Public Health Research Consortium

Addressing child health inequalities:

How best can we exploit child health data collected in the early years?

REVISED FINAL REPORT

19th September 2019

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The work was undertaken by the authors as part of the Public Health Research Consortium. The Public Health Research Consortium is funded by the Department of Health and Social Care Policy Research Programme. The views expressed in the publication are those of the authors and not necessarily those of the Department of Health and Social Care. Information about the wider programme of the PHRC is available from www.phrc.lshtm.ac.uk

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ACKNOWLEDGEMENTS

The authors are grateful to the Centre for Longitudinal Studies (CLS), University of Liverpool for the use of these data and to the UK Data Service for making them available. However, neither CLS nor the UK Data Service bear any responsibility for the analysis or interpretation of these data

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What this study adds:

- Health inequalities have their origins in early childhood and the development of population linked datasets that track the health of all children from birth provide the opportunity to inform policies to reduce health inequalities.
- Using longitudinal data from a contemporary cohort (the Millennium Cohort Study), we focused on the main child health and development outcomes (overweight/obesity, socio-emotional problem behaviour, school readiness and cognitive performance), identifying the predictive capacity and the different causal pathways linking early risk factors from 9 months to 5 years, and the outcomes. We found that a set of predictive risk factors from the perinatal period and early infancy had a good prediction of a measure of early child development age 3; and that language disability, socioemotional behavioural problems and overweight/obesity at age 11 can also be predicted with moderate discrimination using data routinely collected in the first 3 years of life.
- Regarding the causal pathways between early risk factors to health and development outcomes, the increased risk of socioemotional behavioural problems, poor cognitive performance and being overweight/obese in adolescents growing up in disadvantaged socio-economic conditions (SECs) is partly explained by exposure to early adverse experiences. These findings stimulated us to further explore which factors would indeed explain social inequalities in one of the most emerging health concerns among children in the UK, which is socio-emotional problem behaviour (i.e. mental health). We showed that around two-thirds of the social inequality in adolescent mental health is explained by risk factors in the early years, such as perinatal and maternal mental health factors.

Abstract

Introduction

Age 2 – 3 years is a crucial development stage when problems with speech, behaviour, and child development become visible, yet there is time to intervene to make a difference. In England the roll-out of the integrated 2.5-year-old health check provides the opportunity to use data collected in the early years to predict which children may have health difficulties in later childhood; and to understand how early life factors and so called "adverse childhood experiences" (ACEs) might lead to subsequent inequalities in health outcomes.

Methods

Longitudinal analysis using nationally representative contemporary data (Millennium Cohort Study), and datasets with more detailed information on early child development (e.g. the MRC Wirral Child Development Study - WCHADS). Predictive risk models were used to explore the relationship between measures collected in early childhood, and a range of subsequent health and development outcomes up to the age of 11/14 years (depending on data availability). Then causal mediation methods were used to understand which early childhood factors mediate inequalities in subsequent child health outcomes, with a particular focus on the mediating role of ACEs.

Results

In the predictive risk models (PRMs) we found that language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 years are common health problems that can be predicted with moderate discrimination using data routinely collected in England in the first 3 years of life. In addition, perinatal and infant risk factors collected at around the time of birth can be used as good predictors of measures of early child development such as school readiness at age three. Using causal mediation analyses we found that ACEs experienced by age five years explained about one sixth of the social inequality in risk of behavioural problems, cognitive disability and overweight/obesity in U.K. adolescents. By contrast we found that around two-thirds of the social inequality in adolescent mental health is explained by a broader range of early years risk factors identified by the age of 3 years relating to perinatal; individual child; family; peer relation; and neighbourhood level factors.

Discussion

New child health datasets being developed in England have the potential to be used to predict which children are more likely to develop poor health outcomes in later childhood. In terms of explaining health inequalities in later childhood, the contribution of ACEs was relatively small, whereas a broader range of early life risk factors, particularly related to the perinatal period, appear important in explaining subsequent inequalities in child mental health.

Executive Summary

Background/Introduction

Health inequalities have their origins in early childhood and the development of new population linked datasets that track the health of all children from birth provide the opportunity to inform policies to reduce health inequalities[1]. In England, for example, the roll-out of the integrated 2.5-year-old health check[2,] in 2015 means that routinely data collected during pregnancy and in the early years could be used to predict which children may develop health difficulties in later childhood[3]. To do this, however, it is necessary to understand how well variables collected in early childhood might predict important subsequent child health outcomes. In addition, the concept of "adverse childhood experiences" (ACEs) has recently gained popularity, but it is unclear how early exposure to ACEs predicts inequalities in later child health outcomes; and what other early years exposures may also be important[4].

Aims

The overarching research aim of our project was to determine how researchers can best exploit data collected in pregnancy and the early years, with a focus on the new Integrated Review, to improve child health and reduce inequalities.

The project comprised four main objectives:

1.To review how early years childhood data have been used in other settings to predict subsequent child health outcomes.

2.To use existing longitudinal datasets to assess the predictive value of routinely collected child health and development measures collected in pregnancy and up to age 2-3 years.

3.To identify the social patterning of ACEs and analyse the extent to which ACEs and other early years factors explain the association of SECs and adolescent health outcomes.

4. To draw out the policy and practice implications of 1-3

Methods

The project addressed the broad aim and our objectives with the four main empirical analyses presented in this report. To address objective 1, we examined the policy context for the new data collection for children in the UK and reviewed the international literature on risk prediction to identify the most promising approaches. Objective 2 was addressed by conducting longitudinal analyses of nationally representative contemporary data (Millennium Cohort Study), two of which used predictive risk models (PRMs). In these we explored the predictive value of data collected in early childhood for three exemplar outcomes: overweight/obesity, limiting long-standing illness and child socio-emotional problem behaviour (age 11 years old; the latest MCS sweep available when performing the data analysis). We then used similar approaches to understand how data collected around the time of birth in maternity datasets could be used to predict early child development measured by school readiness at age three years. Objective 3 was addressed by studies undertaking causal mediation analyses applied to Millennium Cohort Study data to understand which early childhood factors mediate social inequalities in important subsequent child health outcomes (age 14 years old), with a particular focus on the mediating role of ACEs as currently conceptualised. Finally, objective 4 was addressed by pulling together policy and practice recommendations that follow from our empirical studies.

Key findings and conclusions

<u>Policy context and review of previous predictive models in childhood</u>

The antenatal period and first 2 or 3 years are crucial stages that influence children's subsequent development and health outcomes. By age 3 years, many physical, cognitive and emotional development problems are apparent, but there remain opportunities to intervene to improve child outcomes[5]. There is increasing recognition of the need to collect better early years' data to identify children most at risk early, in order to facilitate more appropriate referral to services and early intervention programmes. Accordingly, the National Health Service (NHS) in England has been developing an improved national maternity services dataset, to collate routinely collected sociodemographic and perinatal information[6]. In addition, in 2015, a new 'integrated universal health check' was introduced for children aged between 2 and 3 years in England to provide a more complete picture of children's health and development[7].

A central challenge in using these new datasets is to accurately identify children most in need of additional support to achieve their greater long-term health and developmental potential and then to decide the most appropriate combination of universal and targeted service[8]. Predictive risk models (PRMs), used widely for applications such as cardiovascular risk prediction, have not been extensively assessed to inform child public health interventions. A few previous studies have investigated this and have suggested the utility of using data collected at birth to predict poor child health outcomes. One study using a UK cohort showed that maternal age was a poor predictor of child health and development up to age 5 and that prediction was improved by including data on mother's smoking status during pregnancy, education level, mental health and financial status[9]. An Australian study using linked early childhood data to identify children with poor development at school entry showed that a model with six perinatal predictors (maternal age, smoking, parity, marital status and both parents' occupation) demonstrated similar discrimination to a model including 22 predictors, predicting developmental vulnerability[10]. A Brazilian study using the 2004 Pelotas Birth Cohort looked at IQ at age 6 and the final model included 12 predictor variables from the first year of life, which had good predictive discrimination[11]. A summary of the literature identified in this field can be found in study 1 and Appendix 1 of this document.

Recently the concept of "adverse childhood experiences" (ACEs) has gained popularity as a way of framing the public health implications of childhood harmful experiences[12]. These experiences typically include abuse, neglect, and indicators of possible household dysfunction affecting children (parental mental health problems, including alcohol and drug abuse). Increasingly, however, the concept has been expanded by some commentators to include other factors including social and economic dimensions such as family instability and parental separation, low parental education, child poverty, parental unemployment, and lone parenthood[12]. Various adverse childhood exposures and risk conditions captured in the first few years of life in datasets in the UK have been labelled as ACEs and have been associated with poor subsequent health outcomes. However, there is currently a lack of understanding of how adverse socio-economic conditions structure the risk and consequences of ACEs[4]. Furthermore, there has been some conflation of directly harmful exposures, such as child abuse, and the broader concept of adverse childhood socioeconomic conditions (SECs). It is therefore important to develop a more causally informed understanding of how disadvantaged childhood SECs structure the subsequent risk of experiencing ACEs, and the impact this has on health outcomes, in order to develop appropriate public health policies.

<u>Secondary analyses of longitudinal datasets</u>

Study 1: How well can poor child health and development be predicted by data collected in early childhood?

These analyses showed that language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 can be predicted with moderate discrimination using data routinely collected in England up to the age of 2-3 years, making use of the new maternity dataset and the data collected in the new Integrated review. Addition of further variables, identified in the

literature that mostly are not routinely collect in health services, adds very little to discriminatory capacity.

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

This analysis identified a set of predictive risk factors from the perinatal period and early infancy that can predict early child development as measured by school readiness at age 3 with a good level of accuracy. The analysis found the most important variables in predicting school readiness related to socioeconomic conditions (social class, maternal education, family income) and ethnicity. A model using just six variables from the perinatal period and early infancy performed similarly well suggesting it is possible to predict school readiness at age 3 using data collected at birth.

Study 3: How do adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

About a sixth of the increased risk of socioemotional behavioural problems, poor cognitive performance and being overweight/obese in adolescents growing up in disadvantaged SECs in the UK was explained by exposure to ACEs. Preventing ACEs in the early years is likely to reduce inequalities in important child health outcomes.

Study 4: How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study?

Using nationally representative data we show that around 1 in 10 young people have mental health problems by age 14 in the UK. There were stark social inequalities whereby the risk of mental health problems was around four times higher for children growing up in adverse SECs compared to highest SECs. Around two-thirds of this increased risk was explained by early years risk factors identified by the age of 3 years, related to perinatal, child, family, peer relations and neighbourhood characteristics.

<u>Research, policy and practice recommendations</u>

How well can poor child health and development be predicted by data collected in early childhood?

- New child health datasets have been developed for the whole population of children in England, and our analysis shows that language disability, socioemotional behavioural problems and overweight/obesity in English children aged 11 years can be predicted with moderate discrimination using these data.
- While many of the variables used in our analysis should be available in routine data, other variables such as breastfeeding status and early measures of maternal mental health are more difficult to capture and may be of relatively poor quality in routine data collection systems.
- Further research is needed to identify what could increase the predictive power of these models at these and other ages in population-based databases. In addition, assessments are needed of how the dynamics of predictive algorithm models can be used in health services to identify children more likely to benefit from additional early years support.
- Furthermore, we require a better understanding of how predictive risk modelling tools could be used in the context of specific child health systems, for instance, in the UK, what proportion of children would go on to receive specialist intervention? What proportion of those would benefit from this and what would be the magnitude of any benefits?

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

- The existing literature, and our findings, indicate that predictive risk models could plausibly be used to identify a group of children in England at high risk of poor early child development who may benefit from early intervention. If implemented as part of a “proportionate universalism” approach PRMs could mitigate socioeconomic inequalities by providing early years settings

with a mechanism for directing their resources to those children at highest risk of poor cognitive development. With new child and maternity datasets now being collected electronically in England, it may be possible to apply a PRM at population level through the use of linked administrative datasets as has been done in Australia.

- Further research is needed to test the external validity of predictive risk models for early child development, for example in another cohort or with linked administrative datasets. 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. 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. Investment in early intervention would be required, which would have opportunity costs for services locally.

How do adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

- The increased risk of socioemotional behavioural problems, poor cognitive performance and being overweight/obese in adolescents growing up in disadvantaged SECs in the UK is partly explained by exposure to ACEs.
- Our analysis supports our previous contention that conflating concepts relating to social circumstances with ACEs is conceptually confusing and may lead to the importance of SEC.
- A policy focus on preventing ACEs is likely to reduce inequalities in important child health outcomes.
- From a policy perspective it is important to separate modifiable childhood SECs from specific harmful exposures.
- Efforts to improve child health outcomes should focus on universal primary prevention of childhood adversities and early identification and appropriate interventions to reduce subsequent modifiable harms.
- In parallel actions on the social determinants of health and other important mediators of child health inequalities such as perinatal risk factors are necessary to reduce modifiable socioeconomic inequalities.

How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study?

- We found that nine percent of children had mental health problems by age 14 in a nationally representative UK child cohort. The risk was much greater in disadvantaged children, and about two thirds of this excess risk was explained by early childhood factors up to age 3 years.
- Future research should investigate specific pathways, critical/sensitive periods for these exposures, and other countries with different socioeconomic context.
  Efforts to reduce inequalities in adolescents mental health problems should focus on reducing socioeconomic inequalities and action to address the early years mediators identified in our study, particularly on perinatal factors and family factors such as maternal mental health problems.
  From a public health policy perspective, our results support the need for an early years prevention focus to ensure a safe and healthy pregnancy, a nurturing childhood and support for families in providing such circumstances in which to bring up children. In the UK it is concerning that funding for early years provision has been disproportionately cut in some of the most disadvantaged areas; and that child poverty - a major socio-economic determinant of child mental health - is currently increasing.

1 Introduction/Background

Childhood disadvantage has significant human costs. There is a large body of evidence demonstrating that early disadvantage tracks forward, to influence health and development in later life. The economic costs of health inequalities, which have their origins in childhood, are staggering[12, 13]. Improving child health and reducing health inequalities early are thus priorities at local, national and international levels. There is a clear need for public policy to shift investment to the early years of children's lives, and to invest in interventions for which there is good evidence of its effectiveness[3].

But the current data systems available to inform population level interventions to support children are not fit for purpose[7]. A key priority is to collect better data and link data on children in the early years across organisations. This will allow better identification of children who could benefit from early intervention and help to track changes over time. Furthermore, longitudinal datasets would facilitate evaluation of services and policies for their effects on early measures of disadvantage that predict subsequent health and social outcomes.

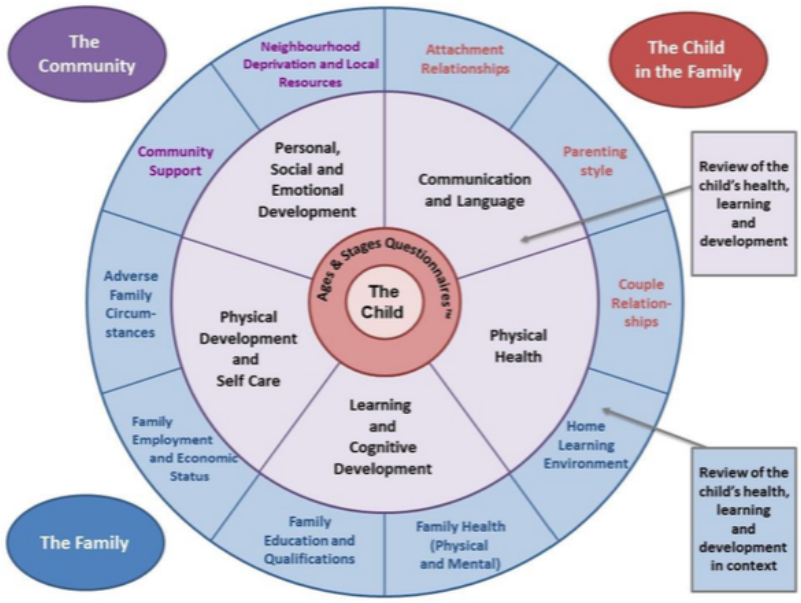
Age 2-3 years is a crucial stage when problems with physical, cognitive and emotional development become visible, yet when there is still time to intervene to make a difference both for individuals and populations. By this age, marked inequalities in child health and development are apparent[1]. In recognition of this, in September 2015, the Government started the implementation of an "Integrated Review" that combines the Healthy Child Programme review (2 1/2-year check) carried out by Health Visitors, and the Early Years Foundation Stage progress check that is completed in a nursery or childcare setting (between 2-3 years)[2,7].

The Healthy Child Programme (HCP) is the universal public health programme for all children and families. It consists of a schedule of reviews, immunisations, health promotion, parenting support and screening tests that promote and protect the health and wellbeing of children from pregnancy through to adulthood. The health, wellbeing and development of the child at age two has been identified as one of the six high impact areas where health visitors can have a significant impact on health and wellbeing and improving outcomes for children, families and communities. The HCP Review is health focused incorporating aspects of child development, including social and emotional wellbeing6[7].

The Early Years Foundation Stage (EYFS) progress check at age two is the statutory framework setting the standards for all early years providers for learning, development and care for children from birth to age five. The EYFS Progress Check at age two is a statutory point of assessment within this framework. To carry out the EYFS Progress Check at age two, early years practitioners must review a child's progress when they are aged between 24 and 36 months and provide parents with a short-written summary of their child's development in the prime areas: Personal, Social and Emotional Development, Communication and Language and Physical Development[14].

The new Integrated Review draws upon the content of both reviews. In practice this may mean that data from the EYFS and HCP reviews are collected separately and combined at a later stage. There has been also developed a new child health population measure to be collected utilising the Ages and Stages Questionnaire (ASQ; see figure 1.)[15, 16]. The ASQ[15] are completed by parents, either at home in advance of the review or with the support of the early years setting. The ASQ can also be completed in conjunction with health visitors during the review, and cover five domains of development: Communication, Gross Motor, Fine Motor, Problem Solving and Personal-Social development.

Figure 1. Integrated Review assessment coverage (source NCB 2015)



The stated purpose of the Integrated Review is to:

1. Identify the child's progress, strengths and needs at this age in order to promote positive outcomes in health and wellbeing, learning and behaviour.

2. Facilitate appropriate intervention and support for children and their families, especially those for whom progress is less than expected.

3. Generate information which can be used to plan services and contribute to the reduction of inequalities in children's outcomes.

Integrating the health and education reviews has the potential to give a more complete picture of the child by drawing together the parents' views and concerns about their child's progress, the early years practitioner's detailed knowledge of how the child is learning and developing, based on day-to-day observation in their early years setting, and the health visitor's expertise in the health and development of young children[8]. This data could be used to identify children who would benefit from early intervention. Furthermore, if used creatively, it could also provide an opportunity to assess the effects of current policies and inform intervention strategies to improve health and reduce inequalities.

On the other hand, there are several possible pitfalls. There is the risk that the most vulnerable children may miss out on assessment, and that the review process takes up time and resource but adds little to the understanding of population or individual needs. Indeed, there is a tension as to how the results of the review will be used to fulfil contrasting requirements at the individual and population level. The purpose is both to identify children at risk, and to provide appropriate referral and signposting, as well as to inform population health needs. But there is a risk that the review may drift into use as a screening tool at local levels, without fulfilling the necessary criteria[15]. Poor predictive value of data collected in the integrated review is of concern if it leads to inappropriate referral, wasted resources and potential harm in terms of parental anxiety. At the same time, it is unethical to assess a child, identify a potential problem requiring further investigation or intervention and yet not act on that information.

Considering these issues, this project tried to understand what data collected in early childhood can and can't be used for. But before the dataset can be exploited for the intended purposes, analyses are required to better understand the predictive value of the full range of child development indicators collected in the Integrated Review at age 2-3 years for later inequalities in health and development. Sophisticated and reliable prediction models have been applied to cardiovascular disease over the last decade, but these approaches have not often been used to identify characteristics (e.g., maternal, partner, child and community) that accurately identify those children most at risk for poorer developmental outcomes in the future[4, 8, 9].

The Integrated Review was introduced against a background of important developments in policy and services for children in this age range:

- Transfer of public health commissioning duties to local authorities
- The Health Visitor Implementation Programme
- Expansion of entitlement to free early education for two-year-olds
- Development of a public health population measure for children aged two to two-and-a-half
- Considerations of the role of children's centres in delivering the early years agenda

This is within a context where children in the UK have poor health compared to other Western European countries[17], and there are large inequalities in life chances. This is a critical moment for children and families in the UK, facing changes to preventative services in the community at the same time as levels of child poverty increasing. Important changes include the transfer of public health commissioning duties to local authorities; the Health Visitor Implementation Programme; the expansion of entitlement to free early education for two-year-olds; and the impact of cut backs to the role of children's centres in delivering the early years agenda[12, 17].

The Government's Integrated Review has been implemented to capture a snapshot of population child health and development at age 2-3 in England, combining data from the Early Years Foundation Stage Progress Check and the Healthy Child Programme health and development review[14-17]. A key step to improving child health and reducing inequalities is to establish data systems that can track longitudinal child health and development trajectories for whole populations. The analyses undertaken in this project help clarify the utility of using population level data on early child development to predict health and social problems in later childhood.

This project builds links to the PHRC project "How does educational achievement impact on health and health inequalities? An analysis of trajectories to inform policy options and development" headed by Professor Russell Viner.

2 Project Aims/ Objectives

The overarching research aim of our project was to determine how researchers can best exploit data collected in pregnancy and the early years, with a focus on the new Integrated Review, to improve child health and reduce inequalities.

The project comprised four main objectives:

1.To review how early years childhood data have been used in other settings to predict subsequent child health outcomes.

2.To use existing longitudinal datasets to assess the predictive value of routinely collected child health and development measures collected in pregnancy and up to age 2-3 years.

3. To identify the social patterning of ACEs and analyse the extent to which ACEs and other early years factors explain the association of SECs and adolescent health outcomes.

4. To draw out the policy and practice implications of 1-3

3 Design/Methods

The project addressed the broad aim and our objectives with the four main empirical analyses presented in this report.

To address objective 1, we examined the policy context for the new data collection for children in the UK and reviewed the international literature on risk prediction to identify the most promising approaches.

