The future of neonatology

Neena Modi[1], Nicola J Robertson[2], Mark Hanson[3], Paolo De Coppi[4], Allyah Abbas-Hanif[5], Mark Turner[6]

1 Section of Neonatal Medicine, School of Public Health, Chelsea and Westminster Hospital campus, Imperial College London, London, UK

2 Department of Neonatology, EGA Institute for Women's Health, University College London, London, UK

3 Emeritus Professor of Human Development and Health and British Heart Foundation Professor of Cardiovascular Science, University of Southampton

4 Specialist Neonatal and Paediatric Surgery, Great Ormond UCL Institute of Child Health, 30 Guilford Street, London, UK

5 Department of Primary Care and Public Health, School of Public Health, Imperial College London, London, UK and Faulty of Pharmaceutical Medicine, Royal College of Physicians of London, London, UK

6 Chief Executive Office, Conect4children Stichting; and Emeritus Professor of Neonatology, University of Liverpool

Correspondence to N Modi; n.modi@imperial.ac.uk

Keywords: Neonate; Infant Newborn; Child Health Policy; Medicines; Devices; Diagnostics; Medial Training; Patient Empowerment

Introduction

We welcome the report of the Lancet Child and Adolescent Health Commission on the Future of Neonatology with contributions from a broad range of stakeholders including clinicians, parent and patient groups, and representatives from regulatory and other bodies from around the world (1). We write as UK authors of the report of the Commission. We are glad to have opportunity to raise awareness of the important issue of optimising and safeguarding newborn health, and to highlight and expand on some of the points made by the Commission. Improving newborn health is a moral imperative, not least because we are living in a period of uncertainty, with war zones affecting even basic neonatal care, but also because trajectories of health and disease are established in early development. A substantial proportion of the population have their future life-long health disrupted by processes operating in early development (2). Hence, if the lasting damage poor newborn health is inflicting on individuals and societies is to be curbed, identification of the biological mechanisms that define these pathways should be cardinal scientific and political goals. The early determinants of diseases encompass physical and mental health, but curiosity, innovation, resilience, cognition, and higher executive functions, positive attributes that enhance human potential, and offer a gateway to a better future, also have their roots in early life (3, 4). Newborn health is therefore also the route to improved population mental and physical wellbeing, and a pathway to sustainable economic resilience.

Despite these opportunities, that would benefit communities everywhere, babies have long been disadvantaged in benefiting from biomedical research and the equitable delivery of healthcare. It is shocking that only one new medicine, surfactant, has ever been specifically developed for a newborn disease, and that the majority of medicines used in newborn care are still prescribed off-label or off license which means that efficacy, dose, and safety are uncertain (5). Over two-thirds of Cochrane neonatal reviews are inconclusive because the relevant studies have either not been done or are methodologically weak (6). Low- and middle-income countries that shoulder the greatest burden of neonatal mortality and morbidity have the lowest representation in research that meets their needs; for example, a review of financing interventions to improve equity in the utilisation of services highlighted the lack of studies targeting newborns (7). Globally, the evidence-base for much fundamental newborn care such as preterm nutritional, immunomodulatory and neuroprotective strategies that result in optimal long-term health is highly insecure (8). Similarly, although

significant technical advances have been made in robotic surgery the only laparoscopic instruments available for neonates have been adapted from fetal surgery (9). The majority of devices used in newborn care have not been developed to address their needs but are hand-me-downs from other age groups and specialities (10). It is also morally unacceptable that globally each year, around 2.3 million infants die in the neonatal period, the majority from preventable or treatable conditions.

The root causes of a problem of this magnitude will clearly be multifactorial. The Commission unpicks the complex and interrelated determinants of the neglect of newborn healthcare and biomedical research, and identifies sectors, public and commercial, where the greatest responsibilities lie. The report sets out a series of remedies, recognising that causes operate in varying degrees across high-, middle-, and low-income settings and hence so too, must actions.

