Developing routinely recorded clinical data from electronic patient records as a national resource to improve neonatal health care: the Medicines for Neonates research programme

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Scientific summary

The Medicines for Neonates research programme

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Scientific summary

Background

Data obtained from electronic patient records (EPRs) have potential to advance patient care and to improve health services. Although this is an acknowledged national goal, problems in realising this aspiration have involved difficulties in data extraction, population coverage, regulations around holding identifying information, uncertain data quality and patient trust.

Approximately 80,000 newborn infants are admitted annually for neonatal specialised care, a high-cost NHS service. Three circumstances placed neonatal specialised services in a favourable position to realise the potential of clinical data: (1) a strong professional desire to develop a standardised Neonatal Data Set, evidenced by a series of working groups of the British Association of Perinatal Medicine dating from the 1990s to the present; (2) a specialist commercial EPR supplier working closely with clinicians; and (3) a national reorganisation of NHS neonatal services over 2003–12 into managed clinical networks and the consequent frequent transfer of infants in accordance with their clinical needs to neonatal units providing different levels of care, which provided impetus to share clinical data.

Members of the Medicines for Neonates research group were closely involved in these initiatives and developed this proposal with the aim of utilising point-of-care, clinician-entered EPR-derived clinical data to improve newborn care and services. The Medicines for Neonates applied research programme is based on the principle that information should be recorded once and not repeatedly, recorded to a high standard, and made available to support multiple outputs.

Objectives

We conducted six inter-related workstreams to:

1. secure agreement for the use of EPR data as a national resource, evaluate and improve neonatal EPR data quality, and develop and test their utility to support multiple outputs
2. test the hypothesis that EPR data are of comparable quality to research data
3. test the hypothesis that neurodevelopmental assessment at the age of 2 years, conducted during routine NHS follow-up and recorded in EPRs, can reliably identify children with neurodevelopmental impairments
4. test the hypothesis that trial-based and other economic evaluations of perinatal interventions can be reliably conducted using EPR data
5. develop and test methods to link EPRS with other NHS data sets
6. involve parents in evaluating parent views of the use of EPR data in research.

We extended our original proposal in two workstreams. In workstream 1, we additionally conducted a systematic review of databases holding data on infants admitted to neonatal units, utilised EPR data to conduct national surveillance of severe necrotising enterocolitis (NEC) (a feared gastrointestinal inflammatory disease predominantly affecting preterm neonates), and tested the use of EPR data in supporting clinical services by evaluating mortality. In workstream 3, we additionally assessed the social communication skills at the age of 2 years of very preterm children using a parent-completed questionnaire, and conducted a systematic review and meta-analysis to determine the sensitivity and specificity of early developmental assessment in identifying school-age cognitive deficits. *Figure a* illustrates the relationships between workstreams and chapters.