Objective 2 was addressed by conducting longitudinal analyses of nationally representative contemporary data (Millennium Cohort Study), two of which used predictive risk models. In these analyses we explored the predictive value of data collected in early childhood for three exemplar outcomes: overweight/obesity, limiting long-standing illness and child socio-emotional problem behaviour. We then used similar approaches to understand how data collected around the time of birth in maternity datasets could be used to predict early child development measured by school readiness at age three years.

Objective 3 was addressed by studies undertaking causal mediation analyses applied to Millennium Cohort Study data to understand which early childhood factors mediate social inequalities in important subsequent child health outcomes, with a particular focus on the mediating role of ACEs as currently conceptualised.

Finally, objective 4 was addressed by pulling together policy and practice recommendations that follow from our empirical studies.

Data

This project used the Millennium Cohort Study (MCS): a nationally representative large-scale longitudinal survey of babies born in the year 2000. Accurate estimates are provided for the prevalence of health damaging risk factors experienced in the early years of life for roughly 19,000 children in the UK. Data has been collected for children at 9 months, 3, 5, 7, 11 and 14 years of age. The MCS contains information on children's physical development, language development, physical and mental health, communication and cognitive development, using a mixture of validated measures, for example the strengths and difficulties questionnaire, and individual questions asked of parents which can be mapped against the domains in the integrated review (figure 1). For example, if we take the

"communications and language" domain the MCS collects data on whether parents can understand their child when they speak, if their child can understand family and friends and respond, and if they have concerns about their child's language development. For the studies presented in this project, we utilised data from the preschool years (sweep 1, 2 and 3) and school years (sweep 5 and 6).

General statistical approach

To assess the predictive value of particular combinations of risk factors we conducted regression analyses to determine how measures collected up to 2-3 years predict outcome classification at later time points (16). Fitted regression models were used to calculate the fitted probabilities, and then outcomes were classified as positive based upon particular cut-off values. For a cut-off and set of variables, we compared the sensitivity and specificity, and ROC curves. The area under the ROC curve (AUC) was then calculated to provide a measure of the discrimination ability of the model.

Adverse childhood experiences (ACEs) were identified based on previous literature and available at sweep 1 and 2 in the MCS (for example, verbal and physical maltreatment; parental drug use; maternal domestic violence, parental divorce, maternal mental illness, and alcohol abuse). We explored the social patterning of ACEs individually and in combination and used counterfactual mediation analysis to estimate the total effect of SECs on odds of health problems at age 14. We identified in the literature the main risk factors up to age 5 years old (sweep 1, 2 and 3) for mental health problems in the adolescence. Then we also estimated the counterfactual effect mediated through such factors on social inequalities in adolescent mental health at age 14.

4 Main Findings

This section includes the four main outputs of this project. There are two manuscripts aiming to assess the utility of data collected in the early years for risk prediction of later health and developmental outcomes. The other two manuscripts explored the extent to which early factors, in particularly adverse childhood experience, mediate social inequalities in health outcomes in the adolescence.

Paper 1. Straatmann VS, et al. (2018). How well can poor child health and development be predicted by data collected in early childhood? J Epidemiol Community Health; 72:1132–1140. doi:10.1136/jech-2018-211028.

Paper 2. Camacho CL, et al. (2019). Development of a Predictive Risk Model for School Readiness at age 3 years using the UK Millennium Cohort Study. BMJ Open, 9: e024851.

Paper 3. Straatmann VS, et al. (2019). How do early adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK? – Under review

Paper 4. Straatmann VS, et al. (2019). How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study? J Epidemiol Community Health; 0:1–12.

4.1 How well can poor child health and development be predicted by data collected in early childhood?

How well can poor child health and development be predicted by data collected in early childhood?

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Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/ jech-2018-211028).

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Abstract

Background Identifying children at risk of poor developmental outcomes remains a challenge but is important for better targeting children who may benefit from additional support. We explored whether data routinely collected in early life predict which children will have language disability, overweight/obesity or behavioural problems in later childhood. Methods We used data on 10262 children from the UK Millennium Cohort Study (MCS) collected at 9 months, 3, and 11 years old. Outcomes assessed at age 11 years were language disability, overweight/obesity and socioemotional behavioural problems. We compared the discriminatory capacity of three models: (1) using data currently routinely collected around the time of birth; (2) Model 1 with additional data routinely collected at 3 years; (3) a statistically selected model developed using a larger set of early year's risk factors for later child health outcomes, available in the MCS—but not all routinely collected. Results At age 11, 6.7% of children had language disability, 26.9% overweight/obesity and 8.2% socioemotional behavioural problems. Model discrimination for language disability was moderate in all three models (area under the curve receiver-operator characteristic 0.71, 0.74 and 0.76, respectively). For overweight/obesity, it was poor in model 1 (0.66) and moderate for model 2 (0.73) and model 3 (0.73). Socioemotional behavioural problems were also identified with moderate discrimination in all models (0.71; 0.77; 0.79, respectively). Conclusion Language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 years are common and can be predicted with moderate discrimination using data routinely collected in the first 3 years of life.

Background

The antenatal period and first 2–3 years are crucial stages that influence children's subsequent development and health outcomes. By age 3 years, many physical, cognitive and emotional development problems are apparent, but there remain opportunities to intervene to improve child outcomes.[1–3] There is increasing recognition of the need to collect better early years' data to identify children most at risk early, in order to facilitate more appropriate referral to services and early intervention programmes.[4] Accordingly, the National Health Service (NHS) in England has been developing an improved national maternity services dataset, to collate routinely collected

sociodemographic and perinatal information. In addition, in 2015, a new 'integrated universal health check' was introduced for children aged 2–3 years in England to provide a more complete picture of children's health and development.[3–5]

A central challenge in using these new datasets is to accurately identify children most in need of additional support to achieve their greater long term health and developmental potential and then deciding the most appropriate combination of universal and targeted service.[6 7] Predictive risk models, used widely for applications such as cardiovascular risk prediction,[8–10] have not been extensively assessed to inform child public health interventions. One previous study using a UK cohort showed that maternal age was a poor predictor of child health and development up to age 5 and that prediction was improved by including data on mother's smoking status during pregnancy, education level, mental health and financial status.[11] An Australian study using linked early childhood data to identify children with poor development at school entry showed that a model with six perinatal predictors (maternal age, smoking, parity, marital status and both parents' occupation) demonstrated similar discrimination to a model including 22 predictors, constituting a more statistically parsimonious set of perinatal characteristics for predicting developmental vulnerability.[12]

In the context of the new datasets being collected in England, the aim of this study was to explore how early childhood characteristics predict three important developmental outcomes: language disabilities (cognitive outcome), overweight/obesity (physical outcome) and socioemotional behavioural problems (behavioural outcome) in later childhood (11 years). To address this aim, we used data from the UK Millennium Cohort Study (MCS), a nationally representative study of infants born in the early 2000s in the UK, which provides a rich data source on the social context and measures of health for children growing up in the UK.13 We assess the predictive capacity of a model using data routinely collected in maternity services; determine how the model's performance improves when this is updated with information collected at age 2–3 years and compare the performance of the enhanced model with a third model using a larger range of early life risk factors for adverse child health collected in MCS.

Methods

Data source and study population The MCS is a nationally representative sample of children born in the UK between September 2000 and January 2002 and followed up at intervals (sweeps) to the present date. We chose the MCS as it captures a wide range of data on the social context for children growing up in the UK and provides actual measures of both early and late child health outcomes that can be used to develop predictive models. The MCS study oversampled children living in disadvantaged areas and those with high proportions of ethnic minority groups, and non-response weights were used to address sample attrition. Further information on the cohort and sampling design can be found in the cohort profile.[13] Interviews were carried out by trained interviewers in the home with the main respondent (usually the mother).

We used data from three sweeps when the children were aged 9 months, 3 years and 11 years. Information was collected from 18818 infants (91% of the 20646 in the target sample), and analysis was restricted to 18296 singleton children. Cognitive, physical and behavioural outcomes We investigated outcomes at 11 years old, an important transition stage between childhood and adolescence marked by the end of primary school. Cognitive ability was evaluated through the British Ability Scale Second Edition (BAS II) Verbal Similarities test, a validated standardised assessment of verbal reasoning and knowledge, normed for children and adolescents from 3years to 11 years of age.[14, 15] We defined children as having language disability if they scored –1.25 SD below the normed mean score for the sample.[16–18] Overweight/obesity was derived from the body mass index (BMI), using the age and sex-specific International Obesity Task Force cut-offs.[19] The Strengths and Difficulties Questionnaire (SDQ—maternal report) was used to assess child socioemotional behaviour. The SDQ is a 25 item measure that asks parents to rate their child's behaviour over the previous 6 months using five subscales: peer problems, conduct disorders, hyperactivity, emotional problems and prosocial

behaviour.[20] As in previous studies,[21 22] we used the total difficulties score (excluding the prosocial behaviour subscale), dichotomised at the validated 'borderline-abnormal' (17–40), cut-off score, indicating socioemotional behavioural problems.20 Potential predictors We outline predictors used in this study, grouped as perinatal (MCS first sweep-9 months), age 3 years (MCS second sweep) and earlier measures of language, SDQ and BMI at age 3 (figure 1). The full details of the coding of the predictors are provided in the online supplementary material.

Modelling approach We developed three models: Model 1: using variables in the MCS that are also currently collected routinely around the time of birth in maternity services in England (15 items). These data have been collected in the NHS in England and collated in the Maternity Services Data Set from April 2015 onwards.[23] Model 2: using variables collected in maternity services (model 1) plus additional information collected at age 3 years in MCS which capture the five central domains included in the new integrated 2.5-year-old health check in England: (1) personal, social and emotional development, (2) communication and language, (3) physical health, (4) learning and cognitive development and (v) physical development and self-care)2 (23 items (15 items of model 1 plus 8 items)). Model 3: a model including 30 perinatal, family/environmental and early childhood factors up to age 3 years, selected from risk factors for later child health and development problems identified in studies worldwide.[24–29] Items included in this model overlap all items of model 1 and 18 items of model 2, since we did not include all variables capturing domains of the Ages and Stages Questionnaire (ASQ) which are represented by other instruments.

We applied a statistical selection to the saturated model (30 items), and a predictive model was developed based on statistical parsimony for each outcome. Figure 1 shows the complete description of items included in each model. Statistical analyses First, we assessed the prevalence (%) for all potential predictor and outcome variables. Relative risks (RRs) and 95%CI for outcomes at 11 years were estimated using Poisson regression for all predictors included in models 1, 2 and 3. To develop model 3, we began with a saturated model containing the full range of 30 variables listed above and then selected a smaller number of variables using forwards and backwards stepwise selection ($p \leq 0.1$ for inclusion and $p > 0.11$ for exclusion). Sampling and response weights were not used for receiver-operator characteristic (ROC) analysis. The predicted probability of poor child development was calculated from these regression models. Predictive risk modelling was performed using a ROC curve which is a graphical plot that illustrates the diagnostic ability of a binary classifier system as its discrimination of true positives (ie, sensitivity) versus the fraction of false positives (ie, 1-specificity).[30] For each model, we assessed the probability cut-off point to obtain the optimal maximised probability cut-off using a function of the difference between true positive rate and false positive rate over all possible cut-point values. The optimal maximised cut-off is the point where the sensitivity and specificity curves intersected and classifies most of the individuals correctly.31 Area under the receiver operating characteristic curve (AUROC) indicates the model's overall capacity to discriminate between those who have or do not have the outcome. This provides an indication of how well the models perform in terms of the probability that a random pair of one child with the poor outcome and one without would be correctly ranked by the predicted probabilities from the model. A guide for classifying the accuracy of a diagnostic test is AUC values of '0.90–1=excellent', '0.80–0.90=good', '0.70–0.80=moderate', '0.60–0.70=poor' and '0.50–0.60=fail'.[31 32] The integrated discrimination improvement (IDI) for model 2 compared with model 1 and model 3 with model 2 were also calculated. The IDI assesses discrimination without relying on cut-off points and compares the average difference in predicted risk for children with poor health or development with those which do not have poor health or development. The IDI improvement is greater when the second model correctly assigns individuals to higher or lower probabilities of having the outcome in comparison to the first model.[33] Calibration's accuracy of the models was assessed using the Hosmer-Lemeshow goodness-of-fit χ^2 statistic. In this statistic test, the null hypothesis is that predicted proportion equals the observed proportion within ranked groupings (deciles) of predicted risk and a high p value suggests good calibration of predicted and observed risk.[34] Dominance analysis, a method for assessing the relative weight of predictive variables in a multivariable regression, was used to estimate the standardised dominance score (SDS) to rank the importance of each variable in each model.[35]

All analyses were conducted in Stata SE V.13.0 (Stata, 2014). Multiple imputation Multiple imputation by chained equation was performed to impute missing data using the 'mi impute chained' command in Stata SE V.13.0 (Stata, 2014). We used data of predictors and the three outcomes at age 11 to shape the imputation process of the other risk factors included in the three models above (imputed sample, n=10262). We generated 20 datasets, with 200 iterations per imputed dataset. Results were calculated by averaging the results across the 20 imputed datasets using Rubin's rules.[36] Results from the imputed sample are reported below and for the complete case sample are provided in the supplementary material.

Results

At 11 years, 6.7% (95% CI 6.3% to 7.2%) of children had language disability; 26.9% (95% CI 26.1% to 27.8%) overweight/obesity and 8.2% (95% CI 7.6% to 8.7%) had socioemotional behavioural problems. Prevalence of outcomes stratified by risk factors is shown in the online supplementary material. With regard to the statistical selection method applied to develop model 3, the language disability and overweight/obesity models included 14 variables, and 22 variables were selected for the socioemotional behavioural problems model (figure 1).

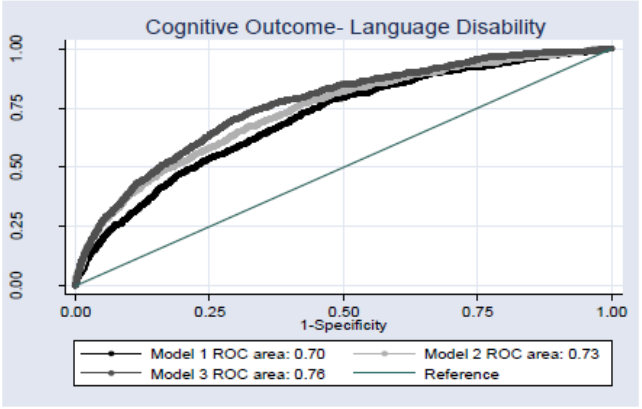
Model 1 (15 items): child's sex and birth weight; mother's ethnicity, age at birth, longstanding disabilities/illness, pre-pregnancy BMI, alcohol consumption and smoking in pregnancy, and symptoms of depression and anxiety at birth; gestational age at birth, breastfeeding initiation, type of delivery, Index of Multiple Deprivation (IMD), language spoke at home, and parent's employment status.

Model 2 (23 items): model 1 + parent's concerns of child speech, and understanding of child speaking; child's longstanding disabilities/illness, hearing problems, walking ability, language disability, socioemotional behavioural problems, and overweight /obesity at age 3.

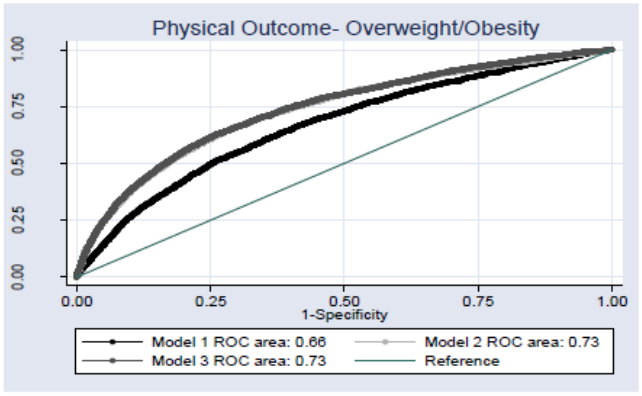
Model 3 (30 items): child's sex and birth weight; maternal education at birth, ethnicity, age at birth, pre-pregnancy BMI, alcohol consumption and smoking in pregnancy, longstanding disabilities/illness, symptoms of depression and anxiety at birth, general health at birth, and mental health disorders at child's age 3; family income, IMD, lone parenthood, number of siblings in household, language spoke at home, gestational age at birth, and breastfeeding initiation; parenting style; parent's employment status, educational disagreements of the child, involvement with child's reading at age 3, relationship-closeness with child at age 3, relationship-conflicts with child at age 3, help child to practice sports at age 3, and regular bed times at age 3; child's language disability, social-emotional behavioural problems, and overweight/obese at age 3.

- **Statistical selection:**
- **Language disability (14 items):** child's sex; maternal education at birth, ethnicity, and age at birth; family income, IMD, number of siblings in household, gestational age; parent's educational disagreements of the child, involvement with child reading, and relationship-closeness with child at age 3; child's language disability, socioemotional behavioural problems, and regular bed times at age 3.
- **Overweight/Obesity (14 items):** child' sex; maternal education at birth, ethnicity, pre-pregnancy BMI, alcohol consumption and smoking in pregnancy, longstanding disabilities/illness, and general health at birth; IMD, parent's employment status, parenting style, parent's involvement with child reading; child's regular bed times, and overweight/obese at age 3.
- **Socioemotional Behavioural Problems (22 items):** child's sex and birth weight; maternal education at birth, ethnicity, age at birth, pre-pregnancy BMI, smoking in pregnancy, longstanding disabilities/illness, symptoms of depression and anxiety at birth, general health at birth, and mental health disorders at age 3 of child; family income, IMD, lone parenthood, language spoke at home, parent's employment status, involvement with child reading, and relationship-conflicts with child at age 3; parenting style, child's regular bed times, language disability, and social-emotional behavioural problems at age 3.

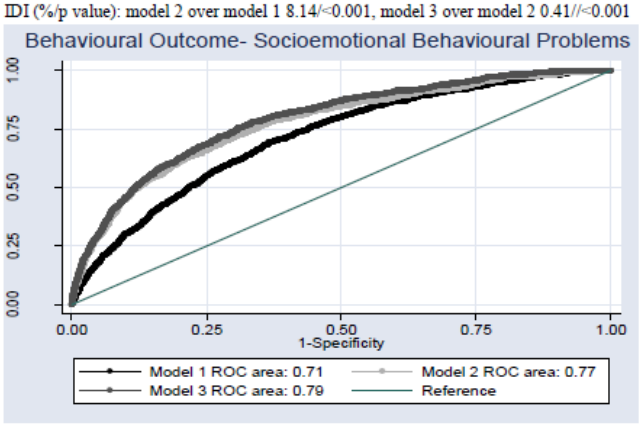
Figure 2 shows the ROC curve for each outcome in separate panels, with model 1 in black, model 2 in light grey and model 3 in dark grey: Language disability was identified with moderate discrimination ability for model 1 (AUROC: 0.70 95%CI 0.68 to 0.72), model 2 (AUROC: 0.73, 95%CI 0.71 to 0.75) and model 3 (AUROC: 0.76, 95%CI 0.74 to 0.78). Overweight/obesity was identified with poor discrimination in model 1 (AUROC: 0.66, 95%CI 0.65 to 0.67) and moderate discrimination for models 2 (AUROC: 0.73, 95%CI 0.72 to 0.74) and model 3 (AUROC: 0.73, 95%CI 0.72 to 0.74). Socioemotional behavioural problems were also identified with moderate discrimination in all models (model 1: AUROC: 0.71, 95%CI 0.69 to 0.73; model 2: AUROC: 0.77, 95%CI 0.75 to 0.79; model 3: AUROC: 0.79, 95%CI 0.77 to 0.80, respectively). IDI indicated that model 2 resulted in a significant improvement in discrimination over model 1, particularly for overweight/obesity and socioemotional behavioural problems with 8.14% and 6.26% more children being correctly reclassified by model 2 compared with model 1, respectively. The IDI improvement was smaller for model 3 compared with model 2 for all outcomes but remained significant (figure 2).



IDI (%/p value): model 2 over model 1 3.27/<0.001, model 3 over model 2 1.55//<0.001



IDI (%/p value): model 2 over model 1 8.14/<0.001, model 3 over model 2 0.41//<0.001



IDI (%/p value): model 2 over model 1 6.26/<0.001, model 3 over model 2 2.01//<0.001

Figure 2 AUC and IDI of language disability, overweight/obesity and socioemotional behaviour problems at age 11 for UK children. AUC, area under the curve; IDI, integrated discrimination improvement; ROC, receiver-operator characteristic.

Sensitivity, specificity, positive predictive value, negative predictive value, percentage of positives and correctly classified for all models are shown in table 1. Model 2 was the most accurate model for all outcomes, which means that this model had the best correct classification of children with health and development problems.