However, the report opens with a salutary tale of the manner in which newborn health has been casually regarded as optional. This was the abrupt cessation of a phase 2b trial of recombinant IGF1 for the prevention of bronchopulmonary dysplasia, a heterogeneous condition that affects around 50% of very preterm babies. This decision, when many babies had been recruited, was made solely for business reasons and in the absence of any safety or efficacy issues. The decision to stop represented a triumph of financial interests over patient benefit, and a deep disrespect for parents who had consented to the participation of their babies because they believed the study would advance the care of other children yet to be born. This decision acted as a catalyst for the release of the anger and frustration felt by many neonatologists, which led to the Commission. A biotech has recommenced the IGF1 study, in partnership with a pharmaceutical firm, but the experience is but one of several instances that speak to the fragility of neonatal research and development pipelines.

How does newborn biomedical research and healthcare come to be in this situation? The Commission identifies multiple causes, rooted in historical attitudes, misplaced paternalism, vested commercial interests, clinician bias, poor research literacy, and ineffective communication of science to both public and policy-makers. The Commission recognises that the responsibility for the neglect of newborn health and wellbeing, and the solutions, lie with multidisciplinary healthcare professionals, researchers, regulators, funders, industry, educators, parents and their representatives, and politicians. The report is a call to action.

The historical perspective

Over the course of societal evolution, perceptions of newborn infants shifted gradually from that of possessions of economic worth to their parents and society, to that of individuals in need of protection. Historic abuses conducted in the name of science, brought to light in the Nuremberg trials, led to a polarised view in which the imperative was to protect patients from the dangers of medical research, which was viewed as experimentation, not as a means to improve healthcare. Infants, above all patient groups, were regarded as highly vulnerable.

Recognition of clinical research as an effective, objective means of improving care initially came slowly but was then propelled into acceptance with the birth of evidence-based medicine (11). Similarly, research ethics are not immutable and continue to evolve but the realisation that infants also have a right to benefit from research was delayed in recognition and is still not universally appreciated (12, 13). This is also shown by the automatic categorisation of all newborn research, even comparative effectiveness studies comparing treatments already in wide use, as “high-risk” by some research ethics committees. Yet, one might ask, what protections are offered to infants against the unregulated experimentation that constitutes much of routine, yet non-evidence-based care?

This situation has similarities with the relative under-representation of women in biomedical research. A recent example was the failure to include pregnant women in COVID-19 trials even though there was no a priori biological reason to do so (14). This led to increased COVID-19 mortality and morbidity in pregnant women and the varying guidance issued about vaccination around the world likely fuelled vaccine hesitancy and mistrust of government advice. In this regard, we are heartened that the MESSAGE project which involves ensuring that sex and gender are considered in research is being adopted by the UK National Institute of Health and Care Research (15) and suggest that this initiative should be expanded to ensure that research also drives age-based equity, so that infants do not continue to be disadvantaged.

Financial considerations

One consequence of regarding all newborn research as “high-risk” is higher insurance and indemnity cover which acts as a disincentive for universities and industry, respectively the

major sponsors of public sector and commercial studies. Another major disincentive is that though the demand for newborn medicines, diagnostics, and devices is large, the market is unpredictable and insecure. This is because the greatest need for treatments for common neonatal conditions is in low- and middle-income countries that are unable to afford even minimal costs. In high-income settings, able to pay for treatments for rare diseases, the number of newborn patients is small. Additionally, health economic assessments to-date, have largely been unable to account adequately for long-term outcomes.

Ascertainment of long-term outcomes of interventions in fetal or neonatal life, and infancy is important as their effects may not be apparent until many years later. The majority of pregnancy and newborn studies require or would benefit from long-term follow-up but funders in the main are understandably reluctant to foot the bill. However, long-term follow-up is also clinically desirable, hence an obvious solution would be for research funders and health service providers to collaborate to establish unified national networks for follow-up assessments. This would be financially efficient and have the added advantages of improving the quality of assessments by conducting them to research standards and enabling more realistic assessment of the costs and benefits of fetal and neonatal treatments; the burden of separate assessments for research and clinical purposes imposed upon infants and families would also be reduced (16).

