ORIGINAL ARTICLE

Designing the landscape for technological development in neonatal neurocritical care

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ABSTRACT

Objectives To identify current 'gaps' in clinical practice or therapeutic knowledge of the care of neonatal neurointensive care patients and to determine the impact healthcare technologies can have on improving outcomes.

Design The Cambridge Institute for Manufacturing's (IfM) roadmapping methodology.

Setting Cambridge, UK.

Participants 16 delegates were selected through professional networks. They provided coverage of academia and clinical skills, as well as expertise in neonatology, engineering and technology development.

Main outcome measures A 'strategic landscape' has been developed with 'landmarks' identified as 'trends or drivers', 'patient pathway experience and unmet needs' and 'enabling project or resources'. Priorities were voted on by delegates.

Results 26 strategic 'landmarks' were identified, and of these 8 were considered 'trends or drivers', 8 'patient pathway experience and unmet needs' and 10 as 'enabling project or resources'. Of these, five priorities for the future of neonatal neurocritical care were identified by a voting process: real-time video monitoring for parents; individualised management of preterm infants in neonatal neurocritical care based on real-time multimodal monitoring; continuous electroencephalogram monitoring for early seizure diagnosis; neuroprotection: understanding basic mechanisms; and sleep measurement.

Conclusions Through the use of the IfM methodology, a list of priorities has been developed for future work into improving the experience and possible outcomes of newborn infants with brain injuries and their families. While not an exhaustive list, it provides the beginning for a national conversation on the topic.

BACKGROUND

Neonatal brain injury is a significant cause of death, disability and financial cost for families and health systems.[1] Around 1 in 10 newborn infants are born before 37 weeks' gestation, equating to around 60 000 infants/year in the UK.[2] While the survival of very preterm infants (<32 weeks' gestation) has increased over the past 20 years, the incidence of lifelong neurodisability has remained relatively constant. Around 50% of extremely preterm infants (<28 weeks' gestation) will have some degree of cognitive impairment or behavioural difficulties.[1] Globally it is estimated that around 15 million babies are born prematurely, and the complications of preterm birth are the leading cause of death in children under 5 years.[3] The cost of preterm birth in the UK was estimated at £2.9 billion in 2009.[4] Term infants are also at risk of brain injury at birth, the most common disorders hypoxic-ischaemic encephalopathy (HIE) and perinatal arterial ischaemic stroke affecting around 1 in 1000 and 1 in 2500 births, respectively.

In 2015 the Department of Health issued a challenge to the medical establishment to reduce the number and severity of brain injuries suffered in this population.[5] While access to good-quality obstetric care can reduce the risk of HIE,[6] the incidence has remained frustratingly static in recent years.[7] Therapeutic hypothermia represents the first neuroprotective therapy for infants with HIE, yet even with hypothermia over half treated infants are still at risk for moderate-severe cerebral palsy or death.[8]

No single intervention can ameliorate neonatal brain injury given the complex interaction between pathological processes, developmental trajectory, genetic susceptibility and environmental influences. However, a dedicated brain-orientated approach to the management of adults with brain injury has been shown to improve clinical outcome.[9] Neonatal neurocritical care is a relatively new concept, bringing together a multidisciplinary team of healthcare professionals providing a brain-orientated approach to the care of high-risk infants.[10]

Neonatal intensive care has always been a technology-driven specialty, with the need for continuous non-invasive physiological monitoring, point-of-care blood sampling and portable brain imaging. Further innovation is required if further progress is going to be seen in this high-risk patient group.

To open the discussion on the topic of improving the care of neonatal brain injury, the National Institute of Health Research (NIHR) Brain Injury Healthcare Technology Co-operative (HTC) set out to explore the gaps that currently exist in neonatal neurocritical care and to identify opportunities for future projects to fill these gaps. In order to do this, the Cambridge Institute for Manufacturing's (IfM) landscaping methodology was chosen. The IfM landscaping methodology provides a rigorous and systematic method of investigating strategic level processes in order to improve those processes.[11] Landscaping is often used in industry[12]; however, it remains underutilised in the healthcare environment.