Table 1. Test properties of maximised cut off probability for language disability, overweight/obese and socioemotional behavioural problems at age 11. Millennium Cohort Study, 2001-2012, United Kingdom (imputed data, N=10,262)

Test properties	**Maximised cut offs**								
	Cognitive Language disability (%)[1]			Physical Overweight/obese (%)[2]			Behavioural Socioemotional problems (%)[3]		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Sensitivity	57.0	55.8	68.5	64.2	66.7	68.2	60.7	62.2	69.6
Specificity	71.6	77.4	71.62	60.7	69.1	67.6	70.3	79.3	74.0
PPV	12.7	15.2	14.89	37.6	44.3	43.7	15.4	21.0	19.2
NPV	95.8	96.0	96.9	82.2	84.9	85.2	95.3	95.9	96.5
% of positives	30.3	24.8	31.1	46.0	40.5	42.0	32.2	24.1	29.5
Correctly classified	70.6	75.9	71.4	61.7	68.5	67.8	69.5	77.9	73.7

PPV: positive predictive value; NPV: negative predictive value; correctly classified: true positives plus true negatives; % of positives: total of children classified as positive, even if it is true or not. [1]maximased cut offs used for language disability (model 1: 0.08, model 2: 0.08, model 3: 0.07); [2]maximased cut offs used for overweight/obese (model 1: 0.24, model 2 0.26, model 3: 0.25); [3]maximased cut offs used for socioemotional behavioural problems (model 1: 0.09, model 2: 0.09, model 3: 0.08)

Table 2. Multivariable associations between factors included in Model 2 and language disability, overweight/obese and socioemotional behavioural problems at age 11. Millennium Cohort Study, 2001-2012, United Kingdom (imputed data, N=10,262)

Model 2[2]						
Outcomes –Age 11	**Cognitive-Language disability**		**Physical- Overweight / obese**		**Behavioural- Socioemotional problems**	
Predictors	Relative Risk (95% CI)	SDS/ Ranking*	Relative Risk (95% CI)	SDS/ Ranking*	Relative Risk (95% CI)	SDS/ Ranking*
Mother ethnicity		0.017/10		0.006/11		0.005/17
White	Ref		Ref		Ref	
Mixed	0.99 (0.50-1.95)		0.77 (0.53-1.10)		1.74 (0.96-3.15)	
Indian	0.37 (0.19-0.71)		1.25 (0.94-1.67)		0.86 (0.44-1.67)	
Pakistani	1.13 (0.70-1.85)		1.32 (1.04-1.68)		0.94 (0.54-1.63)	
Bangladeshi	1.64 (0.96-2.82)		1.12 (0.79-1.59)		0.98 (0.48-1.98)	
Black	0.73 (0.43-1.25)		1.34 (1.13-1.58)		1.23 (0.74-2.03)	
Other	0.61 (0.25-1.47)		0.81 (0.56-1.17)		0.36 (0.12-1.04)	
Mother's age at birth		0.020/9		0.002/14		0.003/7
14-19 years old	1.16 (0.77-1.74)		0.87 (0.73-1.05)		1.37 (0.98-1.91)	
20-24 years old	1.27 (0.92-1.73)		0.93 (0.82-1.05)		1.48 (1.11-1.97)	
25-29 years old	1.02 (0.75-1.40)		0.90 (0.81-1.01)		1.26 (0.99-1.62)	
30-34 years old	1.05 (0.78-1.43)		0.97 (0.87-1.07)		1.01 (0.79-1.30)	
35-63 years old	Ref		Ref		Ref	
Language spoke at home		0.026/8		0.001/15		0.010/14
Only English	Ref		Ref		Ref	
English and additional language	0.64 (0.43-0.95)		0.98 (0.84-1.13)		0.70 (0.48-1.02)	
Not English	0.61 (0.39-0.95)		0.93 (0.72-1.21)		0.37 (0.18-0.75)	
Parents employment status		0.142/2		0.015/5		0.064/4
Both parents in work	Ref		Ref		Ref	
One parent in work	1.13 (0.90-1.51)		1.08 (0.90-1.12)		0.89 (0.91-1.54)	
Neither parent in work	1.98 (1.12-4.18)		1.32 (0.96-1.41)		1.93 (1.19-2.32)	
Deprivation- IMD		0.068/5		0.020/4		0.026/9
1 quintile- highest	Ref		Ref		Ref	
2 quintile	1.45 (0.98-2.22)		1.13 (0.97-1.31)		0.84 (0.60-1.19)	
3 quintile	1.66 (1.12-2.45)		1.14 (0.99-1.31)		1.03 (0.75-1.41)	
4 quintile	1.57 (1.07-2.31)		1.15 (1.00-1.33)		1.40 (1.04-1.88)	
5 quintile- lowest	1.84 (1.28-2.66)		1.23 (1.06-1.42)		1.10 (0.81-1.49)	
Child gender		0.009/14		0.013/6		0.023/11
Male	Ref		Ref		Ref	
Female	1.30 (1.10-1.54)		1.15 (1.06-1.24)		0.71 (0.60-0.83)	
Child birth weight		0.008/16		0.001/17		0.001/20
Normal (>=2.5 to <=4.5 kg)	Ref		Ref		Ref	
Low (<2.5 kg)	0.92 (0.65-1.30)		1.00 (0.84-1.20)		1.19 (0.88-1.62)	
High (>4.5 kg)	1.19 (0.71-1.99)		1.10 (0.83-1.34)		0.70 (0.33-1.48)	
Gestational age		0.001/22		0.001/16		0.001/23
Term, 37-41 weeks	Ref		Ref		Ref	
Preterm, 23-36 weeks	1.50 (1.03-2.17)		1.00 (0.85-1.19)		1.01 (0.70-1.45)	
Post-term, 42-43 weeks	0.79 (0.59-1.05)		1.10 (1.00-1.22)		0.97 (0.78-1.21)	
Smoking in pregnancy		0.017/11		0.026/3		0.067/2
None	Ref		Ref		Ref	

1-10 cigarettes/day	1.01 (0.78-1.31)		1.15 (1.03-1.29)		1.18 (0.98-1.43)	
11-20 cigarettes/day	0.94 (0.63-1.41)		1.34 (1.14-1.57)		1.63 (1.24-2.13)	
> 20 cigarettes/day	1.71 (1.04-2.28)		1.38 (1.04-1.83)		1.31 (0.83-2.05)	
Alcohol consumption in pregnancy		0.016/12		0.010/7		0.004/19
No	Ref		Ref		Ref	
Yes	0.94 (0.75-1.16)		0.88 (0.81-0.95)		0.95 (0.80-1.14)	
Breastfeeding initiation		0.029/7		0.008/8		0.004/18
Yes	Ref		Ref		Ref	
No	1.05 (0.87-1.27)		1.00 (0.91-1.10)		0.94 (0.81-1.10)	
Maternal depression or anxiety		0.009/15		0.007/9		0.071/6
No	Ref		Ref		Ref	
Yes	1.08 (0.90-1.30)		1.06 (0.98-1.16)		1.33 (1.13-1.57)	
Type of delivery		0.001/19		0.002/12		0.001/22
Normal	Ref		Ref		Ref	
Assisted (forceps, vacuum, breach)	1.17 (0.80-1.70)		0.90 (0.79-1.01)		1.00 (0.71-1.40)	
Planned caesarean	1.18 (0.88-1.58)		1.06 (0.93-1.20)		0.81 (0.63-1.04)	
Emergency caesarean	1.03 (0.80-1.34)		0.99 (0.89-1.11)		1.07 (0.86-1.32)	
Other	1.10 (0.26-4.61)		0.82 (0.47-1.43)		1.17 (0.57-2.37)	
Mother BMI before born		0.007/17		0.291/2		0.017/12
Normal	Ref		Ref		Ref	
Overweight/ obese	1.26 (1.05-1.52)		1.85 (1.70-2.00)		1.32 (1.13-1.53)	
Mother disability or illness		0.004/21		0.006/10		0.025/10
No	Ref		Ref		Ref	
Yes	0.88 (0.72-1.07)		1.07 (0.98-1.17)		1.26 (1.08-1.46)	
Hearing problems age 3		0.008/20		0.001/23		0.007/16
No	Ref		Ref		Ref	
Yes	0.93 (0.64-1.36)		1.12 (0.97-1.29)		1.10 (0.83-1.46)	
Concern about child's speech age 3		0.043/6		0.001/21		0.066/3
No	Ref		Ref		Ref	
Yes	1.60 (1.23-2.08)		1.01 (0.90-1.15)		1.59 (1.30-1.95)	
Understands child's speech age 3		0.108/3		0.001/20		0.046/5
Always	Ref		Ref		Ref	
Sometimes	0.97 (0.64-1.47)		0.75 (0.57-0.98)		0.88 (0.60-1.30)	
Rarely	2.16 (1.35-3.46)		1.10 (0.68-1.76)		1.08 (0.63-1.85)	
Walk up steps age 3		0.011/13		0.002/13		0.010/15
Yes	Ref		Ref		Ref	
With help	1.00 (0.57-1.76)		0.79 (0.59-1.07)		1.07 (0.73-1.57)	
No	1.67 (1.08-2.58)		1.28 (1.00-1.63)		1.27 (0.86-1.88)	
Child disability or illness age 3		0.004/18		0.001/22		0.031/8
No	Ref		Ref		Ref	
Yes	1.09 (0.87-1.35)		0.96 (0.88-1.05)		1.36 (1.16-1.60)	
Naming vocabulary disability age 3		0.362/1		0.001/19		0.015/13
No language disability	Ref		Ref		Ref	
Language disability	2.51 (1.95-3.23)		0.98 (0.86-1.13)		1.10 (0.83-1.45)	
SDQ age 3		0.094/4		0.001/18		0.502/1
No related problems	Ref		Ref		Ref	
Behavioural problems	1.39 (1.12-1.72)		0.98 (0.87-1.10)		2.68 (2.22-3.23)	
BMI age 3		0.001/23		0.589/1		0.001/21
Normal weight	Ref		Ref		Ref	

Overweight/obese	0.92 (0.73-1.17)	2.47 (2.28-2.67)	1.05 (0.88-1.27)
Hosmer-Lemeshow/ p value**	5.19/ 0.737	4.65/ 0.794	14.42/ 0.071

[2]Model 2 includes information collected in maternity services in England plus correspondent factors assessed in MCS at age 3 that are collected on 2.5 year old health check in England; *Standardised Dominance Statistic (SDS) and weighted ranking of predictive risk variables; **Calibration analyses

Table 2 presents the multivariable associations between risk factors and language disability, overweight/ obesity and socioemotional behavioural problems at age 11, calibration and dominance analyses for model 2 (model with the best correct classification of children for all outcomes). Those results for models 1 and 3 can be found in the online supplementary material. The Hosmer-Lemeshow goodness-of-fit tests indicate adequate calibration in model 2 for all outcomes (Hosmer-Lemeshow/p value: language disability 5.19/0.737; overweight/obesity 4.65/0.794; socioemotional behavioural problems, model 2 14.42/0.071). Dominance analyses for model 2 showed that the top four most relevant factors for socioemotional behaviours at age 11 years were socioemotional behavioural problems at age 3 (0.502), smoking in pregnancy (0.067), parental concerns about child speech at age 3 (0.066) and neither parent in work (0.064). The most dominant factors for language disability at age 11 were naming and vocabulary disabilities at age 3 (0.362), neither parent in work (0.142), parental concerns about understanding of child speech at age 3 (0.108) and socioemotional behavioural problems at age 3 (0.094). For overweight/obesity at age 11, overweight/obesity at age 3 (0.589), maternal pre-pregnancy BMI indicating overweight/obese (0.291), smoking in pregnancy (0.026) and greater deprivation of area of residence (0.020) were the most important items. Sensitivity analyses of AUROC not including prior measures of the outcome show similar findings to our main results, with moderate discrimination in models 2–3 for socioemotional behavioural and language problems, but lower discrimination for obesity/overweight (about 68% for models 2 and 3—see online supplementary material). In dominance analyses, when we remove prior measures of the relevant outcome, the second, third most influential variables and so on rise in the rank of importance (online supplementary material). Repeating the analysis including all of the variables from the ASQ in model 3 did not alter the model selection or change the results.

Discussion

Using UK data from the MCS, we show that information collected in the first 3 years of life can be a potential tool to predict adverse health and developmental outcomes at age 11 with moderate accuracy. The discriminatory capacity of a model using data collected in maternity services in England is improved when updated with data routinely collected at 2–3 years (particularly earlier measures of the relevant outcomes), but addition of wider set of perinatal, family/environmental and early childhood factors up to age 3 years did not alter risk prediction. The first 3 years of life provide a unique opportunity to intervene and improve child development and subsequent adult outcomes.[7] There has been a raft of policies promoting the benefits of early intervention, but the research base to support effective targeting of these initiatives is still emerging. Child health policy recommendations in the UK apply the principles of proportionate universalism, with universal services provided for all families and, in addition, progressively more intensive support targeted at those with greater need.[6 7] In a technical sense, we would like to be able to find a set of characteristics (eg, maternal, partner, child and community) that accurately identify those children most at risk for poorer developmental outcomes, to help plan improved services for their future development. While it is true that relative concentrations of poorer outcomes are higher in disadvantaged populations, to our knowledge, there has been little systematic work examining the extent to which these outcomes are predicted by risk factors earlier in the life course.

The existing studies that have investigated this and have similarly demonstrated the utility of using data collected at birth to predict poor child health outcomes. Chittleborough and colleagues[11] used a prospective, regional birth cohort in England to explore the predictive value of maternal age, compared with a model using six predictors (mother <20 years, low maternal education, single parent, financial difficulties, depression, smoking in pregnancy) for child development outcomes up to age 5 years. Predictive capacity was improved in this study by including other data, but was still classified as poor (AUROC=0.67). The authors concluded that, even though maternal age is used to target early years child health programmes in many countries, these interventions will have little impact at a

population level, since the majority of at risk children will miss out on intervention if young maternal age is the sole or main means of identifying eligibility for the programmes.[11] A recent study from Australia used linked administrative perinatal datasets linked to data from the Australian Early Development Census to assess whether poor child development at age 5 could be predicted at a population level.[12] A model with six perinatal characteristics (low maternal age, mother's marital status (never married, widowed, divorced or separated), mother and father's occupation (home duties, students, pensioners, unemployed), high number of previous pregnancies resulting in births≥20 weeks and smoking in second half of pregnancy) had poor discrimination for boys (AUROC=0.68) and moderate discrimination for girls (AUROC=0.72). The authors suggest that even with poor-moderate capacity of the models, if these six characteristics were used for targeting intensive support services and the programme targeted families with at least three of the six perinatal risk factors, approximately 10% of families in the population would be identified as needing an intensive intervention soon after birth.[12]

Building on these findings, our study shows that risk predictions were not substantially improved using a wider range of variables in the first 3 years of life and that these data also have moderate predictive value for outcomes at 11 years. Socioeconomic factors and early measures of the relevant outcomes were the most important predictive indicators for child health and development at age 11 years. However, removing the early measure of the outcome from the analysis did not impact greatly on prediction, especially for language disabilities and socioemotional behavioural problems (as tested in our sensitivity analyses). Despite the high prevalence of overweight/obesity, it is to have been expected that predictive power for this outcome would be lower without age 3 years measurement, due to biological influences.[25] Recent findings from predictive modelling studies in high-income countries, in the UK and Australia[37] and in the USA38 corroborate the importance of social factors for later child health and development outcomes, even in high-income countries. Another study from Brazil (a middle-income country), using the 2004 Pelotas Birth Cohort, assessed a predictive model of early life factors for a cognitive outcome (low IQ) at age 6 years. Twelve risk factors were included in the final model and dominance analyses showed that social factors were the most important predictors.[39]

A strength of our study is the use of a large, contemporary UK cohort. A wide range of information is collected in the MCS, which allowed us to explore a large set of demographic, perinatal and early childhood risk factors. Measured BMI, validated assessments of language disability and socioemotional behavioural problems in children were also advantages. The MCS thus allowed us to consider what might be achieved through linkage of administrative datasets in the UK and to assess what added predictive value extra data collection might provide.

A limitation of our study is the lack of an external validation sample. In addition, missing data and attrition are common to all cohort studies, but the similar results in complete case and imputed datasets in our study offer reassurance that the risk of bias is minimised. We note that model 2 in our analysis included early measures of the prior problem, and it could be the case that much of the predictive value in the model could be explained by these early measures. However, repeating the analysis without these measures suggests that this is not the case (online supplementary material). We based most of our results on maternal self-reported data and decisions were made around categorising prediction variables. We have used cohort data from the nationally representative MCS and we expect that the predictors identified in the MCS would predict outcomes similarly in the general population. However, it is unclear the extent to which these models can be reproduced in routinely collected data. Further limitations include concerns about how similar the measures in the MCS are to those used in health services, since MCS data variables are aimed at research and to capture a picture of a representative sample of all UK children. Furthermore, we do not have detailed data on any intervention or specialised services that children may have accessed, that may have attenuated the associations in our study. Further research is needed to assess the utility and impact of predictive risk models for child health and development outcomes in routine practice. We have

used cohort data from the nationally representative MCS, but it is unclear the extent to which these models can be reproduced in routinely collected data.

While many of the variables used in model 1 in our analysis should be available in routine data, other variables such as breastfeeding status and early measures of maternal mental health are more difficult to capture and may be of poor quality in routine data collection systems. Furthermore, we require a better understanding of how predictive risk modelling tools could be used in the context of specific child health systems, for instance, in the UK, what proportion of children would go on to receive specialist intervention; what proportion of those would benefit from this and what would be the magnitude of any benefits. In the UK and the USA, there have been some attempts to target services on the basis of child and family characteristics, and our study provides evidence as to which variables are likely to be useful for this purpose in clinical and public health practice.[40 41] As many high-income countries collect these sort of data, it would be instructive to test how well they predict the same outcomes. The use of such tools raises ethical issues, for instance being labelled high risk could be stigmatising and any population level targeting approach would generate false positives (and false negatives), that would have opportunity costs for services locally. Predictive risk models have the potential to promote a shift towards early intervention and could be adapted to move beyond an individualised risk paradigm towards the development of more supportive services for families based on need. PRM approaches using linked routinely collected data could be developed to identify geographical areas of disadvantage suitable for enhanced service provision, following a proportionate universal approach, facilitating enhanced provision without individuals being singled out or stigmatised. The implementation of risk prediction tools to guide policies would have to be carefully considered to ensure families were appropriately counselled and supported. Future research should evaluate the impact of any approaches informed by predictive risk models using routinely collected data on (inequalities in) health and wellbeing for children and families.

Conclusion

New child health datasets have been developed in England, but it remains a challenge to harness these population-level administrative datasets to improve outcomes for children. Our analysis shows that language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 years can be predicted with moderate discrimination using data routinely collected in England. Addition of further variables identified in the literature that mostly are not routinely collect in health services does not add considerable improvement on discriminatory capacity of health and development problems in later childhood. Further research is needed to identify what could increase the predictive power of these models at these and other ages in population-based databases such as MCS as well as assess how the dynamics of predictive algorithm models can be used in health services to identify children more likely to benefit from additional early years support.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, UCL Institute of Education.

Contributors

VSS carried out the statistical analyses, drafted the initial manuscript, reviewed and revised the manuscript. AP and SH participated in the drafting of the initial manuscript, reviewed and revised the manuscript. BB participated in the drafting of the initial manuscript, reviewed and revised the

manuscript. MW contributed to the conceptualisation of the study, participated in the drafting of the initial manuscript, reviewed and revised the manuscript. CL conceptualised and designed the study, participated in the drafting of the initial manuscript, reviewed and revised the manuscript. DT-R conceptualised and designed the study, coordinated, drafted the initial manuscript, reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding

This work was supported by the UK Public Health Research Consortium (PHRC). The PHRC is funded by the Department of Health and Social Care Policy Research Programme. The views expressed in this paper are those of the authors and do not necessarily reflect those of the Department of Health and Social Care. Information about the wider programme of the PHRC is available from http://phrc.lshtm.ac.uk/. AP is funded by The Wellcome Trust (205412/Z/16/Z), the Medical Research Council (MC_UU_12017/13) and the Scottish Government Chief Scientist Office (SPHSU13). BB is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Health Research and Care (CLAHRC NWC). The NIHR had no role in the study design, data collection and analysis, decision to publish or preparation of the article. This report is independent research arising from research supported by the NIHR. DTR is funded by the MRC on a Clinician Scientist Fellowship (MR/P008577/1).

Competing interests

None declared. Patient consent Not required. Ethics approval Ethical approval for each wave of the MCS was granted by NHS Multicentre Research Ethics Committees. No further ethical approval was required for this secondary analysis of MCS data. Provenance and peer review Not commissioned; externally peer reviewed. Data sharing statement All MCS data used in this analysis are available from UK Data Service, University of Essex and University of Manchester: http://doi.org/10. 5255/UKDA-SN-4683-4; http://doi.org/10.5255/UKDA-SN-5350-4; http://doi.org/10. 5255/UKDA-SN-7464-3.

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

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

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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.

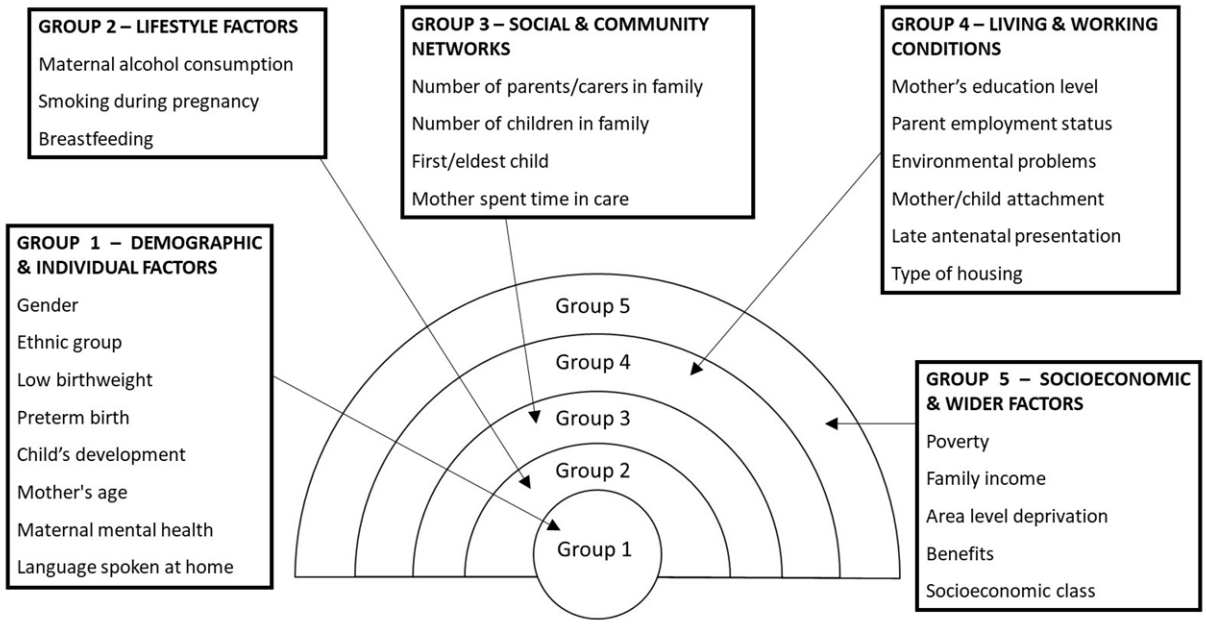

Figure 1 Rainbow Model showing determinants of school readiness (adapted from Dahlgren and Whitehead, 1991)

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'

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

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

Group 5 – Socioeconomic and Wider Factors

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

Statistical analyses

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

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

A multivariable logistic regression model including all 29 variables was reduced using automated forward and backwards stepwise selection (using a cut off p-value of 0.1). Dominance analysis (repeated regression analyses on subsets of variables) was used to produce a ranking and weighting for each predictor in model 1[40]. These rankings were used to specify a more parsimonious model (model 2) containing the top 6 predictors, selected to maximise parsimony and performance. The integrated discrimination improvement (IDI) using the complete case sample from model 1 was

[1] Being on leave from work is classed as being in employment

calculated to assess difference in performance between models as the percentage change in individuals being correctly assigned by the model[41].