Clinician bias and paternalism

Clinicians of all disciplines strive to do their best for their patients. But what they believe to be best, may not be effective, or safe. Neonatal medicine is replete with examples of strongly held views that were ultimately shown to be harmful when put to the test of objective evaluation. Classic examples include the advice to place infants on their fronts, rather than their backs to sleep, and the routine use of 100% oxygen for neonatal resuscitation. These practices led to the death or damage of countless thousands of infants until research showed them to be harmful. This major barrier to improved newborn care, namely the reluctance of doctors, nurses and allied health professionals to put their strongly held beliefs to the test of randomisation, persists (17). This reluctance extends to professional organisations that are slow to modify guidance in the light of new evidence or to recommend participation in randomised controlled trials as best practice in favour of adherence to consensus-based guidelines. Thus, for example it took a quarter of a century before the use of antenatal

steroids for threatened preterm labour was incorporated into professional guidelines with the resulting death or damage to countless thousands of babies. Other adverse consequences flow from clinician and organisational promulgation of guidelines for which there is inadequate evidence. An example is the multi-million-dollar judicial awards made to families on the basis that formula *causes* necrotising enterocolitis. These legal ruling have resulted in companies divesting from their infant research and development pipelines and - in an ironic similarity to the formula industry in the 1970s and 80s - to the unfettered expansion of an increasingly aggressive human milk industry (18, 19). Neonatal healthcare professionals act as gatekeepers in deciding whether or not they will inform parents about research studies relevant to their infants. This is paternalism, the view that they know best, and that it is legitimate to deny parents the right to make informed choices. Paternalism can also operate within teams, with dominant groups excluding other members in decision-making about research (20, 21). In all other spheres of medical practice in the UK and many countries around the world, paternalism has been rejected; surely it is time to apply the same principles to clinical research?

The importance of strengthening neonatal translational research

Translational research is essential to bridge the gap between basic science and clinical application. A prime example of successful translational research in neonatology is therapeutic hypothermia for moderate-severe hypoxic-ischaemic encephalopathy. This was a significant advance where multiple randomised controlled trials built upon a strong foundation of preclinical studies (22, 23). However, other experience is less salutary, with researchers awarded funding for clinical trials in the absence of preclinical justification or in the face of negative large animal work. Erythropoietin did not augment therapeutic hypothermia neuroprotection in two large animal models (24, 25), but a phase 3 randomised controlled trial nonetheless went ahead, based mainly on rodent preclinical studies (26). Similarly, though studies of deeper and longer cooling in preclinical models led to adverse outcomes, trials in human neonates went ahead (27, 28). Further challenges threaten advances in neonatal medicine; in 2025 the United States National Institutes of Health announced prioritisation of human-based research, with the necessity of including mixed approaches in all preclinical studies to validate relevance to human disease. Another aspect of this problem is the need to strengthen the scientific foundations of neonatal

pharmacology. Models that more accurately capture neonatal physiology including advanced preclinical models, in silico approaches, and neonatal biobanks should be incentivised for both academic and private sector evaluation. These tools, alongside harnessing AI innovation, would accelerate the identification of optimal dosing, safety profiles and mechanisms of action, reducing reliance on extrapolation from adults or older children.

The adult stroke community recognised the disconnect between preclinical success and clinical failure in 1999 and published a series of recommendations from the Stroke Therapy (or Treatment) Academic Industry Roundtable (STAIR) committee to improve the design, conduct, and translation of preclinical and clinical stroke research (29). The neonatal world needs similar rigorous guidelines to optimise successful clinical translation of therapies.

