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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Title: Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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ABSTRACT

Objective: To identify and report the screening tools used for early identification of developmental delay in Low-and Middle-Income Countries.

Design: Systematic review

Data sources: Four bibliographic databases: Medline (1946 - Week 4 February 2018), Embase (1974 - 06 March 2018), Scopus (1823 - March 2018), and PsycINFO (1987 to April Week 4 2019) were searched using standard methods.

Eligibility criteria: Peer-reviewed original articles published in English addressing validated culturally sensitive developmental screening tools among children aged < 5 years were included in this review.

Data extraction and synthesis: Two authors performed the full-text reviews and extraction of data. PRISMA statement was used to guide the systematic review. Methodological quality was assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies-2 and Newcastle-Ottawa Scale for cross-sectional studies. Data extraction and analysis were performed using MS Excel. Meta-analysis was not possible due to the heterogeneity of the study setting and findings.

Results: We identified 2707 articles, of which thirteen studies from seven countries, reporting twelve screening tools, were selected for qualitative synthesis. Two cultural contexts were explored; Asian (5 countries) and African (2 countries). Study sites included tertiary hospital, primary healthcare centre, nursery and community. Nine general screening tools, two motor tools and one speech and language tool were identified. Half of them found

to be parent-completed ones. Five screening tools (Ages and Stages Questionnaire-2, Infant Neurological International Battery, Language Evaluation Scale Trivandrum, Lucknow Development Screen 0-3, and New Delhi – Development Screening Questionnaire) reported relatively higher sensitivity (83.3%-100%) and specificity (73.1%-88.7%).

Conclusions: Limited number of culturally sensitive developmental screening tools were validated for children aged <5 year in Low-and Middle-Income Countries. Revising existing screening tools in different ethnic and cultural settings and subsequent validation with normative value should be a research priority.

PROSPERO registration number CRD42018095232

Key words: Developmental delay, Disability, Screening, Early diagnosis, Rehabilitation, Low and Middle-Income Countries

Strengths and limitations of this study

- This review puts together extensive literature searches on original studies conducted among under-5 children from LMICs reporting validity of developmental screening tools in early diagnosis of developmental delay.
- Meta-analysis was not possible due to the heterogeneity of the study setting and findings.
- Critical evaluation of the available screening tools in terms of diagnostic accuracy was not possible to perform due to the unavailability of the necessary information.

INTRODUCTION

Developmental delay is a condition where children exhibit significant variation in achieving developmental milestones as expected for their actual or adjusted age.[1-3] Complications at birth including premature birth; brain trauma and encephalitis; severe medical problems after birth; inborn metabolic errors; genetic or chromosomal abnormalities; inadequate stimulation; malnutrition; iron deficiency anaemia; chronic illness; adverse environmental, familiar and psychological states may lead to developmental delay.[4-6] Although the condition itself may not be permanent, it can provide a foundation for recognizing children who might have more severe and permanent health conditions i.e. developmental disabilities. Apart from developmental delay, developmental disability is considered as a severe, chronic disability originating at birth or during childhood, expected to continue indefinitely, and substantially restricts the individual's functioning in several major life activities.[2, 7] Examples of developmental disabilities include autism spectrum disorder, behavioural disorders, cerebral palsy, down syndrome, foetal alcohol syndrome, intellectual disability, etc. As a predictive of above-mentioned learning, movement and behavioural disorders, the developmental delay can be easily identified during the preschool period (i.e. before the age of 5 years).[8] There is a long-term financial impact on society in terms of healthcare, educational support and other special services related to developmental delay and/ disability. This is because the affected children require substantial resources and increased cost over their lifespan compared to those without such conditions.[9] This further accentuates the significance of early identification to initiate appropriate interventions and/ rehabilitations with the intention of preventing further delays, stimulating emerging skills and creating a more encouraging and protective surroundings.[5]