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

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

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

Ethics and Patient and public involvement

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

Results

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

	Complete Cases (n=9,487)		Imputed Data (n=13,650)	
Is Child School Ready?	**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	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	
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)	13.6 (3)
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)[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).

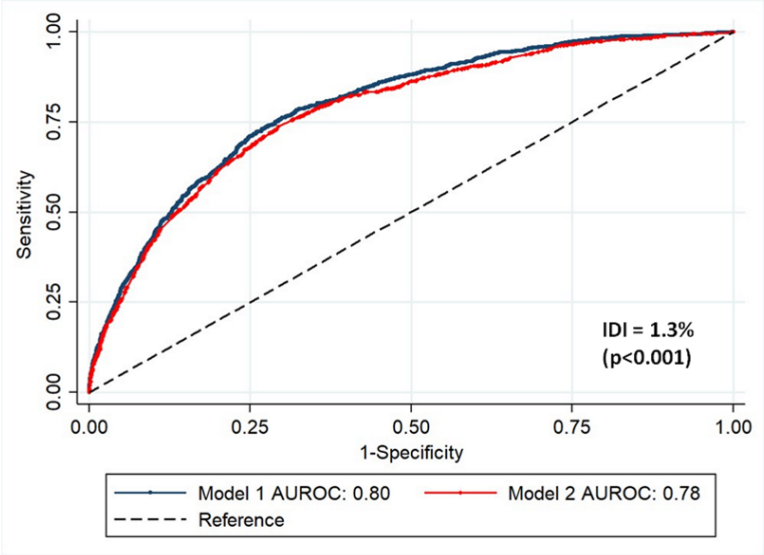

Figure 2 ROC curves for models 1 (13 predictors) and 2 (6 predictors), showing AUROC and IDI

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

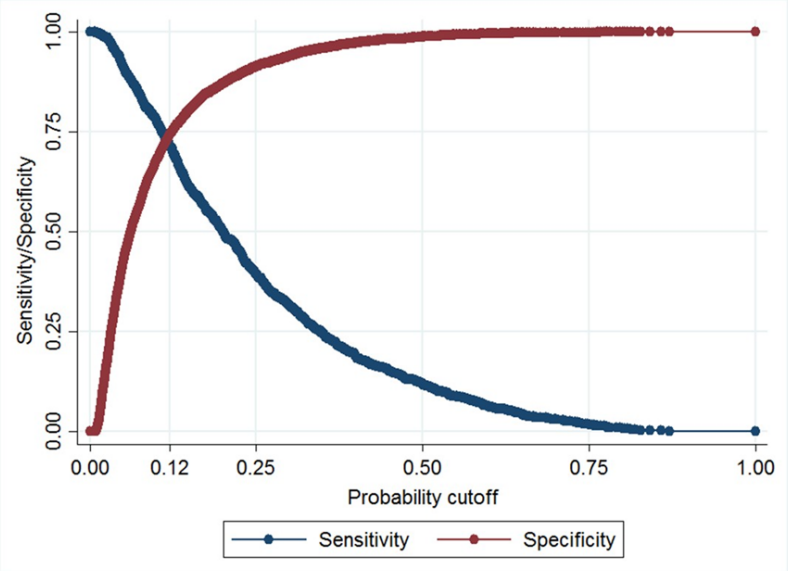

Figure 3 Maximized probability cut off of sensitivity and specificity of model 1

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

Discussion

Findings

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

Comparison with previous studies

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

The model reported here has good predictive strength, and compares favourably to similar PRMs, which with one exception[17], achieved only fair or poor discrimination[14,15,18,48]. Chittleborough et al used the ALSPAC UK birth cohort to test the predictive validity of 2 models for ECD[14]. They used a different outcome measure (School entry assessment aged 4-5) and used 6 predictors in their model,

which appear to be chosen a priori, rather than by a statistical routine. They found that maternal age alone failed to predict ECD (AUROC~0.5), and a model with 6 predictors achieved only poor discrimination (AUROC=0.67). Camargo-Figuera et al used IQ as a measure of ECD and developed a PRM with 12 predictors using the Brazilian Pelotas birth cohort; their model had good discrimination (AUROC=0.8) and calibration, with sensitivity and specificity of 72% and 74% respectively[17]. We believe the use of a representative cohort for model development, stepwise regression to select predictor variables and dominance analysis to specify a simplified model contributed to the good performance of this PRM.

Strengths and Limitations

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

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

Policy Implications

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

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[48].

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; this could lead to stigmatisation of families and unnecessary use of resources. 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.

Further research is needed to test the external validity of predictive risk models for ECD for example in another cohort or with linked administrative datasets. 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. 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. Investment in early intervention would be required, which would have opportunity costs for services locally. A substantive evaluation of the effectiveness of any predictive model using routinely collected data on health and well-being for children and families should be done prior to implementation.

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

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

Competing Interests

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

Contributors

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

Data Sharing

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

Acknowledgements

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

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4.3 How do early life adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

(New draft)

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Abstract

Background. We assessed how early life adverse childhood experiences (ACEs) measured up to five years mediate the relationship between childhood socio-economic conditions (SECs) and socioemotional behavioural problems, cognitive disability, and overweight/obesity in adolescence.

Methods. We used longitudinal data from the U.K. Millennium Cohort Study. Outcomes assessed at age 14 years were socioemotional behavioural problems, cognitive disability and overweight/obesity. The main exposure was maternal education at child birth, which was used to estimate the relative index of inequality. Potential mediating ACEs reported by parents were verbal and physical maltreatment; parental drug use; domestic violence; parental divorce; maternal mental illness; and high frequency of parental alcohol use. Counterfactual mediation analysis was performed to assess total, natural direct and indirect effects and proportion mediate by ACEs on adolescent health inequalities.

Results. The total effect of a hypothetical intervention changing all children from high to low SECs at birth was RR 5·16 (95% CI 3·37, 7·86) for socioemotional behavioral problems, RR 4·75 (3·00, 7·53) for cognitive disability and RR 1.79 (1·49, 2·15) for overweight/obesity. Overall 18% of the total effect of SECs on socioemotional behavioural problems was mediated through ACEs measured by age five years. For cognitive disability and overweight/obese the proportions mediated were 13% and 19% respectively.

Conclusion. ACEs measured up to age 5 years in the MCS explained about one sixth of inequalities in adolescent health outcomes.

Introduction

The concept of "adverse childhood experiences" (ACEs) has gained popularity as a way of framing the public health implications of a range of harmful childhood experiences (1,2). These typically include abuse, neglect, and indicators of possible household dysfunction affecting children such as parental mental health problems and alcohol and drug misuse (2). Although the prevalence of ACEs varies on the basis of the definitions used, there is a clear association with a range of health outcomes across the lifecourse (3). Findings from a cross-sectional UK survey of people aged between 18–70 years showed that almost half of those surveyed reported at least one ACE whilst 12% reported 4 or more ACEs (4).

The preschool period is a crucial stage of development that influences children's subsequent development and health outcomes (5). For example, our recent study has shown that inequalities in adolescent mental health outcomes can be explained by early life perinatal, individual child, family, peer relation and neighbourhood-level factors (6). In this context detrimental experiences framed as ACEs may be particularly important in the early years (7). Furthermore, the role of early life ACEs in explaining socio-economic inequalities in later health is unclear. Many ACEs are socially patterned and are more commonly experienced by children growing up in disadvantaged social conditions. Thus, factors such as family dysfunction may be important mediators on the pathway between childhood SECs and later inequalities in health outcomes (7–9). However, there has been a conflation of socioeconomic factors and ACEs in some studies, which makes it difficult to differentiate these factors in relation to the contribution to pathways to worse health. Some studies, for example, have included measures of SECs such as economic hardship, poverty and deprivation within their definition of ACEs measurement (10,11). By contrast other authors have adjusted for SECs whilst testing for associations between ACEs and later health outcomes (4,12–15). We raised concerns that this might lead to the importance of socioeconomic conditions being overlooked when considering ACEs (16).

We therefore believe it is important to develop an understanding of how childhood SECs structure the risk of experiencing adversities, and the impact this has on health outcomes, in order to develop appropriate public health strategies and policies (2,17). Therefore, this study aims to explore the social patterning of ACEs measured in the preschool period in the latest UK birth cohort, and the extent to which these adversities mediate causal pathways between childhood SECs and three important adolescent health outcomes: socioemotional behavioural problems, cognitive disability, and overweight/obesity.

Methods

The Millennium Cohort Study (MCS) is a large nationally representative cohort study of 18,818 children born in the United Kingdom between 2000-2002 and followed up at six intervals to the present date. In order to address our research question, we used data from baseline (9 months), ages 3, 5 and 14 years old. Survey interviews were carried out in the home with the main respondent (parents- almost always the mother). The study oversampled children living in disadvantaged areas and in those with high proportions of ethnic minority groups by means of a stratified cluster sampling design.

Measures

Health outcomes: behavioural, cognitive and physical

We investigated outcomes at 14 years old, captured in the latest MCS data sweep. The Strengths and Difficulties Questionnaire (SDQ—maternal reported) was used to assess adolescent socioemotional behaviour. The SDQ is a 25-item measure that asks parents to rate their child's behaviour over the previous 6 months using five subscales, each with five items: peer problems, conduct disorders, hyperactivity, emotional problems, and prosocial behaviour. We used the total difficulties score (which excludes the prosocial behaviour items) using validated cut offs used in previous studies (18,19) for which a score of 0–16 indicates 'normal to borderline behaviour' and 17–40 indicates

'socioemotional behavioural problems' (20). Word activity was assessed as a proxy of cognitive ability. The adolescents received 20 different words in English and five possible synonyms for each and were asked to match each word to its correct synonym. We applied a widely used score cut-off (21–23) of –1.25 standard deviations below the normed mean score for the sample to define children as having vocabulary/cognitive disabilities. Overweight/obese was derived from the body mass index (BMI), using the age and sex-specific International Obesity Task Force cut-offs (24).

Measurement of Socioeconomic Condition (SEC)

The level of maternal education at birth was our primary exposure of interest, used as a measure of childhood SECs. The highest qualification attained by the mother was established by questionnaire at the first sweep (1. 'Degree plus=higher degree or first-degree qualifications'; 2. 'Diploma=in higher education'; 3. 'A-levels'; 4. 'General Certificate of Secondary Education (GCSE) grades A–C'; 5. 'GCSE grades D–G'; 6. 'None of these qualifications'). Maternal educational level has been used in previous studies exploring inequalities in child health (25,26) and represents a more stable measure of SECs as compared to income, which could be fluctuated at times. It also encompasses a range of non-economical social attributes, e.g. general and health-related knowledge, literacy, and problem-solving skills; prestige; influence over others and one's own (27).

Adverse Childhood Experiences (ACEs) in the preschool period

Seven parental-reported potentially mediating ACEs experienced by the child up five years were captured in the MCS: physical maltreatment; verbal maltreatment; parental drug use; high frequency of parental alcohol use, domestic violence, parental divorce and maternal mental illness. The full details of coding of the potential mediators is provided in Text box 1.

Analysis

First, we estimated the prevalence of the health outcomes at age 14. We then assessed the distribution of our health outcomes and ACEs according to level of maternal education at birth using the chi-squared test ($\chi 2$). For descriptive purposes, we operationalised ACEs variables by combining categories that distinguished the most adverse scenarios (binary variables) (see description in the Text box 1). According this operationalisation, we presented the frequency of children that have 1, 2, 3, 4 or more ACEs by level of maternal education at birth.

Secondly, we undertook formal mediation analysis using the counterfactual framework to assess the amount of social inequality in health outcomes at age 14 attributable to ACEs suffered up to the age five, whilst adjusting for baseline demographic factors (child sex, maternal ethnicity and maternal age at birth). In the mediation analysis we used the naturally occurring coding of the mediators in the MCS (multicategory variables), shown in supplementary material (S2), to maximise power to capture mediation through our block of ACEs. We scaled the education measure in order to derive a measure of the relative index of inequality (RII). The RII compares the risk of poor health outcomes between children of lowest and highest SECs, taking into account the distribution of education level in the study population by ranking the maternal education groups from lowest to highest and allocating a score (ranging from 0-1) that represents the midpoint of the category's range in the cumulative distribution(28). We used this scaled measure in our regression models to derive the RII, which summarizes the relative risk across the socio-economic gradient in the population (28,29). We estimated the Relative Risk (RR) and 95% Confidence Interval (CI) for the Natural Direct Effect (NDE), Natural Indirect Effect (NIE) and Total Effect (TE) (formulas are shown in the supplementary material S1) for the Direct Acyclic Graph (DAG) outlined in Figure 1, considering all ACEs. We calculated the proportion mediated and 95% CI for each group of mediators applying the formula: (RRNDE*(RRNIE-1)) / (RRNDE*RRNIE -1)(30). Analysis were conducted in Stata/SE V.15 (Stata Corporation) and in medflex package of R software(31). R V.3.4.4.

Robustness tests

To explore exposure-mediator interaction we repeated the analysis allowing for all 2-way interactions between maternal education and the mediators in the model and used the Akaike Information Criterion (AIC) to compare model fit. We repeated the counterfactual mediation analysis using equivalised family income as an alternative measure of childhood SECs. We also repeated our analysis without the alcohol variable, since our variable only captures the frequency of parental alcohol consumption, and not the volume. It is thus possible that our variable may not reflect an adverse experience for the child. We also explored the mediating ACEs effect in inequalities in other outcomes such as smoking, alcohol and cannabis experimentation at age 14. Finally, we repeated the main analysis with multiple imputed datasets.

Results

11,169, 10,645 and 10,825 children who participated in the first and the latest sweeps of MCS had data on socioemotional behavioural problems, cognitive disability and overweight/obese at age 14, respectively. Around two-thirds (N= 6,499 [socioemotional behavioural problems]; 5,393 [cognition]; 6,306 [overweight/obese]) had data on all exposure, outcome, mediators and confounders of interest, i.e. the complete case population to each outcome.

At age 14 years, 8·7% (95%CI 7·9, 9·7) of children had socioemotional behavioural problems, 6·0% (95%CI 5·2, 7·0) had cognitive disabilities, and 24·6% (95%CI 23·3, 25·9) were overweight/obese, with a clear social gradient in all outcomes (Table 1). In our study, 50% of children had experienced one or more ACEs, 16·4% two or more, 5·4% three or more, and 1·4% four or more ACEs. According to the binary operationalisation of our ACEs variables, the most prevalent ACEs was verbal maltreatment at age 5 (36·5%), followed by high frequency of parental alcohol consumption at age 5 (8·2%). There were also significant social gradients evident in many ACEs, apart from verbal and physical maltreatment, and use of drugs. All socially patterned ACEs were more common in children growing up in more disadvantaged circumstances, apart from high frequency of alcohol consumption, which was more common in more socially advantaged families (Table 1). The social patterning of the ACEs using the natural categories coding available in the MCS (multicategories) can be found in supplementary material (S2).

The results of the counterfactual mediation analysis are illustrated in Figure 2. Taking socioemotional behavioural problems as an example, the total effect of a hypothetical intervention moving all children from high to low SECs on adolescent mental health was RR 5·16 (95%CI 3·37, 7·86). The natural direct effect (RR 3·85, 95%CI 2·48,5·97) is the increase in socioemotional behaviour problem risk comparing low to high SEC that we would observe if the ACES mediators remained as in the top end of the SEC hierarchy; and the natural indirect effect is the increased risk of socioemotional behavioural problems we would see if the SECs were fixed at top of the SEC hierarchy, but the ACEs mediators were fixed at those that would naturally occur at low SECs (RR 1·33, 95% CI 1·18,1·51), compared to if they remained at the high SEC levels.

There was a significant indirect effect of SECs on our outcomes of interest via ACEs experienced up five years, indicating statistically significant mediation. Respectively, 18% (9·9, 28·1), 13% (3·7, 26·2) and 19% (8·7, 32·7) of the total effect (TE) of SECs on risk of socioemotional behavioural problems, cognitive disability and overweight/obese at age 14 years was mediated through adversities measured in the MCS by the age five (details in supplementary material S3).

Robustness tests and additional analyses

For the counterfactual mediation analysis, a model that included all exposure-mediator interactions had a worse fit on the basis of AIC (results are nor shown). Conclusions were similar when we repeated the analysis using RII on the basis of family income as the main SEC measure, instead of maternal education (supplementary material S4). Regarding the analysis excluding the mediating variable of frequency of parental alcohol consumption, we found an attenuation on the proportion mediated by

ACEs for socioemotional behaviour problems (18% 95%CI 9·9, 28·1 versus 11·8 95%CI 6·4, 18·7) and cognitive disability (13% 95%CI 3·7, 26·2 versus 7·5 95%CI 0·9, 16·5) outcomes at age 14, but the results were very similar. There was no mediation by ACEs for overweight/obese when removing the alcohol variable (NIE RR 1·03 95% CI 0·99, 1·07) (supplementary material S5). There was no mediating effect of ACEs experienced up five years for the other health risk behaviours at age 14 (details in supplementary material S6). Analysis using multiple imputed datasets (supplementary material S7) showed similar patterns with the main analysis.

Discussion

Using nationally representative data from the UK, we show that most of the ACEs captured in the MCS by the age of 5 years, with the exception of parental alcohol consumption, are more common in more disadvantaged children, and they explain under a fifth of inequalities in mental health (17%), cognitive ability (13%), and overweight/obesity (18%) at age 14 years.

Comparison with previous studies

The stark inequalities in adolescent health outcomes illustrated in our study corroborate other studies (32–35). In our study the most prevalent ACEs were verbal maltreatment and high frequency of alcohol consumption at age 5 and 1.4% of children had experienced 4≥ ACEs. Ours is one of the first studies to quantify the ACEs in the preschool period using rich cohort data. The prevalence of ACEs in our study is not directly comparable with other studies which have focussed on self-report in adulthood. For instance, Bellis and colleagues (4) observed a prevalence of 12.3% for 4≥ ACEs in a retrospective cross-sectional survey of 1500 residents and 67 substance users aged 18–70 years in a relatively deprived and ethnically diverse UK population. These differences may be explained by different operationalization of ACEs variables and the fact that in our study we used estimates of ACEs restricted to the preschool period (i.e. up to five years), while most of other studies looked at ACEs up to age 18 years.

Most of the ACEs considered in our study were more common in children growing up in disadvantaged circumstances. Using the National Survey of Children's Health (NSCH), Slopen and colleagues (36) examined differences in ACEs by family income, race, ethnicity, and birthplace among children in the United States. Corroborating our findings, the authors found that higher family income was associated with fewer ACEs. Moreover, this relationship showed a gradient, with higher income resulting in progressively lower odds of experiencing childhood adversity. A longitudinal study in Scotland has also demonstrated the inverse, graded relationship between various ACEs and family socioeconomic status whereby low-SES children were more likely to experience maltreatment (37).

To our knowledge this is the first study to assess how ACEs in the preschool period mediate the association between SECs and adverse health outcomes in adolescence. Our recent study also showed the importance of other early life risk factors such as perinatal risks (e.g. maternal smoking pregnancy, breastfeeding, gestational age at birth and child birth weight) for inequalities in adolescent mental health (6). Given the lack of a clear understanding of how disadvantaged SECs structure the risk and consequences of ACEs, our study brings a more causally informed interpretation of how it might be responsible for the generation of health inequalities. In many studies poor SECs is considered an ACE in itself, (10,11) and in many others SECs are adjusted for as potential confounders of the association between ACEs and health outcomes (4,12–15). Our analysis supports our previous suggestion that conflating indicators relating to social circumstances with ACEs is conceptually confusing and may lead to the importance of SEC being neglected (16).

There are few studies disentangling the role of ACEs in generating health inequalities. A forthcoming systematic review suggests that out of almost 3,000 papers, only 6 attempted to explain ACEs with reference to childhood socio-economic conditions (38). For example, a study from the US using a nationally representative sample of 95,677 parents of children 0 to 17 years of age examined, cross-

sectionally, the patterning of ACEs according to household income and how that is associated with children's health and developmental outcomes. ACEs influenced negatively a broad range of investigated health and development outcomes, however, it was not confined to the most disadvantaged children but rather extended up the income spectrum (39). Another cross-sectional survey conducted in the US (N=7,470), looked at long-term effects of ACEs on health in conjunction with socioeconomic disadvantage, and found that socioeconomic status partially influenced the ACEs effects on the health outcomes (40).

Strengths and Limitations

A key strength of our study is the use of secondary data from a large, contemporary UK cohort, which measures a wide range of information, which allowed us to explore a range of ACEs experienced in the first five years of life. This study adds to the literature by being the first to formally test the mediating role of ACEs lived through a key stage of live (i.e. first infancy) on social inequalities in adolescent health outcomes using counterfactual methods. The use of validated measures of adolescent mental health, cognitive performance and overweight/obesity is also a strength of our study.

A potential limitation of our study is the parental-reported nature of the variables used to capture ACEs and health outcomes. Most literature has also used parent-reported data on ACEs, so there is a greater chance of underreporting and underestimating the mediated effect on these findings. In this study we were interested in quantifying the impact of adversities experienced in the preschool period. Our findings may be considered as the minimum impact of ACEs on inequalities in health outcomes. Future research may focus on analysing the cumulative mediating role of ACEs up to age 18 years, and the importance of experiences at specific stages of childhood (i.e. school age) for health inequalities. Other outcomes could also be assessed such as somatic health conditions and school attendance. Arguably, different sets of ACEs can be considered for different outcomes – as the pathways between socioeconomic disadvantage and language delay vs obesity are likely to be different.