The specific aims of the exercise were to identify current 'gaps' in clinical practice or therapeutic knowledge, and to determine what impact healthcare technologies can have on improving outcomes across the patient journey in the neonatal 'neurocritical care' unit, create ideas for areas of future research and service development projects, and encourage wider collaboration between the key stakeholders in the field.

METHODOLOGY

Roadmapping is a process originally developed in the high-tech business sector in the 1970s initially at firm and then at industry levels.[11] It brings together people with a strategic level of knowledge around a sector to identify opportunities and difficulties within a system. These are then targeted as areas to address in order to achieve a desired outcome.[12]

While there are many types and variations of roadmapping, with different levels and types of analysis, an 'agile' approach is advocated at the start, iterating as a learning process. 'Fast-start' workshop methods[11] enable diverse groups of stakeholders to explore issues of common interest and to cocreate strategies for tackling these. The 'S-Plan' workshop approach[11] is suitable for tackling broad areas in a top-down fashion, initially developing a 'landscape' for the overall domain, and then identifying and prioritising key 'landmarks' (topics) in the landscape for further exploration in small groups.

Roadmapping and the S-Plan approach have been developed and tested in many sectors, but remain an underutilised method within the healthcare field, with its application to neonatal neurocritical care providing a useful demonstration of utility in this domain.

Delegates

Delegates were identified through professional networks. A cross section of academia and clinical skills was achieved, as well as expertise in neonatology, engineering and technology development. All the clinicians apart from R R-R had specific interests in perinatal brain injury, with relevant publications in the field; the engineers, physicists and neuroscientists had expertise in advanced MRI (JS), signal processing (PS), optical imaging (JH, RC) and biomarkers (PY). Details and affiliations of the delegates are given in online supplementary appendix 1.

Preparatory work

These participants brought their expertise and their preparatory work looking into the following questions:

- Why do we need to take action (particularly regarding developing needs)?
- How can the patient pathway experience be developed to respond to these needs?
- What enabling projects and resources are required to deliver that pathway experience?

Workshops

Delegates attended a 5-hour facilitated workshop where each participant gave a 2–3 min pitch of their preparatory work. With the aid of the facilitators, each item was identified as fitting one of three possible criteria: either 'trends and drivers', a 'patient pathway experience and unmet needs' or 'enabling project or resources'. Time scales of current, short term, medium term, long term or 'vision' were applied before being added to the landscape. Linkages between the different three aspects were agreed on to form a linkage chart which provides insights into current problems and how to address them.

Delegates then voted on the items to agree on priorities before they were further explored by smaller groups. Their findings were then presented for whole group review.

RESULTS

Through this process 26 items were identified (figure 1). Of these 8 were considered 'trends or drivers', 8 'patient pathway experience and unmet needs' and 10 as 'enabling project or resources'. These crossed all the time scales and showed a broad range of subjects, from a lack of robust way to measure neurological damage to the use of three-dimensional printing in neonatal care (figure 1). To further develop the ideas, linkages between items were discussed and agreed on during the workshop and were further considered after the

