

Brussels, 25 May 2021

COST 064/21

## DECISION

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Subject: Memorandum of Understanding for the implementation of the COST Action “Maximising impact of multidisciplinary research in early diagnosis of neonatal brain injury” (AI-4-NICU) CA20124

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The COST Member Countries will find attached the Memorandum of Understanding for the COST Action Maximising impact of multidisciplinary research in early diagnosis of neonatal brain injury approved by the Committee of Senior Officials through written procedure on 25 May 2021.

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## **MEMORANDUM OF UNDERSTANDING**

For the implementation of a COST Action designated as

**COST Action CA20124**  
**MAXIMISING IMPACT OF MULTIDISCIPLINARY RESEARCH IN EARLY DIAGNOSIS OF NEONATAL  
BRAIN INJURY (AI-4-NICU)**

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to improve neurological outcomes for infants with brain injury through the provision of AI-enhanced neuromonitoring technologies. The AI4NICU network will create a pan-European partnership to accelerate research by focusing effort, building consensus on protocols and best practice, and providing open data and algorithms. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

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**OVERVIEW**

**Summary**

Five in every 1000 babies born each year have a condition linked to brain injury. For newborn term infants, lack of oxygen is a common cause of injury; for premature infants, an immature cardiovascular system can lead to brain injury. These injuries can result in death, cerebral palsy, or neurodevelopmental delay. Early diagnosis is essential for risk stratification and targeted neuro-protective strategies. Central to an early diagnosis is continuous brain monitoring.

The AI4NICU Action will create a pan-European multidisciplinary network with the clinical and technical expertise required to bring artificial intelligence (AI)-enabled decision-support tools to the neonatal intensive care unit (NICU). These AI tools build on existing cot-side technologies, such as the electroencephalogram, by including machine-learning algorithms to detect biomarkers of brain injury.

Neuro-physiological data sets are limited in size and scope and not freely available; AI4NICU will develop the tools necessary to acquire, pool, share, and manage data. These data are often complex and noisy, and standards for developing and appraising machine-learning algorithms are lacking; AI4NICU will create a framework to develop, test, and compare these algorithms. A lack of coordinated effort, sometimes exacerbated by a disconnect between clinicians and scientists/engineers, impedes progress; AI4NICU will expand the research community, consolidate existing fragmented efforts, and create and enhance productive synergies.

Working with all stakeholders, AI4NICU will identify roadblocks to clinical implementation and propose designs for clinically useful prototypes. This Action will address the urgent, unmet need to reduce the potentially catastrophic life-long consequences of neonatal brain injury.

<p><b>Areas of Expertise Relevant for the Action</b></p> <ul style="list-style-type: none"> <li>● Medical engineering: Databases, data mining, data curation, computational modelling</li> <li>● Computer and Information Sciences: Machine learning algorithms</li> <li>● Electrical engineering, electronic engineering, Information engineering: Statistical data processing and applications using signal processing (eg. speech, image, video)</li> <li>● Clinical medicine: Paediatrics</li> <li>● Clinical medicine: Clinical neurology</li> </ul>	<p><b>Keywords</b></p> <ul style="list-style-type: none"> <li>● neonatal brain</li> <li>● machine learning</li> <li>● decision support</li> <li>● brain injury</li> <li>● diagnostics</li> </ul>
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**Specific Objectives**

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

- Develop guidelines and standard-operating procedures for data acquisition and management.
- Create an open-science framework for data and machine-learning algorithms.
- Establish criteria for assessing machine learning performance in neonatal brain injury applications.
- Host a data-science competition to crowdsource solutions.
- Explore the pathway to neonatal intensive care unit integration to expedite transition from academic prototypes to industry-ready systems.

Capacity Building

- Knowledge exchange: Develop a joint research agenda on the use of ML for NBI by establishing an interdisciplinary research community of ML engineers, statisticians, computer scientists, neonatologists, nurses, and clinical neurophysiologists.
- Equality, diversity, and career development: Encourage and increase participation of female researchers, researchers from Inclusiveness Target Country, researchers from newly established research groups, Early Career Investigators (ECI), and teams from countries with less capacity in the field of NBI diagnostics.
- Expand the network through: 1) training opportunities, 2) promotion of the Action's outputs, such as open-access data sets, standards and best-practice in data management and ML model development, and 3) open-science competitions in ML-NBI applications.
- Sustainability: Investigate concrete ways to ensure the sustainability of the network beyond the Action by curating new ideas for future collaborative and interdisciplinary research.

## TECHNICAL ANNEX

### 1. S&T EXCELLENCE

#### 1.1 SOUNDNESS OF THE CHALLENGE

##### 1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

**Background and medical context.** Neonatal brain injury (NBI) is a serious concern for clinicians and parents worldwide [1–3]. Brain injuries during the neonatal period include stroke, intracranial haemorrhage, seizures, central nervous system infection, and hypoxic ischaemic encephalopathy (HIE). HIE, the most common form of injury for term infants with an incidence rate of between 1 to 3 per 1,000 live births [3,4], is caused by a lack of oxygen and blood supply to the brain. The devastating consequences of HIE include death, cerebral palsy, epilepsy, and significant intellectual disability [1–4]. Of the 2.9 million neonatal deaths per year worldwide, 1 million are caused by a lack of oxygen at birth [5].

Infants born prematurely are also susceptible to NBI. The rapid growth of the preterm brain makes it particularly vulnerable in an extra-uterine environment. Preterm birth, which accounts for over 1 million deaths each year, is increasing [6]. The most common form of injury for preterm infants is intraventricular/periventricular haemorrhage. Up to 1 in 3 infants born <32 weeks of gestation are at risk of NBI and for infants born <28 weeks this risk increases to 1 in 2 [2]. The injury can cause clinical instability resulting in immediate difficulties such as prolonged ventilation and increased risk of infection. For those preterm infants with NBI that survive, 1 in 10 will develop a permanent disability such as blindness, deafness, learning difficulties, behavioural disorders, and cerebral palsy [7].

The social and economic consequences from NBI is extremely high. Birth asphyxia accounts for 50 million disability-adjusted life years and is one of the leading causes of mortality and morbidity [8]. Neonatal intensive care unit (NICU) costs in the EU are estimated at over €2,000 per day, with an average duration of admission of 10 days. For moderately and severely disabled children, indirect costs of care are enormous: €800,000 over the child's lifetime [9]. Life-long disabilities can place further strain on already stretched health services. The burden placed on families and carers is immeasurable. *Much of this could be prevented through early targeted interventions.* Essential to these targeted medical interventions is early identification of at-risk infants — but without a quantifiable metric of brain health, early identification remains a significant challenge.