Another limitation is that the MCS, as with many other studies, does not have data on all risks considered as ACEs (e.g. sexual abuse, incarceration of adults in the household, etc). MCS questions on parental alcohol consumption at ages 3 and 5 only evaluated frequency without quantifying the volume, and we therefore undertook a robustness test removing this variable from our mediating block. Sampling and response weights were used for descriptive analysis to account for the sampling design and attrition to age 14, however, these cannot account for item missingness. In this analysis the sample was large, and the internal associations, which were the targets of inference within the sample population, are likely to be valid. Although we used modern methods for causal mediation analysis, and adjusted for a range of potential confounders, the assumption of complete adjustment of confounding is still required for causal interpretation of our estimates.

Policy and practice implications

The increased risk of socioemotional behavioural problems, cognitive disability and overweight/obesity in adolescents growing up in disadvantaged SECs in the UK is partly explained by ACEs measured up to five years of age. Preventing ACEs in the early years is likely to reduce inequalities in important child health outcomes. From a policy perspective it is important to separate modifiable childhood SECs from specific harmful exposures. Efforts to improve child health outcomes should focus on universal primary prevention (41) of childhood adversities and early identification and appropriate interventions to reduce subsequent modifiable harms (8,11). In parallel actions on the social determinants of health and other important mediators of child health inequalities such as perinatal risk factors (6) are necessary to reduce modifiable socioeconomic inequalities.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, UCL Institute of Education.

Funding

This work was supported by the UK Public Health Research Consortium (PHRC). The PHRC is funded by the Department of Health and Social Care Policy Research Programme. Information about the wider programme of the PHRC is available from http://phrc.lshtm.ac.uk/. The views expressed in this paper are those of the authors and do not necessarily reflect those of the Department of Health and Social Care. DCTR is funded by the MRC on a Clinician Scientist Fellowship (MR/P008577/1).

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Text Box 1. Description of early adverse childhood experiences at ages 3 and 5

- **Verbal maltreatment (Age 5)** - the main responder was questioned about *'How often shouts at child when naughty? Daily, often [about once a week or more], sometimes [once a month], rarely or never'.*
  Dichotomized: daily, often *versus* sometimes/rarely/never [Ref]

- **Physical maltreatment (Age 5)** - the main responder was questioned about *'How often smacks the child when naughty? Daily, often [about once a week or more], sometimes [once a month], rarely or never'.*
  Dichotomized: daily, often *versus* sometimes/rarely/never [Ref]

- **Parental divorce (Ages 3 and 5)**[1] - the main responder was asked about marital status to identify occurrence of divorce or legal separation (*'Divorced, legally separated, 1st marriage, remarried, 2nd or later married, single, never married or widowed'*).
  Dichotomized: divorced/legally separate *versus* single/widowed/married [Ref]

- **Maternal metal illness (Ages 3 and 5)**[1] - Kessler 6 (K6)[¥] scale was used to assess maternal mental health in the last month asking the responders how often they felt depressed, hopeless, restless or fidgety, worthless, or that everything was an effort. Respondents answered on a five-point scale from 1 (all the time) to 5 (none of the time). We reversed and rescaled all items from 0 to 4 for analysis purposes, so that high scores indicate high levels of psychological distress. We used validated cut offs for severe mental illness [*'yes (scores >=13) /no'*]

- **High frequency of parental alcohol use (Ages 3 and 5)**[1] - the main responder responded a question about the usual frequency of alcohol consumption (*'Every day, 5-6 times per week, 3-4 times per week, 1-2 per week, 1-2 per month, less than once a month or never'*).
  Dichotomized: every day and 5-6 times per week *versus* 3-4 per week/1-2 per week/1-2 per month/never [Ref]

- **Domestic violence (Ages 3 and 5)**[1] - the main responder was asked about the use of force by the partner in relationship (*'Yes, no or do not want to answer'*
  Dichotomized: yes/do not want to answer *versus* no [Ref]

- **Use of drug (Age 5)** - the main responder was asked about the use of recreational drugs in past 12 months (*'regularly, occasionally, cannot define or never'*).
  Dichotomized: regularly *versus* occasionally, cannot define and never [Ref]

[1]Information measured at ages 3 and 5 were treated as two independent variables in the models

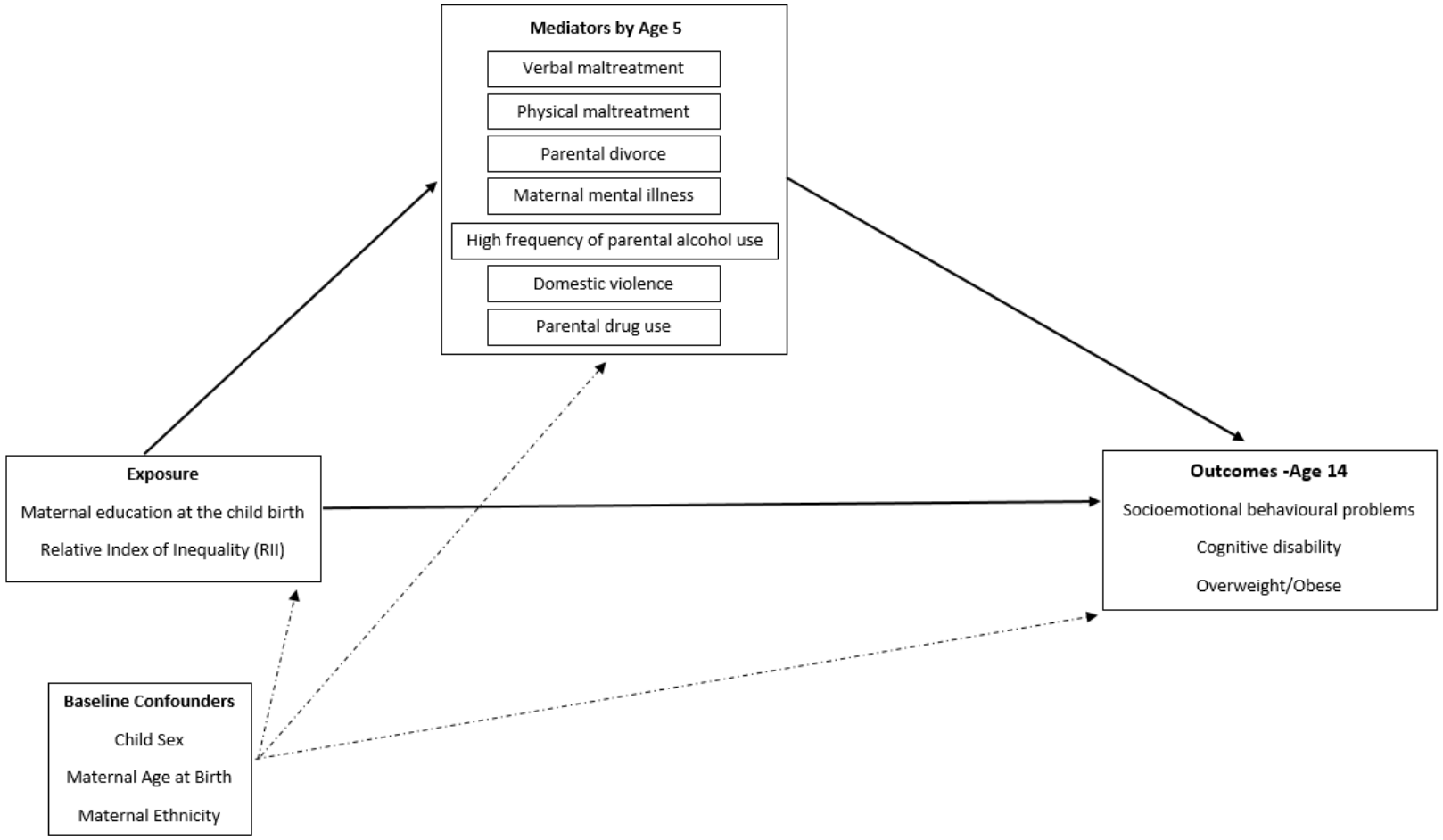
[¥]Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SLT et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychological Medicine 2002; 32(6), 959–976.

Table 1. Health outcomes at age 14 years old and early adverse childhood experiences by maternal educational level at birth

Maternal educational level at birth	Total	Degree Plus	Diploma	A level	GCSE A-C	GCSE D-G	None	p-value
	%	%	%	%	%	%	%	
Outcomes								
Social emotional behavioural problems	8.7	3.5	7.0	6.4	8.4	15.3	15.4	*<0.001*
Cognitive disability	6.0	2.5	4.9	4.2	6.5	9.1	9.9	*<0.001*
Overweight/obese	24.6	16.7	23.9	21.0	26.5	30.0	30.8	*<0.001*
ACEs*[1]								
Verbal maltreatment age 5	36.5	34.1	37.5	38.6	38.6	35.6	32.9	*0.067*
Physical maltreatment age 5	1.4	0.8	1.0	1.2	1.5	1.3	2.2	*0.309*
Parental divorce age 3	3.4	1.0	3.6	3.1	3.9	3.7	5.5	*<0.001*
Parental divorce age 5	2.1	4.7	4.7	3.9	4.3	4.9	8.7	*<0.001*
Maternal mental illness age 3	2.3	0.5	1.1	1.2	2.5	3.9	5.0	*<0.001*
Maternal mental illness age 5	2.4	0.6	1.9	1.1	2.3	4.7	5.1	*<0.001*
High frequency alcohol use age 3	7.3	13.3	9.7	8.9	5.2	4.4	3.3	*<0.001*
High frequency alcohol use age 5	8.2	13.9	9.7	7.9	7.2	5.6	3.4	*<0.001*
Domestic violence age 3	3.3	2.6	4.5	2.6	2.9	4.3	5.1	*0.018*
Domestic violence age 5	4.1	3.0	3.1	3.6	4.1	5.1	6.2	*0.048*
Use of drugs	0.8	0.5	0.9	0.4	0.7	0.8	1.6	*0.317*
1 or > ACEs	50.8	49.2	53.7	52.6	50.3	51.5	50.5	*0.660*
2 or > ACEs	16.4	16.1	16.4	14.4	15.2	18.4	19.9	*0.198*
3 or > ACEs	5.4	5.3	5.7	3.5	6.1	3.8	6.1	0.185
4 or > ACEs	1.4	1.1	1.7	0.9	1.6	0.5	2.1	0.210

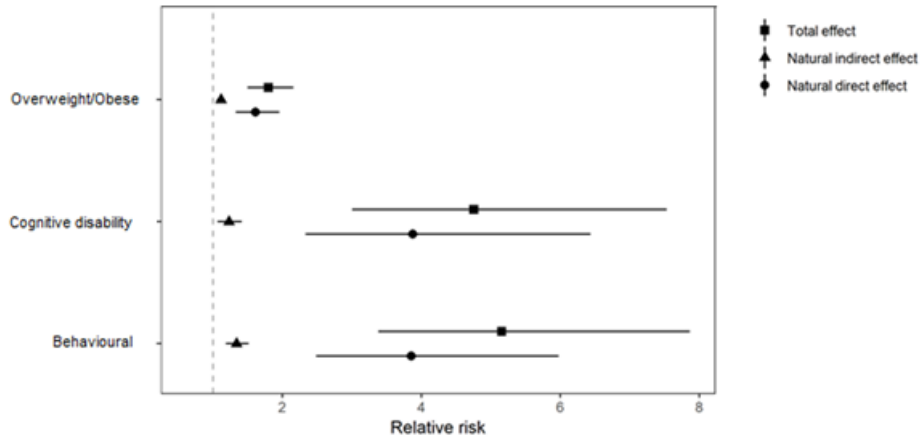
*For the purposes of descriptive analysis the ACEs were dichotomized as outlined in Text box 1

Figure 1. DAG of the natural direct effect of the exposure to outcomes at age 14, and the natural indirect effect throughout mediators by the age 5. Model adjusted for potential baseline confounders.



**RII: calculated by ranking the six educational groups for maternal education from the lowest to the highest within the same category and allocating a score (ranging from 0-1) that equals the midpoint of the category's range in the cumulative distribution*

Figure 2. Counterfactual mediation analysis. Relative Risk (RR, 95%CI) of Natural Direct Effect (NDE, 95%CI), Natural Indirect Effect (NIE, 95%CI), Total Effect (TE, 95%CI) for RII by all ACEs for behavioural, cognitive and overweight/obese outcomes at age 14.



4.4 How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study

How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study

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Abstract

Background. Reducing inequalities in adolescent mental health is a public health priority, yet the pathways that link social conditions to mental health outcomes in the early years are unclear. We aimed to evaluate the extent to which early years risk factors explain social inequalities in adolescent mental health in the UK.

Methods. We analysed data from 6,509 children captured in the UK Millennium Cohort Study. The main outcome was mental health problems at age 14 (Strengths and Difficulties Questionnaire-SDQ). The main exposure was maternal education at birth, used as a measure of childhood socioeconomic conditions (SEC), and used to calculate the relative index of inequality. Using causal mediation analysis, we assessed how perinatal; individual child; family; peer relation; and neighbourhood level factors measured up to age three years mediated the total effect (TE) of SECs on adolescent socioemotional behavioural problems, estimating the proportion mediated and natural indirect effect (NIE) via each block of mediators, and all mediators together.

Results. Children of mothers with no qualification were almost four times as likely to have mental health problems compared to degree plus level (RR 3·82 95%CI 2·48,5·88). Overall 63·9% (95%CI 50·2,77·6) (NIE RR 1·97 (95%CI 1·63,2·37)) of the TE (RR 4·40 95%CI 3·18,6·07) of social inequalities on risk of adolescent mental health problems was mediated by early life factors.

Conclusions. About two thirds of the social inequality in adolescent mental health was explained by early years risk factors measured by age three, highlighting the importance of public health interventions in this period.

What is already known on this subject?

Adolescent mental health is in crisis in the UK, with stark inequalities and concerning signs of deterioration at a population level. It is unclear; however, which factors mediate social inequalities in adolescent mental health.

What this study adds?

Using robust methods for causal inference in observational data we show that around two-thirds of the social inequality in adolescent mental health is explained by early years risk factors identified by the age of 3 years.

Policy implications

The implications of this are that public health policies to improve mental health in the UK should address modifiable socioeconomic inequalities and focus more on early years prevention.

Background

Adolescent mental health is poor in the United Kingdom (UK), and there are concerning indications that the situation may be deteriorating, with UK universities reporting a dramatic rise in students reporting mental health conditions over recent years [1]. There are stark inequalities in mental health, with the most disadvantaged children experiencing worse mental health and subsequent consequences over the course of their lives [2, 3]. A systematic review on prevalence of youth mental health disorders, using worldwide data from the last forth decades, evidenced that 10%–20% of children and adolescents suffer from mental disorders, and half of all mental illnesses initially manifest by 14 years of age [4]. In the UK, according to the most recent population level data from the Office for National Statistics [2], 1 in 8 children aged 10 to 15 reported social-emotional behavioural problems in 2011-2012.

It is essential to understand the drivers of inequalities in adolescent mental health, and to clarify factors associated with risk and resilience in order to inform prevention efforts [1]. A recent systematic review of the association between socioeconomic conditions (SECs) and child mental health outcomes found that 1 in 5 children experience poor mental health, and those living in disadvantaged childhood socio-economic conditions (SECs) were approximately 2 to 3 times more likely to develop mental health problems than their peers from more socioeconomically advantaged families. The authors also found that 52 (out of 55) studies reported a graded inverse relationship between SEC and child mental health outcomes, whereby lower socio-economic status is associated with greater adverse mental health outcomes [5].

Whilst the association of adverse SECs with worse child mental health is well-established, we lack understanding of the complex pathways linking social conditions to mental health outcomes [1]. There are a number of plausible mechanisms: Children growing up in disadvantaged SECs may be exposed to more traumatic events and stressors (e.g., witnessing violence, frequent moves), which in turn may increase their risk of mental and behavioural problems [6-8]; the strain of financial stress may also lead to family conflict and potentially disruption (e.g., divorce or separation of parents); or may influence parenting behaviours, including increased use of harsh discipline methods, lack of affection and support, or inadequate supervision [7-9]. In addition, children growing up in disadvantaged SECs may be more likely to reside in more disadvantaged neighborhoods with higher levels of crime, exposing them to suboptimal physical and social environmental conditions that may adversely influence their mental health [6].

Despite of an increasing recognition of the crucial influence of the early years of life to promote positive future health and wellbeing later in life, there is little evidence as to how risk factors at this

early stage impact adolescent mental health. Mäntymaa and colleagues categorise risk factors for child psychopathology as: (i) risks in the infant or child; (ii) risks affecting the parents and (iii) risks in the family and social context.7 However, the interplay of these mechanisms, and their differential impact by SECs is poorly understood. This study therefore aims to explore the social gradient in poor adolescent mental health and the extent to which it is explained by preschool risk factors, using a contemporary UK cohort.

Methods

Study design and population

The Millennium Cohort Study (MCS) is a large nationally representative cohort sample study of 18,818 children born in the United Kingdom between Sept 1, 2000 and Jan 11, 2002. To date it includes six sweeps: 9 months, 3, 5, 7, 11 and 14 years old, and we used data from 3 sweeps (9 months, 3 and 14 years old). We included all singleton children with complete data provided by the main respondent (almost always the mother). The study oversampled children living in disadvantaged areas and in ethnic minority groups by means of a stratified cluster sampling design. Further information can be found in the cohort profile or online (www.cls.ioe.ac.uk/mcs). Ethical approval for the MCS was received from a Research Ethics Committee at each sweep [10].

Measures

Mental Health Outcome

Our outcome was adolescent socioemotional behavioural problems assessed using maternal reported Strengths and Difficulties Questionnaire (SDQ) when the cohort participants were aged 14 years. The SDQ is a screening tool that has been translated into many languages, has been implemented in mental health settings in many countries around the globe, and is considered a validated and easy to administer measure for emotional and behavioural problems in a number of settings [13]. The SDQ is a 25 item measure that asks parents to rate their child's behaviour over the previous 6 months using five subscales, each with five items: peer problems, conduct disorders, hyperactivity, emotional problems, and prosocial behaviour. We used the total difficulties score (which excludes the prosocial behaviour items) using validated cut-offs widely used in previous studies [11, 12], for which a score of 0 to16 indicates 'normal to borderline behaviour' and 17 to 40 indicates 'socioemotional behavioural problems' [13].

Measurement of socio-economic circumstances (SECs)

Our primary exposure of interest was the highest qualification attained by the mother around time of MCS child's birth, used as a measure of childhood SECs at the birth of the cohort child (1. 'Degree plus=higher degree or first degree qualifications'; 2. 'Diploma=in higher education'; 3. 'A-levels' (exams taken around 18 years); 4. 'General Certificate of Secondary Education (GCSE - exams taken around age 16 years) grades A–C'; 5. 'GCSE grades D–G'; 6. 'None of these qualifications'). Level of maternal educational qualifications is a commonly used measure of childhood SECs in social epidemiological studies [8, 14-16]. The supplementary material provides more information about the education system in the UK (S1). It was coded as a categorical variable for the first step of our analysis (results available in the supplementary material). We also repeated the analysis using family income (see robustness tests below).

In a second step, we calculated the relative index of inequality (RII), which compares the risk of mental health problems between children of lowest and highest socioeconomic status, taking into account the educational distribution, by ranking the six maternal educational groups from the lowest to the highest and allocating a score (ranging from 0-1) that equals the midpoint of the category's range in the cumulative distribution. The RII is a regression-based index which summarizes the relative inequality across the distribution of SECs, taking into the size of the population and the relative

disadvantage experienced by different groups. For instance, if 24% of the mothers had none formal education, they would be allocated a score of 0.12, and if the next group of mothers constituted 42%, they would be allocated a score of 0.45 (0.24 + 0.42/2) etc. Using this score as a continuous exposure variable in the regression model, its estimated coefficient expresses the RII, with a similar interpretation to a relative risk (RR) [17].

Potential Mediating Risk Factors

We identified five categories of early childhood risk factors considered as potential mediators of the social gradient in adolescent mental health based on literature reviews and mapped onto data available in the MCS [6-8]. The potentially mediating risk factor blocks were ordered from proximal to distal influences in the child [4] (Figure 1) and were reported by the main responders. The full details of the coding of these mediators are provided in the supplementary material (S2).

1. Perinatal factors: maternal smoking and consumption of alcohol in pregnancy; preterm birth; duration of breastfeeding (<4 months) and low birth weight [5 items];

2. Child individual factors: delayed school readiness, long-term disabilities or illness, cognitive disabilities [3 items];

3. Family factors: maternal mental health problems, high levels of parent-child conflict, harmful parenting style and lone parenthood [4 items];

4. Peer relation factors: low time spent with friends per week, experience of being bullied or bullying other peers [3 items];

5. Neighbourhood factors: poor neighbourhood conditions and perceived safety [2 items].

Analysis and Statistical Modelling

We estimated the prevalence of mental health problems at age 14 by maternal education; and tested univariate associations between our mediators of interest and child mental health. Then the analysis progressed in two stages. First, we ran sequentially adjusted Poisson regression models to assess how the RR for the association between childhood SECs and child mental health changed on adjustment for the blocks of potentially mediating factors, added individually, and then all together, whilst adjusting for potential baseline confounders (child sex, maternal ethnicity and maternal age at birth). We evaluated the change in RRs comparing mothers with the highest qualifications to those with the lowest calculated as 100x (RR-aRR)/ (RR-1). Sampling and response weights were used in all analyses to account for the sampling design and attrition at age 14.

Second, we undertook a counterfactual mediation analysis to formally assess the amount of social inequality in mental health at age 14 explained by each mediating block, using the RII as the exposure. We estimated the RRs and 95%CI for the Natural Direct Effect (NDE), Natural Indirect Effect (NIE) and Total Effect (TE) (more information in the online supplementary material, S3) for each block of mediators individually and all blocks together (six models described above) using the medflex package in R software. This package fits natural effect models, a novel class of counterfactual models to directly parameterize the path-specific effects of interest, in the presence of multiple mediators, taking into account interactions between the variables included in the mediating blocks [18]. We calculated the proportion mediated and 95%CI for each block of mediators applying the formula: (RRNDE*(RRNIE-1)) / (RRNDE*RRNIE -1) [19]. All analyses were conducted in Stata/SE V.15 (Stata Corporation) and R V.3.4.4.

Robustness tests

We used multiple imputation by chained equation [20] in order to check whether there are differences in descriptive and associative results of complete cases and imputed samples. We did additional

descriptive analysis comparing baseline cases and complete cases for child sex, maternal ethnicity and maternal education.

