BMJ Global Health

Neurodevelopmental screening for neonates less than 44 weeks gestation in low-income and middle-income countries: a systematic review

Benjamin J S al-Haddad [1,2] Elisabeth Olson [2] Erin Reardon [3] Emmanuel Bonney [2,4]

To cite: al-Haddad BJS, Olson E, Reardon E, *et al*. Neurodevelopmental screening for neonates less than 44 weeks gestation in low-income and middle-income countries: a systematic review. *BMJ Glob Health* 2025;**10**:e017683. doi:10.1136/bmjgh-2024-017683

Handling editor Fi Godlee

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjgh-2024-017683).

Received 24 September 2024
Accepted 16 March 2025

[1]Department of Pediatrics, University of Minnesota Twin Cities, Minneapolis, Minnesota, USA
[2]University of Minnesota Masonic Institute for the Developing Brain, Minneapolis, Minnesota, USA
[3]Libraries, Emory University, Atlanta, Georgia, USA
[4]University of Minnesota Twin Cities School of Kinesiology, Minneapolis, Minnesota, USA

Correspondence to
Dr Benjamin J S al-Haddad; haddad@umn.edu

ABSTRACT

Introduction With global improvements in neonatal survival, more small and sick newborns in low-income and middle-income countries (LMICs) are at increased risk of neurodevelopmental disability and delay. While there is increased recognition of the importance of early identification of neurodevelopmental differences and timely initiation of therapy, little is known about standardised neonatal neurodevelopmental screening tools in these settings.

Methods We performed a systematic review to determine what standardised neurodevelopmental assessments had been used in LMICs for neonates before 44 weeks corrected gestational age and published in the literature. We excluded short-term clinical assessments designed for specific pathologies. We performed the search across seven databases, screened studies for eligibility and inclusion and extracted bibliographic data, country, patient characteristics, assessments and study aims. Results were summarised in tabular and graphical presentation.

Results There were 2477 records screened, yielding 67 studies for inclusion. Studies in Asian countries made up 65.7%, while Latin America and Africa made up 19.4% and 16.4%, respectively. Physicians and paramedical staff performed the screening assessments in only 16.4% of studies, and 92.5% of studies used inpatient recruitment. The Neonatal Behavioural Neurological Assessment (25.4%) was the most frequently used screening tool followed by the General Movements Assessment (22.4%), the Hammersmith Neonatal Neurological Examination/Dubowitz (16.4%) and the Neonatal Behavioural Assessment Scale (10.4%).

Conclusions We did not identify any one neonatal neurodevelopmental screening assessment that is rapid, globally validated, identifies targets for intervention, has high predictive prognostic value and does not require neonatal or kinesiologic expertise or uncommon equipment. Such an assessment, in concert with evidence-based intervention, therapeutic delivery platforms, established referral pathways and trained personnel would improve functional outcomes for high-risk small and sick neonates in LMICs.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ With the improvements in neonatal survival in many low-income and middle-income countries (LMICs), there are increased numbers of small and sick newborns at high risk for lifetime neurodevelopmental disability.

WHAT THIS STUDY ADDS

⇒ This systematic review provides comprehensive evidence about published uses of standardised neonatal neurodevelopmental screening examinations used in low-income and middle-income countries to identify newborns with neurodevelopmental differences that may benefit from therapeutic interventions. There is a need to strengthen birth to childhood neurodevelopmental health systems in LMICs to improve early detection, care and support services for children and their families.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the most used assessment tools globally in LMICs and serves as a reference for the state of neonatal neurodevelopmental screening in these settings for research, clinical practice and policy.

INTRODUCTION

With global improvements in neonatal survival, the number of children experiencing neurodevelopmental delay and disability may be increasing.[1 2] Since the early 2000s, when neonatal survival was signalled as a neglected area, it has become a global health priority and neonatal mortality rates have decreased significantly.[3–6] More neonates at high risk for neurodevelopmental delay and disability (neonates born small for gestational age, with low birth weights, preterm and who experienced early infection or perinatal asphyxia) are surviving beyond the perinatal and neonatal periods.[7] In 2019, the WHO

published Survive and Thrive: transforming care for every small and sick newborn, signalling an extension in global neonatal health thinking towards neurodevelopmental flourishing.[8] Beyond survival, a newborn's neurodevelopmental health in the critical first days of life is an important indicator of their developmental outlook across the lifespan.[9] Concurrent with these increases in survival, there is evidence of increased prevalences and incidences of neurodevelopmental disability such as cerebral palsy (CP).[10 11] It is estimated that conditions arising in the neonatal period are the number one cause of disability-adjusted life-years globally.[12] While CP prevalence in many high-income countries has declined, there is little published data on the trend in low-income countries because of a lack of population surveillance, rare routine developmental screening, weak healthcare provision systems and stigma.[13] However, secondary evidence suggests that as neonatal mortality continues to decline with improvements in care for infants born preterm and with birth asphyxia, increasing numbers of surviving infants have neurodevelopmental delays and disabilities.[11 14–16]

Early neurodevelopmental assessment of neonates in low-income and middle-income countries (LMICs) can improve functional outcomes and provide essential epidemiological data in these settings. However, very little is known about neurodevelopmental screening tools and practices used by clinicians and researchers for neonates in LMICs. Early screening is crucial for early identification of neurological differences and timely initiation of therapy. The first months to years of life may be the most dynamic brain plasticity period of the human lifespan, and developmental outcomes may be most optimised with earlier therapy.[1 17 18] Yet, in many global settings, barriers including long distances, absence of transportation, weather, seasonal work patterns, financial barriers and absence of local paediatric developmental expertise prevent access to routine periodic developmental screening. Consequently, many families struggle to bring their infants to healthcare facilities for developmental surveillance. Predischarge identification of neonates who may benefit from early therapy is highly desirable because (1) families may not be able to identify and seek care for developmental concerns until much later, (2) earlier identification and intervention improve neurodevelopmental outcomes and (3) early identification of developmental differences can make it possible for families to provide some therapy at home.[17 19–23]

Over the last 70 years, a wide array of clinical assessments to evaluate early neonatal central nervous system function and development have been promulgated.[1 24–26] Since the 1960s, when the first systematic neurological assessments of newborns appeared, new tools have subsequently been elaborated to evaluate global development and neurologic function, particular developmental domains (ie, gross motor skills) and to identify relevant therapeutic indications.[26] Despite the application of numerous standardised screening instruments in different populations globally, there is little published data on the uses of neonatal neurodevelopmental assessments in LMICs.[10 11]

Our main objective was to determine which standardised neonatal neurodevelopmental screening examinations had been used and published for neonates before 44 weeks corrected gestational age in LMICs to determine which, if any, would be most appropriate for wide-scale clinical screening. Further, we aimed to examine published assessment use through time, across geographical regions and to characterise the types of assessments and how they were used.[4 27] Lastly, an exploratory aim was to contextualise these findings in relation to early intervention therapies.