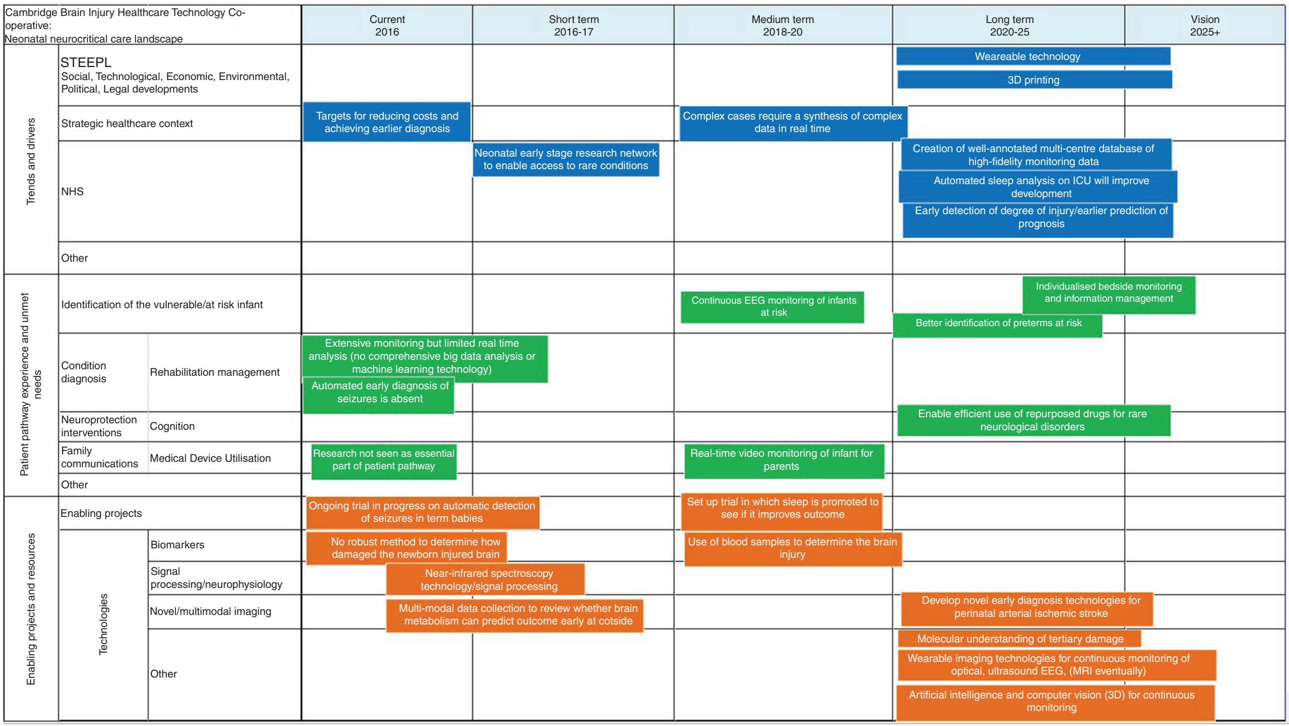

Figure 1 Landscape. 3D, three-dimensional; EEG, electroencephalogram; ICU, intensive care unit; NHS, National Health Service; PAIS, perinatal arterial ischaemic stroke.