In the last few decades, successful implementation of World Health Organization's (WHO's) key health services[10] regarding "The Countdown to 2015 Initiatives" resulted in

the reduction of the neonatal mortality rate from 37 deaths per 1000 live births in 1990 to 19 per 1000 live births in 2016, worldwide with a projection of further future reductions.[11, 12] Among the survivors, more than 250 million under-5 children from Low-and Middle-Income Countries (LMICs) are not fulfilling their developmental potential in cognitive, motor, and social-emotional domains due to poor nutrition, poverty and conflicts.[4, 13, 14] In addition to them, there is an undetected number of surviving children suffering from various forms of developmental delay presumably due to brain injury during the foetal, perinatal and post-neonatal period.[15] Nation-wide population-based retrospective studies conducted in Taiwan discovered that, with time, while the neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing (as shown in Fig. 1).[16, 17]

In LMICs, parents and caregivers with strong cultural beliefs regarding health not only remain ignorant of the child's developmental deficit but also about the future impact of the condition.[18] The perspective on developmental disability varies from one culture to another. Along with economic, geographical, social factors, it often becomes a barrier to healthcare accessibility for children with disability.[19] In Chinese culture, having children with disability is often considered shameful for the family. In Southeast Asian cultures, parents often face social deprivation due to the stigma related to developmental disability.[20] Moreover, cultural believe often holds control over treatment approaches for developmental delay or disabilities, including: (1) whether to seek help or not; (2) which treatment option to choose; (3) parental expectations for their child; (4) interpersonal relationship between caregiver and healthcare professionals, etc.[21] One of the biggest challenges in early identification of developmental delay or disability is providing culturally sensitive screening tools, which not only include cultural perception of delay and/or disability but also easily adaptable across the various cultural/ nation.[22] Among the developmental

domains, social development is culturally specific and difficult to adapt, whereas the gross motor domain is easier to adapt culturally.[23]

Developmental screening is the first step of the comprehensive diagnostic procedure for secondary prevention and early identification of developmental delay.[24-26] A validated developmental screening tool is thus very important. The standardized tools available from western countries provide well-validated assessment in their own settings. However, the transfer of such western-based tools to non-western countries is linked with substantial limitations in terms of score interpretation and feasibility of their use in resource-constrained settings such as in LMICs.[22] In the developed countries, early identification of developmental delay is considered as mandatory part of good healthcare practice which is recommended by the American Academy of Paediatrics.[25] Benefits of early identification developmental delay are as follows: (1) augmenting child's future cognitive, motor, and social development while the nervous system is still pliable and receptive; (2) leading to definite diagnosis and effective therapy for conditions where definitive treatment is available; (3) improving overall outcome of the child for conditions that cannot be reversed; (4) reducing long term disability; (5) improving quality of life of the child; (6) enabling families to be resourceful for successful functioning; and (7) reducing the social cost.[9, 25, 27–29] In contrast, in LMICs, most teaching and training programs of health professionals are still concentrated on acute illness and growth aspects of children rather than a developmental perspective, resulting in limited attention in developmental delay.[25] Also, in these geographical areas, strong cultural beliefs and superstitions regarding child healthcare and development may be present among parents. The combined effect of these two factors often results in overlooking or delayed the diagnosis of developmental concerns.

The purpose of this study was to look for the screening tools which have been used and validated for early identification of developmental delay in LMICs, to report how effective they are for early identification of developmental delay in terms of validity, and to identify areas for future research.

METHODS

Data sources and search strategy

To locate items on screening tools for early identification of developmental delay among children in low and middle-income countries, literature searches were undertaken by an experienced medical librarian (Dr. Catherine King) in four bibliographic databases. The databases searched were: OVID Medline (1946 - Week 4 February 2018), OVID Embase (1974 - 06 March 2018), SCOPUS (1823 - March 2018), and PsycINFO (1987 to April Week 4 2019). Search terms included database-specific thesaurus terms where available such as 'Mass Screening', 'Diagnosis', 'Surveys and Questionnaires', 'Neurodevelopmental Disorders', 'Motor Disorders', 'Cerebral Palsy', 'Cognitive Dysfunction', and 'Communication Disorders' as well as relevant associated text word terms. These were combined with low and middle-income country terms and infant, child and adolescent terms. To minimize the introduction of bias, no publication date and language limits were used. The date of the latest search was 03.05.19. The Medline search strategy could be found online as Supplementary Table S1.