METHODS

Literature search

We conducted a systematic search using a combination of controlled vocabulary and natural language keywords following best practices from the Cochrane Handbook for Systematic Reviews of Interventions.[28] The search strategy was designed by a health sciences librarian (ER) and encompassed the concepts of neurological examinations, screenings or assessments; neonates; and LMICs and resource-poor settings. The Cochrane EPOC Review Group's LMIC search filter[29] was adapted for use in this search strategy. See online supplemental appendix A for the verbatim search strategy with Boolean operators. The search strategy was developed in Ovid MEDLINE and then translated and executed across six additional databases and registers from their inception to 30 January 2023: Embase via OVID (final search executed on 22 February 2023), Scopus, Web of Science, Cochrane Library, Global Index Medicus and ClinicalTrials.gov.

Eligibility criteria

All studies, regardless of date or language of publication, that took place in LMICs defined by the World Bank[30] in which a neurological, neurobehavioural or neurodevelopmental assessment was performed on neonates less than 44 weeks corrected gestational age were included. We did not include Sarnat, Thompson or Bilirubin Induced Neurological Dysfunction score examinations as these were designed for short-term clinical information rather than general neurological functioning.

Study selection

The search results from all databases were compiled on 22 February 2023 and deduplicated in EndNote V.X9[31] by ER, then imported into Covidence.[32] Records were screened independently against the eligibility criteria by two reviewers (BJSa-H and EB) and conflicts were resolved through consensus discussion. After title and abstract screening, ER retrieved full texts for the remaining records. Two authors, BJSa-H and EB, reviewed the full texts against the inclusion criteria, with discrepancies resolved by consensus. The screening and inclusion process is shown in figure 1.[33]

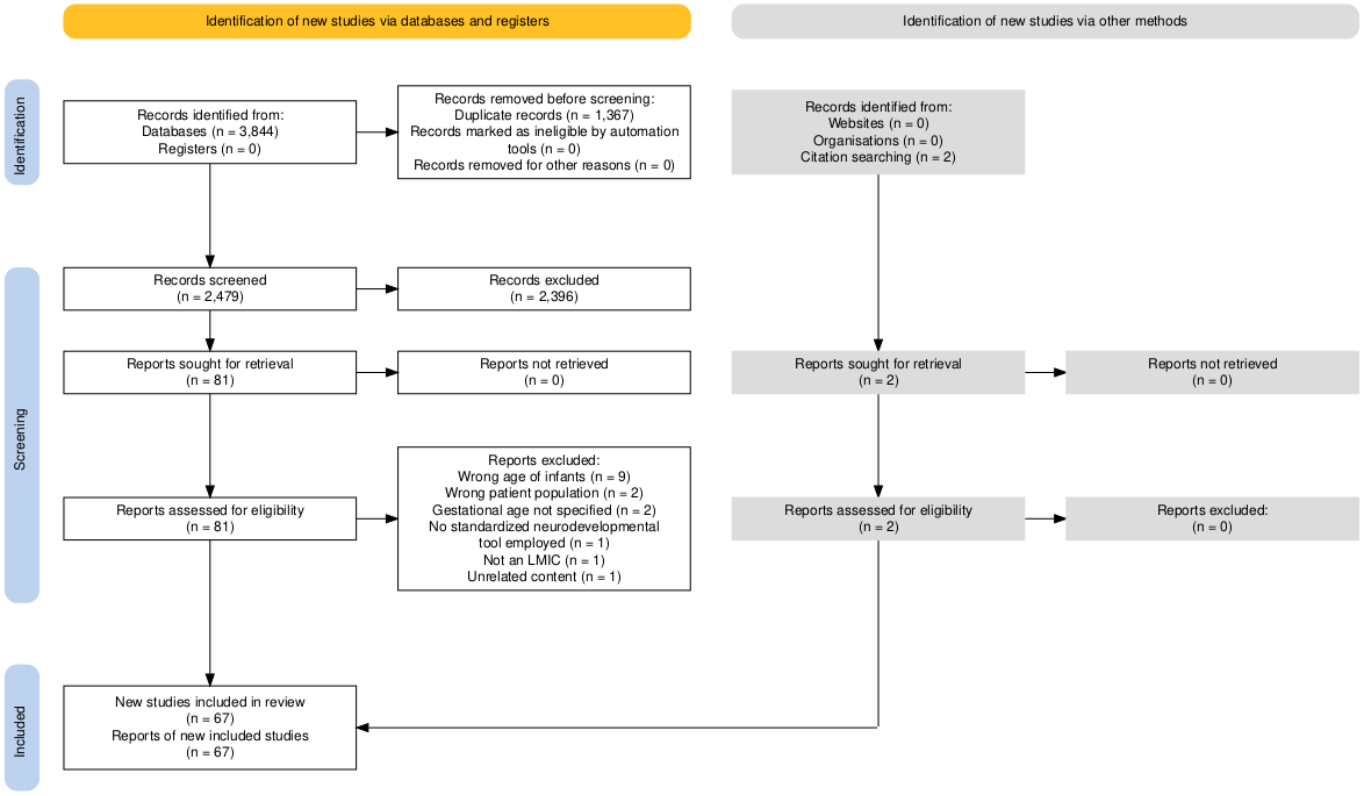


Figure 1 PRISMA diagram. Figure shows the number of studies identified, screened and included in the systematic review. LMIC, low-income and middle-income country; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data collection

The data extraction form function in Covidence was used to extract data. Extracted data were verified by two coauthors (BJSa-H and EO). Data extracted included the following: (1) title, (2) lead author, (3) year of publication, (4) country or countries in which the study was conducted, (5) number of study subjects, (6) gestational age range of subjects at birth, (7) study inclusion and exclusion criteria, (8) study aim(s), (9) neonatal neurologic assessment tool(s) used, (10) personnel who administered the assessment, (11) corrected gestational age at the time of the assessment administration, (12) chronological age at the time of the assessment and (13) location of patient recruitment. If the required data were not available in the English language abstract, this was noted as such in the data extraction table.

Analytical framework

We aimed to aggregate all the literature on standardised neonatal neurodevelopmental screening examinations for neonates before 44 weeks corrected gestational age in LMICs to serve as grounding for comparing assessments. We summarised study characteristics to understand how, where and by whom the examinations were conducted. Our focus was to enumerate assessments to consider how well they could be widely applied in basic newborn care settings outside of research and specialised care contexts.

