Childhood outcomes after perinatal brain injury: a population-based linkage study

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Abstract

Aim: To conduct a retrospective population-based matched cohort study to investigate health and educational outcomes after perinatal brain injury.

Background:
Perinatal brain injuries can have devastating consequences for children, parents, and society as a whole. Advances in neonatal care have dramatically improved short-term survival in this population. However, there are considerable gaps in our knowledge about the long-term impact of perinatal brain injuries. This project will utilise existing routine data to explore childhood outcomes after perinatal brain injury, in order to understand the prognosis of this population in addition to their health and educational needs, and to ultimately inform health policy and resource provision.

Design:

Workstream 1: Creating a matched cohort
Infants with perinatal brain injury will be identified using a pre-existing definition that maps to the National Neonatal Research Database (NNRD). Preterm infants with brain injury will be matched 1:1 with infants in the NNRD using propensity scores accounting for a range of confounders. Term infants with brain injury will be matched on sex, year of birth, birth weight, gestation, and multiplicity, using a 1:3 algorithm, to infants in the general population using Office of National Statistics (ONS) data.

Workstream 2: Health outcomes
The matched cohort will be linked to ONS mortality data, Hospital Episode Statistics data and the Mental Health Services Dataset at NHS Digital to acquire longitudinal outcome data. This will enable investigation of the impact of perinatal brain injuries on the risk of neurodisabilities; all-cause mortality; mental health and behavioural conditions, and chronic health conditions up to the age of 13 years.

Workstream 3: Academic outcomes
The matched cohort created will be linked to the National Pupil Database. This will enable investigation of how perinatal brain injury impacts school performance on national tests, special educational needs, and school attendance up to the age of 13 years.

Workstream 4: Patient and public involvement
This crosscutting work stream will involve focus groups with families affected by perinatal brain injury: initially to identify meaningful outcomes measures, and later to explore perception of study results, different communication strategies and to co-develop communication aids.

Anticipated impact for parents, children, and the NHS
Study findings will be corroborated with stakeholders from government, the NHS and families to understand how best to adapt policy, health and education services. Additionally, communication aids co-developed with families will be disseminated for use across neonatal units. The evidence generated by this fellowship will enable accurate family-centric discussions about what the future may hold as well as informing clinical practice throughout the NHS. This study will help us to understand the impact of national quality improvement initiatives targeting brain injury, facilitate service planning, and provide essential insight into how we can best support these children to reach their full potential.

Background and Importance

What is the problem being addressed?

Perinatal brain injuries can have devastating consequences for children, families and society as a whole.(1) As such, reducing the number of infants with perinatal brain injury is a current governmental priority. Over 3000 infants suffer a perinatal brain injury in England every year and in 2015 the Department of Health declared a national ambition to halve the rates of perinatal brain injury by 2030.(1, 2)

Advances in neonatal care and the adoption of innovative neonatal treatments have considerably impacted the survival of these infants.(3-5) However, our knowledge about childhood health and educational outcomes across the life course after perinatal brain injury, and how this has changed over time, is limited by a paucity of population-level research. As such there is a dearth of evidence underscoring the decisions of policymakers, the NHS, schools, healthcare professionals and parents – in their aspiration to support affected children to reach their full potential.

Why is this research important?

Parents on the neonatal unit have understandable questions about prognosis after perinatal brain injury, the likely health and educational outcomes of their children, and how they can best support their children. This population-study will provide the most complete picture of how children's lives are affected by perinatal brain injury and as such it will provide essential information to answer parents' questions accurately and in a meaningful family-centric manner. Such information is also vital to inform clinical practice and facilitate optimum service planning within the NHS to meet the needs of these children and their families through to adulthood, and ultimately to improve their future health outcomes.