In addition to bibliographic database searches, we manually checked the reference lists of articles included in the full-text review. We also contacted experts in the field to identify any additional studies or information.

Selection criteria

Study inclusion criteria were: (1) Children aged less than 5 years who were at risk of developmental delay; (2) Original studies (both observational and experimental); (3) Study where single, as well as multiple developmental domains, were examined; (4) Studies conducted only in LMICs. The exclusion criteria were: (1) Studies conducted on diagnosed cases of developmental delay; (2) Studies focusing on autism spectrum disorder and other behavioural disorders; (3) Studies conducted among HIV exposed children; (4) Studies on developmental delay among children aged more than 5 years; (5) Interventional studies on developmental delay; (6) Studies on developmental delay published before 1946; (7) Article published in languages other than English; (8) Conference papers, letter to the editor, protocols, systematic reviews and ongoing studies; (9) Study conducted among children of eligible ethnic origin but in different country settings (i.e. children adopted from LMICs but study conducted in higher income countries).

LMICs consist of countries belonging to three World Bank income groups (low, lower-middle, upper-middle, and high) of WHO's Member States. The classification is based on the estimated per capita gross national income. We have used the World Bank's country classifications by income level (2018-2019) in this review.[30, 31]

Study selection, data extraction and quality appraisal

We carried out the following steps to decide on the studies: (1) Searching the above-mentioned databases using similar search strategy; (2) Deduplication and merging search results using the EndNote bibliographic software; (3) Examining titles and abstracts to remove obviously irrelevant reports; (4) Retrieving and examining the full text reports of eligible studies; (5) Making final decisions on study inclusion and proceeding for data collection. Extracted information included: publication year, the country where the study was

conducted, the name of the screening tool, the reference standard tool(s) against which the screening tool was validated, study design, study setting, sample size, sampling technique, the age of the participants, selection criteria and sensitivity-specificity of the screening tools. Disagreements have been resolved through discussion. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, including 27- item PRISMA checklist to guide the systematic review.[32] The quality of the selected studies was assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies-2[33] (Supplementary Table S2) and Newcastle-Ottawa Scale for cross-sectional studies[34] (Supplementary Table S3).

Data analysis

Individual study findings were reported including the country, study design, study setting, sample size, sampling technique, proportions and age range of participants, sensitivity-specificity of the developmental screening tools etc. Data extraction and analysis were performed using MS Excel. We were unable to perform a meta-analysis due to the heterogeneity of the study setting and findings.

Patient and Public Involvement

No patient involved.

Protocol registration and ethical approval

The protocol of this systematic review has been registered in PROSPERO (registration number CRD42018095232). As this systematic review did not directly involve human or animal subjects, or access to medical records; ethical approval was not required.

RESULTS

Search results

The initial search retrieved 2707 records. We have found 2698 records from four bibliographic databases (1313 from OVID Medline, 1012 from OVID Embase, 287 from Scopus and 86 from PsycINFO). Nine records were located by reviewing the reference lists of fully extracted articles and consulting expert researchers in this area. There were 2211 unique records once duplicates were removed. Following the screening of title and abstracts for articles, which described the validation of tools to screen out developmentally delayed children, 41 articles were selected for further evaluation. After further review, 13 articles were selected for inclusion in study.[35-47] A PRISMA flow diagram has been prepared to illustrate the study selection process (as shown in Fig. 2).