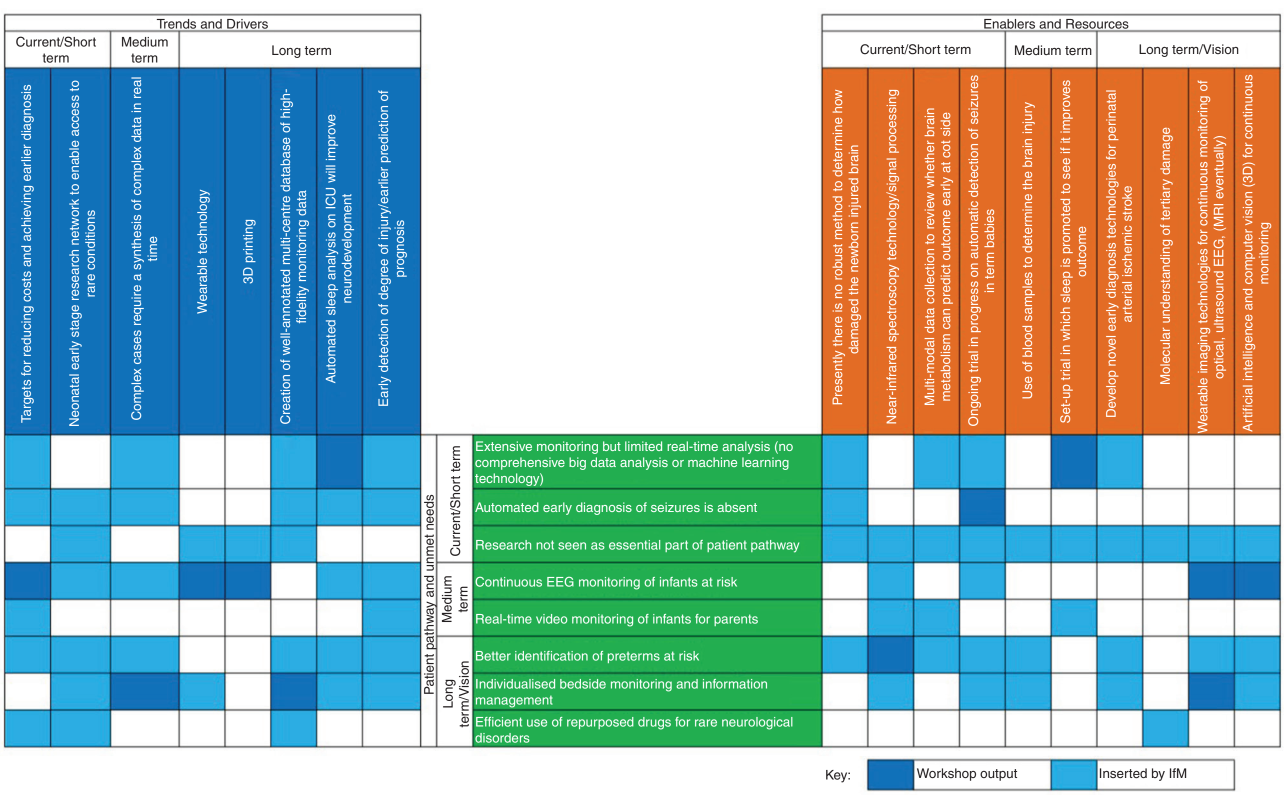

Figure 2 Linkage chart. 3D, three-dimensional; EEG, electroencephalogram; ICU, intensive care unit; IfM, Institute for Manufacturing; PAIS, perinatal arterial ischaemic stroke.

session (figure 2). Of these, five priorities for the future of neonatal neurocritical care were identified by a voting process (online supplementary appendix 2). These were the following:

- Real-time video monitoring for parents.
- Individualised management of preterm infants in neonatal neurocritical care based on real-time multimodal monitoring.
- Continuous electroencephalogram (EEG) monitoring for early seizure diagnosis.
- Neuroprotection: understanding basic mechanisms.
- Sleep measurement.

Groups of delegates further expanded and developed these ideas using a preset structure (figure 3). The results were as follows:

Real-time video monitoring for parents

Delegates identified that at present parents are often unable to visit their baby due to childcare issues with other children, work commitments or distance from home. This was identified as a risk for maternal and paternal depression and parents bonding, which could be addressed by real-time video monitoring in the neonatal unit. It was acknowledged that while this has been used in some settings, it is far from widespread and remains an area of inconsistency. The opportunity this provides for the observation of behaviours for research and teaching purposes was emphasised with delegates, highlighting the possible insights that could be gained into neonatal brain injury.

Data security, ethical considerations and infrastructure installation were seen as key barriers to be addressed. The use of pre-existing system such as FaceTime, Skype or similar live techniques was a possible way of addressing these issues with minimal investment. If videos were to be stored for research or teaching purposes, then storage of very large quantities of data would have to be considered and a specialist system might need to be developed. Ethical and legal aspects are likely to need to be addressed, as well as education for staff and parents. The impacts that this might have on acute scenarios such as resuscitation, as well the possible added challenges that the use of a possible audio element would bring, were seen as areas that need further consideration.

Individualised management of preterm infants in neonatal neurocritical care based on real-time multimodal monitoring

For the second priority delegates considered the use of monitoring in the neonatal neurocritical care unit. They identified that preterm infants in intensive care have a number of physiological parameters such as heart rate, blood pressure and peripheral oxygen saturation measured continuously. An alarm is triggered if a recording goes above or below a preset threshold, alerting staff to acute deterioration in a single system. But the assumption is that each parameter is independent, so subtle changes in multiple parameters go unnoticed. Delegates emphasised that although there appears success of intelligent monitoring in adults, there has not yet been a large-scale clinical demonstration of neonatal multiparameter monitoring. They hypothesised that this may be due to the lack of homogeneity in the neonatal neurocritical care unit, with infants at different stages having very different physiologies, depending on gestational age and condition, and because their resting parameters change substantially as they mature.