Continuous neurological monitoring at the cot-side, with existing technologies such as the electroencephalogram (EEG) and near infra-red spectroscopy (NIRS), can help identify at-risk infants before significant injury occurs. Both monitoring modalities are non-invasive, record continuously, and can be applied easily at the cot-side in the NICU. Long-duration recordings requires distillation of the relevant information; for the EEG, this is achieved by an expert's visual interpretation of recording. But there is a lack of expertise in this speciality in most hospitals and the prohibitive expense of providing a continuous, 24/7 service makes continuous assessment impractical. *Artificial intelligence (AI) decision-support systems can address this gap by intelligently transforming the available data into clinically meaningful information.* Unlike the human expert, these systems can easily scale up to multiple cots in one unit or across multiple clinical centres nationally or internationally. These systems have the potential

to be a truly disruptive technology that will aid critical-care management and facilitate urgent targeted interventions to improve health outcomes [10].

**Machine learning for NBI.** At the heart of these AI-enabled systems are machine learning (ML) algorithms. These algorithms map discriminative patterns in the data through a training process in which data is presented to the algorithms with an associated outcome, such as seizure (yes/no). ML algorithms range in complexity from the simple, such as logistic regression, to the complex, such as deep neural networks. They can process multidimensional data, deal with uncertainty and noise, and provide an objective decision with an associated measure of confidence. Many ML algorithms have been developed for several different NBI applications: for example, detection of seizures [11–13], HIE grading [14,15], detection and prediction of haemorrhage [16], prediction of neurodevelopmental outcome [17], estimation of brain maturation [18,19], and sleep staging (an important indicator of brain health) [20,21]. Most of these algorithms use EEG, as this is considered the gold-standard for continuous monitoring of cerebral function in the NICU. Nonetheless, other physiological signals — such as NIRS to measure cerebral oxygenation, the electrocardiogram (ECG), and other vital signs such as peripheral oxygen saturation, blood pressure, and heart rate — are also useful biomarkers of NBI, both individually and in combination [22]. Unfortunately, little progress has been made on the transition of these ML models to the clinic.

Development of a robust, accurate solution for NBI ready for clinical integration is hindered by multiple factors. First, there are diverging approaches for assessing performance of ML algorithms. An important aspect of any assessment framework are the metrics employed, which can differ from publication to publication. Different strategies for training and testing can distort the bias and variance of the generalisation error. Database size and scope differ a lot among published studies and important clinical information (such as aetiology, gestational age, or medication history) may be missing. Standards for dichotomising brain injury or neurodevelopmental outcome are also lacking. All these factors prohibit cross-study generalisation, comparison of results, and the selection of the best performing algorithms for a designated group of patients. This also weakens the conclusions about the translational usefulness of the developed techniques.

Second, progress is thwarted by a lack of publicly available datasets and computer code for the state-of-the-art algorithms. Open data sets can draw in the wider scientific community. This can be a game-changer in progressing the development of algorithms as development can spread from a handful of research groups to tens of thousands of researchers working on the same problem. For example, open data in speech and image processing have been particularly helpful in progressing applied ML research [23].

These challenges can be overcome by closer interaction between all stakeholders: neonatologists, clinical neurophysiologists, nurses, biomedical engineers, computer scientists, data scientists, statisticians, parent and public involvement groups, and industry. Standard protocols for performance assessment, guidelines for data harmonization and management, and wider access to neonatal data, will lead to technological advances, improve technology readiness levels, and expedite translation towards cot-side implementation.

### 1.1.2. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The overarching aim of this COST Action is to improve neurological outcomes for infants with NBI through the provision of enhanced neuro-monitoring technologies in the NICU; at the heart of these AI-technologies are cutting-edge ML algorithms. The interdisciplinary AI4NICU network will create a pan-European partnership that will share learning, resources, and pool data to create curated open-access

databases. Coordinated effort, consensus on protocols and best practice, and open data and algorithms will accelerate research in this field.

Europe is facing major health challenges which need to be addressed to ensure a secure future and a sustainable, competitive economy. The Covid-19 pandemic has placed further pressure on health-care services and the economy. The life-long consequences of NBI can have devastating effects on the health of European citizens and place additional economic strain on health systems.

The solutions are likely to be beyond the scope and resources of any single country and must be addressed collectively. Hence, there is a need for better coordination of research within Europe, around the world, and between academia and industry. Many researchers are working in the field of ML model development for NBI. As mentioned previously, there is active research in seizure detection, HIE grading, and sleep staging for example [11–15,20,21]. Much of this effort is scattered at a national level, or at best individual European efforts. These fragmented efforts — using different clinical protocols for acquiring and managing data, different techniques for testing algorithm performance, and locked data sets and algorithms — lack reproducibility and therefore utility to others. The lack of synergies impedes progress.

The rapid and recent development of advanced statistical modelling and ML methods has enormous potential in the data-dense field of neonatal brain research. To maximize the potential of combining the fields of neonatal brain health and ML, several challenges must be overcome. There is currently a lack of optimal understanding and implementation of ML modelling within the NBI field, which can lead to overoptimistic, misleading, or sometimes erroneous results. Few concerted efforts so far have been made, with notably exceptions such as a multi-centre clinical validation of a seizure-detection algorithm [10,13] or the INFANS training network for ECIs, and a limited community currently exists beyond isolated groups. We group several technical challenges as follows.

#### **Data characteristics:**

- Small cohort numbers make inference difficult. Data sets from a limited number of patients, especially for low gestational-age preterm groups, make it difficult to assess performance and potential utility.
- Diverging data acquisition protocols. Different hardware parameters such as sampling frequency, duration of recordings, and placement of sensors, are some examples that increase variability across different data sets.
- Lack of a data management plans, including the lack of adoption of FAIR (Findable, Accessible, Interoperable, and Reusable) data principles.
- Lack of open data sets to build ML models and compare different approaches.
- No central location to collate information on open (and closed) data sets and promote the field to researchers looking for data to build and test new ML models.

#### **Experimental design:**

- Lack of agreement on grading NBI severity and different clinical assessments for neurodevelopmental outcome impedes meta-analysis.
- Different approaches to imbalanced class size — often more normal than abnormal events — and missing data.
- Different experimental design in building and testing ML models — including different methods for pre- and post-processing, model selection, hyper-parameter optimisation, estimation of the generalisation error — reduce repeatability and fair cross-study comparisons.
- Difficulty comparing ML models, as published trained ML models are seldom shared.