Neonatal training and research literacy

In the UK neonatology only became a recognised paediatric speciality in the 1980s, and to this day in many parts of the world it remains within the domain of general paediatrics. There is a clear need to extend recognition of, and clinical training in neonatology worldwide for doctors, nurses, and allied health professionals. Similarly, with the emergence of fetal surgery as a distinct and dedicated area of training within paediatric surgery, and the increasingly defined role of the neonatal surgeon, it would be beneficial to have a dedicated neonatal surgical training pathway. It is recognised that specialised paediatric surgeons are best suited to treat children; we envision a future in which specialist surgeons similarly provide comprehensive care for neonates in recognition of their distinct physiological, developmental and healing responses. There is also the need to improve understanding of clinical research methods among these professional groups, including recognition of the harms that can result from consensus, opinion, or belief-based practice, and the right of infants to benefit from research (30). This is a responsibility of the professional bodies who define standards of training and assessment. Research training pathways exist in only a few countries such as the UK. Yet here and to even greater extent in low- and middle-income countries, over-stretched healthcare systems often have no option but to prioritise care delivery to the detriment of research and development. A further difficulty is that though publicly-funded healthcare systems hold clinical academics in high regard, this is not necessarily the case in systems funded by private insurance or with for-profit providers where clinical research is regarded as a second-class career pathway, with poor pay and esteem.

Approaches to strengthen and harmonise training exist. The long-established NOTE (Neonatal Online Training and Education) programme, based at the University of Southampton is one such example with its curriculum aligned with the recently updated European Union commissioned syllabus for neonatal training in Europe (https://moodle.neonataltraining.eu/mod/page/view.php?id=374). In neonatal surgery the need to strength centralization following the guided of GIRFT will help training, beside improving neonatal surgical outcomes. (GIRFT Neonatology: "Neonatology – GIRFT Programme National Specialty Report" (Adams, Harvey, Sweeting) January 2022; Getting It Right First Time). Specifically, this could be achieved with neonatal surgical services co-location with Level 3 NICU, specialist paediatrics, specialist children's surgery/anaesthesia and maternity services — consistent with commissioning standards. (GIRFT; GIRFT Paediatric General Surgery & Urology: "Paediatric General Surgery and Urology – GIRFT Programme National Specialty Report" (Kenny) February 2021). These initiatives represent an exemplar for a structured approach to improving training. We urge that they be extended to strengthen knowledge of research methods and that understanding of research methods is promoted in training for all allied healthcare professionals.

The need for neonate-focussed regulation

The regulation of neonatal research and development represents another example of trying to fit a square peg into a round hole; in other words, to adopt processes designed for adult studies rather than consider neonatal needs directly. An example is the 2017 Medical Devices Regulation (2017/745), created by the European Union with the laudable aims of protecting patients, replacing three previous directives, and harmonising practice across member states. However, the financial and administrative costs have adversely affected neonatal research and development because this is largely conducted by small and medium enterprises. The Regulation has placed at risk devices such as tracheal occlusion balloons, atrial septostomy catheters, and extracorporeal membrane oxygenation pumps. Following a letter by European paediatric, perinatal and parent organisations the EU Commission extended the time to comply with the new regulation. However, this is no more than a temporary expediency and what is needed is recognition that much neonatal research and development is not carried out by large multinationals able to shoulder the expense of new regulatory requirements and ensure that legislation does not have unintended adverse

consequences. The European Medicines Agency has recently established an advisory group for paediatrics and similar initiatives are required to safeguard and strengthen neonatal device development (31).

Other regulatory mechanisms must also evolve. Offering label extensions for drugs developed for neonates at post marketing stages would lower commercial risk and reward companies that invest in this vulnerable group. Similar to paediatric use marketing authorisations in Europe and Best Pharmaceuticals for Children Act provisions in the United States, but tailored for neonates, such frameworks could normalise the inclusion of newborns in development pathways rather than treating them as exceptions. A default position of inclusion, with scientific justification required for exclusion, would realign incentives across academia, industry, and regulators.

Research ethics

The need to harmonise recognition and application of the principles of newborn research ethics across countries is another area of need, but one that will be difficult to achieve given widely differing legal frameworks and societal attitudes. However, what is within reach is to advocate for national research ethics services and remove the requirement for researchers to obtain approval from every hospital or facility that participates in a clinical research study. The Commission also urges research ethics committees to question the exclusion of infants from clinical trials in the absence of any scientific of biological rationale, adopt proportionate risk assessment, and seek the views of frontline neonatal physicians and parents in making decisions about the level of risk involved in any individual study. The Commission also urges research ethics committees to recognise the legitimacy of a variety of forms of consent. An example is opt-out consent for comparative effectiveness trials evaluating treatments that are already in wide use which reduces the burden placed on researchers, the anxieties placed on parents and carers and presents the research appropriately as an ethical approach to improve patient care (32). Other approaches that merit consideration in specific circumstances such as time critical neuroprotective therapies include verbal (with a continuing consent process and follow up within 24h with written consent), deferred, and waived consent (33). Another achievable recommendation is to require the inclusion of neonates in research as the default approach unless there is clear scientific justification for

their exclusion, a principal that has been successfully used to counter the strong and longstanding bias against the participation of women in clinical research (15).

