1.5 (11)
Yes	1.15 (0.98,1.34)	
Child developmental milestones		
Developmental score	1.10 (1.07,1.13)	2.8 (10)
GROUP 2 - LIFESTYLE FACTORS		
Duration of breastfeeding		
6 months or more	1	3.6 (9)
6 weeks - 6 months	1.17 (0.92,1.48)	
One week or less	1.15 (0.90,1.48)	
1 - 6 weeks	1.22 (0.96,1.57)	
Never	1.58 (1.29,1.95)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS		
Number of children in family		
One child	1	7.1 (6)
Two or three children	1.40 (1.19,1.63)	
Four or more children	2.48 (1.94,3.16)	
GROUP 4 - LIVING & WORKING CONDITIONS		
Maternal education		
Degree plus	1	16.7 (2)

Diploma	0.88 (0.61,1.26)	
A levels	1.13 (0.80,1.59)	
GCSE A-C	1.34 (1.01,1.78)	
GCSE D-G	1.72 (1.23,2.39)	
None	1.74 (1.28,2.38)	
Workforce status		
Both parents in work	1	
One parent in work	0.94 (0.78,1.12)	6.5 (7)
Neither parent in work	1.21 (0.93,1.57)	
Housing tenure		
Owner occupied	1	
Private rented	1.18 (0.90,1.54)	5.5 (8)
Social housing	1.43 (1.18,1.72)	
Other	0.96 (0.69,1.35)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS		
Social class		
Managerial & professional	1	
Intermediate	0.98 (0.75,1.29)	
Small employers & own account	1.32 (0.87,2.00)	17.6 (1)
Lower supervisory & technical	1.50 (1.06,2.13)	
Semi-routine & routine	1.77 (1.38,2.27)	
Never worked & long-term unemployed	2.19 (1.53,3.15)	
Annual income		
£33,000+	1	
£22,000-£33,000	1.33 (1.02,1.72)	11.9 (4)
£11,000-£22,000	1.67 (1.30,2.14)	
£0-£11,000	2.14 (1.60,2.87)	
ROC Analysis	AUROC = 0.79 (95% CI 0.78,0.80)	

SUPPLEMENTARY FILE 3

Integrated discrimination improvement (IDI) analysis was run using Stata function 'idi', which compares the discrimination ability between two logistic regression prediction models. In the first stage of this analysis, the IDI of a PRM with just the strongest predictor variable (social class) was compared to a model with all 13 predictors. Adding the additional 12 predictors lead to a 7.3% increase in IDI. In each subsequent analysis, an additional predictor variable was added according to the ranking of variables from the dominance analysis (Table 1).

Predictor	Weighting	Rank
Social Class	17.38	1
Ethnic group	14.66	2
Maternal education	13.55	3
Income band	12	4
Gender	9.54	5
Number of children	7.84	6
Parent's employment	6.9	7
Housing type	5.65	8
Child development	3.9	9
Breastfeeding	3.9	10
Mother's age at birth of first child	2.87	11
Low birth weight	1.42	12
Mental health	0.38	13

Table 1 - Results of the dominance analysis for model 1

The full results of integrated discrimination improvement (IDI) analysis are shown in Table 2.

Variables included	IDI (%)	p	1-IDI
1	7.3%	<0.00001	92.7%
2	5.3%	<0.00001	94.7%
3	3.8%	<0.00001	96.2%
4	3.5%	<0.00001	96.5%
5	2.3%	<0.00001	97.7%
6	1.3%	<0.00001	98.7%
7	1.0%	<0.00001	99.0%
8	0.9%	<0.00001	99.1%
9	0.6%	0.00001	99.4%
10	0.6%	0.00001	99.4%
11	0.2%	0.01402	99.8%
12	0.0%	0.52356	100.0%

Table 2 - Results of integrated discrimination improvement analysis for 12 models

A 6-predictor model was chosen as this offered the optimal balance between parsimony and discrimination.