### Clinical utility:

- Scattered efforts from different research groups mean the most pressing clinical need is not always addressed first.
- Clear understanding of the roadblocks to clinical implementation is often lacking. These can include commercial constraints, social and ethical issues, and lack of comprehensive stakeholder involvement.
- Reported research metrics are often not translatable to clinical use.
- Design of decision-support systems is not clear. To maximise clinical impact, an evaluation is needed to determine how best to present information to the clinician.

## 1.2 PROGRESS BEYOND THE STATE-OF-THE-ART

### 1.2.1 APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE-OF-THE-ART

Coordinated and collective effort can overcome the challenges relating to data, experimental design, and clinical utility. This Action will bring together the necessary expertise in key areas such as clinical NBI management and applied ML research to create a mature scientific network. Adherence to the plan outlined by each working group will enable harmonisation of data sets, creation of data management plans, protocols for experimental design (developing and testing of ML models), and a clear roadmap for clinical integration of ML models for NBI diagnostics. Knowledge exchange within the network and promotion of state-of-the-art to a wider audience will help grow and strengthen the research community and accelerate progress. A clear consensus-based pathway, with the necessary protocols and guidelines, will enhance existing individual research efforts and accelerate progress in the field. The AI4NICU network will overcome multiple outstanding limitations:

**Focus:** current research efforts are fragmented with different levels of activity on different aspects of ML applications for NBI [11–22]. Through discussion and consensus building, AI4NICU will highlight key research areas of high clinical priority. Focusing on these areas will build critical mass and accelerate development.

**Reproducible and comparable research:** much of the published work in this field is not reproducible and it is difficult, if not impossible, to compare across independent studies. This Action will deliver a number of measures to address these shortcomings: data harmonisation, through protocols for data acquisition and management, will enable fair comparison across studies; protocols and guidelines for the development and testing of new ML models will help standardised performance assessment and therefore inter-study comparisons; and open data sets to benchmark and compare methods will permit both reproducible and comparable research.

**Validation and knowledge discovery:** most methods are tested and validated on small data sets, and rarely are these data sets multi-centre. AI4NICU will develop data harmonisation protocols and management plans that will allow for pooling of data sets. Also, the scale of pooled data sets opens the possibility for inference and knowledge discovery, something not possible with limited data.

**Availability:** freely-available data can attract a wider research community, particularly for many biomedical-engineering and machine-learning groups that do not have access, or have only limited access, to real-world clinical data. Proof-of-concept testing is no longer encouraged for publication in many biomedical engineering journals. Currently there is only 1 open-access data set and it is limited to



the specific application of neonatal seizure detection [24]. Research is therefore limited to those groups with their own data sets. AI4NICU will provide federated data access, by providing a central location to search and access open data (and algorithms) relating to NBI.

**Accelerating progress:** ML competitions can accelerate progress. Solution crowdsourcing has the potential to evaluate many more ML models than any single centre can afford. For example, a seizure prediction challenge organised by the American Epilepsy Society ran for 3 months, attracted over 600 participants, with the amount of workhours matching the time-equivalent of 40 four-year PhDs [25]. AI4NICU will organise the first ML competition in NBI diagnostics.

**Decision support tools:** we have very few examples of AI-enabled decision support tools (ML models in a complete computer system) in the NICU. Therefore, it is not clear how best to design these tools to maximise support for the treating clinician. AI4NICU will discuss and propose design concepts, using feedback from surveys and interaction with industry network members.

**Towards clinical translation:** again, because of the limited integration of AI-enabled tools in the NICU, there are many issues to uncover. For example, the network will consider issues such as the robustness of the algorithms to cases outside the typical ranges; risk assessments; and potential societal and ethical issues. These issues will be considered with stakeholder involvement, including medical insurance companies and patient and public involvement (PPI) groups for example.

**Future directions:** new and emerging clinical applications will be proposed and aligned with predictive modelling tasks. The AI4NICU network will allow for interdisciplinary discussion and European and international coordination on an unprecedented scale.

AI4NICU will exploit the diverse expertise of all members and create a trusted knowledge-sharing platform for ground-breaking NBI research. By sharing this knowledge with industry, AI4NICU will be a driver of technological innovation in NBI diagnostic tools with the potential to greatly improve neonatal clinical decision support. Ultimately, AI4NICU will innovate the diagnosis and management of a global and very pressing healthcare issue, improving NBI outcomes and thus reducing the socioeconomic and financial burden of NBI-associated disorders on European healthcare bodies.

## 1.2.2 OBJECTIVES

### 1.2.2.1 Research Coordination Objectives

This Action will create a network of clinicians, engineers, and scientists to facilitate the development of AI decision-support tools for NBI. These tools consist of specialised ML models, developed from specific data sets. Timely information on brain health will aid critical care and help with neuroprotective strategies. To accomplish this, this Action will:

1. **Develop guidelines and standard-operating procedures for data acquisition and management (Working Group 1, WG1).** Main outcomes: Handbook for Data Protocols and Management and a benchmark open-access data set.
2. **Create an open-science framework for data and ML algorithms (WG3).** Main outcome: Access-portal to search, download, and upload data and algorithms for NBI applications.
3. **Establish criteria for assessing ML performance in NBI applications (WG2).** Main outcomes: scientific publications with computer code; standards for NBI applications.

4. **Host a data-science competition to crowdsource solutions (WG3).** Main outcome: high-performing ML models with insight on top performing methods.
5. **Explore the pathway to NICU integration to expedite transition from academic prototypes to industry-ready systems (WG2).** Main outcomes: publication on ethical concerns with AI-enable support tools in the NICU; design concepts based on survey of the end-users (clinicians).

#### 1.2.2.2 Capacity-building Objectives

The Action will pursue the following objectives to build capacity:

- **Knowledge exchange.** Collaborative exchange to develop a joint research agenda on the use of ML for NBI by establishing an interdisciplinary research community of ML engineers, statisticians, computer scientists, neonatologists, nurses, and clinical neurophysiologists.
  - Emphasis will be placed on bridging the sometimes large 2-way knowledge gap between clinicians and engineers/data scientists. Workshops, training schools, and conferences will include introductory sessions and ensure throughout that terminology and basic definitions and concepts are clearly defined.
- **Equality, diversity, and career development.** Encourage and increase participation of female researchers, researchers from Inclusiveness Target Country (ITCs), researchers from newly established research groups, Early Career Investigators (ECI), and teams from countries with less capacity in the field of NBI diagnostics. The Action will aim for gender balance in leadership roles and actively encourage ECI to leadership roles where appropriate — for example as deputy leaders in the Working Groups.
- **Expansion.** Expand the network through 1) training opportunities, such as training schools and STSMs for ECIs, workshops, and conferences, 2) promotion of the Action's outputs, such as open-access data sets, standards and best-practice in data management and ML model development, and 3) open-science competitions in ML-NBI applications.
- **Sustainability.** Investigate concrete ways to ensure the sustainability of the network beyond the Action by curating new ideas for future collaborative and interdisciplinary research and finding the appropriate instruments to fund them.