Parents, patients, the public, and societies

Patient and public advocacy can be a powerful force for change. The inclusion of parents, people with lived experience of ill-health during the neonatal period, and the public, also makes for better and higher impact research. This principle is now firmly embedded in the work of funding bodies such as the UK National Institute for Health Research and acknowledged by professional organisations such as the European Society for Paediatric Research (34). Parent-patient-public involvement and engagement tailored to the situation, is essential to grow trust in science and research processes (35). The dangers of poor public understanding of science and scientific method is illustrated by the rise of vaccine hesitancy that is leading to a resurgence in outbreaks of measles and other infectious diseases in many parts of the world, including the United States. A particularly salutary example of the need for trust in science is the lasting legacy of the Tuskegee Syphilis Study. This was a 40-year medical research project conducted by the United States Public Health Service commencing in the 1930s. The study involved unethical experimentation on African-American men and added immeasurably to the troubled history of racism and distrust of government in the United States (36). The Commission therefore rightly urges professional organisations to support the involvement of patients, parents and the public in advocating for better newborn research and care and in collaborating to speak with a collective voice. Fortunately in this aspect, parent-led and patient support organisations in the UK have been instrumental in advancing neonatal care by partnering with professional societies and research networks. Their participation in multicentre collaborative studies and advisory panels has ensured that research and service development remain aligned with the real-world needs and experiences of families affected by neonatal conditions (doi: 10.1016/j.jpedsurg.2017.05.033. doi: 10.1007/s00383-024-05865-z; doi: 10.1055/s-0039-3400284).

A global issue

The issues raised by the Commission are global and for this reason a major recommendation is the creation of a Global Alliance for Innovation in Newborn Health (GAINH) consisting of four major components:

(i) The establishment of a Neonatal Global Financing Facility to provide a predictable market for industry through pooled procurement. It might also advise on conflicts of interest relevant to adverse commercial influences on newborn health (37). Other market shaping approaches such as extended exclusivity, and priority review vouchers can also create incentives for industry. Lessons from rare disease and vaccine markets show that even small, high risk patient groups can attract substantial research and development investment if the right structures are in place. However, the primary purpose of such a facility would be to support low- and middle-income countries to initially pay a fraction of the costs of newborn products, with the proportion increasing as their economies grow

(ii) Establishment of a Global Neonatal Research Network to help to tackle inequities across low-, middle- and high-income countries, improve research efficiency, and reduce research waste. The network would consist of a core group of neonatal facilities worldwide funded to deliver studies to common protocols by trained staff. An additional aim would be to promote the establishment of coordinated research pathways from pre-clinical exploration, through to pilot or feasibility studies and efficacy trials. These would be followed by health technology assessments to evaluate effectiveness and global generalisability, and ultimately incorporation into policy, implementation at scale and determination of impact. When combined with use of real-world data, digital technologies, and innovative study designs, such a network could substantially reduce costs and time to achieve patient benefit. This could start in the UK based, on an ethos similar to the NICHD Eunice Shriver Network, funded centrally and, importantly, run independently of the academic system where self-interest may be perceived.

(iii) Partnership with professional bodies to strengthen neonatal training, address the global neonatal skills shortage, improve research literacy for all neonatal healthcare professionals, and define career pathways for neonatal physician-scientists.