For the mediation analysis to have a causal interpretation, we assume that sufficient adjustment for confounding has been achieved and that there is no post-treatment confounding (supplementary material) [19]. To explore exposure-mediator interaction we repeated the analysis allowing for all 2-way interactions between maternal education and the mediators in the model and used AIC to compare model fit.

We repeated our first step regression analysis using RII as the exposure variable for the purposes of comparison with the counterfactual mediation analysis. The second step (counterfactual mediation analysis) was also repeated using equivalised family income as an alternative measure of childhood SECs.

Results

10,264 children who participated in the first (9 months) and the latest (14 years) sweeps had data on mental health at age 14. Data on cohort member's mental health (main outcome) and maternal education at birth (main exposure) were available for 9,962 participants. Around two-thirds (n=6,509) had full data on all exposure, outcome, mediators and confounders of interest, i.e. the complete case population.

9% (95%CI 7·9, 10) of children had mental health problems by 14 years. There was a clear social gradient in mental health problems, whereby the proportion of children reporting problems increased as childhood SEC level decreased, as measured by maternal educational qualification level (Figure 2). All characteristics of the study population, except child sex and long-term disability or illness at age 3, were associated with childhood SECs (Table 1).

Table 1. Characteristics of the complete case study population, by level of maternal education at birth of child (N =6,509)

	Degree Plus	Diploma	A level	GCSE A-C	GCSE D-G	None	Total	p-value
	%	%	%	%	%	%	%	
Adolescents mental health problems at age 14	3·1	7·0	5·9	9·7	14·3	14·4	8·9	<0·001
Child's sex								0·701
Male	50·2	51·2	46·2	50·2	48·3	47·9	49·6	
Female	49·8	48·8	53·8	49·8	51·6	52·1	50·4	
Maternal age at MCS birth								<0·001
14-24	26·5	41·5	47·5	52·6	71·4	61·3	47	
25+	73·5	58·5	52·5	47·4	28·6	38·7	53	
Maternal ethnicity								<0·001
White	91·7	94·4	93	94·6	92·6	86·2	92·8	
Non-white	8·3	5·6	7	5·4	7·4	13·8	7·2	
Smoking in pregnancy								<0·001
No	96·6	90·1	88·9	79·1	66·3	53·7	82·3	
Yes	3·4	9·9	11·1	20·9	33·7	46·3	17·7	
Alcohol consume in pregnancy								<0·001
None	34·7	48·4	54	59·7	69·1	73·7	53·9	
Any unit per week	65·3	51·6	46	40·3	30·1	26·3	46·1	
Gestational age at birth								0·007
Preterm	4·6	5·8	3·4	5·9	5·8	6·7	5·4	
Regular term	95·4	94·2	96·6	94·1	94·2	93·3	94·6	
Child's birth weight								<0·001
Low weight	3·6	5·4	4·7	5·5	6·4	8·9	5·3	
Normal+	96·4	94·6	95·3	94·5	93·6	91·1	94·7	
Breastfeeding at least 4 months								<0·001
Yes	64·3	40·3	41·9	26·9	17·9	15·8	37·2	
No	35·7	59·7	58·1	73·1	82·1	84·2	62·8	
Cognitive disability at age 3								<0·001
No	98·5	97·7	97·7	96	94·2	88·9	96·2	
Yes	1·5	2·3	2·3	4	5·7	11·1	3·8	
School readiness at age 3								<0·001
Average, advanced or very advanced	96·6	96·1	95·1	91·4	85·4	79·7	92·1	
Very delayed or delayed	3·4	3·9	4·9	8·6	14·6	20·3	7·9	
Child long term disabilities or illness at age 3								0·063
No	85·7	85·2	88·7	84·6	83·7	80·6	85	
Yes	14·3	14·8	11·3	15·4	16·3	19·4	15	
Maternal mental health problems								<0·001
No	89·1	87·3	86·5	81·6	81·6	70·6	83·7	
Yes	10·9	12·7	13·5	18·4	18·4	29·4	16·3	

Parenting style								<0·001
Firm discipline plus fun	59·9	56·3	54·6	47·1	42	37·4	51	
Education negligence or excess of rules	40·1	43·7	45·4	52·1	58	62·6	49	
Child-parents conflict relationship								0·001
Low conflicts	47·5	47·5	47·8	47·7	45·5	36·5	46·5	
High conflicts	52·5	52·5	52·2	52·3	54·5	63·5	53·5	
Lone Parenthood								<0·001
No	98·3	95·6	92	87·5	83·7	76·2	90·2	
Yes	1·7	4·4	8	12·5	16·3	23·8	9·8	
Child's time spend with friends								0·027
Any time per week with friends	99·4	100	98·5	99·4	99·4	98·7	99·3	
Not at all	0·6	0	1·5	0·6	0·6	1·3	0·7	
Being bullied								<0·001
Not being bullied	95·7	96·1	94·3	93·5	89·5	86·6	93·5	
Some true or certainly true	4·3	3·9	5·7	6·5	10·5	13·4	6·5	
Fights or bullies other peers								<0·001
Not fights or bullies	90·7	89·3	88·4	85·6	78·4	69·6	84·1	
Some true or certainly true	9·3	10·7	11·6	14·4	21·6	30·4	15·9	
Neighbourhood conditions								<0·001
Not at all or nor very common neighbourhood problems	50	44·1	43·7	39·8	29·2	27·4	41·1	
Fairly or very common neighbourhood problems	50	55·9	56·3	60·2	70·8	72·6	58·9	
Neighbourhood safety								<0·001
Very safe	95·1	93·3	90·5	85·5	81·9	76·4	87	
Fairly safe	5·1	6·7	9·5	14·5	18·1	23·6	13	

In the univariate regression, adolescents of mothers with no qualifications were more than four times as likely to have had mental health problems than adolescents of mothers with degree level qualifications or higher (RR 4·48 [95%CI 2·91,6·88]) (Table 2). Younger maternal age at MCS birth, smoking in pregnancy, absence of alcohol consumption in pregnancy, less than 4 months of breastfeeding; cognitive disabilities, school readiness delayed, long term disabilities or illness at age 3; maternal mental health problem diagnosis, high conflicting relationship of children-parents, lone parenthood; being bullied or fights/bullies other peers; poorer neighbourhoods conditions and lower safety were statistically associated with an increased RR for adolescent mental health problems at age 14 years (Table 2).

Table 2. Prevalence of mental health problems at age 14 and univariate RRs (N = 6,509)

	Total %	Adolescents with mental health problems %	RR (95% CI)
Maternal education			
Degree plus	6·4	3·1	1·00
Diploma	7·6	7·1	2·26 (1·44,3·54)
A levels	6·7	5·9	1·88 (1·13,3·15)
GCSE A-C	41·2	9·7	3·09 (2·10,4·55)
GCSE D-G	17·5	14·4	4·60 (2·98,7·09)
None	20·6	14	4·48 (2·91,6·88)
Child's sex			
Male	53·9	9·7	1·18 (0·95,1·48)
Female	46·1	8·2	1·00
Maternal age at MCS birth			
14-24	67·8	11·5	1·93 (1·55,2·41)
25+	32·2	6·1	1·00
Maternal ethnicity			
White	93·5	8·9	1·00
Non-white	6·5	9·8	1·11 (0·70,1·76)
Smoking in pregnancy			
No	62·2	7·2	1·00
Yes	37·8	15·1	2·06 (1·66,2·54)
Alcohol consume in pregnancy			
None	64·6	10·4	1·00
Any unit(s) per week	35·4	7·1	0·69 (0·56,0·86)
Gestational age at birth			
Preterm	6·2	9·8	1·11 (0·75,1·65)
Regular term	93·8	8·9	1·00
Child's birth weight			
Low weight	92·5	11·5	1·34 (0·91,1·96)
Normal+	7·5	8·8	1·00
Breastfeeding at least 4 months			
Yes	19	5·3	1·00
No	81	10·7	2·08 (1·59,2·73)
Cognitive disability at age 3			
No	90·3	8·5	1·00
Yes	9·7	19·7	2·33 (1·65,3·30)
School readiness at age 3			
Average, advanced or very advanced	83·7	8·3	1·00
Very delayed or delayed	16·3	14·8	1·72 (1·26,2·34)
Child long term disabilities or illness at age 3			
No	76·5	8·1	1·00
Yes	23·5	13·8	1·73 (1·34,2·23)
Maternal mental health problems			
No	67·5	7·3	1·00
Yes	32·5	16·5	2·25 (1·81,2·79)
Parenting style			
Firm discipline plus fun	44·9	8·1	1·00
Education negligence or excess of rules	55·1	9·8	1·19 (0·98,1·44)
Child-parents conflict relationship			
Low conflicts	23·2	4·7	1·00
High conflicts	76·8	12·2	2·61 (2·08,3·27)

Lone Parenthood			
No	76·6	7·9	1·00
Yes	23·4	15·4	1·95 (1·49,2·54)
Child's time spend with friends			
Any time per week with friends	98·7	8·9	1·00
Not at all	1·3	16·4	1·86 (0·86,4·01)
Being bullied			
Not being bullied	86·3	8·4	1·00
Some true or certainly true	13·7	16·2	1·89 (1·28,2·80)
Fights or bullies other peers			
Not fights or bullies	65·1	6·9	1·00
Some true or certainly true	34·9	19·5	2·76 (2·17,3·50)
Neighbourhood conditions			
Not at all or nor very common neighbourhood problems	26·7	6·0	1·00
Fairly or very common neighbourhood problems	73·3	10·9	1·84 (1·45,2·34)
Neighbourhood safety			
Very safe	80·9	8·3	1·00
Fairly safe	19·1	12·9	1·60 (1·19,2·15)

Table 3 shows the distribution of the sample in terms of maternal education, and the extent to which the elevated RR of mental health problems in 14-year-old adolescents with mothers with no qualifications (RR 3·82, 95%CI 2·48, 5·88, after adjustment for confounders) was attenuated when adjusting separately for each block of mediators. There was a 40·8% reduction to aRR 2·67 (95% CI 1·68, 4·23) adjusting for perinatal factors (model 1); a 12·7% reduction (aRR 3·46, 95%CI 2·22, 5·39) adjusting for child factors (model 2); a 25·8% (aRR 3·09, 95%CI 1·96, 4·89) and 26·9% (RR a3·06, 95%CI 2·00, 4·58) reduction for family (model 3) and peer relation factors (model 4) respectively; and a 13·8% reduction adjusting for neighbourhood factors (model 5, aRR 3·43, 95%CI 2·16, 4·94). In model 6, adjusted for all blocks, the RR was attenuated by 64·8% (aRR1·99, 95%CI 1·22, 3·26).

Table 3. Regression models for mental health problems at age 14. Covariate estimates using complete case analysis (N =6,509)

		RR (95%CI)*						
		Baseline**	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Maternal education	**Diploma**	2·08 (1·32,3·27)	1·88 (1·19,2·98)	2·06 (1·31,3·22)	2·09 (1·33,3·29)	2·06 (1·26,3·05)	2·04 (1·22,2·97)	1·89 (1·20,3·00)
	A levels	1·71 (1·03,2·85)	1·55 (0·92,2·59)	1·71 (1·03,2·84)	1·68 (1·01,2·78)	1·68 (1·01,2·80)	1·66 (1·00,2·75)	1·55 (0·93,2·60)
	GCSE A-C	2·70 (1·83,3·98)	2·21 (1·46,3·33)	2·60 (1·76,3·83)	2·50 (1·68,3·72)	2·57 (1·64,3·33)	2·52 (1·60,3·27)	2·02 (1·32,3·11)
	GCSE D-G	3·73 (2·41,5·77)	2·79 (1·74,4·49)	3·46 (2·21,5·40)	3·39 (2·17,5·28)	3·28 (2·15,4·85)	3·37 (2·20,4·98)	2·36 (1·44,3·87)
	None	3·82 (2·48,5·88)	2·67 (1·68,4·23)	3·46 (2·22,5·39)	3·09 (1·96,4·89)	3·06 (2·00,4·58)	3·43 (2·16,4·94)	1·99 (1·22,3·26)
Perinatal Factors								
Smoking in pregnancy			1·47 (1·12,1·92)	-	-	-	-	1·23 (0·94,1·61)
Alcohol consume in pregnancy			0·92 (0·74,1·13)	-	-	-	-	0·90 (0·74,1·10)
Gestational age at birth			0·95 (0·65,1·38)	-	-	-	-	0·87 (0·58,1·29)
Child's birth weight			1·16 (0·77,1·76)	-	-	-	-	1·17 (0·78,1·75)
Breastfeeding at least 4 months			1·35 (1·01,1·80)	-	-	-	-	1·21 (0·91,1·61)
Child Individual Factors								
Cognitive disability			-	1·64 (1·11,2·41)	-	-	-	1·45 (0·99,2·12)
School readiness			-	1·15 (0·82,1·62)	-	-	-	1·01 (0·73,1·40)
Child long term disabilities or illness			-	1·59 (1·24,2·04)	-	-	-	1·47 (1·15,1·87)
Family Factors								
Maternal mental health problems			-	-	1·61 (1·33,3·29)	-	-	1·52 (1·19,1·93)
Parenting style			-	-	1·00 (0·81,1·23)	-	-	1·02 (0·83,1·25)
Lone Parenthood			-	-	1·27 (0·95,1·71)	-	-	1·15 (0·85,1·55)
Child-parents conflict relationship			-	-	2·20 (1·70,2·84)	-	-	1·85 (1·43,2·39)
Peer Relations Factors								
Child's time spend with friends			-	-	-	1·97 (0·95,3·90)	-	1·70 (0·91,3·20)
Being bullied			-	-	-	1·35 (0·94,1·96)	-	1·15 (0·79,1·67)
Fights or bullies other peers			-	-	-	2·22 (1·75,2·83)	-	1·76 (1·39,2·23)
Neighbourhood Factors								
Neighbourhood conditions			-	-	-	-	1·51 (1·18,1·94)	1·35 (1·07,1·72)
Neighbourhood safety			-	-	-	-	1·20 (0·88,1·65)	1·05 (0·78,1·41)
Proportion attenuated (%) * **			40·8	12·7	25·8	26·9	13·8	64·8

*All models were adjusted for baseline confounders (maternal age birth, child sex and maternal ethnicity) - omitted table results; **Adjusted only for baseline confounders - omitted table results;*** Proportion of RR attenuated by comparison of Baseline Model with Models 1-6.

The counterfactual mediation analysis results were shown in Figure 3 and detailed in Table 4 (Log-RR results was presented in the supplementary material (S4)). Overall 34% (19·9,47·5), 16% (7·8,24·2), 28% (17·2,38·3), 26% (18·8,34·2) and 17% (10·3,24·2) of the TE of SECs on risk of mental health at age 14 years in UK children were mediated through exposure to perinatal, child individual, family, peer relations and neighborhood factors, respectively. Considering all blocks of early risk factors together, 63·9% (50·2, 77·6) of the TE of SEC on risk of adolescent mental health problems was mediated. The TE of low (hypothetical at the bottom of the educational hierarchy) versus high SECs on children mental health was RR 4.40 (95%CI 3.18, 6.07). The natural direct effect (RR 2·23, 95%CI 1·55,3·20) is the increase in mental health risk comparing low to high SEC that we would observe if the mediators remained as in the top end of the SEC hierarchy; and the natural indirect effect is the increased risk of mental health problems we would see if the SECs were fixed at top of the SEC hierarchy, but the mediators were fixed at those that would naturally occur at low SECs (RR 1·97, 95%CI 1·63,2·37).

Table 4. Natural Direct Effect (NDE), Natural Indirect Effect (NIE), Total Effect (TE) and proportion mediated for exposure maternal education at birth mediated by blocks of risk factors for adolescents mental health at age 14. (N=6,509)

Blocks of Mediators	Effect	RR (95% CI)	Proportion mediated [% (95% CI]
Perinatal	NDE	3·29 (2·29-4·71)	34·1 (19·9-47·5)
	NIE	1·36 (1·18-1·56)	
	TE	4·48 (3·21-6·25)	
Child individual	NDE	3·90 (2·76-5·48)	16·1 (7·8-24·2)
	NIE	1·14 (1·06-1·22)	
	TE	4·45 (3·19-6·19)	
Family	NDE	3·45 (2·45-4·89)	27·9 (17·2-38·3)
	NIE	1·30 (1·15-1·40)	
	TE	4·40 (3·16-6·10)	
Peer relation	NDE	3·50 (2·50-4·86)	26·4 (18·8-34·2)
	NIE	1·25 (1·17-1·34)	
	TE	4·38 (3·16-6·07)	
Neighbourhood	NDE	3·89 (2·78-5·45)	17·3 (10·3-24·2)
	NIE	1·15 (1·08-1·22)	
	TE	4·49 (3·22-6·28)	
All blocks	NDE	2·23 (1·55-3·20)	63·9 (50·2-77·6)
	NIE	1·97 (1·63-2·37)	
	TE	4·40 (3·18,6·07)	

NDE: Natural direct Effect ; NIE: Natural Inrect Effect; TE: Total Effect

Robustness tests

The results for our descriptive analysis, and step 1 analysis were similar in our multiply imputed sample (S5, S6 and S7 supplementary material), with 57% attenuation of the SEC effect in the model adjusted for all mediators. Baseline cases and complete cases sociodemographic characteristic are show in S8. For the counterfactual mediation analysis a model that included all exposure-mediator interactions had a worse fit on the basis of AIC (results are not shown). The pattern of results was similar using RII as the exposure for the first step of the analysis (supplementary material S9). Repeated counterfactual analysis using RII on the bases of income, instead of maternal education presented similar pattern of results (S 10).

Discussion

Using nationally representative data we show that around 1 in 10 young people have mental health problems by age 14 in the UK. There were stark social inequalities whereby the risk of mental health problems was around four times higher for children growing up in adverse SECs compared to highest

SECs. Around two-thirds of this increased risk was explained by early years risk factors identified by the age of 3 years, related to perinatal, child, family, peer relations and neighbourhood characteristics.

The inequalities in adolescent mental health identified in our study corroborate a systematic review of 55 studies that demonstrated an inverse relationship between socioeconomic status and mental health problems in children and adolescents. In the systematic review children and adolescents in socioeconomically disadvantaged populations were 2 to 3 times more likely to develop mental health problems and the persistence over time was strongly related to higher rates of mental health problems [5].

Our study suggests that efforts to reduce inequalities in adolecent mental health problems in the UK should focus on reducing socioeconomic inequalities and concerted action to address modifiable risk factors that mediate the increased risk associated with low SECs [6]. Understanding the role of risk factors in infancy and early childhood in explaining inequalities in adolescent mental health is critical to inform effective interventions, and our study is one of the first to attempt to decompose the contribution of different blocks of risk factors using counterfactual mediation analysis. The first 2 to 3 years of life is the period of maximum brain growth and of formation of emotional regulatory patterns that affect later mental health outcomes [21], and our analysis suggests that around two thirds of the inequality in mental health outcomes in adolescence can be explained by early years perinatal, child, family and neighbourhood level factors.

Our analysis suggests that addressing inequalities in perinatal risk factors is important to reduce inequalities in mental health in later life. Perinatal factors alone were the most influential block, mediating 34% the association of SEC and mental health at age 14 years, with significant associations between maternal smoking in pregnancy and shorter duration of breastfeeding, and increased risk of adolescent mental health problems. It is likely that prenatal exposures such as maternal alcohol and tobacco smoking impact adversely on early child neurodevelopment, as suggested in a recent systematic review [22], with subsequent impacts on risk of mental health problems later in life [23]. Other studies have also suggested that shorter duration of breastfeeding is an independent predictor of mental health problems through childhood and into adolescence [24]. Possible mechanisms include effects of breastfeeding on: neuroendocrine aspects of the stress response [25]; impacts on attachment [26] and infant temperament [27]; and direct effects of maternal milk on neurodevelopment [28]. The lengthy time from perinatal exposure to the development of mental health problems makes it particularly difficult to establish precise causal pathways, especially because the ways in which risk factors interplay are very complex, and the many intervening factors make it difficult to isolate effects of a single, specific factor [29].

Family factors alone mediated 27% of the inequality in child mental health, indicating another important target for public health intervention. One of the main perspectives guiding research into the pathways mediating the association of SECs and child mental health has been a focus on family factors. A recent systematic review showed that from 59 studies, parent depression, conflict between parents, parenting practices, and adolescent resilience were identified as important mediators of the relationship of socioeconomic status and psychosocial outcomes in adolescent's outcomes [6].

Strengths and limitations

A key strength is that this study used secondary data from a large, contemporary UK cohort, which measures different indicators of SEC. A wide range of information is collected in the MCS, which allowed us to explore a range of pre school risk factors for adolecents mental health problems over time. This study adds to the literature by being the first study to formally test the mediating role of different risk factors of social inequality of adolescents' mental health with methodological

robustness, using counterfactual methods. We aimed to assess multiple early years risk factors in order to put some bounds around the contribution of early years factors, which is a methodological challenge, and we used two approaches which showed similar results. The use of a validated measure of adolescent mental health is also a strength of this study.

A potential limitation of our study is the main responder self-reported nature of the mental health outcome. In addition, the co-occurrence of risk factors and protective factors makes the identification of the specific elements responsible for the onset and continuity of mental health problems challenging. Although we were able to explore a wide range of potential mediators, arranged into blocks, we were limited to data collected in the MCS. Thus, data about potentially mediating childhood adversities such as sexual abuse and parental criminality were not included in our analysis. We were unable to adjust for genetic risk factors for mental health problems which may partially explain some inter-generational transfer of risk [30] and epigenetics influences [31]. Early distal factors (i.e. non-specific factors that affect the likelihood of subsequent risks) work together with proximal causes (which directly impinge on the individual) through a probabilistic chain that is likely to be influenced by issues such as dosage, context and timing [4]. Furthermore, the impact of early years factors may be mediated by policy relevant targets for interventions at subsequent time points, although the focus of this study is on what can be done in the early years.