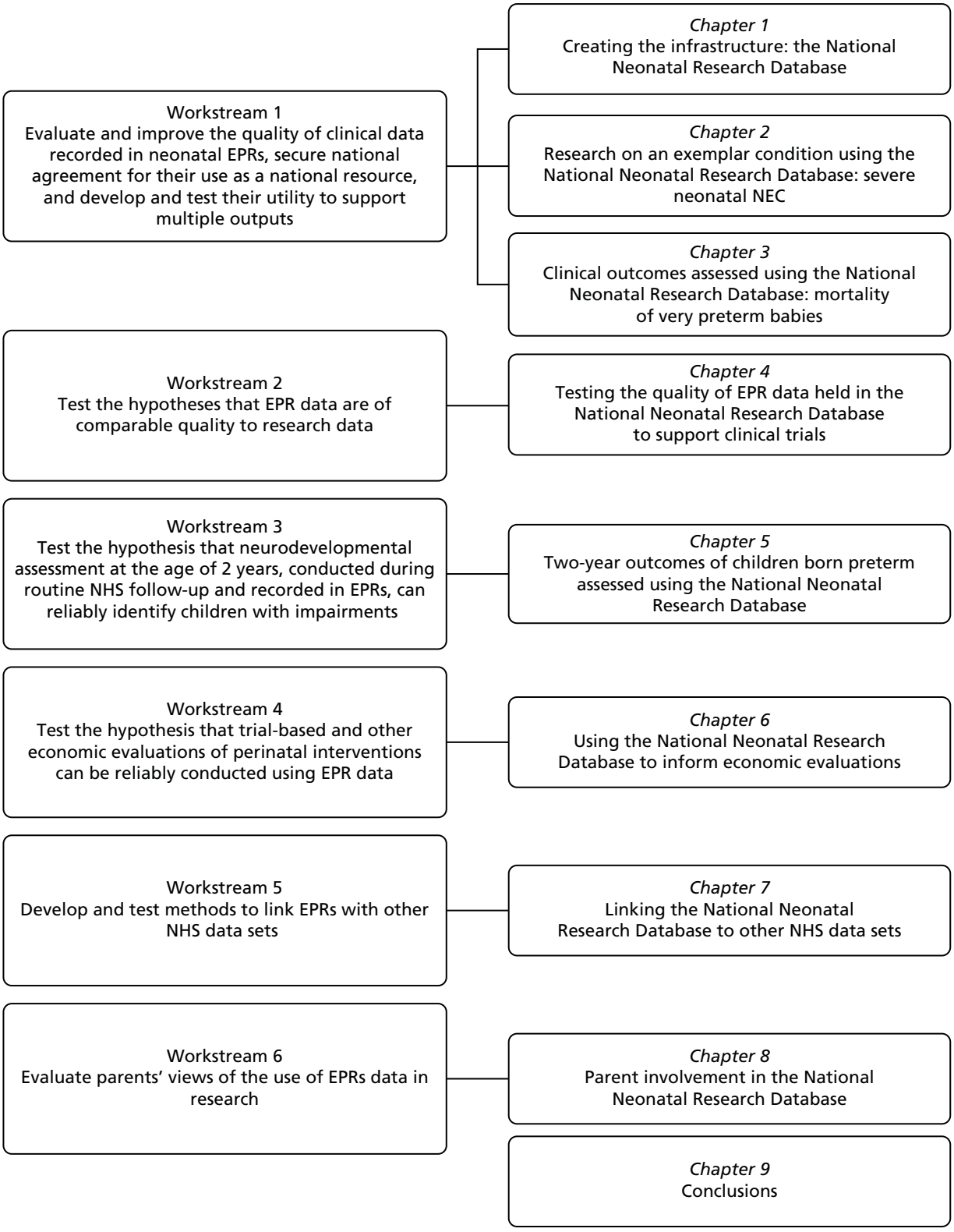

FIGURE a Relationships between medicines for neonates workstreams and chapters.

Methods

The Medicines for Neonates research programme ran for the period 1 July 2009 to 31 March 2015. In workstream 1, we obtained regulatory approvals to receive quarterly extracts of predefined data from neonatal EPRS through collaborative arrangements with the commercial supplier, the NHS trust hosting the Medicines for Neonates programme and the University research sponsor. We completed multiple application stages and public consultations leading to the submission of the defined data set for approval by the Health and Social Care Information Centre (now known as NHS Digital) as an NHS data standard. We developed algorithms and standard operating procedures for data management. We conducted a series of evaluations and addressed our research hypotheses using EPR data. We carried out a literature search of existing neonatal databases covering the period 1 January 2000 to 15 March 2015. We identified all cases of NEC requiring surgery or resulting in death over the complete 2-year period 2012–13 and we assessed variation in incidence across neonatal networks in England.

In workstream 2, we assessed the quality (completeness and accuracy) of EPR data in comparison with demographic, process and outcome variables obtained as part of a Health Technology Assessment-funded multicentre randomised clinical trial [i.e. Probiotic in Preterm infants Study (PiPS)]; Costeloe KL, Bowler U, Brocklehurst P, Hardy P, Heal P, Juszczak E, *et al.* A randomised controlled trial of the probiotic Bifidobacterium breve BBG-001 in preterm babies to prevent sepsis, necrotising enterocolitis and death: the Probiotics in Preterm infantS (PiPS) trial. *Health Technol Assess* 2016;**20**(66)].

In workstream 3, we employed a standard assessment tool [Bayley Scales of Infant and Toddler Development, third edition (Bayley-III scales)] to evaluate the neurodevelopmental status at the age of 2 years of children who were born before 32 weeks' gestation, and compared this with categorisation derived from EPR data recorded in the course of routine NHS follow-up. We evaluated the children's social communication skills as measured on a parent-completed questionnaire [Quantitative Checklist of Autism in Toddlers (Q-CHAT)] against normative data. We conducted a search on MEDLINE through the PubMed interface covering English-language literature published between 1 January 1990 and 31 March 2012 to determine the predictive validity of early developmental assessment in identifying cognitive deficit at school age.

In workstream 4, we compared health-care resource utilisation for infants recruited to the PiPS trial using three data sources: the PiPS trial case report forms, EPR-derived data and a combination of information from these two sources. Resource inputs captured by each data source were primarily valued using national tariffs and expressed in GBP (2012/13 prices). We estimated the level of agreement between the data sources and the level of precision of incremental cost-effectiveness for the probiotic evaluated in PiPS. For comparisons within trial by data source, differences in resource use and costs were tested using the independent sample *t*-test for continuous variables, the chi-squared test for categorical variables and the Mann–Whitney *U*-test for medians. For comparisons between the data sources, the levels of agreement in resource use and cost estimates for alternative combinations of data sources were estimated using the Lin concordance correlation coefficient.