(iv) Provision of a platform for advocacy to draw the attention of global and local funders, regulators, policy makers, and society to the importance of neonatal studies to improve health across the life course. Global entities such as the

Partnership for Maternal, Newborn and Child Health hosted by the WHO, Saving Newborn Lives, Gates Foundation, and Global Financing Facility for Women, Children and Adolescents already have a focus on newborn health, targeting advocacy, clinical training, research funding, and health systems. GAINH would complement these activities by promoting recognition of research as a route to improved newborn health and tackling barriers.

Conclusions

We believe the Commission's proposals and those we describe here are feasible. However, addressing the many challenges that are compromising the future of neonatology will require concerted action by actors across all sectors. We accept too that though a paradigm shift is warranted and possible in some countries, a more pragmatic goal in others may be a series of small, sustainable, incremental changes. The report of the Commission is a first step. We hope that it will help inspire activities across the globe.

Disclosures

The authors are UK contributors to the Lancet Commission on the Future of Neonatology.

Acknowledgments

We acknowledge gratefully the immense work of the Commission, the many contributors worldwide, and the support of the editors of the Lancet Child and Adolescent Health in bringing the report to fruition

Funding

None

References

1) De Luca D, Modi N, Davis P, et al The Lancet Child & Adolescent Health Commission on the future of neonatology. Lancet Child Adolesc Health. 2025 Aug;9(8):578-612. doi:10.1016/S2352-4642(25)00106-3. Epub 2025 Jun 25

2) Sales WB, Maranhão EF, Ramalho CST *et al.* Early life circumstances and their impact on health in adulthood and later life: a systematic review. BMC Geriatr 2024; 24:978 https://doi.org/10.1186/s12877-024-05571-4

3) Pentecost M, Keaney J, Moll T, Penkler M, editors. The handbook of DOHAD and society: past, present, and future directions of biosocial collaboration. Cambridge University Press; 2024

4) Poston L, Godfrey KM, Gluckman PD, Hanson MA, editors. Developmental origins of health and disease. Cambridge University Press;2nd. Edition 2022 Dec 22

5) Costa HTML, Costa TX, Martins RR, Oliveira AG. Use of off-label and unlicensed medicines in neonatal intensive care. PLoS One 2018; 13: e0204427

6) Lai NM, Ong JM-J, Chen K-H, et al. Decreasing number of conclusive neonatal reviews: increasing role for shared decision-making? Neonatology 2020; 117: 125-26

7) Bou-Karroum L, Iaia DG, El-Jardali F, et al Financing for equity for women's, children's and adolescents' health in low-and middle-income countries: A scoping review. PLOS Global Public Health 2024; 4(9):e0003573

8) Varrio T, De Luca D, Kuitunen I. Evidence certainty in neonatology-a metaepidemiological analysis of Cochrane reviews. Eur J Pediatr. 2025;184(2):191. doi: 10.1007/s00431-025-06023-w

9) Shen LT, Tou J Application and prospects of robotic surgery in children: a scoping review: World Journal of Pediatric Surgery 2022;5:e000482.

10) Melvin T, Dooms MM, Koletzko B, et al Orphan and paediatric medical devices in Europe: recommendations to support their availability for on-label and off-label clinical indications Expert Rev Med Devices 2024; 21(10):893-901

11) Claridge JA, Fabian TC. History and development of evidence-based medicine. World J Surg. 2005 May;29(5):547-53. doi: 10.1007/s00268-005-7910-1

12) Modi N, Vohra J, Preston J, et al; Working Party of the Royal College of Paediatrics and Child Health. Guidance on clinical research involving infants, children and young people:

an update for researchers and research ethics committees. Arch Dis Child 2014; 99(10):887-91

13) Modi N Consent and the continuing evolution of clinical research ethics Arch Dis Child Fetal Neonatal Ed 2021; 106:230-31

14) Modi N, Ayres-de-Campos D, Bancalari E, et al Equity in coronavirus disease 2019 vaccine development and deployment. Am J Obstet Gynecol 2021; 224:423-7

15) MESSAGE: Medical Science Sex & Gender Equity; https://www.messageproject.co.uk/; last accessed 190825