## 2. NETWORKING EXCELLENCE

### 2.1. ADDED VALUE OF NETWORKING IN S&T EXCELLENCE

#### 2.1.1. ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

The European Commission (EC) has been supporting brain research through Horizon 2020 programmes for many years. Investments have been directed at better understanding of brain function and dysfunction, developing methods for diagnosis, prevention, treatment, as well as care and support. AI4NICU will build upon these initiatives to further cutting-edge research and technological innovation in the area of NBI.

- AI4NICU will enhance 2 Marie Skłodowska-Curie Innovative Training Networks, the INFANS network (INtegrating Functional Assessment measures for Neonatal Safeguard, GA:813483) and the PARENT network (PremAtuRe nEwborn motor and cogNitive impairmentTs: Early diagnosis, GA:956394). Both training networks will develop AI algorithms for NBI using an Open Science approach. The INFANS network aims to develop new technologies and methods for neonatal brain monitoring, with a particular focus on EEG and NIRS. The PARENT network

(starting November 2020) aims to develop diagnostic and prognostic tools for motor and cognitive impairments for preterm infants with NBI. These tools will harness ML and data fusion methods on biomarkers, neuroimaging, and clinical data to predict neurodevelopmental delay.

These projects will provide training for 30 early-stage researchers (ESRs). The AI4NICU Action will complement and enhance the projects by providing guidelines and procedures for data life-cycle management and harmonization of algorithmic development and validation. In addition, the ESRs will be encouraged to join and contribute to the network through the STSMs, workshops, and training schools. These targeted events will provide learning and networking opportunities for the ESRs to strengthen their research and enhance career development.

- The ALBINO project (Effect of ALlopurinol in addition to hypothermia for hypoxic-ischemic Brain Injury on Neurocognitive Outcome, GA:667224) is a clinical trial of a drug to limit damage caused by hypoxic-ischemic NBI. The secondary aim of this large, multi-centre trial includes the development and validation of physiological biomarkers of NBI.

The recently ended (2020) Digi-NewB project (Non-invasive monitoring of perinatal health through multiparametric digital representation of clinically relevant functions for improving clinical intervention in neonatal units, GA:956394), collected a wealth of physiological data from over 700 newborn infants. The project aimed to develop a computer-based decision support system for early detection of sepsis and tracking of neurobehavioural maturation.

For both these projects, the AI4NICU Action will help with data life-cycle management and validation of detection and regression algorithms. In addition, value will be obtained by pooling the outputs, where available, from these projects to harmonize data and ML methods for NBI and build networking opportunities for future collaborative projects.

- OXYPREM (High-precision oxygen monitor for preterm infants, GA:888943) is a recently concluded (2020) initiative by an SME to bring a new brain-monitoring device to market. The device, a NIRS machine, was designed specifically for preterm infants and therefore has many advantages over conventional systems designed for adults. ML methods applied to data from existing technologies can greatly increase the utility of the device by making it a 'smart' device, capable not only of recording data but also providing clinically useful interpretations of the data.

Other pan-European research projects have and are collecting physiological data across multiple European NICUs. For example, the HiP trial (Management of Hypotension In the Preterm Extremely Low Gestational Age Newborn, GA:260777) has acquired EEG and NIRS from preterm neonates. The SafeBoosc-III trial (Safeguarding the brain of our smallest children—a phase III randomised clinical trial on NIRS monitoring) is acquiring NIRS from preterm neonates. And the ANSeR study (Algorithm for Neonatal Seizure Recognition, a clinical validation of ML algorithm in the NICU) has acquired EEG data from term neonates in the NICU. The AI4NICU Action will provide guidelines and tools for maximising the utility of these datasets through management and pooling of digital assets and providing guidance on the development and assessment of new ML algorithms on existing datasets.

## 2.2. ADDED VALUE OF NETWORKING IN IMPACT

### 2.2.1. SECURING THE CRITICAL MASS AND EXPERTISE

AI4NICU aims to accelerate the development of AI-enabled decision support tools for NBI diagnosis. It will add value to existing European projects by avoiding unnecessary duplication, pooling data sets, and creating productive synergies. The network's objectives require expertise in both technical and clinical professions. The AI4NICU proposers have expertise in the areas of ML, signal processing, computer science, biomedical engineering, mathematical modelling, multivariate statistics, neonatology, neurology, clinical neurophysiology, and commercialisation of AI support tools for the NICU. This group also has strong representation from major research centres with track records in NBI research. Many proposers have existing interdisciplinary collaborations, with existing data sets and portfolios of developed algorithms in NBI diagnostics. Some proposers have experience with managing and sharing databases, creating data-science competitions, and working closely with medical device companies to licence ML algorithms.

AI4NICU will build capacity beyond the network of proposers. A key aim is to involve more ECIs. This will be achieved by recruiting ECIs from the relevant European Innovative Training Networks (outlined in Section 2.1.1); through workshops, training schools, and calls for STSM; and other dissemination activities, as organised by Working Group 4. The proposers will recruit new members from their own networks. Data science competitions and open-data sets (Working Group 1 and 3) will expand the research community by attracting those not currently working in NBI field. The network will aim to provide gender and geographical balance throughout its activities and in leadership roles (outlined in the Capacity Building Objectives, provided by Working Group 4). Building capacity to critical mass will enable AI4NICU to go beyond what isolated efforts can achieve alone.

## 2.2.2. INVOLVEMENT OF STAKEHOLDERS

Stakeholders who are AI4NICU proposers and who will actively participate in the network's activities:

- Research-active clinicians and scientists with an interest in NBI. New protocols and standards for data acquisition and management (Research Coordination Objective 1, RCO1) will maximise utility of recorded data. Large, multi-centre data sets (RCO2) will allow for new insights on NBI.
- Engineers and computer/data scientists with expertise in signal processing, applied statistics, and ML development who will develop the ML models for NBI diagnostics. Access to data sets (RCO2) in an accessible and interoperable format (RCO1), and established criteria for developing and testing (RCO3) will accelerate progress to develop robust and accurate ML models. Data-science competitions (RCO4) will help benchmark new methods and generate interest in NBI applications in the wider ML research community.
- Clinicians and healthcare professionals, such as neonatologists, clinical physiologists, and NICU nurses. Participation in the design of the decision-support tools (RCO5) will help maximise the utility of these tools, and ultimately help the clinician in diagnosis and treatment of NBI.
- Industry, including SMEs, will provide business acumen for AI4NICU and guidance on how to prepare the technology for commercial uptake. Entrepreneurship will be encouraged within the network. A clear pathway from academic model to clinical implementation (RCO5) will assist commercial interests in developing and profiting from novel NBI diagnostic.