Quality assessment

Studies were evaluated using established study quality criteria by two coauthors (EB and BJSa-H).[34] These included the following: (1) study design and sampling methods were appropriate for the study question, (2) sample size calculations were used, (3) the response rate was reported and above >70% if applicable, (4) participant characteristics were clearly defined and presented, (5) administration of screening tool(s) or measure(s) was clearly defined, (6) CIs were reported, (7) for case–control studies: cases and controls were clearly defined and comparable and (8) for cohort studies: groups were comparable at baseline and losses to follow-up were reported. Studies were categorised as low, medium or high risk of bias. A low risk of bias was assigned to studies where all or most of the above criteria were fulfilled, and those that were not fulfilled were thought unlikely to alter the conclusions of the study. Medium risk of bias was assigned to studies where some of the above criteria were fulfilled, and those not fulfilled were thought unlikely to alter the conclusions of the study. A high risk of bias was assigned to studies where few or no criteria were fulfilled, and the conclusions of the study were thought likely or very likely to alter with their inclusion.[34]

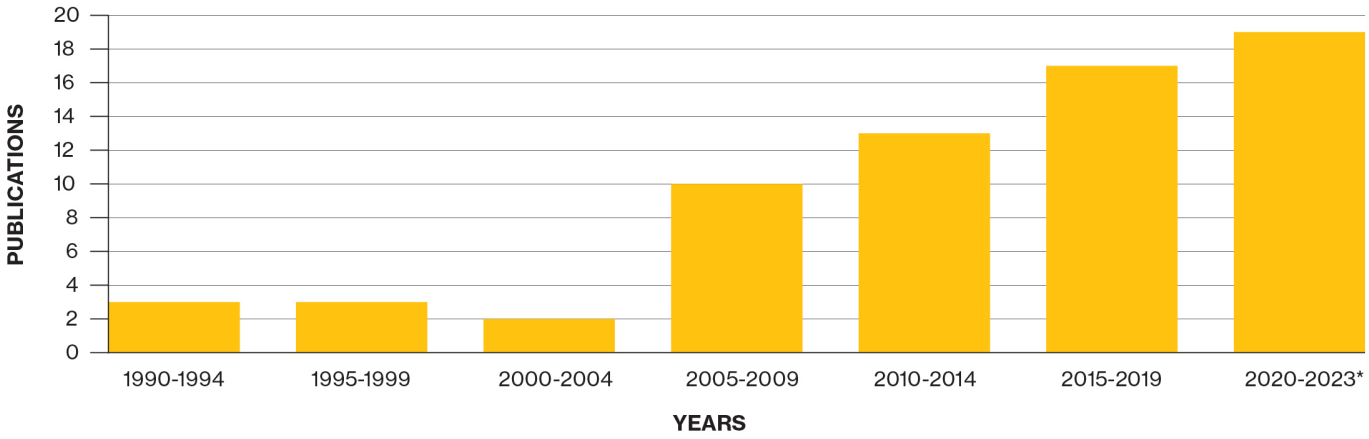


Figure 2 Number of published studies with standardised neonatal neurodevelopmental assessments from 1990 to 2023. *The 2020–2023 range stops in February 2023 and is shorter than the other 5-year categories.

Patient and public involvement

Patients and the public were not involved in any way in this study.

RESULTS

The initial database search generated 3844 records (2477 after duplicates were removed). Of these, 2396 were excluded after title and abstract screening. The full texts of 81 papers were subsequently assessed for inclusion. Out of these studies, 16 were deemed ineligible and were excluded, leaving a final sample of 65 studies. Two additional studies referenced in the initial 65 studies were added. See figure 1 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram. Two versions (one abbreviated (B1) and one complete (B2)) of the data extraction tables can be found in online supplemental appendix B.

The temporal distribution of studies demonstrated that six studies took place before the year 2000. 25 of the studies took place between 2000 and 2015 and 36 were completed after 2015. See figure 2 for the temporal distribution of studies. Table 1 describes the geographical regional distribution of studies, patient recruitment sources, the profession or role of the assessor and the evaluation instruments used in the included studies. Figure 3 shows the geographical distribution of the included studies by the assessment tools used. While studies varied greatly in risk of bias, the individual study elements that may have led to bias were not likely to influence the data collected for this review.

Among the studies included in this review, there were four broad categories of study objectives. 28 studies had objectives that were exploratory, descriptive or intended as benchmarking an assessment in a previously unpublished neonatal population. 19 studies focused on prenatal exposures and neonatal neurological outcomes. 17 studies used neonatal neurological screening assessments to study the effects of perinatal and postnatal exposures. Three studies used neonatal assessments to predict later neurodevelopment.

DISCUSSION

Summary of main results

Our objective was to generate comprehensive evidence of neonatal neurodevelopmental screening practices in LMICs to date. This systematic review found 67 publications on neurodevelopmental screening of neonates in LMICs. Since the initial studies appeared in the 1990s, there has been a steady increase in the number of articles published; indeed, during the 3.5-year period from 2020 to the beginning of 2023, more articles were published than in any previous 5-year increment. Almost two-thirds of the studies took place in Asia, with most conducted in China and India. The most frequently published assessment was the Neonatal Behavioural Neurological Assessment (NBNA), which was exclusively used in China and was developed based on the Neonatal Behavioural Assessment Scale (NBAS) and the Amiel-Tison Neurological Assessment at Term. Only 16.4% of studies were performed in Africa. The most geographically widely used assessments were the Hammersmith Neonatal Neurological Examination (HNNE)/Dubowitz Examination and the General Movements Assessment (GMA). Almost all the neonates in the studies were recruited from inpatient health facilities, and most studies did not describe the role or profession of the assessor. Among the remaining studies, healthcare providers including physicians and therapists only made up 16.4% of the assessors administering the examinations. Remarkably, only 4.5% of the studies aimed to use neonatal assessments to predict later neurodevelopmental outcomes.

Common standardised neonatal neurodevelopmental examinations

Among the 15 different neonatal neurodevelopmental examinations that were identified in the literature, the 6 most geographically widespread included the HNNE/

Table 1 Characteristics of included studies

Region*		n	%
	Asia	44	65.7
	Latin America	13	19.4
	Africa	11	16.4
Assessor†			
	Not described	25	37.3
	Trained/certified/expert evaluator	22	32.8
	Researcher	12	17.9
	Medical doctor	8	11.9
	Paramedical staff‡	3	4.5
Recruitment source§			
	Inpatient	62	92.5
	Not described	3	4.5
	Outpatient	2	3.0
	Community sample	2	3.0
Assessment instrument			
	Neonatal Behavioural Neurological Assessment	17	25.4
	General Movements Assessment	15	22.4
	Hammersmith Neonatal Neurological Examination/Dubowitz	11	16.4
	Neonatal Behavioural Assessment Scale (Brazelton)	7	10.4
	Prechtl Neonatal Neurological Examination	5	7.5
	Test of Infant Motor Performance	6	9.0
	Amiel-Tison Neurological Assessment at Term	2	3.0
	Other	7	10.4

*Two studies were multinational.
†Some assessments were performed by more than one role.
‡Paramedical staff included physical therapists and occupational therapists.
§Some studies used multiple recruitment sources.