An understanding of the sequelae of perinatal brain injury, specifically how and when children are affected, would inform enhanced developmental surveillance across the NHS (to detect issues) and would enabled the design of targeted multidisciplinary interventions to support children as needed.(6) In the preterm population, who for example are prone difficulties with inattention and mathematics, education packages for teachers have raised awareness of these challenges and children benefit from delayed school entry and additional Special Educational Needs (SEN) support in these areas.(7, 8)

Our PPI work, in collaboration with BLISS and the meningitis research foundation, consistently highlighted that evidence about the long-term impact of brain injuries

(particularly the unseen impact on mental health and schooling) was a frequently overlooked parental priority. It matters to the people most affected.

Review of the existing evidence

Perinatal brain injuries are a leading cause of childhood death and disability globally. The lifelong morbidities resulting from these perinatal insults have far-reaching implications for affected children, families and the global burden of disease.(9-12) In 2015, the incidence of perinatal brain injuries across England was 3.5 per 1000 live term births and 25.9 per 1000 live preterm births.(1)

The Department of Health commissioned the Neonatal Data Analysis Unit to develop a standardised definition of perinatal brain injuries, through expert consensus. This includes a range of discrete but not mutually exclusive diagnoses and clinical signs such as: hypoxic ischaemic encephalopathy (HIE), perinatal stroke, central nervous system (CNS) infections, preterm brain injuries such as intraventricular haemorrhage (IVH) and white matter changes, seizures and kernicterus.(1, 4) These categories are considered together for the purpose of this study as per the Department of Health definition, and indeed by neonatal researchers and parents.

Hypoxic ischaemic encephalopathy

HIE, also known as birth asphyxia, refers to a range of neurological signs and symptoms seen secondary to poor oxygenation and perfusion of the brain. The incidence of HIE in the UK is 2.6 per 1000 live births. Therapeutic hypothermia has been standard of care for term infants with moderate to severe HIE since 2009.(13) Studies have consistently shown that infants with moderate to severe HIE have high mortality and morbidity: and even amongst those without severe disability studies have demonstrated persistent subtle impairments in cognitive, neuropsychological, educational and behavioural functioning.(3, 14-18) Since the introduction of therapeutic hypothermia the rate of death or moderate to severe disability at is 44% at 18-22 months and 53% at 6-7 years.(13) Around 35% have moderate to severe disability and 17% have cerebral palsy.(13, 14, 19-21)

HIE has the best long-term population data (to age 6-7 years) compared to other brain injuries. However, these longer-term studies were small (including a total of 274 children receiving therapeutic hypothermia), underpowered to detect certain longer-term outcomes, and there was high (9-54%) loss to follow-up.(14, 19, 22) Additionally, there has been little

consideration of school age outcomes beyond 7 years of age or functional childhood outcomes such as mental health and educational performance, across the spectrum of HIE.

Perinatal stroke

Perinatal strokes are diagnosed in 0.14 per 1000 live births in the UK, typically presenting with seizures.(1, 23) Studies exploring outcomes after perinatal stroke highlight that around 3-5% of infants subsequently die and 60% have neurological deficits that emerge over time.(24, 25) However, no studies to date have explored the educational or broader health and mental health outcomes of children after perinatal stroke.

Central nervous system infections

CNS infections including meningitis and encephalitis occur in 0.7 per 1000 live births in the UK.(1) In 1999 the British Paediatric Surveillance Unit highlighted that although cases of neonatal meningitis had remained stable up to up to 1997 and mortality had reduced, this had not translated into reduced childhood morbidity over the previous 10 years.(26, 27) Group B streptococcus is the commonest cause of neonatal meningitis and a recent review highlights that amongst survivors, 32% had neurodevelopmental impairment at 18 months, including 18% with moderate or severe neurodevelopmental impairment.(28) There have been no recent population studies of the long-term outcomes of children after neonatal CNS infections and no studies to date have explored, functional outcomes at school.(26, 27)

Preterm brain injury

Preterm brain injuries such as intraventricular haemorrhages (IVH) i.e. bleeding into the ventricles or cystic periventricular leucomalacia (cPVL) (the development of cysts in the white matter) occur as a result of structural vulnerabilities in the premature brain. The incidence of IVH amongst preterm infants is 58.3 per 1000 preterm births and the rate of cPVL is around 12.4 per 1000 preterm births.(1)