Summary of the included studies

All of the thirteen studies included for qualitative synthesis were original articles published in English, with a publication date range from 1997 to 2017 inclusive. Six studies originated in "South Asia",[35, 36, 42-44, 47] three studies from "East Asia and Pacific",[39-41] three studies from "Sub-Saharan Africa",[38, 45, 46] one study from the "Middle East and North Africa"[37] region of the World Bank. No eligible studies were found from the "Latin America and Caribbean", or "Europe and Central Asia" region. In total, twelve developmental screening tools were used in seven countries. Among the twelve screening tools, Language Evaluation Scale Trivandrum for 0-3 years LEST (LEST 0-3) focuses on language domain; Infant Neurological International Battery (INFANIB) and Little Developmental Coordination Disorder Questionnaire (Little DCDQ) work on motor domains. The remaining tools are general developmental screening tools. A brief description of the selected screening tools is provided in Table 1.

Table 1: Brief description of the selected screening tools

	Ages and Stages Questionnaire (ASQ)	Development Screening Questionnaire (DSQ)	Infant Neurological International Battery (INFANIB)	Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Lucknow Developmental Screen (LDS)	Mongolian Rapid Baby Scale (MORBAS)	New Delhi – Development Screening Questionnaire (ND-DSQ)	Parent Evaluation of Developmental Status (PEDS)	Rapid Prescreening Denver Questionnaire (R-PDQ)	Road to Health Booklet Developmental Checklist (RTHB-DC)	Ten Questions (TQ)
Country of Origin	USA	Bangladesh	USA	India	Canada	India	Mongolia	India	USA	USA	South Africa	Multiple
Study Country	India	Bangladesh	Iran	India	South Africa	India	Mongolia	India	Thailand	India	South Africa	Benin
Concerned Age	1–66 months	birth to 24 months	0 to 18 months	0 to 3 years	3-5 years	birth to 24 months	0 to 42 months	9 to 18 months	birth to 8 years	0-6 years	14 weeks to 6 years	2 to 9 years
Parent-Reported Version	Yes	No	No	No	Yes	Yes	No	Yes	Yes	No	No	Yes
Questionnaire Type	Q & A	Q & A	Not found	Chart	Q & A	Chart	Written	Q & A	Q & A	Q & A	Checklist	Q & A
Number of Questionnaires	21 age sets	24 age sets	Single	Single	Single	Single	Single	2 age sets	Single	4 age sets	Single	Single
Number of items	30 items	8 questions per set	20-items	33 items	15 items	27 item	161 item	20 items	10 items	25 items	21 items	10 items
Developmental Domain	Communication, gross motor, fine motor, problem solving, personal-social	Gross motor, fine motor, vision; hearing, cognition, socialization, behaviour, and speech	Gross motor	Speech and language	Gross motor, fine motor	Motor, mental, language, social	Cognitive, receptive communication, expressive communication, fine motor, gross motor, social-emotional, adaptive behavior	General screening tool (domains not explicitly mentioned)	Global /cognitive, speech / expressive language, receptive language, behaviour, social-emotional, school, self-help, fine motor, gross motor, other	Gross motor, fine motor activity, personal-social, language	Gross motor, fine motor, communication, vision, hearing	Vision, hearing, seizure, cognition, motor

Participant characteristics

All the studies involved males and females, age range 0 to 5 years. The smallest sample size was 53 and the largest was 643. The studies explored the following cultural contexts: Asian (Bangladesh, India, Iran, Mongolia, and Thailand) and African (Benin, South Africa). Selection criteria used for participation in those studies are stated in Table 2.