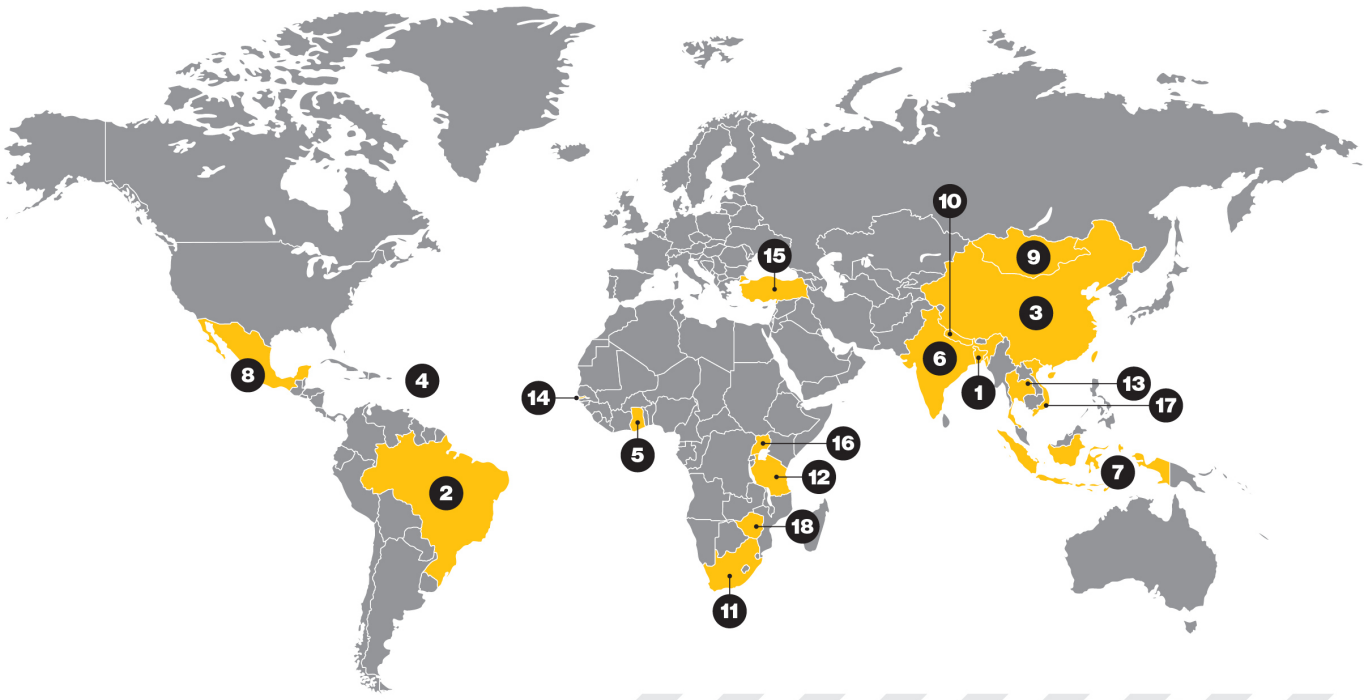
Dubowitz Examination, the GMA, NBAS, the Test of Infant Motor Performance (TIMP), the Prechtl Neonatal Neurological Examination (NNE) and Screening Examination and the Amiel-Tison Neurological Assessment at Term (ATNAT). While not used to date outside of China, the NBNA has been used in at least 17 publications. Below, we discuss the histories and examination frameworks for these commonly used assessments. See table 2 for basic characteristics of neonatal assessment tools.

Hammersmith Neonatal Neurological Examination

The HNNE was initially developed by Dr Lilly Dubowitz and Professor Victor Dubowitz in 1981 and was revised into the current version in 1998 by Dr Eugenio Mercuri.[35] The test is recommended to be completed at term age for preterm neonates and around 2 weeks of age in term neonates.[36] It consists of 34 items divided into 6 categories: posture and tone, tone patterns, reflexes, movements, abnormal signs/patterns, and orientation and behaviour.[35 37] Items are scored from 1 to 5 and then converted to optimality scores based on a normal distribution to categorise neonates as above the 10th percentile or below the 10th percentile.[38] The examination requires 15–20 min to administer and training for the HNNE requires 4 hours.[35] The sensitivity and specificity of the HNNE for neurodevelopmental delay were 64% and 73%, respectively, when performed earlier than recommended and were 50% and 77% when performed at the recommended ages.[39]

General Movements Assessment

The GMA was developed in the early 1990s by Professor Heinz Prechtl and his colleagues.[40] It is a standardised, qualitative assessment that uses a video recording of an infant to observe and assess spontaneously generated movement patterns from birth up until 60 weeks corrected gestational age.[41–43] The GMA evaluates the presence or absence of specific characteristics of general movements (GMs) that can then be used to assess the integrity of the central nervous system.[44] During the preterm and writhing periods, GMs can be classified into one of four categories: normal, poor repertoire, cramped-synchronised or chaotic.[43 45] If the nervous system is impaired, the quality of GMs differs and movement patterns appear



	1. Bangladesh	2. Brazil	3. China	4. Dominica	5. Ghana	6. India	7. Indonesia	8. Mexico	9. Mongolia	10. Nepal	11. South Africa	12. Tanzania	13. Thailand	14. The Gambia	15. Turkey	16. Uganda	17. Vietnam	18. Zimbabwe
Amiel-Tison Neurological Assessment at Term (ATNAT)					●							●						
Developmental Assessment Scales for Indian Infants (DASII)					●													
General Movements Assessment (GMA)	●	●	●		●	●				●	●			●				
Hammersmith Neonatal Neurological Examination / Dubowitz Examination (HNNE)		●	●	●	●	●					●	●			●	●		
Infant Neurological International Battery (INFANIB)			●															
Mongolian Rapid Baby Scale								●										
Morgan Neonatal Neurobehavioral Examination (MNNE)					●													
Neo Neuro and Up							●											
Neonatal Behavioral Assessment Scale (NBAS)			●		●				●	●			●					
Neonatal Behavioral Neurological Assessment (NBNA)			●															
Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS)		●																
Neurobehavioral Assessment of Preterm Infant (NAPI)					●													
Prechtl Neonatal Neurological Examination (NNE)				●			●										●	
Test of Infant Motor Performance (TIMP)		●	●											●				
Touwen Screening Newborn Neurological Examination (TNNE)							●											

Figure 3 Geographical distribution of standardised neonatal neurodevelopmental assessments. Figure 3 illustrates the standardised neonatal neurodevelopmental examinations that have been published in the literature in populations from low-income and middle-income countries.

more monotonous and may be categorised as cramped-synchronised.[43] The GMA requires 5–10 min to perform and has high sensitivity and specificity (reportedly up to 100% and 92.5 to 100% over the age range, respectively) to predict CP at a much earlier age than was previously possible.[40 43 46] Certification to perform the GMA requires a 4-day course and passing an examination administered through the General Movements Trust.[43]