Severe IVH and cystic PVL are widely accepted to be associated with increased risk of neurodisability above and beyond the risk posed by prematurity alone.(29) Amongst survivors of severe IVH the adjusted odds ratio for moderate to severe neurodevelopmental impairments is 1.39 and the risk ratio for cerebral palsy at 5 years is 3.43 (after adjusting for gestation.(30, 31) However the evidence of the effects of IVH and cystic PVL on more specific school-age outcomes including cognitive development, language abilities, executive function and academic attainment is conflicting. (30, 32-43) Cognitive scores at 2 years (which is the focus of most neonatal studies) do not necessarily correlate with school-age

cognitive outcomes. The long-term effect of these injuries on cognitive development is thought to change over time under the increasing influence of environmental factors.(43) Prematurity has also been associated with longer-term mental health issues including inattention, peer relationship problems and emotional disorders: however the extent to which preterm brain injuries such as IVH contribute to this risk is unknown.(44)

The associations put forward in the literature, require further exploration, using a contemporary population dataset specifically exploring brain injuries across the spectrum of prematurity, in a cohort study capable of adjusting for key confounders, with adequate follow-up throughout childhood to explore school-age outcomes and outcome trajectories.

Kernicterus

Kernicterus is a rare type of perinatal brain injury that occurs secondary to hyperbilirubinaemia. Long-term outcomes after kernicterus can include athetoid cerebral palsy, hearing loss, cognitive delays visual paralysis and dental issues.(12, 45)

Seizures

Seizures are a non-specific yet common indicator of a neurological insult that is seen across types of perinatal brain injury but their prognostic value as an indicator of later childhood impairment, in isolation, is unclear.(1, 46)

Long-term follow up

Our definition of perinatal brain injury includes markers of potential brain injury, as brain injuries are difficult to definitively diagnose during the neonatal period, and as such long-term follow up of these infants throughout childhood is essential for accurate diagnosis.

Most neonatal studies utilise a composite measure of mortality and neurodevelopmental impairment at 18-24 months as their primary outcome. It is however becoming increasingly clear that 2 year outcome measures are poorly predictive of childhood function (except for the most severely impaired) across the spectrum of neonatal conditions.(47, 48) The poor predictive value of neurodevelopmental testing at 2 years, is thought to be underpinned by measurement error, difficulties in infant testing (i.e. observing a child at one time point), changes in function throughout childhood, difference in inherited developmental patterns and environmental influences.(49-51)

Whilst the prevalence of severe neurodisability amongst some neonatal cohorts remains stable between 6 to 11 years, more subtle impairments and mental health effects may not become apparent until later childhood.(17, 52) Functional impairment as a result of neonatal insults is fluid: it can evolve or even diminish throughout childhood. Therefore exploration of longer-term childhood trajectories is essential to gain an accurate picture of how children's lives are affected by perinatal brain injuries.

A systematic review of parental perception of neonatal research highlights that short-term outcomes are too often prioritised over the more meaningful long term functional outcomes.(53)

Communicating with families

A lack of evidence of the significance of markers of perinatal brain injuries, and the resulting prognostic uncertainty, has direct implications for clinicians and families. Studies exploring parental experiences of communication about brain injuries on the neonatal unit highlight three key issues: fragmented and contradictory communication; difficulty in understanding complex therapies such as therapeutic hypothermia; and uncertainty about prognosis.(54) This contributes to discordance between clinicians and families and potentially long-lasting psychologically distress for families.(55-58)

There has been relatively little research into the most effective way of communicating prognosis after perinatal brain injury to parents.(54, 55, 57-59) The lack of research in this area and the prognostic uncertainty surrounding perinatal brain injuries has resulted in huge variation in communication practices.(54, 55, 59, 60) As such, there is a need for family-centred communication resources, containing standardised evidence-based information, to support families and healthcare professionals.