In workstream 5, we obtained approval to receive NHS numbers and infant identifiers from the Confidentiality Advisory Group of the Health Research Authority and requested permission from all NHS trusts in England to receive these as extracts from their EPR data. We obtained Hospital Episode Statistics (HES) data from the Health and Social Care Information Centre (now NHS Digital) (https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics). We conducted two studies, utilising HES data covering the financial years 2005/6–2009/10, and HES and EPR-derived data for the calendar year 2010. We identified all individual birth episodes in HES, examined the completeness of HES recording and compared the total number of births with Office for National Statistics birth registrations. We used a deterministic approach to link the NNRD and HES records using the NHS number as a common unique identifier. We created a birth cohort of all infants born in English NHS hospitals and discharged during the period 1 April 2007 to 31 March 2008.

In workstream 6, we undertook a review of literature concerning public understanding of health data use for research purposes and contemporary e-health policy, identified relevant parameters and involved parents with previous experience of a child in neonatal care to assist in the design of a questionnaire directed at the parents of infants admitted to neonatal units. Materials were made available in eight languages in addition to English. These parents informed the research team of key questions regarding the routine use of babies' clinical data for research purposes and, thus, contributed to the content of the questionnaire. We recruited 29 NHS hospitals in England with neonatal care units as research sites. Research nurses approached parents to explain the study, provide written information and obtain consent.

Patient and public involvement (PPI) was a component of workstreams 1, 5 and 6.

Results

In workstream 1, we created a National Neonatal Research Database (NNRD) containing a defined extract from real-time, point-of-care, clinician-entered EPR NHS neonatal units and made this available for a variety of outputs. We achieved incremental coverage with data from 90% of English NHS neonatal units in 2010, 100% of English NHS neonatal units from 2012 onwards, and neonatal units in Wales from 2012 onwards. Scottish neonatal units joined in 2016.

We established a UK Neonatal Collaborative comprising all NHS Trusts providing neonatal specialised care, each of which provided Caldicott Guardian and Lead Neonatal Clinician approval for their data to be held in the NNRD. We created a new NHS Information standard, the Neonatal Data Set (ISB1595), comprising the predefined data held in the NNRD. We showed incidence of severe NEC to range from 7.55 per 1000 admissions [95% confidence interval (CI) 4.94 to 11.55] to 1.70 (95% CI 0.80 to 3.61), with no strong evidence of variation by network from the national average.

In workstream 2, we set out to test the hypothesis that EPR data are of comparable quality to research data; our results demonstrate that following data cleaning and merging, most key data items derived from EPR systems are of comparable quality to research data. We found completeness of data in the NNRD to be generally good. We assessed 2257 episodes of care from 1258 infants. Major discordance rates were low for 14 out of 15 patient characteristics, 9 out of 12 process measures and 10 out of 11 outcomes. The prevalence of adverse outcomes was < 6% with the exception of bronchopulmonary dysplasia (49.0%) and medical treatment for patent ductus arteriosus (20.3%). Specificity was > 85% for all outcomes, with the majority being > 90%. Specificity was high (> 85%) for all outcomes, sensitivity ranged from 50% to 100%, positive predictive values (PPV) ranged from 58.8 (95% CI 40.7 to 75.4) for a report of a porencephalic cyst to 99.7 (95% CI 99.2 to 99.9) for survival to discharge. Patient characteristics and the majority of NNRD items tested compare well against case report form (CRF) data. A small number of important outcomes are not currently reliably recorded in the EPRs.

In workstream 3, we recruited 190 children. We set out to test the hypothesis that neurodevelopmental assessment at the age of 2 years, conducted during routine NHS follow-up and the results of which are recorded in EPRs, can reliably identify children with neurodevelopmental impairments. The results demonstrate that neurodevelopmental assessment conducted during NHS follow-up has low sensitivity but high specificity for identifying children with neurodevelopmental impairments. Clinical neurodevelopmental data underestimated population prevalence of impairments following preterm birth by between 30% and 50%. We assessed the social communication skills of 141 very preterm children and found that they displayed greater social communication difficulties and autistic spectrum behaviours at 2 years than the general population. The systematic literature review revealed that neurodevelopmental assessment at approximately 2 years has low sensitivity but high specificity for identifying later school-age cognitive deficits.