Delegates saw a need to develop a greater understanding of how to interpret and exploit this monitoring in order to maximise survival and minimise resultant morbidity. To gain this understanding a multicentre analysis of monitoring, including longitudinal data with clinical annotations, was recommended. This analysis would also need to consider the outcome of the children after discharge from the neonatal neurocritical care unit to provide a fuller picture of the importance of these observational trends. To be able to do this, a large central database is likely to be required to collect a unified data set from each child. This would again be likely to need a sophisticated network infrastructure to collect high-quality, high-resolution data, to validate these data and to provide final analysis. Delegates however saw the potential benefits as significant, as has been demonstrated in improving outcomes in adult neurocritical care.

Continuous EEG monitoring for early seizure diagnosis

The third group developed further the idea of the use of continuous EEG in the neonatal neurocritical care unit. Delegates stated that at present clinical presentations of seizures can be subtle and are easily missed and can cause long-term disability, and that interventions are of high impact with associated side effects. The importance of the reduction of seizure burden was emphasised. To do this, delegates stated that there is a need for predicting onset of seizures and objectively detecting them in order to improve the patient's neurodevelopmental outcomes.

Delegates saw the expansion of the use of video EEG as vital to improving the care of the newborn at risk of seizures. The use of standard EEG caps in the neonatal neurocritical care unit was advocated, and the development of algorithms to correctly analyse clinical and subclinical seizures was seen as important and would improve standardisation across units. The ability to monitor continuously for seizure activity therefore was seen as a gateway to developing an evidence base for a wider range of interventions which would further improve outcomes for these vulnerable patients.

Neuroprotection: understanding basic mechanisms and long-term neurological outcome

The fourth group emphasised the importance of understanding the underlying basic mechanism of perinatal brain injury and its impact on long-term development

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<table>
<tr><td>Proposed Project:
What problem are we going to solve?</td><td colspan="2"></td><td>Team Members:</td></tr>
<tr><td>Why should we do this?</td><td colspan="2"></td><td rowspan="3">We have a need/opportunity for:</td></tr>
<tr><td>What is the scale of the problem?</td><td colspan="2"></td></tr>
<tr><td>Required outcomes and timing to complete</td><td colspan="2"></td></tr>
<tr><td>Staged deliverables and dates</td><td colspan="2"></td><td rowspan="3">Because</td></tr>
<tr><td>What is she missing today, for example information?</td><td colspan="2"></td></tr>
<tr><td>Current relevant research and other activities</td><td colspan="2"></td></tr>
<tr><td>Key actions (including proposed team to address)</td><td>Actions:</td><td>Team Members:</td><td rowspan="3">Actions to deliver:</td></tr>
<tr><td>Resource requirements (financial and manpower)</td><td colspan="2"></td></tr>
<tr><td>Other enablers and barriers</td><td colspan="2"></td></tr>
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Figure 3 Priority proforma.

in order to develop novel neuroprotective strategies. Delegates identified this as an area where improved knowledge of specific aspects of neuroprotection offers opportunities for reducing the impact of brain injury. Five areas were identified. These were the following:

- Inflammatory process, including its effects on the blood–brain barrier and the consequent leaking of reactive astrocytes and microglia.
- Genomics, in particular extreme phenotypes and the impacts of rare disorders.
- Novel delivery of therapies: intravenous and across the blood–brain barrier or directly at target cells in the brain.
- Long-term follow-up of these children: the use of electronic health records across the National Health Service, and across the patient's life for long-term outcome data, such as cerebral palsy.

Delegates highlighted current research into diagnostic imaging, animal models and human cell-based models as promising; however, further investigation was emphasised in the following areas: (1) additional therapies for hypothermia for term infants with HIE, such as the use of erythropoietin, (2) personalised medicine for rare genetic disorders and (3) the development of an integrated infrastructure including imaging, genetics, trials and laboratory investigations in this population. The possible resource implications of this were acknowledged, but delegates stated that there appears to be a unique opportunity to considerably improve outcomes and reduce the suffering of this vulnerable population group and their families.