Aim

1. **To conduct a retrospective UK population-based matched cohort study to investigate outcomes of children with perinatal brain injury**

Objectives

1. **To link routine national data to create a longitudinal matched cohort of children with perinatal brain injury**
2. **To determine childhood morbidity, mortality and academic attainment after perinatal brain injury, in the UK, between 2008-2021**

Study Design and Methods

Inclusion criteria

This study will include infants:

- Born between January 21st 2009- December 31st 2020
- Admitted to a neonatal unit in England
- Meeting the Department of Health definition of perinatal brain injury prior to discharge from the neonatal unit
- Children aged 13 years and under

Exclusion criteria

- Infants born outside of England
- Infants with congenital: infections, encephalopathies or brain abnormalities
- Infants with seizures from neonatal abstinence syndrome or hypoglycaemia
- Participants who have opted out of data sharing
- Participants born before 2008, aged over 13 years
- We will be unable to identify and account for those who:
    - Emigrate (although the numbers are thought to be negligible)
    - Do not attend state school

Databases

1. The National Neonatal Research Database (NNRD): contains care data for all neonates admitted to NHS neonatal units across England, Wales and Scotland. Its population coverage is internationally unique with 100% coverage since 2012 and high representative coverage since 2008.(61) The NNRD contains infant *NHS number*, *date of birth*, *sex* and *postcode*.

2. The Personal Demographic Service (PDS): (controlled by NHS Digital) contains demographic data for all NHS patients including *forename*, *surname*, *postcode* (including changes), *date of birth*, *sex*, and *NHS number*.

3. Office for National Statistics (ONS) death registration data: is accessible through the PDS, for all children across England and Wales. NNRD and ONS data have previously been linked to investigate survival of extremely premature infants.(62)

4. Hospital Episode Statistics (HES): is controlled by NHS Digital and contains all data pertaining to NHS hospital admissions, outpatient appointments and emergency department attendances across England.(63) It has been extensively utilised to investigate longitudinal population health outcomes because it is uniquely positioned to do so with its universal coverage and patient-level data.(63, 64) NNRD and HES data have previously been linked.(62)

5. Mental Health Services Dataset (MHSDS): controlled by NHS Digital, contains individual level data for all children accessing mental health care across the community, outpatient and inpatient settings in England.

6. The National Pupil Database (NPD): is controlled by the Department for Education. It contains detailed information on the educational attainment, special educational needs and attendance of children at state schools across England between the ages of 5-18 years. The NPD has previously been linked to health data.(65)

Workstream 1: Creating a matched cohort of infants with perinatal brain injury

Definition of perinatal brain injury:

Infants with perinatal brain injuries of all gestational ages (cohort 1) will be identified from the NNRD using a pre-existing definition that was developed through expert consensus and maps to NNRD data items. This includes infants with HIE, perinatal stroke, CNS infections, IVH, white matter changes, seizures and kernicterus born in England between January 2008 and December 31st 2020 (n=43, 582).

Identifying controls

A preterm control cohort (cohort 2) will be identified from the NNRD using propensity score matching (for gestation, birth weight Z score, sex, mode of delivery, maternal smoking, antenatal steroid treatment, antenatal magnesium sulphate treatment, surfactant treatment, month/ year of birth) at the NNRD population level. Cohort 2 will be matched 1:1 to the number of preterm infants <34 weeks with brain injuries (n=16, 175). Additional confounders affecting outcomes in premature infants with brain injuries necessitate more complex matching to create a balanced comparable cohort for meaningful analysis. A term control cohort will be identified from ONS data matched on sex, year of birth, gestation, birth weight and multiplicity, using a 1:3 algorithm (cohort 3; n= 82,221).

Methods:

1. Infants meeting the Department of Health definition will be identified within the NNRD. The pseudonymised neonatal care data for this cohort will be transferred to the ONS Secure Research Service (SRS). Preterm infants (born before 34 weeks) will be propensity score matched to a comparator group of infants.

2. The NNRD reliably captures data items such as date of birth, postcode, and infant NHS number, but it does not reliably hold the *child's registered name*. Additionally the NNRD contains the infants' *postcodes at birth*, but does not capture *postcode changes* throughout childhood. Therefore the NNRD cohorts will be linked to the

PDS, using *NHS number*, *date of birth*, *sex* and *postcode at birth*: to identify registered *forename* and *surname*, and *postcodes changes*.