Neonatal Behavioural Assessment Scale

The NBAS also known as the Brazelton NBAS was developed by Dr Berry Brazelton and his colleagues in the 1970s to assess newborns' neurological functioning and its contribution to the infant–parent interaction.[47 48] The NBAS can be used as a neurobehavioural assessment and additionally as a clinical intervention instrument for improving mother–infant bonding.[48] The instrument is

Table 2 Characteristics of neurodevelopmental assessment tools

Assessment	Training time	Administration time	Equipment required	Screening target	Estimated predictive accuracy
HNNE	4 hours	15–20 min	Visual target, rattle, reflex hammer	Neurodevelopmental delay	Sens=50% Spec=77%
GMA	4 days	5–10 min	Video recording equipment	Neurodevelopmental delay	Sens=100% Spec=92.5%
NBAS	1–2 days	45 min	Rattle, red ball, flashlight, soft cloth	Neurological function and parent-neonate bonding	–
TIMP	2 days	20–45 min	TIMP Kit (rattles, balls, etc), stopwatch	Motor development primarily may predict cognitive and language outcomes	Sens=45% Spec=74%
NNE	–	45 min (modified version)	Light source, cotton ball	Neurologic function	Sens=44% Spec=90%
ATNAT	–	5 min	Black and white Bull's eye target	Neurologic function/ neurodevelopmental delay	Cohen kappa=0.83
NBNA	2 weeks	10 min	Soft cloth, simple objects	Neurodevelopmental delay	Sens=84.6% Spec=82.6%

ATNAT, Amiel-Tison Neurological Assessment at Term; GMA, General Movements Assessment; HNNE, Hammersmith Neonatal Neurological Examination; NBAS, Neonatal Behavioural Assessment Scale; NBNA, Neonatal Behavioural Neurological Assessment; NNE, Prechtl Neonatal Neurological Examination; Sens, sensitivity; Spec, specificity; TIMP, Test of Infant Motor Performance.

built on 28 behavioural items and 18–20 reflex items.[48] Certification for general use requires a 1-day to 2-day course.[49] The reflex items are scored on a 4-point scale, and the behavioural and supplementary items are scored on a 9-point scale.[50] The exam does not produce a single total score but rather assesses each developmental area and examines how the infant integrates these into its environment.[51] The scale requires 20–30 min to administer, is suitable for use with healthy full-term newborns a few hours after birth up to 2 months postpartum and can also be used with stable preterm infants from 35 to 36 weeks' gestational age.[47 51] There is little known about the sensitivity and specificity of the assessment for predicting neurodevelopmental outcomes later in childhood.

Test of Infant Motor Performance

The TIMP was developed in the late 1980s and early 1990s by Drs Gay L Girolami and Suzann Campbell for use by occupational and physical therapists to assess motor function in infants from 32 to 34 weeks gestational age to 4 months after term or around 57 weeks corrected gestational age.[52 53] The instrument was designed to reflect maturation, degree of medical complications, and to particularly assess postural control and alignment relevant for early infant functional movements.[52] Certification in the TIMP requires around 15 hours of instruction and is primarily designed for paediatric-oriented therapists.[54] The TIMP consists of 42 components that test motor development and requires 20–45 min to administer.[55 56] 13 items are scored dichotomously based on spontaneous observation of the infant's movements, and the remaining 29 items are scored on a rating scale based on the infants' movements in response to examiner positioning manoeuvres.[53] Evidence suggests that when performed at 7 days of age, the TIMP has sensitivity of 45% and specificity of 74% for performance at less than the fifth percentile on the Alberta Infant Motor Scale at 12 months of age.[57] Although designed to focus on the motor domain, there is evidence that the TIMP may also predict cognitive and language outcomes at 2 years of corrected age.[58]

Prechtl Neonatal Neurological Examination

The NNE was published in 1964 by Professors Heinz Prechtl and David Beintema and outlined a detailed method for neurological assessment of the newborn designed predominantly for physicians to be used after 2 days of life.[59] Concurrent with the publication, there was a shorter screening examination composed of seven items including Moro response, resistance to passive movement, state, posture, eyes and spontaneous motor activity which could be summated to either normal, suspect or abnormal. There is evidence suggesting that the assessment sensitivity and specificity for 2-year mental and physical development are 44% and 90%, respectively.[60]

Amiel-Tison Neurological Assessment at Term

The ATNAT was developed by Dr Amiel-Tison and published in 1982 through several iterations based in part on the earlier work of Drs Thomas and Saint-Anne-Dargassies.[61 62] The assessment is composed of 35 items in 10 domains including cranial assessment, sensory function, spontaneous motor activity, passive muscle tone, axial motor activity, primitive reflexes, palate and tongue evaluation, stability during assessment, feeding autonomy,

medical status and infant status at the time of the examination.[63] The components are noted and then synthesised into four possible results for term neonates: normal (or optimal), mildly abnormal, moderately abnormal or severely abnormal (or non-optimal).[63] In contrast, abnormal preterm neonatal results are categorised in two ways: either mild/moderately abnormal or severely abnormal. If a neonate has a normal result with their first testing on day of life 1 or 2, no further assessments are required. However, if there are some abnormal results, the assessment is repeated over the next several days to categorise into mild, moderate or severely abnormal. The ATNAT is supposed to take 5 min to complete and has been taught in a small group setting with a master examiner teaching the assessment with several neonates. The ATNAT performed at term has been found to have excellent correlation (Cohen's kappa coefficient=0.83) with moderate to severely abnormal neurological outcome at 12–15 months but may also have a high false positive rate.[64]

Neonatal Behavioural Neurological Assessment

The NBNA was developed in China by Dr Bao *et al.* in 1991 and was based on the assessments developed by Brazelton and Amiel-Tison with some additional items. The NBNA is composed of 20 items including 6 behavioural components, 4 passive tone components, 4 active tone components, 3 primary reflex items and 3 general assessment items. Each component is scored as 0, 1 or 2 for a possible total of 40 points. The assessment was standardised across 12 cities in China and was designed for clinical assessment of asphyxiated newborns. The creators of the NBNA state that it takes 10 min to complete and requires 2 weeks of training and an examination for proficiency.[65] Published evidence suggests that the assessment has 84.6%–88.9% sensitivity and 82.6%–97.4% specificity for delay at 1–2 years among high-risk neonates who experienced perinatal asphyxia.[66]

Contrasting neonatal neurodevelopmental screening tools for widespread clinical screening implementation