Table 2: Selection criteria used for participation in the studies

Ref.	[35]	[36]	[37]	[38]	[39]	[40]	[41]	[42]	[43]	[44]	[45]	[46]	[47]
Selection Criteria	**Inclusion Criteria** Children living in the study area	**Inclusion Criteria** Children attending the study hospital	**Inclusion Criteria** Children living in the study area	**Inclusion Criteria** Afrikaans, Tswana or English speaking parents or guardian	**Inclusion Criteria** Parents willing to participate	**Inclusion Criteria** Children attending the study hospital	**Inclusion Criteria** Children with apparently normal development	**Inclusion Criteria** Parents completed primary education Parents able to read Hindi Parents living with the child	**Inclusion Criteria** Children attending the study hospital	**Inclusion Criteria** Children living in the study area	**Inclusion Criteria** Children born to mothers enrolled in "Malaria in Pregnancy Preventive Alternative Drugs" trial	**Inclusion Criteria** Afrikaans or English speaking parents Parents visiting the primary health care clinics Parents asked to participate	**Inclusion Criteria** Children whose parents/ primary caregiver gave consent
	Exclusion Criteria Children whose parents did not give consent to participate	**Exclusion Criteria** Children with acute illness Children not accompanied by parents Children whose parents did not give consent to participate	**Exclusion Criteria** Not applicable	**Exclusion Criteria** Children suspected or diagnosed with mental retardation, autism or neuromotor delay	**Exclusion Criteria** Chronically ill children Previous diagnosis of developmental delay	**Exclusion Criteria** Premature children Previous diagnosis of developmental delay Children with a visual/hearing problem The accompanying parent does not understand the Thai language	**Exclusion Criteria** Children with acute and chronic disease Children not accompanied by a caregiver Children with illiterate caregiver	**Exclusion Criteria** Premature children Children with acute severe illness Previous diagnosis of developmental disorder	**Exclusion Criteria** Children without a proper birth record Children not accompanied by a caregiver at the time of evaluation	**Exclusion Criteria** Not applicable	**Exclusion Criteria** Non-singleton births	**Exclusion Criteria** Not applicable	**Exclusion Criteria** Ill children Children uncooperative for testing

Study characteristics

All the included studies were cross-sectional in nature. Among the thirteen studies, seven were conducted in the tertiary hospital,[36, 37, 39-43] two were conducted in the community,[35, 47] and one study each was conducted in a nursery school setting[38] and primary health care clinic setting.[46] In the remaining two studies, screening was done in the community followed by a hospital-based detailed assessment in one[44] and primary health care clinic-based assessment in another.[45]

Validated screening tools

The Ages and Stages Questionnaire (ASQ)

This is a parent-completed questionnaire that could be used as a general developmental screening tool. The ASQ was designed and developed by J. Squires and D. Bricker, at the University of Oregon and can be completed in 12-18 minutes.[48] The questionnaire has 30 items focusing on five domains of child development, named gross motor, fine motor, problem-solving, communication, and personal-social. Obtaining lower scores than the cut off in any domain is considered as "screen positive". The latest version of ASQ, ASQ-3, has 21 sets of questionnaires, appropriate for children aged 1–66 months.[49] In the study by Juneja et al., 2012; a Hindi adaptation of an older version of ASQ, (ASQ-2, which had 19 sets of questionnaires for 4 to 60 months aged children) was used in a convenience sample of 200 children divided into 4 age groups: 4, 10, 18 and 24 months, in a tertiary hospital setting.[43] Each age group consisted of 30 low risk and 20 high-risk children. High-risk status was determined by the presence of any of the following risk factors: prematurity, low birth weight, history of neonatal hospitalization, history of central nervous system infection, history of afebrile seizure, diagnosed cases of developmental disorder and chromosomal abnormalities. Children without these risk factors were treated as being in the low-risk group. Eventually, 4, 10, 18 and 24 months questionnaires of ASQ-2 were validated against

"Developmental Assessment Scales for Indian Infants (DASII)", considered as a reference standard for developmental assessment tool among Indian children.[43] The overall sensitivity and specificity of ASQ-2 for Indian children were found to be 83.3% and 75.4% respectively.