In workstream 4, we set out to test the hypothesis that trial-based interventions and other economic evaluations of perinatal interventions can be reliably conducted using EPR data. The results revealed no statistically significant differences between NNRD data and data collected as part of randomised clinical trials for any resource input or cost category (i.e. that trial-based economic evaluations of neonatal interventions can be reliably conducted using the NNRD). When clinical trial data and NNRD data were compared, the agreement was relatively high for utilisation or cost of hospital stay by level of neonatal care, hospital transfers, retinopathy of prematurity screening and treatment, and surgery. However, for post-mortem examinations and cranial ultrasound scans, agreement fell below an acceptable threshold. The bulk of hospital resource inputs incorporated into a rigorously designed economic evaluation of a neonatal intervention in a UK context can be successfully and accurately extracted from the NNRD. We suggest that these results should be validated against other trials. Comparisons of cost-effectiveness outcomes between the NNRD and clinical trial data sources revealed low probability levels of miscoverage of incremental net monetary benefit when the NNRD acted as the sole source of resource use information. However, separate sensitivity analyses revealed that probability estimates of miscoverage for incremental net monetary benefit increased for both the death and the sepsis outcomes when the NNRD acted as the sole source of resource use information and clinical outcomes.

In workstream 5, we showed that completeness and quality of NNRD data are higher than NHS administrative (HES) data. The completeness of HES birth data varies substantially between hospitals. Approximately one-fifth of babies in HES have missing gestational age data and around 1.5% have a biologically implausible birthweight. We found that 1 in 10 neonates identified in HES is represented in the NNRD. There is > 95% agreement between HES and the NNRD for key items. We achieved linkage between HES and the NNRD for 61.3% of records. Linkage enhances the quality and scope of records substantially.

In workstream 6, we showed that there is a very high level of parent support for the routine use of health data for research purposes. Overall, 70% of the 1291 respondents were in agreement that their infant's clinical data be used for research, which rose to 77% if permission was asked and nearly 80% if identifying information was removed. Attitudes are moderated by level of education, previous children who had required neonatal care, and the degree of intensity of care received by their baby.

Conclusions

We have shown that it is possible to obtain high-quality data extracts from EPRS, achieve total population coverage and make data available as a national resource to support a wide range of outputs, researchers and organisations. Parent support for sharing clinical data for research is strong and underpinned by altruistic motivation.

Implications for health care

The Medicines or Neonates programme has established proof of concept for the use of EPR-derived clinical data in a wide range of research and health service evaluations. This opens the possibility of adapting the road map that we have established for other specialty areas with potential to bring about substantial NHS savings.

This study highlights the potential limitations of clinical data, in particular the necessity for high-quality recording. Clinical data are important to patient care and safety, and utilising routine clinical data for research is a secondary purpose. Completeness and quality checks can be automated for electronic data, and recording processes can be made 'user friendly' and constructed in ways to minimise the likelihood of missing or erroneous entries, which represents a major potential advance over traditional hand-written medical case notes. The development of criteria that provide assurance that data conform to prespecified

completeness and quality criteria would be an important development. This would enhance both patient care and research, each of which contributes to improving patient outcomes. This development would be especially beneficial in relation to research involving Investigational Medicinal Products as these are subject to the most stringent regulatory processes.

We developed and currently maintain the NNRD through academic endeavour, but processes to secure the stability of EPR-derived databases as national resources and their ongoing management are uncertain. A systematic approach to delivering neurodevelopment and neurocognitive screening of very preterm children by appropriately trained health-care personnel at ages that have optimum sensitivity and specificity for the identification of impairment requires consideration and evaluation. Finally, measures to extend public understanding and improve trust in the wider uses of clinical data are likely to be required if the full potential of clinical data are to be realised.

Research recommendations

Our principal recommendations are aimed at extending the benefits of EPR data, the outcomes of the Medicines for Neonates programme and the NNRD. Unlike the EPRs, data is not received in the NNRD in real time. As they are real time, EPR data are not appropriate for service evaluations or research because they change from moment to moment and have not undergone quality assurance processes. In contrast, the NNRD contains data that have been cleaned, merged and locked down in a permanent repository. We suggest testing the use of the NNRD to facilitate the delivery of a large-scale pragmatic national clinical trial and developing and testing methods to quality assure EPR data. The latter include, but are not limited to, involving parents, directing incentives at provider organisations, assigning local lead responsibility and automating certain procedures using machine-learning approaches. We also suggest linking the NNRD to other health, social care and educational data sets to facilitate the acquisition of lifelong outcomes across multiple domains.

Study registration

This study is registered as PROSPERO CRD42015017439 (workstream 1) and PROSPERO CRD42012002168 (workstream 3).

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