AI4NICU stakeholders, who are not among the network of proposers:

- Patient and Public Involvement groups with an altruistic interest in the prevention of NBI. These groups will advise on the design of the decision support tools (RCO5) and provide consultation on the effects of NBI on the family unit, which will be shared with network members through meetings, workshops, and training schools. Charitable and philanthropic organisations who will financially support and advocate AI4NICU to the public, thereby increasing awareness and visibility of the Action and its outputs.

- Insurance companies who provide medical indemnity to clinicians and healthcare providers. A reduction in occurrence and severity of NBI will lead to better health outcomes and therefore help de-risk insurance policies, to the benefit of the insurance company.
- National and European research agencies and policy makers who will use outputs of AI4NICU to prepare documents and guidelines on the use of the ML-based solutions in the NICU (ROC5), and future research activities. These stakeholders will thus facilitate translation of AI solutions to the cot-side.

Special effort will be made to reach-out to clinicians who may have busy clinical loads with little time or interest in research. Dissemination will be made through suitable channels for busy clinicians, such as in Grand Round seminars and professional development workshops. Education will be core part of this dissemination, with emphasis on the evidence-based research to highlight the efficacy of new diagnostics for NBI. For example, by highlighting a recent study which has shown the clinical benefit of using a ML algorithm for neonatal seizure detection [13].

Regulator and industry stakeholders will play a key role in translating the Action's research into commercially viable applications which may benefit the economies of the member countries. We expect that specific academic–industry relationships between AI4NICU members will lead to even further collaborations through joint grant applications (for example under Horizon–Europe's equivalent to the H2020 Industrial Leadership scheme), in addition to the licensing and commercialisation of the decision-support systems. In agreement with the COST Rules for Participation in and Implementation of COST Activities, the benefits of the improved knowledge will be shared with as many companies as possible within the member countries through dedicated dissemination and will not be absorbed by only one or two major groups.

### 2.2.3. MUTUAL BENEFITS OF THE INVOLVEMENT OF SECONDARY PROPOSERS FROM NEAR NEIGHBOUR OR INTERNATIONAL PARTNER COUNTRIES OR INTERNATIONAL ORGANISATIONS

AI4NICU will give European research and development a competitive edge over North American and Asian enterprise. To maximise impact however, an international outlook must be included: application of ML solutions for NBI in NICUs both inside and outside of the EU. The network of proposers includes partners from Ukraine, a near-neighbour country. AI4NICU will expand beyond the group of proposers to include more near-neighbour and international partners, as outlined in the capacity building objectives (Section 1.2.2.2). These partners will ensure that non-EU data, clinical practice, and research methods are included in the core of the network. The development of decision-support systems in an international context will accommodate for any potential regional differences that may exist. In turn, the near-neighbour and international partners will benefit from closer collaboration with EU partners, with all the benefits of working within a large network, such as knowledge transfer, development of standards for data and methods, and building relationships for future collaborative projects.

## 3. IMPACT

### 3.1. IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAK-THROUGHS



### 3.1.1. SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

AI4NICU will build an extensive, interdisciplinary network to advance research in ML model development for NBI. It will connect existing and future research efforts, adding significant value and progress towards the end goal of delivering these technologies to the NICU. The outputs from AI4NICU, with reference to the Research Coordination Objectives (RCO), will have the following impact:

- Protocols and management plans for data sets (RCO1) will ensure that data is accessible, interoperable, and re-usable; this will extend the useful lifespan of the data and increase utility to more researchers and more applications.
  - Tracking impact: number and impact of publications using the same data sets.
- An Open Science framework for data and algorithms (RCO2), clear criteria for developing ML models (RCO3), and benchmark data sets and open competitions (RCO2+4) will 1) increase availability of neonatal physiological data which will increase research interest in this area; 2) accelerate development of accurate and robust ML models, 3) enable cross-study comparison of ML models.
  - Tracking impact: number of publications and performance of algorithms over time; performance will be tracked using the agreed metrics (RCO3).
- Mapping a clear route to clinical implementation (RCO5) by engaging with end-user clinicians and other stakeholders will 1) avoid roadblocks from ethical or commercial concerns, 2) progress systems along technology readiness levels, and 3) make these systems more attractive to industry.
  - Tracking impact: technology readiness levels of ML-prototype systems; commercial uptake from spin-outs or industry.

AI4NICU's impact will expedite translation from academic prototypes to clinically robust models suitable for decision-support systems. In the longer term, these systems may be integrated into existing monitoring technologies, such as EEG devices, or developed separately with new stand-alone hardware. SMEs will capitalise on the network's multi-disciplinary and specialised knowledge to ensure commercial success with a high level of uptake in NICUs. This, in turn, will help improve diagnostic accuracy in the NICU.

The potential destructive impact of NBI is alarming — death, cerebral palsy, epilepsy, and cognitive, developmental, and behavioural problems [1–8]. There is a clear, unmet clinical need for smart brain monitoring systems to be available cot-side in NICUs the world over [10]. Mitigating the consequences of brain injury will deliver immeasurable human benefits, positively impacting parents and families of the newborns. The cost savings of avoiding disabilities and treatments, which can last for the patient's lifetime, also reduces the economic burden on health services around the globe.

## 3.2. MEASURES TO MAXIMISE IMPACT

### 3.2.1. KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

**Knowledge Creation.** New knowledge will be created by developing the protocols and management plan for neonatal physiological data (RCO1) and the framework to develop, test, and assess

performance of ML models (RCO2+3). These protocols and tools will transform the area of NBI-applied ML by allowing for reproducible, accurate, and robust ML methods. These methods have downstream potential for real clinical impact. Large, multi-centre and open access data sets (RCO2) will help build and train ML models; they will also allow researchers to develop statistical models and inferences to create new knowledge on NBI. Crowdsourcing ML development through a data-science competition (RCO4) will build new knowledge on the best methods to generate accurate ML models for NBI applications. Inclusive engagement between industry, clinicians, and patient-interest groups will generate new designs for decision-support tools for the NICU (RCO5).