Development Screening Questionnaire (DSQ)

The DSQ was designed and developed in Bangladesh, to be administered to mothers of children from birth to 24 months of age to screen their child's neurodevelopmental status. The DSQ has 24 age sets with 8 questions per set related to eight functional domains, named: gross motor, fine motor, vision; hearing, cognition, socialization, behaviour and speech.[44] Any child found to be positive on one or more functional domain is considered "screen positive". In a study conducted in urban Bangladesh, a random sample of 197 children aged 0-24 months was screened in the community with DSQ, and then a detailed developmental assessment was done in a tertiary hospital with the help of the "Rapid Neurodevelopmental Assessment" tool as the reference standard. Overall sensitivity and specificity of DSQ for under 2-year-old Bangladeshi children was found to be 47.1% and 97.2% respectively.[44] Despite moderate sensitivity, the DSQ might be advantageous for resource-poor settings due to its high specificity.

Infant Neurological International Battery (INFANIB)

The INFANIB was established by Ellison and Browning in 1985 to assess the gross motor function of children aged 0 to 18 months. The tool contains 20-items focusing on spasticity, vestibular function, head and trunk, French angles and legs.[50] In the study by Soleimani and Dadkhah, 2006; a consecutive sample of 6150 children were screened using INFANIB and classified as normal, transiently abnormal and abnormal. To validate the tool a random sample of 153 children from the above-mentioned groups were assessed by paediatric

neurologists. It was found that overall sensitivity and specificity of INFANIB for Iranian children were 90% and 83% respectively.[37]

Language Evaluation Scale Trivandrum (LEST 0-3)

Designed and developed at the Child Development Centre of the Trivandrum Government Medical College, India, LEST (0-3) is a 33 items screening tool to screen out language delay among 0 to 3 years old children.[47] The LEST (0-3) was validated against the "Receptive-Expressive Emergent Language Scale" tool as a reference standard in a community sample of 643 Indian children aged 0 to 36 months. To decide on the best possible combination, researchers considered both "one item delay" and "two items delay" as screen positive. When one item delay considered as screen positive, sensitivity and specificity of LEST (0-3) found to be 95.8% and 77.5% respectively. Similarly, when two items delay measured as screen positive, the sensitivity and specificity obtained as 66.7% and 94.8% respectively.[47] It should be noted that the original version of Receptive-Expressive Emergent Language Scale (1971) was used in this study for validation due to the lack of age-appropriate language assessment tool for language delay.

Little Developmental Coordination Disorder Questionnaire (Little DCDQ)

The Little DCDQ was developed by Rithman and colleagues in Canada to assess gross motor and fine motor function of children between 3 to 5 years of age. It is a parent-reported questionnaire with 15 items under three main components, control during execution, fine motor execution and overall coordination.[38] The Little DCDQ was validated against the Movement Assessment Battery for Children-2 as a reference standard in a group of 53 South African pre-schoolers between 3 to 5 years of age, with Afrikaans, Tswana or English speaking parents.[38] With 57.14% sensitivity and 81.25% specificity, Little DCDQ had the potential to be used in South African culture, however, some adjustments would be required.

Lucknow Development Screen (LDS)

The LDS was developed in CSM Medical University, Lucknow, India, using selected milestones from Baroda Development Screening Test. It is a 27 items chart format tool, covering four domains namely motor, mental, language and social. Suitable for children aged 0 to 24 months. The LDS is said to be easily administrable by interviewing parents or caregiver.[36] In a study conducted in India, the LDS tool was validated against the DASII and the Vineland Social Maturity Scale. They administered the tool to mothers of a sample of 142 children, aged between 6 to 24 months, attending Paediatric Outpatients or Neurology Clinic of CSM Medical University, Lucknow, India. The screening tool was translated into Hindi for easy understanding and administration. For 3 children among the sample size of 142, Vineland Social Maturity scale was used as a reference standard, as DASII couldn't be applied to them. It is claimed that the LDS has a great potential to be used as a community screening tool among Indian children, with an overall sensitivity of 95.9% and specificity 73.1%.[36]