3. The remaining un-matched infants (≥ 34 weeks gestation) with perinatal brain injury will be matched in a 1:3 ratio to a comparator group of infants, identified from the ONS.

4. Using *NHS number*, infants *surname*, *forename, sex* and *date of birth*, all 3 cohorts will be linked to ONS mortality records, HES and the MHSDS.

One file containing a list of personals identifiers for linkage to the NPD, will be transferred to the Department for Education. Another file, containing the three pseudonymised cohorts of infants and their health outcomes, will be transferred to the ONS SRS.

4. The following personal identifiers will be used to link to educational data within the NPD: *forename*, *surname*, *date of birth*, *sex* and *postcodes*. A logic model, designed to maximize the chance of a reliable postcode match (given the variation over time), will be used. This model was developed by another study team to improve the linkage of health and NPD data.(65)

5. At each step, we will evaluate the quality of linkage with the data controllers and un-linked cases will be reviewed with a view to amending and maximising the sensitivity of the probabilistic matching algorithms.(65, 66)

Workstream 2: Health and mortality outcomes

Population

The proposed matched cohort includes approximately: 141,978 infants. Maximum proposed follow up would be 13 years and minimum follow up of 1 year. The study would therefore include a total of: 985, 668 person follow-up years (accounting for general population mortality but not excess mortality from brain injuries which estimated at 19%).

Justification of outcomes:

The outcomes proposed have been chosen to collectively reflect parental, researcher, clinician and policymaker priorities as evidenced in the literature and through our PPI work. Where possible, the outcomes are consistent with those used in previous studies and reflect the most prevalent issues affecting our population of interest.

A core outcome set for perinatal brain injury does not exist. However, a minimum set of core outcomes in neonatology (COIN) – which was co-developed with parents through consensus methods – does. (67)Where possible, the study's outcomes incorporate the minimum outcome set put forward by COIN, and utilises the pre-existing Hardelid classification of chronic childhood conditions within HES data.(68-70)

Primary outcome:

- Neurodisability at 2 years, 5 years and 12 years

Secondary outcomes:

- All-cause mortality
- Mental health and behavioural conditions
- Chronic conditions

PRIMARY OUTCOME

1. Neurodisability

Definition: Neurodisability as per predefined ICD codes, for each included child at 2 years, 5 years and 12 years during the study follow-up period (from birth to December 31st 2021)

Data sources: HES, ONS, MHSDS

Analysis: We will undertake a logistic regression to determine the odds ratio (with 95% confidence intervals) of neurodisability (amongst the included population) at age 2 years, 5 years and 12 years, during the study follow-up period.

Covariates: maternal age, ethnicity (most covariates are accounted for in 'a priori' matching)

Subgroup analyses:

- Type of brain injury
- Type of neurodisability
  - Cognitive impairment
  - Language
  - Severe visual impairment
  - Cerebral palsy / gross motor impairment
  - Deafness
- Specific treatments
- Geographic variation

Power calculation

The minimum effect size that can be detected for the primary outcome with 99% power is shown in Table 1, alongside the expected effect size (calculated using Cohen's h).(71) Neurodisability incidence estimates were acquired from the literature.(13, 72-74)

Table 1

Age	Minimum detectable effect size (h)	Expected effect size (h)
2 years	0.030	0.683
5 years	0.036	0.879
12 years	0.105	0.704

SECONDARY OUTCOMES

2. All-cause mortality

Definition: Time to day of death from any cause for each included child during the follow-up period (from birth to December 2021).

Data sources: ONS, HES

Analysis: We will undertake a survival analysis with cox proportional hazards modelling using frailty function to fit hospital as random effect and adjust for predetermined covariates. Follow-up time will be censored. This will be used to estimate the absolute rates (per 1000 person years) and hazard ratios with 95% confidence intervals. The data will be examined for breaches in the proportionality assumption. The cox proportional hazards model was chosen as it permits the inclusion of the whole cohort in the analysis and accounts for the amount of follow up time available for each child.