**Transfer of knowledge.** The Action will promote and foster knowledge exchange within the network through meetings (in person and virtual), workshops, training events, and STSMs. Two training schools will be held for non-expert ML members, one on quantitative analysis of physiological data and the other on ML methods for NBI diagnostics; one training school will be held on the data protocols (RCO1) and another on Open-Science for data and algorithms (RCO2). Workshops will be held on frameworks for developing ML models (RCO2) and on the outcomes from the data-science competition (RCO4). Calls for STSMs will be handled by working group (WG) 4, and cross-discipline missions — for example, a ML expert gaining experience in a clinically-focused centre — will be encouraged in addition to increasing depth within a discipline. WG4 will oversee knowledge exchange by delivering on actionable tasks to ensure that analysis and insights are shared with the network through reports and publications on the Action Web Portal and other channels in addition to the many networking events. Researcher mobility will facilitate knowledge exchange, throughout the network and between Inclusiveness Target Countries (ITC) and non-ITCs, and near neighbour and international countries. WG4 will also coordinate future collaborative funding applications to foster transfer of knowledge and research ideas within the network. AI4NICU will encourage cooperation between academic and industry members, thus progressing the translational aims of the Action. And finally, dissemination activities (again WG4) will ensure transfer of knowledge to the wider community through publicly available reports, documents, open-access data sets, and computer code.

**Career development.** The Action will benefit the careers of all members because 1) the critical-mass effect of the network will progress research and translational agendas much faster than individual effort, 2) the sharing of data, standards, and research ideas, in conjunction with the multiple channels for knowledge exchange, will help generate high-quality research and raise the profile of all network members, and 3) network membership will increase the likelihood of generating funding for future research by improved collaborative grant applications. Special support for career development will be given to ECIs. Training schools, workshops, and networking opportunities with other ECI and senior members will help develop the next generation of scientific leaders in ML and NBI. ECIs will be encouraged to gain leadership experience within the Action (for example as deputy WG leaders) to develop the qualities necessary for building future research groups. ECIs will be encouraged to avail of STSMs to build knowledge and networks for future grant applications, such as COST Action Conference Grants to present results at international conferences and individual fellowships (such as Marie Skłodowska-Curie Actions) to support mobility across Europe to learn new techniques and develop research ideas.

### 3.2.2 PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

The Action Management Committee (Action MC) and WG4 will work closely to actively promote the work of the Action and encourage all its members to participate widely in various dissemination activities. AI4NICU will hold a kick-off meeting to bring the network's participants and stakeholders together to

communicate responsibilities, objectives, and outputs. (If workshops and meetings are not able to take place in person due to local Covid-19 restrictions, they will transfer to the virtual space using appropriate platforms such as Microsoft Teams.) WG4 will be responsible for reporting on AI4NICU progress to the network members, through reports, newsletters, and social media channels.

AI4NICU will ensure results and outputs are disseminated clearly to 1) network members, 2) research communities, including those with an interest in either NBI or biomedical ML applications, 3) clinicians who are not involved in research but are in NBI management, 4) clinical physiologists and technologists who record and interpret EEG, 5) patient and public involvement groups, 6) industry, including SMEs and potential spin-outs arising from the Action, who are not AI4NICU members, 7) insurance companies who provide medical indemnity, 8) national and European research agencies and policy makers, and 10) the general public.

Key deliverables from the Action will published as follows.

- The Handbook on Data Protocols (milestone from WG1) will be freely available as an eBook on the AI4NICU web-portal; revisions will be handled through github/gitlab.
- The first open-access data set (milestone from WG1) will be available on Zenodo, with links on the AI4NICU web-portal.
- Access-portal to the data and algorithms will either be hosted on the AI4NICU web-portal or at an alternative location; this will be determined by WG3.
- Data and code will be hosted on free, open platforms such as Zenodo and github.
- Similarly, location of the data-science competition will be determined by WG3. The competition will be promoted through social media channels, AI4NICU web-portal, and at workshops and conferences.

AI4NICU will use the following dissemination channels:

- **Action Web-Portal:** The AI4NICU website will act as the central hub for disseminating information from all aspects of the Action's activities through both a public profile and an internal profile (intranet, with password-protected access) for AI4NICU members. The web-portal will contain links to all AI4NICU results and outputs, including links to the Access-Portal for Data and Algorithms (as implemented by WG3). Public information will be presented in all major European languages.
- **Social media:** Twitter, LinkedIn, and YouTube accounts will be managed by WG4. In addition to collective dissemination, members will be encouraged to use their own social media to connect to and promote the AI4NICU accounts.
- **Code sharing platforms:** AI4NICU will create a github or gitlab account to share computer code from the project. Members will be encouraged to link and promote this account, which will help others find the freely-available code.
- **Scientific and clinical conferences:** members will present results of the Action and work within the scope of the Action, thus promoting the objectives of the Action. Keynote presentations by senior researchers in the network will also be used to disseminate key results and progress of the Action.
- **Public lectures and interactive workshops:** aimed to the general public, these lectures and workshops will help raise awareness on NBI and the potential for ML solutions. Will integrate with national science festivals.
- **Interviews:** television, radio, and podcast interviews of key network members will inform the general public on AI4NICU goals, objectives, and progress; again, will raise awareness on NBI and ML.
- **Email:** newsletters will be emailed twice a year to members and stakeholders; the newsletter will also be available on the web-portal.



- **Scientific publications:** specific outputs will be published in high-impact clinical and scientific/engineering journals. Will be made freely available under open access licences.

Key performance indicators from these channels — for example, the number of citations for journal publications or the number of forks of computer code repositories — will be tracked and reported in progress reports from WG4.

## 4. IMPLEMENTATION

### 4.1. COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

#### 4.1.1. DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

AI4NICU will be coordinated by an Action Management Committee (MC) formed in accordance with the COST Action “Rules for Participation and Implementation of COST Activities”. The Action MC will meet virtually every 6 months, and in-person once a year at the annual AI4NICU conference, which will be held in different COST Action countries (dependent on pandemic restrictions). At the kick-off meeting, key leadership positions in the Action MC will be appointed, such as the Action-Chair, Action-Vice Chair, and leaders of the 4 Working Groups (WGs). Also appointed will be an ECI representative to ensure ECI challenges and opportunities are at the front of the Action’s agenda. An equality and diversity officer will be appointed to likewise ensure diversity and gender equality throughout the Action’s activities. These members will form the Core Group, and will facilitate the day-to-day management of the Action. Action leadership will also come from members of the participating Inclusiveness Target Countries (ITC) for whom at least one leadership position will be reserved. Care will be taken during the appointments process to ensure gender balance in leadership roles. Additionally, leadership roles for ECIs, such as deputy WG leaders, will be sought.