Our findings suggest that there is currently no single validated clinical screening instrument that can be easily deployed at a low cost across diverse neonatal populations in LMICs. While no neonatal neurodevelopmental assessment (and screening) tool is comprehensive, several characteristics of the current tools are important in considering the design of a future ideal assessment tool for use in low-resource settings. First, the assessment should not require neonatal or kinesiologic expertise or special training to administer. All the major assessments discussed required specialised training lasting from 4 hours for the HNNE to 2 weeks for the NBNA and were targeted at therapists or medical practitioners. In many LMICs, there are very few trained physical and occupational therapists and even fewer therapists trained in neonatal assessment. For example, as of 2017 there were 16 educational programmes for occupational therapy and 31 for physical therapy in Anglophone sub-Saharan Africa, with 9 countries without education programmes for either profession.[67] While developing the neonatal and infant therapy expertise pool within LMICs is crucial for realising the objectives of the Survive and Thrive agenda, these rare resources may be best deployed in providing therapy for neonates and infants rather than in screening sick and small newborns for signs of delay. Second, the ideal assessment should not require uncommon equipment to administer. Some examinations required minimal equipment to administer, including the NNE and ATNAT, while others like the TIMP required proprietary kits (see table 2). Ministries of Health and communities in many low-resource settings lack the resources to devote to specialised purchases. Third, the assessment should be fast enough to allow for healthcare workers to administer easily prior to discharge without adding a large burden to staff that may already be overworked. In considering the reported time needed to perform the assessment, the tools ranged from 5 min for the ATNAT to up to 45 min for the TIMP. Fourth, the assessment should be based on universal human development principles and be standardised to a broad global neonatal population. The assessments considered in this work were validated in variable breadths of populations. Lastly, the assessment should have a high predictive value for intervenable developmental delay. From the perspective of the ability to predict neurodevelopmental outcomes in the first years of life, the assessments performed variably with sensitivities and specificities for outcomes at 12 months and beyond ranging from 44% sensitivity and 90% specificity for the NNE to 100% sensitivity and 100% specificity for the GMA.[40 43 46 60] To begin to improve neurodevelopmental outcomes for high-risk neonates and to generate standardised and comparable data, there is a need to create a valid, reliable and accessible neonatal neurodevelopmental screening instrument that is feasible to use across low-income and middle-income contexts.

Beyond screening: context, opportunities and challenges

While screening and identification are essential first steps in the provision of care for neonates who may benefit from therapy, identification is not sufficient. To connect identification of pathology with therapy, broader healthcare system components including evidence-based intervention, therapeutic delivery platforms, referral pathways and trained personnel must also be addressed. Considering CP as a key example, evidence from developmental basic neuroscience and randomised controlled trials demonstrate that early identification and intervention improve functional outcomes over the life course. Early therapy with active movement is important for continued development of the motor cortex and likely takes advantage of the tremendous neural plasticity at younger ages.[42] Evidence suggests that infant–environment interactions stimulate and regulate the joint development of musculoskeletal and neuromotor systems.[19 42] With CP-specific

early interventions, infants have the greatest chance of gaining the most lifelong function, reducing their disability burden and that of their family over the long term. Evidence shows that infants who receive regular surveillance and therapies like constraint-induced movement therapy or goals-activity-motor enrichment therapy have improved outcomes and less morbidity.[19–23 42 68 69] Importantly, all these effective therapy modalities can be, in major part, delivered by parents and caregivers in the home without costly equipment. Despite these promising therapies, the body of evidence for neonatal-specific therapies is small in low-income, middle-income and high-income countries.

In addition to the need for progress in evidence-based gold-standard therapies for neonates, considerations of how therapy may be delivered are essential. Models of therapeutic delivery platforms exist in low-resource settings. For example, in rural Uganda, community-based interventions have been developed for infants with moderate to severe disability where parents and caregivers receive training on how to provide specialised care and physical therapy for their infants.[70] Relatedly, many healthcare facilities where sick and small newborns are treated may need to establish or strengthen pathways for referral to intervention. When there are effective referral networks in place, the subsequent challenge may be to have a qualified cadre of physical and occupational therapists and other developmental healthcare professionals prepared to provide therapy, teach parents how they might provide therapy at home and oversee functional progress. Ultimately, there is a need for large-scale integration of early neurodevelopmental care for neonates and infants in the health systems of LMICs.

In addition to improved functional outcomes, earlier identification and intervention may also bring significant economic benefits to families, communities and countries. While evidence on the economic effects of any early intervention programme is exceedingly rare in low-resource settings, one recent study of early intervention in Kenya demonstrated a high return on investment when considering cognitive outcomes.[71] More evidence is likely to appear in the coming years.[72 73]

Limitations

There are some limitations that need to be considered when interpreting the findings of this review. First, the current review focused on published journal articles and abstracts and did not include a systematic review of grey literature. Second, publication bias may limit the conclusions that can be drawn from this review as studies that used internationally recognised, standardised screening instruments may be more likely to be published than those that applied locally made tools or clinical screening procedures.

CONCLUSIONS

Over the last 30 years, improvements in neonatal survival have opened up new opportunities for improving the neurodevelopmental outcomes of high-risk newborns. Increasing numbers of studies are being conducted and published assessing neonatal neurodevelopment in LMICs for a variety of uses. While there is no one ideal assessment tool, these studies are evidence of the growing importance accorded to neonatal brain health for infants, families, communities and economies. There exist tremendous opportunities for improvements in both how neonatal neurodevelopmental screening is conducted and in the development of neurodevelopmental care in LMICs.

Acknowledgements We thank Mathew Rezac for his work creating figures 2 and 3 and Nicole Theis-Mahon, MLIS, AHIP for her work with literature retrieval.

Contributors BJSa-H conceived of the idea for the manuscript. ER devised the search strategy and performed the systematic review searches. BJSa-H, EB and EO reviewed the literature for the systematic review and summarised the results. BJSa-H, EO, ER and EB all contributed to writing and critically revising the manuscript. BJSa-H is the guarantor for the work.

Funding BJSa-H has been supported by T32 GM008244 from the National Institute of General Medical Sciences.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval For this systematic review, ethical approval was not needed. There were no human or animal study subjects.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. The complete search strategy can be found in online supplemental file 1 and the full extracted dataset can be found in online supplemental file 1.

ORCID iDs
Benjamin J S al-Haddad http://orcid.org/0000-0003-1398-9527
Elisabeth Olson http://orcid.org/0009-0005-2787-9718
Erin Reardon http://orcid.org/0000-0001-7939-9808
Emmanuel Bonney http://orcid.org/0000-0001-7179-2816

REFERENCES

1 Hadders-Algra M. Early Diagnostics and Early Intervention in Neurodevelopmental Disorders-Age-Dependent Challenges and Opportunities. *J Clin Med* 2021;10:861.
2 Kassebaum N, Kyu HH, Zoeckler L, *et al*. Child and Adolescent Health From 1990 to 2015: Findings From the Global Burden of