Thus, establishing precise causal pathways is challenging. Though we used modern methods for causal mediation analysis, and adjusted for a range of confounders, the assumption of complete adjustment of confounding is required for causal interpretation of our estimates (no unmeasured confounding through exposure-mediator, mediator-outcome and exposure-outcome associations) [32], and the standard methods for assessing these assumptions [33] cannot be applied in the context of multi-dimensional mediators. The individual block estimates need to be interpreted with caution, since our analysis does not take into account the causal ordering of the blocks of mediators. Thus whilst the total proportion mediated by all the blocks is relatively robust, the sum of the individual blocks adds up to more than the total, since the blocks are likely to affect one another, with some intermediate confounding. However, of the individual block estimates, the perinatal block estimate is unlikely to confounded by the other blocks, since the perinatal factors occur first. Missing data is also a limitation. We used a complete case analysis, including 64% of the eligible sample. Sampling and response weights were for the first stage of analysis to account for the sampling design and attrition to age 14, however these cannot account for item missingness. Complete case analyses can be inefficient, particularly in smaller datasets, or if those who were missing data are different (in terms of the associations under study) than those who were included. However, in this analysis the sample was large, and the internal associations, which were the targets of inference within the sample population, are likely to be valid. Further, it is repeating the first stage of our analysis led to similar conclusions when re-ranning the analyses in an imputed sample.

Policy and practice implications

From a public health policy perspective, our results support the need for an early years prevention focus to ensure a safe and healthy pregnancy, a nurturing childhood and support for families in providing such circumstances in which to bring up children. Addressing inequalities in perinatal factors maternal mental health and family functioning with interventions in the pre-pregnancy, antenatal and early years of life should be policy priorities. Whilst this is currently advocated in UK mental health strategy [34], much of the current action is focussed on addressing mental health in schools and improving access to mental health services for children [1]. Whilst these are clearly of critical importance, our results suggest a platform of early investment is required in order to build the foundations for healthy mental health at the population level. In the UK it is concerning that funding for early years provision has been disproportionately cut in some of the most disadvantaged areas

[35]; and that child poverty, a major socio-economic determinant of child mental health is currently increasing [3, 12].

In conclusion, we found that nine percent of children had mental health problems by age 14 in a nationally representative UK child cohort. The risk was much greater in disadvantaged children, and about two thirds of this excess risk was explained by early childhood factors up to age 3 years. Future research should investigate specific pathways, critical/sensitive periods for these exposures, and other countries with different socioeconomic context. Efforts to reduce inequalities in adolescents mental health problems should focus on reducing socioeconomic inequalities and action to address the early years mediators identified in our study, particular on perinatal factors and family factors such as maternal mental health problems. I have a minor comment about the focus on intervention for the child, but not parents.

Paper 4 shows strong effects of maternal mental health and parental conflict, which could be amenable to interventions during and after delivery (or even before pregnancy), and are currently areas of policy priority.

Ethics approval and consent to participate

Ethical approval for each wave of the MCS was granted by NHS Multicenter Research Ethics Committees. No further ethical approval was required for this secondary analysis of MCS data.

Availability of data and material

All MCS data used in this analysis are available from UK Data Service, University of Essex and University of Manchester: http://doi.org/10.5255/UKDA-SN-4683-4; http://doi.org/10.5255/UKDA-SN-5350-4; http://doi.org/10.5255/UKDA-SN-7464-3.

Competing interests

The authors have no financial relationships relevant to this article and no conflicts of interest to disclose.

Funding

This work was supported by the UK Public Health Research Consortium (PHRC). The PHRC is funded by the Department of Health and Social Care Policy Research Programme. The views expressed in this paper are those of the authors and do not necessarily reflect those of the Department of Health and Social Care. Information about the wider programme of the PHRC is available from http://phrc.lshtm.ac.uk/. VSS was granted by the Early Career Research Funding 2017 from the University of Liverpool. DTR is funded by the MRC on a Clinician Scientist Fellowship (MR/P008577/1).

Authors' contributions

Dr VSS carried out the statistical analyses (supported by Drs ETCL and TL), drafted the initial manuscript, reviewed and revised the manuscript. Drs ETCL, KSL, TL, MC, SW and Prof AMNA participated in the drafting of the initial manuscript, reviewed and revised the manuscript. Prof DCTR conceptualized and designed the study, coordinated, drafted the initial manuscript, reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, UCL Institute of Education.

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Figure 1. Logical model of block of perinatal and early life (age 3 years) mediators of SECs and maternal report of mental health problems at age 14 years

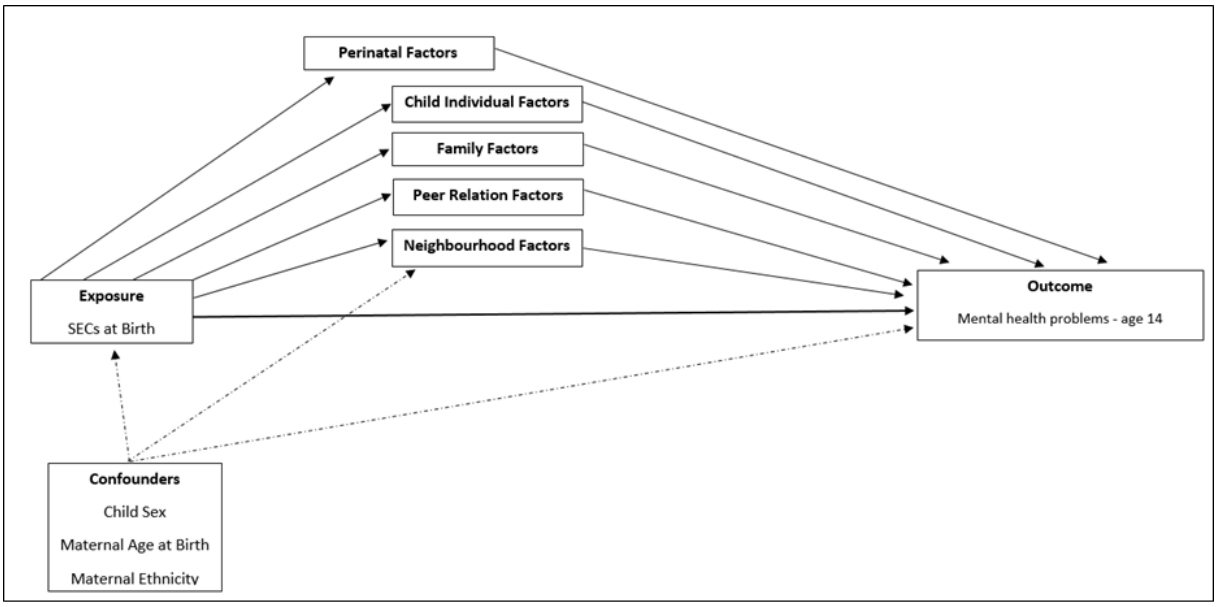


Figure 2. Prevalence (%) and Confidence Intervals (CI95%) of adolescents mental health problems in the UK at age 14 by maternal education at birth (N=6,509)

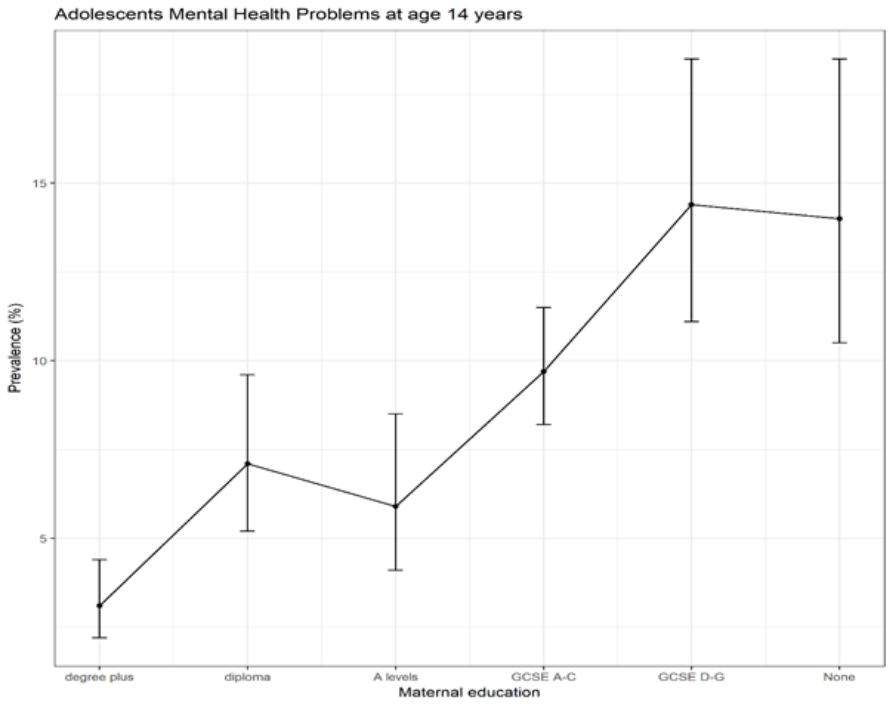
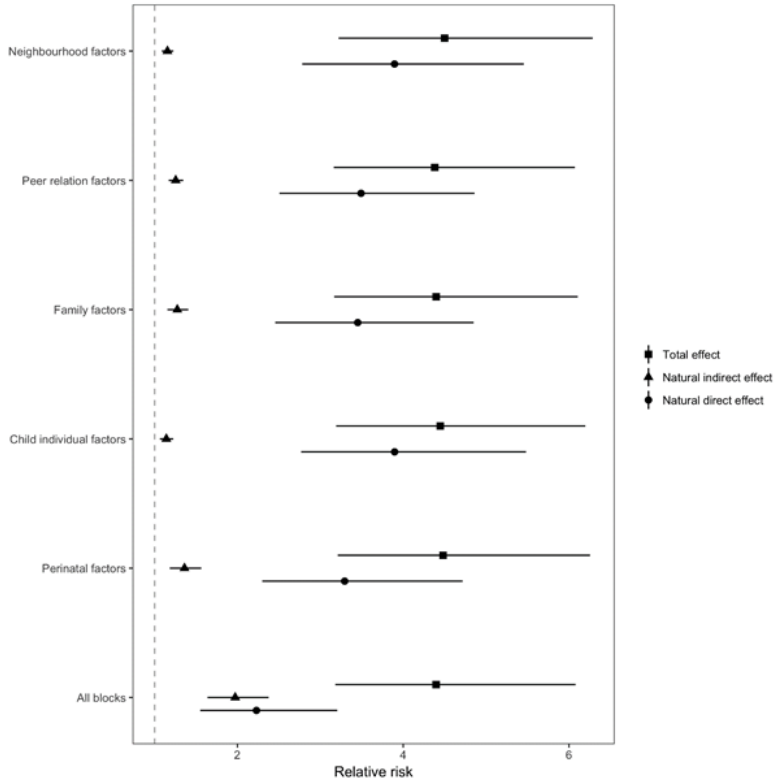


Figure 3. Mediation analysis with a conterfactual approach by block of risk factors (perinatal, child individual, family, peer relations and neighbourhood) in the association of SECs and adolescents mental health at age 14 (Relative Risk and Confidence Intervals [CI95%]) (N=6,509)



5 Contributions to the Consortium Themes

Health inequalities

All analyses presented in this project were relevant to addressing health inequalities. Health inequalities have their origins in early childhood and the development of population linked datasets

that track the health of all children from birth provide the opportunity to inform policies to reduce health indicate that predictive risk models could plausibly be used to identify a group of children at high risk of poor health and developmental outcomes who may benefit from early intervention. If implemented as part of a "proportionate universalism" approach, such models could mitigate socioeconomic inequalities by providing early year's settings with a mechanism for directing their resources to those children at highest risk of poor cognitive development. We also showed that inequalities in child physical and mental health were only partially mediated by adverse childhood experiences (ACEs) experienced during early childhood. A policy focus on preventing ACEs is likely to reduce inequalities in important child health outcomes, but the impact is likely to be relatively small. By contrast, our studies highlight the importance of addressing the broader social determinants of child health as an important policy focus for addressing inequalities across the life course.

Risk and health

A wide range of individual risk factors were included in our longitudinal analyses. In general our analyses highlight the importance of socioeconomic conditions at birth and perinatal risk factors for predicting and explaining the social distribution of later child health outcomes. For example, a model using just six variables from the perinatal period performed well in predicting early child development; and the use of routinely collected data in the first three years of life predicted language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 years. Our analyses show that ACEs as currently conceptualised only partially explain inequalities in later outcomes, and that perinatal factors were important in explaining inequalities in mental health in later childhood.

Translation to policy

There are important messages for policymakers. We found that early risk factors, such as perinatal and maternal factors, can predict health and developmental outcomes, and are part of the causal pathway to generate inequalities later in adolescence. A policy focus on preventing ACEs is likely to reduce inequalities in important child health outcomes, but the impact is likely to be relatively small. By contrast, our studies highlight the importance of addressing the broader social determinants of health as an important policy focus for addressing inequalities across the life course.

Obesity

We used overweight/obesity as an outcome in our analyses. About 26 % of children with 11 years old in the UK were overweight/obesity. Risk of overweight/obesity can be predicted with moderate discrimination using data routinely collected in England.

Methodological development

We demonstrate methodological advances using predictive risk models and counterfactual mediation analyses in this project. Predictive risk models, used widely for applications such as cardiovascular risk prediction, but have not been extensively assessed to inform child public health interventions. Such models were used to explore the relationship between measures collected in early childhood, and a range of subsequent health and development outcomes up to the age of 14 years. Then novel causal mediation methods that can handle multiple mediating pathways were used to understand which early childhood factors mediate inequalities in subsequent child health outcomes, with a particular focus on the mediating role of ACEs.

6 Conclusions

The first 3 years of life provide a unique opportunity to intervene and improve child development and subsequent adult outcomes. There has been a raft of policies promoting the benefits of early intervention, but the research base to support effective targeting of these initiatives is still emerging. Child health policy recommendations in the UK apply the principles of proportionate universalism, with universal services provided for all families and, in addition, progressively more intensive support targeted at those with greater need. In a technical sense, we would like to be able to find a set of characteristics (e.g., maternal, partner, child and community) that accurately identify those children most at risk for poorer developmental outcomes, to help plan improved services for their future development. While it is true that relative concentrations of poorer outcomes are higher in disadvantaged populations, to our knowledge, there has been little systematic work examining the extent to which these outcomes are predicted by risk factors earlier in the life course.

The existing literature, and our findings from the analyses in this report, indicate that the use of predictive risk models could plausibly be used to identify a group of children at high risk of poor child development who may benefit from early intervention. If implemented as part of a "proportionate universalism" approach, this method could mitigate socioeconomic inequalities by providing early year's settings with a mechanism for directing their resources to those children at highest risk of poor cognitive development. With new child and maternity datasets now being collected electronically in England, it may be possible to apply such predictive models at population level through the use of linked administrative datasets as has been done in other developed countries. A criterion for screening programmes is that interventions should be available, it is thus important to further consider the implications of using a predictive risk models to assess early children development in the context of available resources.

Recently the concept of "adverse childhood experiences" (ACEs) has gained popularity as a way of framing the public health implications of childhood harmful experiences[12]. These experiences typically include abuse, neglect, and indicators of possible household dysfunction affecting children (parental mental health problems, including alcohol and drug abuse). Increasingly, however, the concept has been expanded by some commentators to include other factors including social and economic dimensions such as family instability and parental separation, low parental education, child poverty, parental unemployment, and lone parenthood[12]. Various adverse childhood exposures and risk conditions captured in the first few years of life in datasets in the UK have been labelled as ACEs and have been associated with poor subsequent health outcomes. Our analysis suggests that from a policy perspective it is important to separate modifiable childhood SECs from harmful exposures such as ACEs. Efforts to improve child health outcomes should focus on universal primary prevention of harmful ACEs in parallel with actions on social determinants of health (e.g. education) to reduce modifiable socioeconomic inequalities, as well as, early identification and appropriate intervention for children that have had adverse childhood experiences.

Our results support the need for an early year's prevention focus to ensure a safe and healthy pregnancy, a nurturing childhood and support for families in providing such circumstances in which to bring up children. Whilst this is currently advocated in UK mental health strategy, much of the current action is focussed on addressing mental health in schools and improving access to mental health services for children. Whilst these are clearly of critical importance, our results suggest a platform of early investment is required in order to build the foundations for healthy mental health at the population level. In the UK it is concerning that funding for early years provision has been disproportionately cut in some of the most disadvantaged areas; and that child poverty, a major socio-economic determinant of child mental health is currently increasing.

Strengths and limitations

How well can poor child health and development be predicted by data collected in early childhood?

- A strength of our study is the use of a large, contemporary UK cohort.
- A wide range of information is collected in the MCS, which allowed us to explore a large set of demographic, perinatal and early childhood risk factors. Measured BMI, validated assessments of language disability and socioemotional behavioural problems in children were also advantages.
- The MCS allowed us to consider what might be achieved through linkage of administrative datasets in the UK and to assess what added predictive value extra data collection might provide.
- A limitation of our study is the lack of an external validation sample.
- Missing data and attrition are common to all cohort studies, but the similar results in complete case and imputed datasets in our study offer reassurance that the risk of bias is minimised.
- We based most of our results on maternal self-reported data and decisions were made around categorising prediction variables.
- More research is needed to address the challenges of applying the predictive models from MCS to administrative data. Differences include the nature of variables collected (service-recorded vs self-report), data quality (including linkage error), the continuous/dynamic nature of service use by mother and child, and the inherent biases due to links between recording and services responses.
- More research is needed to evaluate impact of using of predictive models applied to routinely collected data on (inequalities in) health and wellbeing for children and families.
- Variable coverage of early years assessment means that the most disadvantaged families may miss out. This is a challenge for predictive risk modelling approaches, and the latest data (appendix 2) indeed shows socioeconomic variation in uptake.

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

How do adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

- Use of secondary data from a large, contemporary UK cohort, which measures a wide range of information, which allowed us to explore a range of ACEs;
- First study to formally test the mediating role of ACEs on social inequalities in important adolescent health outcomes using counterfactual methods;
- The use of validated measures of adolescent mental health, cognitive performance and overweight/obesity (measured, not self-reported) is also a strength of our study;

- A potential limitation of our study is the self-reported nature of the variables used to capture ACEs and health outcomes;
- Missing data are also a limitation;
- A further limitation is that the MCS questions on parental alcohol consumption at ages 3 and 5 do not allow quantification of both frequency and volume of alcohol use, and we therefore undertook a robustness test removing the high frequency of parental alcohol use variable from our mediating block.

How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study?

- A key strength is that this study used secondary data from a large, contemporary UK cohort, which measures different indicators of SEC;
- This study adds to the literature by being the first study to formally test the mediating role of different risk factors of social inequality of adolescents' mental health with methodological robustness, using counterfactual methods;
- The use of a validated measure of adolescent mental health is also a strength of this study.
- A potential limitation of our study is the main responder self-reported nature of the mental health outcome;
- The co-occurrence of risk factors and protective factors makes the identification of the specific elements responsible for the onset and continuity of mental health problems challenging. Although we were able to explore a wide range of potential mediators, arranged into blocks, we were limited to data collected in the MCS;
- Thus, data about potentially mediating childhood adversities such as sexual abuse and parental criminality were not included in our analysis;
- We were unable to adjust for genetic risk factors for mental health problems which may partially explain some inter-generational transfer of risk and epigenetics influences.

<u>Research, policy and practice recommendations</u>

How well can poor child health and development be predicted by data collected in early childhood?

- New child health datasets have been developed in England, and our analysis shows that language disability, socioemotional behavioural problems and overweight/obesity in UK children aged 11 years can be predicted with moderate discrimination using these data.
- While many of the variables used in our analysis should be available in routine data, other variables such as breastfeeding status and early measures of maternal mental health are more difficult to capture and may be of relatively poor quality in routine data collection systems.
- Further research is needed to identify what could increase the predictive power of these models at these and other ages in population-based databases as well as assess how the dynamics of predictive algorithm models can be used in health services to identify children more likely to benefit from additional early years support.
- Furthermore, we require a better understanding of how predictive risk modelling tools could be used in the context of specific child health systems, for instance, in the UK, what proportion of children would go on to receive specialist intervention; what proportion of those would benefit from this and what would be the magnitude of any benefits.

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

- The existing literature, and our findings, indicate that predictive risk models could plausibly be used to identify a group of children at high risk of poor early child development who may benefit from early intervention. If implemented as part of a "proportionate universalism" approach PRMs could mitigate socioeconomic inequalities by providing early years settings with a mechanism for directing their resources to those children at highest risk of poor cognitive development. With new child and maternity datasets now being collected electronically in England, it may be possible to apply a PRM at population level through the use of linked administrative datasets as has been done in Australia.
- Further research is needed to test the external validity of predictive risk models for ECD for example in another cohort or with linked administrative datasets. 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. 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. Investment in early intervention would be required, which would have opportunity costs for services locally.

How do adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

- The increased risk of socioemotional behavioural problems, poor cognitive performance and being overweight/obese in adolescents growing up in disadvantaged SECs in the UK is partly explained by exposure to ACEs.
- Our analysis supports our previous suggestion that conflating concepts relating to social circumstances with ACEs is conceptually confusing and may lead to the importance of SEC being neglected
- A policy focus on preventing ACEs is likely to reduce inequalities in important child health outcomes, but the impact is likely to be relatively small.
- By contrast, our study highlights the importance of addressing the broader social determinants of health as an important policy focus for addressing inequalities across the life course.
- Efforts to improve child health outcomes should focus on universal primary prevention of harmful ACEs in parallel with actions on social determinants of health (e.g. education) to reduce modifiable socioeconomic inequalities, as well as, early identification and appropriate intervention for children that have had adverse childhood experiences**Error! Reference source not found.**.

How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study?

- We found that nine percent of children had mental health problems by age 14 in a nationally representative UK child cohort. The risk was much greater in disadvantaged children, and about two thirds of this excess risk was explained by early childhood factors up to age 3 years.
- Future research should investigate specific pathways, critical/sensitive periods for these exposures, and other countries with different socioeconomic context. Efforts to reduce inequalities in adolescents mental health problems should focus on reducing socioeconomic inequalities and action to address the early years mediators identified in our study, particular on perinatal factors and family factors such as maternal mental health problems.
- From a public health policy perspective, our results support the need for an early years prevention focus to ensure a safe and healthy pregnancy, a nurturing childhood and support

for families in providing such circumstances in which to bring up children. In the UK it is concerning that funding for early years provision has been disproportionately cut in some of the most disadvantaged areas; and that child poverty, a major socio-economic determinant of child mental health is currently increasing.