The Action MC will be responsible for setting and monitoring the Action strategy, such as 1) strategic decisions, 2) establishment and over-arching management of the WGs, 3) approval of the work and budget plan for Grant Periods, and 4) preparation of the Action reports. The WG leaders and deputy leaders will collaborate with the Action MC leaders to plan and coordinate tasks and, when necessary, appoint Task Coordinators. WG meetings will be organised appropriate to their tasks (for example regular virtual meetings and in-person when possible). Each working group will submit an annual report of the progress, deliverables, and impact of the WG activities ahead of the annual conference, thereby facilitating annual Action MC discussions and the planning of the annual work programme. Details of the WGs follow.

**WG1: Data Protocols and Management.** Establish guidelines and standards for 1) acquiring the physiological data in clinical research studies and 2) creating, merging, sharing, and managing databases. Mechanisms for integration between multiple sites and with existing cohort data, and future inter-operability will be investigated.

- ▶ **Task 1.1 (T1.1): Guidelines for data acquisition.** Detailed descriptions and standard operating procedures (SOPs) on how to record physiological signals not included in most clinical practice,

such as EEG and NIRS. Guidelines will include details on recording hardware/software specifications with specifics for common devices.

► **T1.2: Guidelines for processing and storing data.** Guided by FAIR principles, this task will consider multiple issues in creating a database: how to convert from proprietary format to an open format; what open format to use, e.g. EDF, json, HDR; data quality, e.g. is the data complete? clean? or accurate?; what metadata to include; how to link separate files, e.g. EEG and NIRS from 1 infant; ensuring privacy and data protection, e.g. what clinical metadata will be GDPR compliant?

► **T1.3: Data lifecycle management.** In consultation with relevant stakeholders, a data management plan will be detailed. This plan will consider multiple maintenance aspects: where to store, e.g. use existing hosting open-data sites such as OpenAIRE/Zenodo, figshare, or github for example; what licence should be used; do we need version control, e.g. DataLad; and what simple analytic tools should be included to describe the data.

**Milestone (M1.1):** Handbook on Protocols and Management of NICU-Generated Data (publicly available on Action website and promoted through dissemination channels).

► **T1.4: Design of benchmark dataset.** Identify a priority area for ML-NBI application, e.g. seizure detection or sleep staging. Consider number of infants, associated clinical information, and data storage parameters (from T1.1). Review existing data sets held individually by network members able and willing to share. Pool data and share openly, following guidelines from T1.2 and T1.3.

**M1.2:** Open-access data set.

**WG2: ML Performance Assessment and Pathway to NICU Integration.** To maximise the utility of ML for NBIs, the Action will consider standards for ML performance assessment (important factors for cross-study compatibility), design factors for decision-support tools constructed from ML models, and the ethical considerations required for these tools.

► **T2.1: Map ethical and societal issues associated with ML in the NICU.** Review GDPR in relation to data management and open-science plans (WG1 and WG3). Include risk assessment for clinical use of the ML models and balance with potential benefits. Consult with patient and public involvement (PPI) groups.

**M2.1:** Publication (clinical journal) on ethical and societal issues on AI-enabled decision support systems.

► **T2.2: Priority ML applications.** Compile list of ML applications and rank based on clinical importance. Mature projects may rank towards the top; some applications may be important sub-modules of a larger system. Justify selection and detail what is required for each task. Organise workshop on this topic to help gain understanding of future trends.

► **T2.3: Best practice for assessing ML methods.** Evaluate metrics for assessing performance of ML models. Consider clinical importance of accuracy measures (bias and variance estimation, with confidence intervals) for classification (multi-class), detection, and regression models for specific NBI applications. Develop open source code for the metrics.

**M2.2:** Open-source code (on github/gitlab; in Matlab or Python) with pseudo-code to enable translation to different computer languages (e.g. R, Julia).

► **T2.4: Integration of ML in the NICU.** Survey the end-users (neonatologists and neonatal nurses) about essential and desirable parameters for an AI-enabled decision support tool. Recruit participants to the survey through the Action's network and associated colleagues and at high-profile Action events, such as the first AI4NICU conference. Investigate concepts for user-interface design and system architecture. Generate visual mock-up of these tools and use as vision to inspire others of the potential for AI-enabled tools.

► **T2.5: Prototype-ready models.** Guidelines for best practice to transition along technology readiness levels (e.g. preferred computer language, documentation, revision history, V-model). Consult with industry (within and outside network) on desired approach.

**WG3: Open Science Framework and Solution Crowdsourcing.** A key output of AI4NICU is the data-science challenge to provide solutions (ML models) for a specific application, promote the work of the Action, and to generate more interest for ML engineers to the area of NBI. This WG will also provide the resources to ensure that data and algorithms follow an Open Science framework.

► **T3.1: Repositories for data and algorithms.** Review existing data repositories: e.g. archives for neuroscience projects, such as EBRAINS for the Human Brain Project and the Data Archive for BRAIN Initiative (DABI); generic scientific solutions, such as figshare and Zenodo (OpenAIRE); or a bespoke solution combining free resources. Review repositories for computer code, which should ideally include version control information, such as github, gitlab, or bitbucket. Select preferred options for both data and code.

► **T3.2: Data federation.** Create an access portal to the data and algorithms. Detail requirements for metadata (consult Handbook, D1.3). Explore options for location of portal, considering ease of use, longevity, and access (open, free).

**M3.1:** Access portal to data and algorithms.

► **T3.3: Data-science competition.** Develop parameters for competition using the benchmark dataset (D1.4). Review hosting options for competition (e.g. Kaggle, DataDriven, CrowdANALYTIX). Seek funding for competition prize through industry or academic sponsorship (optional). Promote competition to engage the wider research community.

**M3.2:** Open competition.

► **T3.4: Analysis and insight of competition.** Collect best performing algorithms and analyse attributes for any common factors (for example, are best solutions deep-learning solutions?).

**WG4: Capacity Building and Dissemination.** An internally focused WG to support network infrastructure and delivery of the results of the Action. Will work closely with the Action MC.

► **T4.1: Monitor progress.** Liaise with Action MC on strategy to disseminate progress and outcomes of the AI4NICU Action within and outside the network using the web-portal, reports, meetings, and conferences.

► **T4.2: Monitor and grow network.** Identify all stakeholders and recruit new members to the network by promoting the network through dissemination channels, international conferences, and the members' own network. Pay particular attention to engaging and retaining clinicians, as many will have busy clinical loads. Promote gender balance, geographical inclusiveness, and ECI engagement throughout all the Action's activities.