Diseases, Injuries, and Risk Factors 2015 Study. *JAMA Pediatr* 2017;171:573–92.
3 Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? *The Lancet* 2005;365:891–900.
4 Lawn JE, Bhutta ZA, Ezeaka C, *et al*. Ending Preventable Neonatal Deaths: Multicountry Evidence to Inform Accelerated Progress to the Sustainable Development Goal by 2030. *Neonatology* 2023;120:491–9.
5 Sharrow D, Hug L, You D, *et al*. Global, regional, and national trends in under-5 mortality between 1990 and 2019 with scenario-based projections until 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. *Lancet Glob Health* 2022;10:e195–206.
6 Hug L, Alexander M, You D, *et al*. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. *Lancet Glob Health* 2019;7:e710–20.
7 Hedstrom A, Ryman T, Otai C, *et al*. Demographics, clinical characteristics and neonatal outcomes in a rural Ugandan NICU. *BMC Pregnancy Childbirth* 2014;14:327.
8 World Health Organization. Survive and thrive: transforming care for every small and sick newborn. 2019.
9 World Health Organization. Reaching the every newborn national 2020 milestones: country progress, plans and moving forward. 2017. Available: https://www.who.int/publications/i/item/9789241512619
10 Olusanya BO, Gladstone M, Wright SM, *et al*. Cerebral palsy and developmental intellectual disability in children younger than 5 years: Findings from the GBD-WHO Rehabilitation Database 2019. *Front Public Health* 2022;10:894546.
11 Niyonshaba B, Kabugo D, Nakiganda C, *et al*. Feasibility, acceptability and preliminary effectiveness of the Hospital to Home discharge and follow-up programme in rural Uganda: a mixed-methods intervention study. *BMJ Glob Health* 2025;10:e015945.
12 World Health Organization. Global health estimates: leading causes of dalys. 2023. Available: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/global-health-estimates-leading-causes-of-dalys
13 McIntyre S, Goldsmith S, Webb A, *et al*. Global prevalence of cerebral palsy: A systematic analysis. *Dev Med Child Neurol* 2022;64:1494–506.
14 Kabugo D, Nakamura H, Magnusson B, *et al*. Mixed-method study to assess the feasibility, acceptability and early effectiveness of the Hospital to Home programme for follow-up of high-risk newborns in a rural district of Central Uganda: a study protocol. *BMJ Open* 2021;11:e043773.
15 Khandaker G, Smithers-Sheedy H, Islam J, *et al*. Bangladesh Cerebral Palsy Register (BCPR): a pilot study to develop a national cerebral palsy (CP) register with surveillance of children for CP. *BMC Neurol* 2015;15:173.
16 Khandaker G, Muhit M, Karim T, *et al*. Epidemiology of cerebral palsy in Bangladesh: a population-based surveillance study. *Dev Med Child Neurol* 2019;61:601–9.
17 Morgan C, Fetters L, Adde L, *et al*. Early Intervention for Children Aged 0 to 2 Years With or at High Risk of Cerebral Palsy: International Clinical Practice Guideline Based on Systematic Reviews. *JAMA Pediatr* 2021;175:846–58.
18 Darling JC, Bamidis PD, Burberry J, *et al*. The First Thousand Days: early, integrated and evidence-based approaches to improving child health: coming to a population near you? *Arch Dis Child* 2020;105:837–41.
19 Martin JH, Chakrabarty S, Friel KM. Harnessing activity-dependent plasticity to repair the damaged corticospinal tract in an animal model of cerebral palsy. *Dev Med Child Neurol* 2011;53 Suppl 4:9–13.
20 Eliasson A-C, Holmefur M. The influence of early modified constraint-induced movement therapy training on the longitudinal development of hand function in children with unilateral cerebral palsy. *Dev Med Child Neurol* 2015;57:89–94.
21 Elkamil AI, Andersen GL, Hägglund G, *et al*. Prevalence of hip dislocation among children with cerebral palsy in regions with and without a surveillance programme: a cross sectional study in Sweden and Norway. *BMC Musculoskelet Disord* 2011;12:284.
22 Morgan C, Novak I, Dale RC, *et al*. Single blind randomised controlled trial of GAME (Goals - Activity - Motor Enrichment) in infants at high risk of cerebral palsy. *Res Dev Disabil* 2016;55:256–67.
23 Morgan C, Darrah J, Gordon AM, *et al*. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. *Dev Med Child Neurol* 2016;58:900–9.
24 Brown N, Spittle A. Neurobehavioral evaluation in the preterm and term infant. *Curr Pediatr Rev* 2014;10:65–72.
25 Gladstone M, Oliver C, Van den Broek N. Survival, morbidity, growth and developmental delay for babies born preterm in low and middle income countries - a systematic review of outcomes measured. *PLoS ONE* 2015;10:e0120566.
26 Ashwal S. Historical aspects of the neonatal neurological examination: why child neurologists are not “little” adult neurologists. *J Hist Neurosci* 1995;4:3–24.
27 Kerber KJ, de Graft-Johnson JE, Bhutta ZA, *et al*. Continuum of care for maternal, newborn, and child health: from slogan to service delivery. *The Lancet* 2007;370:1358–69.
28 Higgins J, Thomas J, Chandler J, *et al*. *Cochrane Handbook for Systematic Reviews of Interventions*. 2023.
29 cochrane effective practice and organisation of care. LMIC Filters; 2023. Available: https://web.archive.org/web/20230904155027/https://epoc.cochrane.org/lmic-filters
30 New World Bank country classifications by income level: 2021-2022, Available: https://blogs.worldbank.org/en/opendata/new-world-bank-country-classifications-income-level-2021-2022
31 The EndNote Team. EndNote. 2013.
32 Covidence systematic review software. Melbourne, Australia: Veritas Health Innovation, Available: www.covidence.org
33 Haddaway NR, Page MJ, Pritchard CC, *et al*. *PRISMA2020*: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. *Campbell Syst Rev* 2022;18:e1230.
34 Banks LM, Kuper H, Polack S. Poverty and disability in low- and middle-income countries: A systematic review. *PLoS ONE* 2017;12:e0189996.
35 Mac Keith Press. Mac Keith Press | Hammersmith Neonatal and Infant Neurological Examinations, Available: https://www.mackeith.co.uk/hammersmith-neurological-examinations/
36 Venkata SKRG, Pournami F, Prabhakar J, *et al*. Disability Prediction by Early Hammersmith Neonatal Neurological Examination: A Diagnostic Study. *J Child Neurol* 2020;35:731–6.
37 Huf IU, Baque E, Colditz PB, *et al*. Neurological examination at 32-weeks postmenstrual age predicts 12-month cognitive outcomes in very preterm-born infants. *Pediatr Res* 2023;93:1721–7.
38 Dubowitz L, Mercuri E, Dubowitz V. An optimality score for the neurologic examination of the term newborn. *J Pediatr* 1998;133:406–16.
39 Howard GT, Baque E, Colditz PB, *et al*. Diagnostic accuracy of the Hammersmith Neonatal Neurological Examination in predicting motor outcome at 12 months for infants born very preterm. *Dev Med Child Neurol* 2023;65:1061–72.
40 Krynauw R, Du Preez JCF, Van Zyl JI, *et al*. The trajectory of general movements from birth until 12 - 14 weeks corrected age in very low birthweight and extremely low-birthweight infants born preterm. *S Afr J Child Health* 2022;16:99–104.
41 Porro M, Fontana C, Giannì ML, *et al*. Early detection of general movements trajectories in very low birth weight infants. *Sci Rep* 2020;10:13290.
42 Novak I, Morgan C, Adde L, *et al*. Early, Accurate Diagnosis and Early Intervention in Cerebral Palsy: Advances in Diagnosis and Treatment. *JAMA Pediatr* 2017;171:897–907.
43 Einspieler C, Prechtl HFR. Prechtl’s assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system. *Ment Retard Dev Disabil Res Rev* 2005;11:61–7.
44 Khurana S, Rao BK, Lewis LE, *et al*. Neonatal PT Improves Neurobehavior and General Movements in Moderate to Late Preterm Infants Born in India: An RCT. *Pediatr Phys Ther* 2021;33:208–16.
45 Prechtl HF. Qualitative changes of spontaneous movements in fetus and preterm infant are a marker of neurological dysfunction. *Early Hum Dev* 1990;23:151–8.
46 Ferrari F, Cioni G, Einspieler C, *et al*. Cramped synchronized general movements in preterm infants as an early marker for cerebral palsy. *Arch Pediatr Adolesc Med* 2002;156:460–7.
47 Barlow J, Herath NI, Bartram Torrance C, *et al*. The Neonatal Behavioral Assessment Scale (NBAS) and Newborn Behavioral Observations (NBO) system for supporting caregivers and improving outcomes in caregivers and their infants. *Cochrane Database Syst Rev* 2018;3:CD011754.
48 Costa R, Figueiredo B, Tendais I, *et al*. Brazelton Neonatal Behavioral Assessment Scale: A psychometric study in a Portuguese sample. *Infant Behavior and Development* 2010;33:510–7.
49 Brazelton Institute. NBO/nbas training. Boston Children’s Hospital. 2024 Available: https://www.childrenshospital.org/research/centers/brazelton-institute-research/training#nbasSep12
50 Loo KK, Zhu H, Yin Q, *et al*. Maternal confidence in China: association with infant neurobehaviors but not sociodemographic variables. *J Pediatr Psychol* 2006;31:452–9.