Sleep measurement

Sleep and its measurement was the final priority developed. Delegates highlighted the difficulties of facilitating high-quality sleep in infants in a busy intensive care setting. They stated that at present clinicians are unable to reliably measure a baby's sleep cycle and therefore are unable to tailor care and interventions (feeding, drugs and so on) to the need of the child. In the longer term the development of a reliable sleep measurement system through the use of monitoring technologies and the opportunity to develop a wearable device were seen as possible ways forward, with high-quality evidence being developed into the effects of sleep on the developing brain. While in theshorter term, research could possibly focus on EEG, or blood markers such as melatonin and cortisol in monitoring sleep cycles.

Delegates again acknowledged that this may require an investment for initial development of the technology as well as for the analysis of the data to find what is normal before being able to detect the abnormal. However, the possible impact that these data could have on future research and care could be considerable.

DISCUSSION

The care of the critically ill newborn infant in the critical care unit is complex and multifaceted. To improve mortality and morbidity, investment will be required and new approaches taken. The use of the IfM landscaping methodology has identified 'gaps' in the care of these children in a systematic way for the first time. However, of 26 possible avenues raised, only 5 were explored further within this exercise. All may need to be considered for discussion by the wider community with cost/benefit analysis as well as ethical considerations discussed by all key stakeholders in this group. Also, this is by no means an exhaustive list and the authors acknowledge that areas of promise may not have been included. The most obvious of these is in the area of automatic seizure detection. It also must be acknowledged that one of the priorities developed is not directly related to the neonatal neurocritical care child but looking at the experience of the parents and their ability to be present in the care of their child (real-time video monitoring). However, if the medical community is to rise to the challenge issued by the Department of Health to improve the outcome of these children and their families, then these results must be considered by healthcare practitioners, researchers, and the management as well as by the industry.

While centralisation of patient care is recommended in many conditions in order to concentrate clinical skills and improve care,[13] a considerable downside of this as identified in this exercise is the difficulty of distance for parents. The difficulty this has caused in the context of maternity care has been documented,[14] but unfortunately methods of overcoming this have not been well described. The delegates identified standardising the use of video monitoring as an improvement in this area. While video monitoring by parents of their children in the form of baby monitors have become routine in society at large,[15] this has yet to become as common in the hospital environment. While concerns were raised regarding the use of such methods, similar systems have been described in other sections of the literature, and when practical issues were overcome patient care improved.[16] The use of patient and public involvement is likely to be important in this particular strand, and its impact on not just patient care but also on the experience of the wider family should be acknowledged.

The use of multimodal monitoring remains a challenge in the neonatal neurocritical care unit. While the system described here of accumulation of a large quantity of observational data would be the first in this setting, the use of large data sets to identify trends and improve patient care has been demonstrated extensively.[17] Although this method of extracting data and knowledge is unquestionably a valid method of moving forward the state of the art, such analyses require considerable investment of time, infrastructure and expertise.[17] Buy-in from multiple centres would be required for this to collect the amount of data required for meaningful results.

The use of continuous video EEGs has revolutionised the management of seizures in the general population.[18] However, its use remains a matter of debate in the neonatal neurocritical care unit. While its use for specific patients where seizure activity is suspected is best practice,[19] evidence is growing that comprehensive use of continuous video EEG in the neonatal neurocritical care unit is able to pick up seizure activity which is missed with normal clinical observation, as well as ruling it out in others where there were clinical concerns.[20 21] While this may provide a significant improvement in patient care and possibly outcomes as identified by the delegates, there remain significant obstacles to overcome. Current practice is time-intensive, with specialist technicians and clinicians needed to apply the EEG and to interpret the results. The use of computer learning and seizure algorithms would make continuous monitoring of large number of infants more feasible. Although it has been an ambition to develop this for many years, only recently with improvements in computer performance has it shown real promise in the neonate.[22]

As stated by the delegates, specific neuroprotective therapies are commonly used in the adult population after brain injury and have shown considerable benefits.[23] In the newborn population cooling is now routinely used in term infants with hypoxic-ischaemic brain injury.[19] The difficulty however comes in diagnosing neurological insults in a timely manner and therefore being able to correctly target appropriate patients.[24] This difficulty also limits any efforts to further subdivide this heterogeneous patient group in order to investigate the effects of adjuncts or of differing cooling regimens on different pathologies.[8] Therefore, development of improved neuroprotection protocols remains a difficult but potentially rich avenue to explore.