Covariates: as per the primary outcome

Subgroup analyses:

- Type of brain injury
- Specific treatments
- Geographic variation
- Temporal trends (year of birth)
- Cause-specific mortality

3. Mental health and behavioural conditions

Definition: First occurrence of any of the conditions below (identified with predefined ICD 10 codes), for an included child, during the study follow-up period (from birth to December 2021 or death whichever occurs first).

Subgroups (the most prevalent childhood mental health conditions):

- Behavioural disorders including conduct disorder
- Emotional disorders such as depression and anxiety
- Hyperactivity disorders e.g. ADHD
- Other disorders e.g. Autism Spectrum Disorders

Data sources: HES, MHSDS

Analysis methods: The survival analysis, covariates and subgroup analyses will be as detailed previously for the all-cause mortality outcome, with the same covariates and subgroup analyses.

4. Chronic health conditions

Definition: First occurrence of any of the conditions below (using ICD 10 codes), for an included child, during the study follow-up period (from birth to December 2021 or death whichever occurs first).

Subgroups: (as per the Hardelid classification)

- Infections
- Cancer and chronic blood conditions
- Cardiovascular conditions
- Respiratory conditions
- Musculoskeletal/ dermatological conditions
- Neurological conditions e.g. epilepsy
- Metabolic/ endocrine/ digestive conditions
- Renal/ genitourinary conditions

Data sources: HES

Analysis: We will conduct a survival analysis and fit a cox proportional hazards model as for the all cause mortality outcomes detailed above, with the same covariates and subgroup analyses.

Workstream 3: Academic outcomes

OUTCOMES

1. Academic attainment

Definition: the mean academic attainment scores of the included population at the early years foundation key stage, key stage 1 and key stage 2, during the study follow-up period (from birth to December 31st 2021).

Data source: National Pupil Database

Analysis: The 3 cohorts will include approximately 97,084 children: at Early Years Foundation Stage (age 4, n= 97,084), at Key Stage 1 (Age 7; n=63,570), and at Key stage 2 (Age 11; n=19,999). These figures account for general population mortality but not excess mortality from brain injury. Loss to mortality across those with brain injuries is estimated at 19%. These figures also do not account for those not in state education, and those who emigrate. The differences in mean academic attainment scores at each of the national curriculum key stages will be analysed by fitting a linear regression models and adjusting for pre-specified covariates.

Covariates: maternal age, ethnicity, season of birth (most covariates are accounted for in 'a priori' matching)

Subgroup analyses: (data permitting)

- Type of brain injury
- Geographic variation (area of birth)
- Temporal trends (year of birth)
- Eligibility for free school meals
- Looked after child

- First language spoken at home
- Fixed term exclusions
- School type (mainstream or special school)

2. Special educational needs

Definition: The occurrence of any special educational need (SEN) on the National Pupil Database SEN register, for included children at age 4 (Early Years Foundation Stage) age 7 (Key Stage 1) and age 11 (Key Stage 2 during the follow-up period.

Data source: National Pupil Database Census

Analysis: We will undertake a logistic regression to determine the odds ratio (with 95% confidence intervals) of special educational needs (amongst the included population) at each key stage. Covariates and subgroup analyses will be as specified for the primary outcome (academic attainment).

Missing data

A sensitivity analysis will be undertaken to assess the effect of missing data. Specifically, the characteristics of linked and unlinked data will be compared to identify and if necessary adjust for potential sources of bias using 'a priori' informed imputation.(71)

Workstream 4: Patient and public involvement

This is a crosscutting workstream to ensure meaningful input from families throughout the fellowship.
The research plan to date has been shaped by detailed feedback from charity representatives and over 30 parents and ex-neonatal unit patients via the Great Ormond Street Parent Advisory Committee, the BLISS Insight and Involvement group, and the Meningitis Research Foundation. To ensure that the methods (using de-identified sensitive data without consent) are acceptable, that the research questions are relevant and that the chosen outcomes are meaningful.