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Outputs / Dissemination

NB: this includes outputs and dissemination resulting from this project up to 31/03/2019 (and forthcoming). For an up-to-date list, including dissemination after the production of this report, please see the PHRC website http://phrc.lshtm.ac.uk.

PUBLICATIONS

Straatmann, V.S., Lai, E.T.C., Campbell, M., Wickham, S., Nybo-Andersen, A.M., Strandberg-Larsen, K. & Taylor-Robinson, D.C. (2019). How do early life factors explain social inequalities in adolescent mental health: Findings from the UK Millennium Cohort Study. Journal of Epidemiology and Community Health, 0:1–12.

Camacho, C., Straatmann, V. S., Day, J. C. &Taylor-Robinson, D. C. (2019). Development of a predictive risk model for school readiness at age 3 years using the UK Millennium Cohort Study. BMJ Open, 9: e024851.

Straatmann, V. S., Pearce, A., Hope, S., Barr, B., Whitehead, M., Law, C., & Taylor-Robinson, D.C. (2018). How well can poor child health and development be predicted by data collected in early childhood? Journal of Epidemiology and Community Health, 72(12), 1132-1140.

Taylor-Robinson, D. C., Straatmann, V. S., & Whitehead, M. (2018). Adverse childhood experiences or adverse childhood socioeconomic conditions? Lancet Public Health, 3(6), E262-E263. (Editorial comment)

SUBMITTED PAPERS

Straatmann, V. S., Law, C., Whitehead, M., Strandberg-Larsen, K. & Taylor-Robinson, D. (2019). How do early adverse childhood experiences mediate the relationship between childhood socio-economic conditions and adolescent health outcomes in the UK?

MANUSCRIPTS IN PROGRESS

Using MCS data:

Straatmann, V.S., Lai, E.T.C. & Taylor-Robinson, D.C. (2019). Childhood social inequalities and domestic violence in the UK: Longitudinal analyses from the UK Millennium Cohort Study.

We are currently developing further analyses using data from the MRC Wirral Child Development Study (WCHADS), which provides in-depth information on early child development that will allow us to explore the relationships between measures of early childhood development at 2-3 years, and a range of subsequent health and development outcomes. The MRC WCHADS study is a longitudinal cohort study following 1233 children from a range of social backgrounds in the Wirral, in the North West of England, and includes 8 research assessment points up to 4.5 years of age. The cohort was particularly designed to capture mental health and development outcomes over time in children. The WCHADS specifically collected data from health visitor checks and used the Parents' Evaluation of Developmental Status (PEDS) questionnaire. The dataset contains detailed information on the child's hearing, speech and language development, vision, public health and community support, health lifestyle, and physical development, which can also be mapped on to the 5 domains measured in the Integrated Review. See here for a related analysis of WCHADS data: https://doi.org/10.1371/journal.pone.0217342

Rutherford, C., Straatmann, V.S., Sharp, H. & Taylor-Robinson, D.C. (2019). How do early childhood factors influence trajectories of mental health? Findings from the Wirral Child Development Study.

CONFERENCE PAPERS AND PRESENTATIONS

Straatmann, V. S., Lai, E. T. C., & Taylor-Robinson, D. (2018). How do adverse childhood experiences explain social inequalities in adolescent health outcomes? findings from the UK millennium cohort study. The Lancet, 392. (Conference abstract)

Camacho, C., Straatmann, V. S., Day, J. & Taylor-Robinson, D. C. (2018). OP14 How well can early child development be predicted in children in the UK? findings from the millennium cohort study. Journal of Epidemiology and Community Health, 72:A7. (Conference abstract)

Straatmann, V. S., Whitehead, M. & Taylor-Robinson, D. C. (2018). RF31 Adverse childhood experiences or adverse socio-economic conditions? assessing impacts on adolescent mental health in the UK millennium cohort study. Journal of Epidemiology and Community Health, 72:A57. (Conference abstract)

Straatmann, V. S., Pearce, A., Law, C., Barr, B. & Taylor-Robinson, D. (2018). How well can poor child health and development be predicted with data collected in early childhood in the UK? Findings from the Millennium Cohort Study. The Lancet, 390:S87. (Conference abstract)

Straatmann, V.S., Campbell, M., Rutherford, C., Wickham, S. & Taylor-Robinson, D.C. (2017). OP61 Understanding social inequalities in child mental health: findings from the UK millennium cohort study.Journal of Epidemiology and Community Health, 71:A31. (Conference abstract)

POLICY AND PRACTICE PRESENTATIONS

- 5/2/2019- Westminster Seminar. Priorities for reducing inequalities in children's health across England. Professor David Taylor-Robinson http://www.westminsterforumprojects.co.uk/agenda/childrens-health-2019-agenda.pdf
- 2/11/2018- Reducing Health Inequalities in Ireland: The Role of Policy: Health inequalities presentation in Trinity College, Dublin https://www.tasc.ie/archive/events/past/2018/11/02/reducing-health-inequalities-in-ireland-the-role-o/
- 30/8/2018- Addressing inequalities in child health. Social medicine society presentation, Copenhagen http://dspm.dk/2018/08/international-forelaesning-aabner-sensommerne-i-dspm/
- Edge Hill festival of ideas – Addressing Inequalities in Child Health video here https://www.youtube.com/watch?v=2_YXry0_H-E&index=1&list=PLBrk-wPNLaVkJV1mYtNtONIYeJYFS0MeT 21/5/2018
- Beyond the North-South health divide: what should we do about inequalities? PHE keynote presentation, Sept 2017 (https://www.youtube.com/watch?v=dN2_1kpiWjU)
- Royal Society of Medicine Child Health Festival presentation https://twitter.com/i/moments/1010855514123784192, 12/6/2018
- 20/9/2017- Chief Medical Officer roundtable on poverty and childhood obesity
- 25/10/2017- RCPCH presentation on Poverty and Child Health – views from the frontline.
- 22/11/17- PHE Health Inequalities Workshop in London – presentation

OTHER DISSEMINATION

- We were engaged in the development process of the Universal Support Tool in Liverpool. We have collaborated with staff at the Granby Child Centre to discuss the way data is being collated, and issues related to the integrated review at children's Centres in Liverpool.
- We held a meeting with the Program Director of National Child and Maternal Health Intelligence Network to ensure links to policy and practice (Helen Duncan in York) and to discuss potential for linking data from maternity records to ASQ data at 2-3 years. Discussions about access to Liverpool data were also introduced.
- 14/9/2018- Submission to UN poverty rapporteur https://www.ohchr.org/EN/Issues/Poverty/Pages/UKVisitSubmissions.aspx

APPENDIX 1

LITERATURE REVIEW BOX WITH STUDIES USING PREDICTIVE RISK MODELLING TO EXPLORE THE ASSOCIATION BETWEEN PERINATAL AND EARLY CHILDHOOD PREDICTORS WITH HEALTH AND DEVELOPMENT OUTCOMES

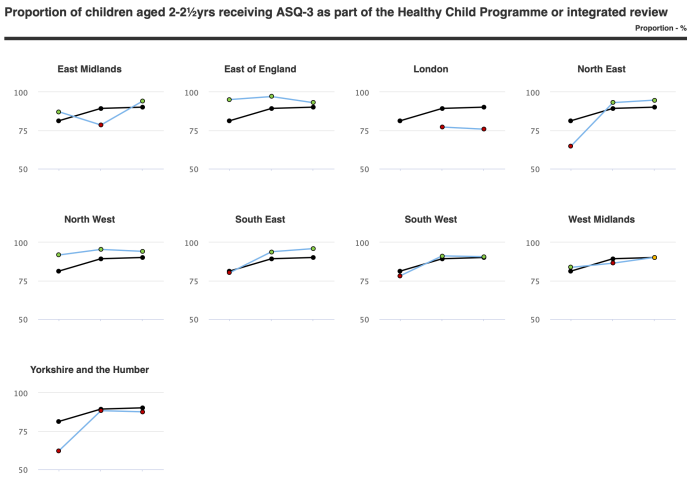
Author, Year, Title	Data set & country	Outcome variable	Predictor variables	Findings
Chittleborough et al (2011) – Young Maternal Age and Poor Child Development: Predictive Validity From a Birth Cohort[8]	ALSPAC birth cohort (UK)	ALSPAC developmental scale (ADS) Top 10% of SDQ School Entry Assessment (SEA)	Maternal age, education, financial difficulty, partner status, smoking, depression	Maternal age fails to predict. Full model poor predictive capability AUROC = ADS: 0.56; SDQ: 0.66; SEA: 0.67
Camargo-Figuera et al (2014) – Early life determinants of low IQ at age 6 in children from the 2004 Pelotas Birth Cohort: a predictive approach[10]	Pelotas birth cohort (Brazil)	Cognitive ability at age 6, IQ test using WISC	Gender, skin colour, number of siblings, employment, income, maternal education, overcrowding, breastfeeding; height-for-age deficit; head circumference-for-age deficit, smoking, maternal perceptions	Good predictive capability AUROC = 0.8, Sensitivity = 72%, Specificity = 74%.
McKean et al (2016) – Predicting Meaningful Differences in School-Entry Language Skills from Child and Family Factors Measured at 12 months of Age[18]	Northumberland cohort (UK), Early language in Victoria Study (ELVS) (Australia)	Poor language outcomes at 4–5 years measured by CELF-P2 (score ≤1.25 SD below the mean)	Child communication behaviours, family history, socio-demographic quintile, maternal education, parental behaviour	Poor-fair predictive capability. AUROC = 0.63 (Model 1), 0.71 (Model 2), 0.73 (Model 3)
Nelson et al (2016) – Predictors of Poor School Readiness in Children Without Developmental Delay at Age 2[19]	Early Childhood Longitudinal Study, Birth Cohort (ECLS-B) (US)	Low academic scores and high problem behaviours at age 5	Gender, language development, parental expectations, parental education, income, family composition, parental health status, food insecurity, parental depression, smoking, shared reading, housing quality, neighbourhood safety	Fair predictive capability AUROC = 0.76 for academic risk
Chittleborough et al (2016) – How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study[9]	Early Development Census (AEDC) Linked population data set (Australia)	AECD – children vulnerable on ≥2 domains	Maternal age, smoking during pregnancy, parity, marital status, and both parents' occupation	Fair-poor predictive capability. AUROC =0.682 males, 0.724 females
Reilly et al (2010) Predicting Language Outcomes at 4 Years of Age: Findings From Early Language in Victoria Study[20]	Melbourne, Australia	Clinical Evaluation of Language Fundamentals-Preschool, language scores, low language status, and specific language impairment	Gender, prematurity, birth weight and order, multiple birth, socioec, maternal mental health, vocabulary, education, and age at child's birth, non–English-speaking background, and family history of speech/language difficulties.	The combined predictors discriminated only moderately between children with and without low language levels or SLIs (area under the curve: 0.72– 0.76); this improved with the addition of late talking status (area under the curve: 0.78 – 0.84).
Peyre et al (2014) Predicting changes in language skills between 2 and 3 years in the EDEN mother–child cohort[21]	Nancy, France	2 years old: CDI-2 3 years old: ELOLA (Evaluation du Language Oral de L'enfant Aphasique) (and NEPSY (A Developmental Neuro PSYchological Assessment)	Gender, gestational age and birth weight, maternal age at birth and alcohol and tobacco pregnancy, Family history of speech and language delay. Breastfeeding Child environmental factor	Exposure to alcohol during pregnancy, earlier birth term, lower level of parental education and lower frequency of maternal stimulation were associated with the declining trajectory. Breastfeeding was associated with the resilient trajectory
Smithers et al (2014) Can Items Used in 4-Year-Old Well-Child Visits Predict Children's Health and School Outcomes?[22]	Australia	Overweight/obesity, asthma, health care/medication needs, general health, mental health problems, quality of life, teacher-reported mathematics and literacy ability	Mandatory (anthropometry, eye/vision, ear/hearing, dental, toileting, allergy problems) and non-mandatory; (Processed food consumption, low physical activity, motor, behaviour/mood problems) items.	Weight or height at 4–5 years predicted overweight/obesity at 6–7 years with 60 % sensitivity, 79 % specificity and 40 % PPV. Mood/behaviour problems at 4–5 predicted mental health problems at 6–7 years with 86 % sensitivity, 40 % specificity and 8 % PPV.

Author, Year, Title	Data set & country	Outcome variable	Predictor variables	Findings
Law et al (2012) Predicting Language Change Between 3 and 5 Years and Its Implications for Early Identification[23]	United Kingdom	*BAS II- at ages 3 and 5 *Language delayed *4 pattern groups of transition of naming vocabulary between 3 and 5 years old.	Maternal education, gestational age, Gross and fine motor (9months), Parental concerns about language development and hearing at 3 years were grouped into "some concerns" or "none/not applicable." And SDQ	The final model (predicting 32% of the variance) included maternal education, pattern construction, behaviour, language concerns, and 3-year vocabulary. Four change patterns were identified: one consistently low (n = 201), one consistently high (n = 12 066), a group that is resilient (n = 572), and one with a declining profile (n = 177).

*INFORMATION FROM REPORTS DEVELOPED BY K. KIERNAN AND F. MENSAH (2010)[24] '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 (PREVIEW PROJECT)' AND J.N. HOBCRAFT AND K.E KIERNAN (2010)[25] '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 (PREVIEW PROJECT)' WERE ALSO RELEVANT.

APPENDIX 2

LATEST DATA FROM PUBLIC HEALTH ENGLAND FINGERTIPS SHOWING COVERAGE OF THE INTEGRATED REVIEW



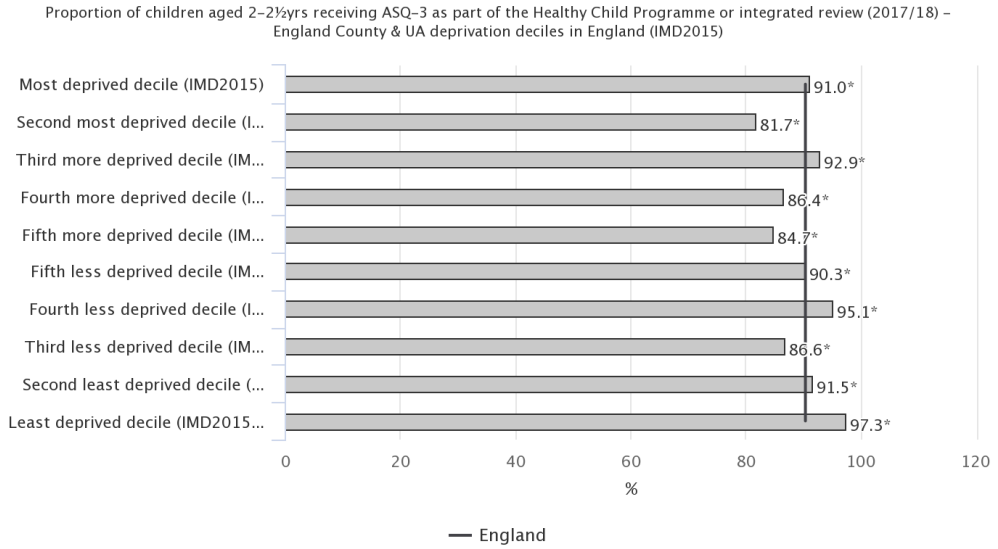
* 2015/16 – 17/18

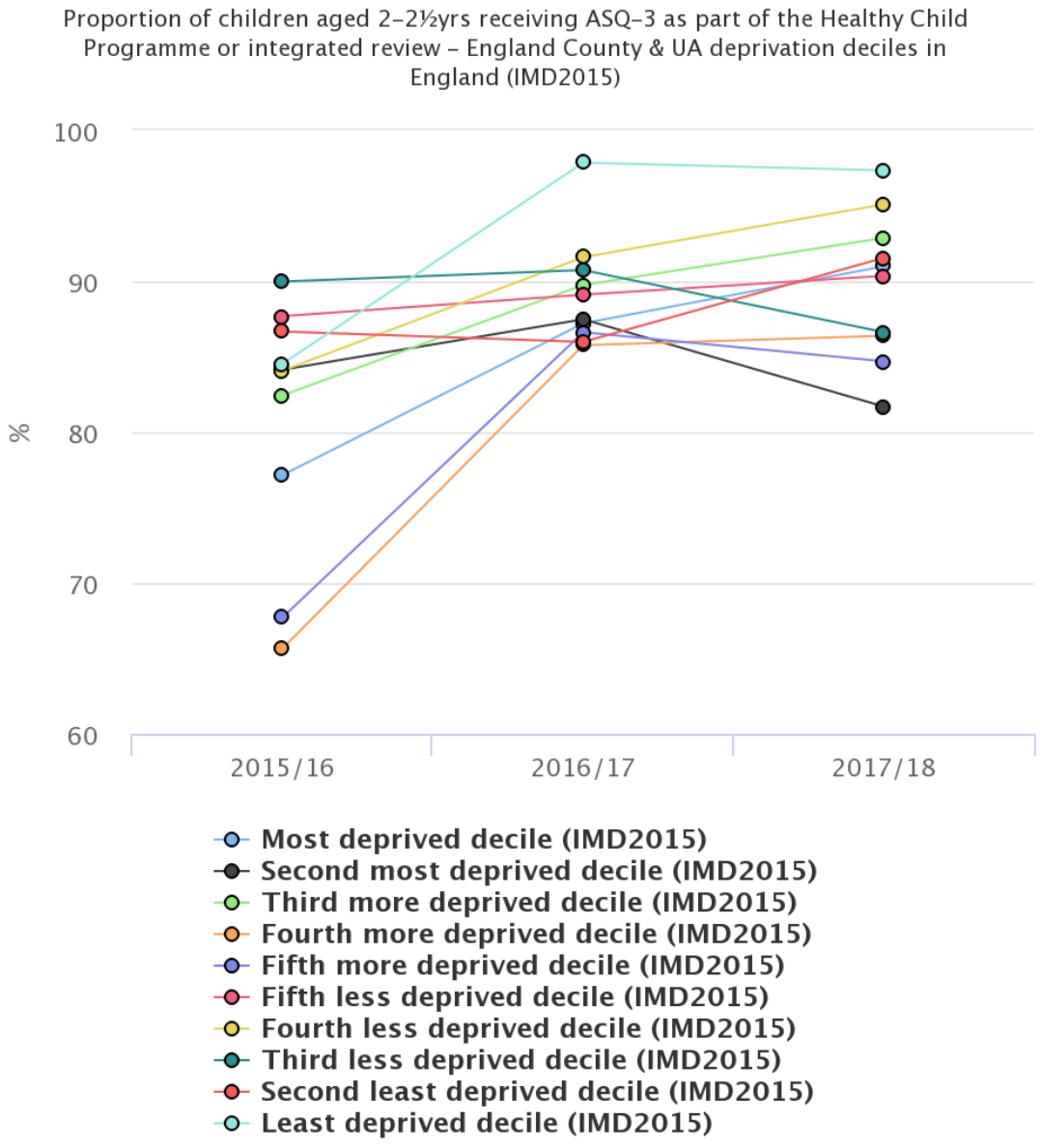
* a note is attached to the value, hover over to see more details

Compared with benchmark: Better | Similar | Worse | Not compared

Recent trends: Could not be | Increasing / worse | Increasing / better | Decreasing / worse | Decreasing / better | No significant | Increasing | Decreasing

Indicator	Period	England	East Midlands region	East of England region	London region	North East region	North West region	South East region	South West region	West Midlands region	Yorkshire and the Humber region
Proportion of children aged 2-2½yrs receiving ASQ-3 as part of the Healthy Child Programme or integrated review	2017/18	90.2	94.2	93.1	75.8	94.8	94.2	96.0	90.7	90.3	87.6
Percentage of children at or above expected level of development in all five areas of development at 2-2½ years	2017/18	83.3	85.1	82.7	84.4	85.6	79.0	86.3	84.4	74.8	86.0
Percentage of children at or above expected level of development in communication skills at 2-2½ years	2017/18	88.8	90.6	88.2	89.1	91.5	85.2	91.3	91.6	78.1	91.5
Percentage of children at or above expected level of development in gross motor skills at 2-2½ years	2017/18	91.5	93.3	90.3	94.2	94.3	88.5	94.3	92.3	79.9	95.0
Percentage of children at or above expected level of development in fine motor skills at 2-2½ years	2017/18	92.0	95.2	90.2	94.5	92.7	88.9	95.2	95.1	80.4	94.7
Percentage of children at or above expected level of development in problem solving skills at 2-2½ years	2017/18	91.9	94.3	90.1	93.6	94.5	88.9	94.7	94.7	80.1	95.3
Percentage of children at or above expected level of development in personal-social skills at 2-2½ years	2017/18	91.3	93.4	90.2	93.0	94.2	89.0	92.8	93.1	79.6	94.8


Proportion of children aged 2–2½yrs receiving ASQ–3 as part of the Healthy Child Programme or integrated review (2017/18) – England County & UA deprivation deciles in England (IMD2015)
Most deprived decile (IMD2015)
Second most deprived decile (I...
Third more deprived decile (IM...
Fourth more deprived decile (I...
Fifth more deprived decile (IM...
Fifth less deprived decile (IM...
Fourth less deprived decile (I...
Third less deprived decile (IM...
Second least deprived decile (...
Least deprived decile (IMD2015...
91.0*
81.7*
92.9*
86.4*
84.7*
90.3*
95.1*
86.6*
91.5*
97.3*
0
20
40
60
80
100
120
%
England


Proportion of children aged 2–2½yrs receiving ASQ–3 as part of the Healthy Child Programme or integrated review – England County & UA deprivation deciles in England (IMD2015)
100
90
80
70
60
%
2015/16
2016/17
2017/18
Most deprived decile (IMD2015)
Second most deprived decile (IMD2015)
Third more deprived decile (IMD2015)
Fourth more deprived decile (IMD2015)
Fifth more deprived decile (IMD2015)
Fifth less deprived decile (IMD2015)
Fourth less deprived decile (IMD2015)
Third less deprived decile (IMD2015)
Second least deprived decile (IMD2015)
Least deprived decile (IMD2015)