While the importance of the other priorities appears to be in standardising care or expanding current technologies, the impact of sleep and sleep measurement on the neonatal neurocritical care unit patient appears to be a novel output from this exercise. Sleep is poorly understood.[25] However, its importance in normal development and recovery from health difficulties has been well explored.[26] The constant interventions, poor day/night cycles and background noise in the intensive care environment have been found to have considerable long-term effects on those unlucky enough to be treated there.[25] While in adult patients it is relatively easy to observe sleep–wake cycles and some effort has been made to improve these,[26] it is a significant challenge in the neonatal neurocritical care unit. Non-invasive monitoring of sleep in the preterm infant may therefore provide vital insights into the effects of environment on these children, as well as allow staff to gain an appreciation of patients' needs and how and when best to intervene.

Next steps

This exercise aimed to bring to the fore a longer list of possible areas for development within the neonatal neurocritical care unit, as well as further developing areas seen as priorities for specific focus. As discussed previously the Brain Injury HTC continues with its programme, and further roadmapping exercises with other stakeholders will also provide valuable insights as well as possible areas of disagreement in priorities.

The next steps would be to individually fully analyse the priorities and possibly the whole landscape in the context of a limited health budget and possible negative outcomes. While that is not within the remit of the roadmapping technique, the question should be posed, and it is our aim that future researchers will pick up this challenge. The Brain Injury HTC has been successful in obtaining funding for a 5-year NIHR MedTech Co-operative with the aim of facilitating some of these discussions especially around the role of technology in moving these elements forwards.

Strengths and weaknesses

The use of the IfM landscaping methodology has considerable methodological benefits. Its structured and transparent methods, visual output and well-documented impacts on processes mean that it provides a significant element of rigour to a strategic level service investigation. In this exercise, it allowed the wide range of experts that participated to provide insights that were not understood before, and the links that were made will drive forward future research and development in this area. However, the lack of a patient/parent representative was notable. Patient and public involvement has been shown to improve the applicability of research and service development.[27] Acknowledging this as a weakness, a further landscaping event with parents and key charity stakeholders is planned and results will be made public.

There are also weaknesses in the IfM methodology that should be acknowledged. The most obvious being that it is dependent on the people who contribute to the session. Additionally elements which have been well discussed in the literature were not seen as priorities or even on the wider landscape in this exercise. These include measuring long-term outcomes within this population,[28] improving neuroimaging[29] and point-of-care testing in order to detect and aid management of neurological insults,[30] among others. The difficulty that any methodology has in trying to draw out possible areas of priority will always be that other areas that show promise will be missed. Readers should consider this paper within the wider research landscape rather then seeing it as a stand-alone piece.

The impact of the session being run by the HTC should be considered especially in view of the apparent focus of the priorities on the possible use of technologies to address difficulties. While each delegate had a 'strategic level' of knowledge of the area, each was also an expert in their own area and therefore there may be a possible bias with regard to the selection of delegates and their areas of expertise or interest influencing the gaps identified. The inclusion therefore of the delegate list is important as is the acknowledgement that a different group may bring further ideas and disagree with the priorities stated here.

CONCLUSION

Care of the newborn infant at risk of brain injury is complex and challenging. Through the use of the IfM landscaping methodology for the first time in an intensive care setting, this paper has illustrated five avenues for advancement in care. This list is in no way exhaustive and tends to be focused on the impact that technological developments could have. While these weaknesses are acknowledged, this paper aims to start the conversation with regard to the future of the newborn infant in the neonatal neurocritical care unit. It invites a discussion of other stakeholders in the area, be they clinicians, researchers, parents, former patients or industry, to bring their perceived 'gaps' and possible solutions to them in order to optimise care for this patient group.

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