► **T4.3: Supporting dissemination.** Periodic review of progress on dissemination activities and adjust as necessary. Ensure key stakeholders—such as non-research clinicians, data scientists, PPI networks, and industry—are targeted in dissemination.

► **T4.4: Training.** Provide central point to organise training schools, workshops, STSMs, and the AI4NICU conference. Review calls for STSMs. Coordinate with other WGs on training schools and workshops. Develop and implement 2 training schools: 1) introduction to quantitative and ML methods for NBI and 2) advanced ML methods for NBI.

**M4:** Training schools on ML methods for NBI applications.

## 4.1.2. DESCRIPTION OF DELIVERABLES AND TIMEFRAME

### **WG1: Data Protocols and Management**

- D1.1: Part I of Handbook: guidelines on recording parameters (year 1, 2<sup>nd</sup> quarter; Y1-Q2).
- D1.2: Part II of Handbook: guidelines for data storage. Examples of prototype datasets, links on Action website (Y1-Q4).
- D1.3: Part III of Handbook with guidelines on data management (Y2-Q4).
- D1.4: Open-access data set of neuro-physiological data, such as EEG or NIRS, recorded from infants in the neonatal intensive care unit (Y3-Q3).

### **WG2: ML Performance Assessment and Pathway to NICU Integration**

- D2.1: White paper with priority ML applications for NBI (Y1-Q4).
- D2.2: Publication on ethical and societal issues on AI-enabled support systems (Y2-Q2).
- D2.3: Open-source code (on github/gitlab) for performance assessment methods in Matlab or Python with pseudo-code to enable translation to different computer languages (e.g. R, Julia) (Y2-Q4).
- D2.4: Publication on clinical support tools for the NICU (Y3-Q4).
- D2.5: White paper containing guidelines and best practice on prototype models (Y4-Q4).

### **WG3: Open Science Framework and Solution Crowdsourcing**

- D3.1: Educational resources on data and algorithm archiving on the Action's website (Y2-Q3).
- D3.2: Access Portal to data and algorithms (Y3-Q1).
- D3.3: Open data-science competition (Y3-Q4).
- D3.4: Scientific publication detailing competition solutions and insights gained (Y4-Q3).

### **WG4: Capacity Building and Dissemination**

- D4.1: Material and report of Training schools on ML methods for NBI applications (Y1-Q4)
- D4.2: Material and report of Training schools on ML methods for NBI applications (Y4-Q2).

## 4.1.3. RISK ANALYSIS AND CONTINGENCY PLANS

AI4NICU addresses the specific challenge of building a unique network connecting two highly active scientific communities, ML and NBI. Potential significant risks to the success of this Action are:

- Failure to agree on a universal framework for best practice, guidelines, and standards due to national ethics, regulation, and legal requirements.
- Failure to develop an adequate and dynamic communication channel between the research communities and among participants.

The associated risks are considered minimal for the following reasons:

- The interdisciplinary interaction and collaboration between clinicians and ML engineers are already established for some members and they will share their experiences to help others. The Action will create a discussion panel to first generate a shared vocabulary. Two training schools will be developed on ML methods for the non-expert (see Section 3.2.1), STSMs will be encouraged to include interdisciplinary learning, and workshops will include introductory sessions on clinical management of NBI and ML methods.
- The clinical community recognises the need for ML approaches to supplement subjective decision making with objective decision support and extract complex information from massive amounts of data.

- Flexibility in standards and definitions will be allowed to adapt for local constraints.
- Public dissemination of the standards, through the relevant conferences and journal articles, and the release of open source tools (protocols, procedures, and methods), data, and open competitions will engage other researchers outside the network, thus creating an incentive for the network to succeed in its goals.

Specific contingency plans are presented in the following table.

	<b>Risk</b>	<b>Contingency Plans</b>
<b>Network</b>	Smaller network membership than expected	WG4 will periodically review the network and, if necessary, run a recruitment drive through various dissemination channels, setting targets for gender, geographical coverage, ECIs, and ITCs. The kick-off meeting will offer an early opportunity to suggest new members and the research conference in the first year to attract members.
	Turnover of network members	Introduction of new members with sufficient expertise throughout the Action (see previous point) will ensure that this knowledge is retained. Researchers with key background knowledge will be targeted to ensure depth of knowledge within the network.
	Stakeholder disinterest	Dialogue with stakeholders during engagement activities will help steer the execution of objectives to ensure maximum impact.
	Workloads and task completion rates	The Action MC will monitor workloads, task completion, and milestones and adjust workloads if necessary.
	Covid-19 distribution	The Covid-19 pandemic may disrupt networking activities, such as in-person meetings, conferences, and workshops. This can be mitigated by transferring meetings to virtual networking platforms and by allowing for flexibility in calendar events.
<b>Science and Technology</b>	Failure to reach consensus on protocols	WG1 and WG2 aim to gain consensus on data protocols and assessment routines for ML models. These groups will work to build consensus and if not achieved will build in flexibility by offering more than 1 option to the standards and protocols.
	Lack of compatibility of research strategies	All groups, with oversight from the Action MG, will ensure that progress is being made towards common strategies. Perceived divergence of research strategies will be adjusted early to allow for long-term cohesion.
	Data compliance and exchange	Data acquisition and storage will adhere to EU GDPR policies. Data, computer code, and results will be shared according to GDPR and the guidelines of the relevant ethics committees. WG1 will ensure that the protocols and standards are in-place for open access licences.

#### 4.1.4. GANTT DIAGRAM

	Year 1				Year 2				Year 3				Year 4			
	Quarter: 1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
MC meetings	K		M		M		M		M		M		M		M	M
WG meetings			M		M		M		M		M		M		M	
Research conference				C				C				C				C
<b>WG1: Data Protocols and Management</b>																
Deliverables		1.1		1.2				1.3				1.4				
Milestones							1.2		1.2							
Training Schools								T1								
<b>WG2: ML Performance Assessment and Pathway to NICU Integration</b>																
Deliverables				2.1		2.1		2.3				2.4				2.5
Milestones						2.1		2.2								
Training Schools (T); Workshops (W)				W2		T2										
<b>WG3: Open Science Framework and Solution Crowdsourcing</b>																
Deliverables							3.1		3.2			3.3				3.4
Milestones							3.1					3.2				
Training Schools (T); Workshops (W)															W3	
<b>WG4: Capacity Building and Dissemination</b>																
Deliverables				4.1												4.2
Milestones				4												4
Training Schools (T); Workshops (W)				T3												T4

MC: Management Committee; WG: Working Group; M: meeting; K: Kick-off meeting

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