Parents will be invited (through these partner charity organisations) to participate in a focus group; with the purpose of ensuring their input shapes the study from the onset. There will be annual meetings with the project advisory group – which will include a parent representative.

In the final year two 90-minute focus groups will be undertaken with a purposive sample of parents of children with perinatal brain injury. Parents from the previous focus group will be invited to participate and additional families via the charity BLISS who will also help run the focus groups. These focus groups will use semi-structured open-ended interview techniques. During these groups we will explore the study results with parents, capturing their thoughts on the results and what they mean for parents whilst also seeking input around how best to communicate these results on the neonatal unit. These discussions will be recorded with parents' consent. Recordings will be anonymously transcribed, uploaded to NVIVO and undergo thematic analysis. The learning

from this will inform the co-production of resources such as lay summaries, information leaflets, info graphics, with parents.

Dissemination, Outputs and Anticipated Impact

Anticipated impact on neonatal care, society and NHS services

Impact on neonatal care

- Equip healthcare professionals with reliable information to counsel families.
- Communication aids will facilitate meaningful family-centred conversations on the neonatal unit
- Help prepare families for their child's future and understanding what additional support may be needed.
- Encourage healthcare professionals consider the long-term impact of various neonatal care decisions.

Impact on the NHS and policymakers

- Help those involved in shaping policy, resource planning and service provision to make informed decisions about how to most effectively support these children whilst maximising the efficiency of services.
- Our findings will inform national guidelines on follow-up after brain injury

Impact on schooling and policymakers

- Equip parents with important information about the academic impact of brain injuries to help them plan their child's future and support them with their educational needs.
- Provide key information and education to teachers about how they can support children with perinatal brain injuries.
- Help the Department for Education in determining resource allocation and the provision of additional educational support

Planned outputs

The study protocol and in particular the methods developed in workstreams 1-3 will be submitted for publication in BMJ Open to share the learning about utilising these datasets amongst the academic community and prevent duplication of effort. The study findings from workstreams 2-4 will be submitted for publication in high impact general medical journals, such as the New England Journal of Medicine and the BMJ, to maximise awareness of the results internationally. The findings from workstream 4 will be submitted for publication in JAMA Pediatrics. This manuscript will also raise awareness of the communication tool (co-developed with parents) amongst neonatologists, which will be disseminated to all UK neonatal units. The study results will be presented at international conferences such as the Royal College of Paediatrics and Child Health annual conference, the Kings Fund annual conference, and the Paediatric Academic Societies meeting in the USA.

Parent and patient dissemination

The results of the study will be more broadly disseminated via press releases targeting the general media, and by utilising the communications team at the Institute of Child Health. Additionally social media platforms will be leveraged to spark and collate discussion about research findings whilst publicising the work. Stakeholders such as BLISS and the Meningitis Research Foundation will also publicise findings to their followers and the general public through their social media channels

Project Management

A detailed project timeline with specific deadlines for each task within each workstream has been developed. A strong network of collaborators underpins this project. In addition the project advisory group will be updated quarterly and meet once a year to lend their wide-ranging expertise to the study and ensure its timely completion.

Data Security

This project has been registered with the UCL Data Protection Team (registration number: Z6364106/2020/08/04). At no point will UCL researchers have access to identifiable information. UCL researchers will only have access to pseudonymised data held within the ONS Secure Research Service. No data will be held by or at UCL. Personal identifiers will only be available to those identifying participants for linkage at the Neonatal Data Analysis Unit and those undertaking data linkages at NHS Digital and the Department for Education. After linkages at these organisations, all identifiers will be removed (only the unique anonymous ID number will be retained) and these pseudonymised data will be securely transferred (using secure electronic file transfer – as per the organisations' information governance toolkits) for secure storage within the ONS SRS. Individuals who have opted out of data sharing at these organisations will not be included. Data sharing agreements between these organisations and UCL will be drawn up following ethical approval.

Ethics

We have full REC and CAG approval for this study.

REC reference: 20/LO/1023

CAG reference:20CAG0107

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