16) Wong HS, Cowan FM, Modi N; Medicines for Neonates Investigator Group. Validity of neurodevelopmental outcomes of children born very preterm assessed during routine clinical follow-up in England. Arch Dis Child Fetal Neonatal Ed 2018; 103(5):F479-F484. doi: 10.1136/archdischild-2016-312535

17) Lammons W, Moss B, Battersby C, Cornelius V, Babalis D, Modi N. Incorporating parent, former patient and clinician perspectives in the design of a national UK double-cluster, randomised controlled trial addressing uncertainties in preterm nutrition. BMJ Paediatr Open 2021 Jun 15;5(1):e001112

18) Neu J, Modi N. When biological causality is determined in a court of law. JAMA Pediatr 2024;178(12):1239-40

19) Modi, N. Repeating the errors of the past: the hazards of a commercial human milk industry. Pediatr Res 2024; 95:1480-82

20) Allegaert K, Mitra S, Smits A, Turner MA Advocating for drug development in newborn infants Early Hum Dev 2024; 199:106136

21) Degl J, Ariagno R, Aschner J, et al The culture of research communication in neonatal intensive care units: key stakeholder perspectives. International Neonatal Consortium. J Perinatol 2021; 41:2826-33

22) Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev. 2013;(1): CD003311. doi:10.1002/14651858.CD003311.pub3

23) Gunn AJ, Laptook AR, Robertson NJ, et al Therapeutic hypothermia translates from ancient history into practice. Pediatr Res 2017; 81(1-2):202-9

24) Pang R, Avdic-Belltheus A, Meehan C, et al. Melatonin and/or erythropoietin combined with hypothermia in a piglet model of perinatal asphyxia. Brain Commun. 2020 Dec 1;3(1): fcaa211

25) Wassink G, Davidson JO, Crisostomo A, et al Recombinant erythropoietin does not augment hypothermic white matter protection after global cerebral ischaemia in near-term fetal sheep. Brain Commun 2021; 29;3(3):fcab172

26) Wu YW, Comstock BA, Gonzalez FF, et al; HEAL Consortium. Trial of erythropoietin for hypoxic-ischemic encephalopathy in newborns. N Engl J Med 2022; 387:148-59

27) Alonso-Alconada D, Broad KD, et al Brain cell death is reduced with cooling by 3.5°C to 5°C but increased with cooling by 8.5°C in a piglet asphyxia model. Stroke 2015; 46(1):275-8

28) Shankaran S, Laptook AR, Pappas A, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Effect of depth and duration of cooling on deaths in the NICU among neonates with hypoxic ischemic encephalopathy: a randomized clinical trial. JAMA 2014; 312(24):2629-39

29) Stroke Therapy Academic Industry Roundtable (STAIR). Recommendations for standards regarding preclinical neuroprotective and restorative drug development. Stroke 1999; 30:2752-8

30) Allegaert K, Mitra S, Smit A, Turner MA Advocating for drug development in newborn infants Early Hum Dev 2024; 199:106136

31) Guerlich K, Patro-Golab B, Barnacle A, et al; European Academy of Paediatrics.

European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children. Acta Paediatr 2023; 112:2440-8

32) Gale C, Hyde MJ, Modi N; WHEAT trial development group. Research ethics committee decision-making in relation to an efficient neonatal trial. Arch Dis Child Fetal Neonatal Ed. 2017; 102(4): F291-F298

33) Modi N. Consent and the continuing evolution of clinical research ethics. Arch Dis Child Fetal Neonatal Ed 2021; 106:230-31

34) Molloy EJ, Mader S, Modi N, Gale C. Parent, child and public involvement in child health research: core value not just an optional extra. Pediatr Res 2019; 85:2-3

35) Folayan MO, Conway M, Russo C, et al Health equity in pediatric drug development: translating aspiration into operation. Ther Innov Regul Sci 2022; 56:991-1003

36) Tobin MJ. Fiftieth Anniversary of Uncovering the Tuskegee Syphilis Study: The Story and Timeless Lessons. Am J Respir Crit Care Med 2022; 205:1145-58

37) Modi N, Hanson M. The commercial determinants of infant and child health. BMJ 2024; 31;387