1
2
3 **SUPPLEMENTARY FILE 4**
4
5

6 Table 1 - Adjusted associations for the predictor variables in model 2 (6 predictors) using
7 complete cases (n=11,146) and multiple imputed data (n=11,879). The weightings and rank are
8 from dominance analysis of the complete case sample.
9

10
11
12
13
14

Predictors	Adjusted OR (95% CI) - complete case	Adjusted OR (95% CI) - multiple imputation	Weighting (rank)
GROUP 1 - DEMOGRAPHIC & INDIVIDUAL FACTORS			
Gender			
Female	1	1	9.9 (5)
Male	1.99 (1.72,2.31)	1.93 (1.68,2.22)	
Ethnicity			
White	1	1	13.7 (4)
Mixed	1.2 (0.77,1.88)	1.26 (0.83,1.90)	
Indian	1.64 (1.09,2.47)	1.72 (1.14,2.59)	
Pakistani and Bangladeshi	2.67 (2.10,3.41)	2.71 (2.11,3.47)	
Black or Black British	2.32 (1.52,3.54)	2.69 (1.80,4.02)	
Other ethnic group	1.98 (1.10,3.58)	2.06 (1.27,3.32)	
GROUP 3 - SOCIAL & COMMUNITY NETWORKS			
Number of children in family			
One child	1	1	9.5 (6)
Two or three children	1.48 (1.27,1.73)	1.45 (1.25,1.69)	
Four or more children	2.89 (2.23,3.75)	2.62 (2.03,3.38)	
GROUP 4 - LIVING & WORKING CONDITIONS			
Maternal education			
Degree plus	1	1	20.5 (3)
Diploma	0.87 (0.58,1.29)	0.88 (0.60,1.28)	
A levels	1.05 (0.72,1.53)	1.06 (0.74,1.52)	
GCSE A-C	1.43 (1.02,1.99)	1.55 (1.14,2.12)	
GCSE D-G	1.78 (1.23,2.58)	2.14 (1.51,3.03)	
None	2.01 (1.44,2.81)	2.42 (1.77,3.30)	
GROUP 5 - SOCIOECONOMIC AND WIDER FACTORS			
Social class			
Managerial & professional	1	1	26.0 (1)
Intermediate	1.17 (0.88,1.55)	1.14 (0.86,1.51)	
Small employers & own account	1.44 (0.91,2.28)	1.52 (0.99,2.33)	
Lower supervisory & technical	2.01 (1.42,2.86)	1.92 (1.37,2.68)	
Semi-routine & routine	2.41 (1.86,3.12)	2.16 (1.68,2.78)	
Never worked & long-term unemployed	3.34 (2.41,4.63)	2.95 (2.14,4.07)	
Annual income			
£33,000+	1	1	20.6 (2)
£22,000-£33,000	1.33 (0.97,1.81)	2.65 (2.01,3.50)	
£11,000-£22,000	1.88 (1.42,2.50)	1.75 (1.32,2.31)	
£0-£11,000	2.98 (2.26,3.92)	1.29 (0.95,1.75)	

15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ROC Analysis	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,146	AUROC = 0.78 (95% CI 0.77 - 0.79) n=11,879
---------------------	---	---

For peer review only

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	3
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	3
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	3-4
	5b	Describe eligibility criteria for participants.	4
	5c	Give details of treatments received, if relevant.	
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4
	6b	Report any actions to blind assessment of the outcome to be predicted.	
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors. <small>temporal ordering in cohort</small>	
Sample size	8	Explain how the study size was arrived at.	5
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	5-6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	6
Risk groups	11	Provide details on how risk groups were created, if done.	
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6-7
Model development	14a	Specify the number of participants and outcome events in each analysis.	10
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	8-10
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	
	15b	Explain how to use the prediction model.	
Model performance	16	Report performance measures (with CIs) for the prediction model.	10
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11-12
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11-13
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	
Funding	22	Give the source of funding and the role of the funders for the present study.	

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.