51 Brazelton TB. *Neonatal behavioral assessment scale*. London and Philadelphia: Spastics International Medical Publications, 1973.
52 Campbell SK, Osten ET, Kolobe THA, *et al*. Development of the Test of Infant Motor Performance. *Phys Med Rehabil Clin N Am* 1993;4:541–50.
53 Campbell SK. Functional movement assessment with the Test of Infant Motor Performance. *J Perinatol* 2021;41:2385–94.
54 Learn the tests. Available: https://www.thetimp.com/learn-the-tests [Accessed 9 Sep 2024].
55 Gower L, Jenkins D, Fraser JL, *et al*. Early developmental assessment with a short screening test, the STEP, predicts one-year outcomes. *J Perinatol* 2019;39:184–92.
56 Campbell SK, Swanlund A, Smith E, *et al*. Validity of the TIMPSI for estimating concurrent performance on the test of infant motor performance. *Pediatr Phys Ther* 2008;20:3–10.
57 Campbell SK, Kolobe THA, Wright BD, *et al*. Validity of the Test of Infant Motor Performance for prediction of 6-, 9- and 12-month scores on the Alberta Infant Motor Scale. *Dev Med Child Neurol* 2002;44:263–72.
58 Peyton C, Schreiber MD, Msall ME. The Test of Infant Motor Performance at 3 months predicts language, cognitive, and motor outcomes in infants born preterm at 2 years of age. *Develop Med Child Neuro* 2018;60:1239–43.
59 Prechtl HFR. The Neurological Examination of the Full-Term Newborn Infant: A Manual for Clinical Use from the Department of Developmental Neurology; Cambridge University Press; 1991.
60 Maas YGH, Mirmiran M, Hart AAM, *et al*. Predictive value of neonatal neurological tests for developmental outcome of preterm infants. *J Pediatr* 2000;137:100–6.
61 Gosselin J, Gahagan S, Amiel-Tison C. The Amiel-Tison Neurological Assessment at Term: conceptual and methodological continuity in the course of follow-up. *Ment Retard Dev Disabil Res Rev* 2005;11:34–51.
62 Amiel-Tison C, Barrier G, Shnider SM, *et al*. A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. *Anesthesiology* 1982;56:340–50.
63 Amiel-Tison C. Update of the Amiel-Tison neurologic assessment for the term neonate or at 40 weeks corrected age. *Pediatr Neurol* 2002;27:196–212.
64 Paro-Panjan D, Neubauer D, Kodrie J, *et al*. Amiel-Tison Neurological Assessment at term age: clinical application, correlation with other methods, and outcome at 12 to 15 months. *Developmental Medicine & Child Neurology* 2005;47:19–26.
65 Bao XL, Yu RJ, Li ZS, *et al*. Twenty-item behavioral neurological assessment for normal newborns in 12 cities of China. *Chin Med J (Engl)* 1991;104:742–6.
66 Bao XL, Yu RJ, Li ZS. 20-item neonatal behavioral neurological assessment used in predicting prognosis of asphyxiated newborn. *Chin Med J (Engl)* 1993;106:211–5.
67 Agho AO, John EB. Occupational therapy and physiotherapy education and workforce in Anglophone sub-Saharan Africa countries. *Hum Resour Health* 2017;15:37.
68 Hägglund G, Andersson S, Düppe H, *et al*. Prevention of dislocation of the hip in children with cerebral palsy. The first ten years of a population-based prevention programme. *J Bone Joint Surg Br* 2005;87:95–101.
69 Rostami HR, Malamiri RA. Effect of treatment environment on modified constraint-induced movement therapy results in children with spastic hemiplegic cerebral palsy: a randomized controlled trial. *Disabil Rehabil* 2012;34:40–4.
70 Nanyunja C, Sadoo S, Kohli-Lynch M, *et al*. Early care and support for young children with developmental disabilities and their caregivers in Uganda: The Baby Ubuntu feasibility trial. *Front Pediatr* 2022;10:981976.
71 Lopez Garcia I, Saya UY, Luoto JE. Cost-effectiveness and economic returns of group-based parenting interventions to promote early childhood development: Results from a randomized controlled trial in rural Kenya. *PLoS Med* 2021;18:e1003746.
72 Garcia IL, Luoto J, Aboud F, *et al*. In-person versus remote (mHealth) delivery for a responsive parenting intervention in rural Kenya: a cluster randomized controlled trial. *BMC Public Health* 2024;24:2421.
73 Palmer T, Clare A, Fearon P, *et al*. Cost-effectiveness of a radio intervention to stimulate early childhood development: protocol for an economic evaluation of the SUNRISE trial in Burkina Faso. *BMJ Open* 2024;14:e080905.