Mongolian Rapid Baby Scale (MORBAS)

The MORBAS is a written developmental screening test, designed and developed in Mongolia. It has 161 items arranged under seven developmental domains, namely gross motor, fine motor, cognitive, expressive language, receptive language, social-emotional and adaptive behaviour. The tool is suitable for children aged 0 to 42 months.[41] In a study conducted in Mongolia, MORBAS was administered in a convenience sample of 150 Mongolian children aged 0 to 42 months and thus validated against the Bayley Scales of Infant and Toddler Development-III. With sensitivity 81.8% and specificity 52.3%,[41] MORBAS could be useful in the long run to screen out children for early intervention and rehabilitation.

New Delhi – Development Screening Questionnaire (ND-DSQ)

The ND-DSQ was developed by Jain and colleagues, at Chacha Nehru Bal Chikitsalaya, a tertiary hospital of northern India. ND-DSQ has 20 items, two age sets (9 months and 18 months) and applicable for children aged 9 to 18 months.[42] The items mentioned were milestone specific. Thus, no explicit mention of the developmental domains was found. In the study by Jain et al., 2017; ND-DSQ was validated against DASII in a convenience sample of 200 children aged 9 and 18 months (with 100 children per age group). It was established that the 9-month questionnaire was 100% sensitive and 87.2% specific for Indian children. Correspondingly, the 18 months questionnaire was validated with 91.4% sensitivity and 88.7% specificity.[42] As a newly developed tool, the ND-DSQ is promising to be useful for Indian and similar cultural settings.

Parent Evaluation of Developmental Status (PEDS)

This tool was developed in 1997 by F. P. Glascoe at Tennessee, USA.51 It is the only screening tool available to date that addresses parent's concern about children's development in the following domains: gross motor, fine motor, cognitive, expressive language, receptive language, behaviour, social-emotional, self-help, school and other.[52] It has ten open-ended questions under ten areas of parental concerns, applicable for children aged 0 to 8 years. The other category allows parents to express concerns not already addressed under previous categories. This unique property makes PEDS unique as a developmental screening tool. In PEDS, parental concerns are labelled as "predictive" (significant) and "non-predictive" (non-significant). Thus, children are screened as low risk, moderate risk and high-risk group if they have no or non-predictive concerns, one predictive concern and two predictive concerns, respectively.[40]

In the study by Chunusuwan et al., 2016; the PEDS- Thai was validated against the "Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level" in a tertiary hospital. A convenience sample of 266 children of 9, 18 and 30 months of age was selected. Screen positive children were assembled as "high risk" (≥ 2 significant concerns) and "moderate or high risk" (≥ 1 significant concern) group. Sensitivity and specificity of PEDS against Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level for the high-risk group was established as 27.7% and 93.0%, respectively. For moderate or high-risk group, the tool was 67.7% sensitive and 60.7% specific.[40] In order to avoid unnecessary/over-referral, the authors suggested to practice second stage evaluation (using Parent Evaluation of Developmental Status: Developmental Milestones, ASQ, Denver-II etc. tools) alongside/after PEDS screening.

In another study by Wantanakorn et al., 2016; they validated the PEDS- Thai against the Mullen Scales of Early Learning tool as a reference standard in a convenience sample of 137 children aged 18 to 36 months in another tertiary hospital. It was found that the PEDS-Thai is a promising tool for Thai cultural backgrounds with overall sensitivity of 92.8% and specificity 49.2%.[39] According to the authors, "the relatively low specificity of PEDS seen here may be because of the excessive concern of parents regarding their child's development, especially who are in relatively high socioeconomic status". The selection bias of participants was mentioned as the major limitation of the study. Thus, they advised further evaluation of the diagnostic performances of the tool using a representative sample of the population.

Rapid Pre-screening Denver Questionnaire (R-PDQ)

The R-PDQ is a general developmental screening tool covering four developmental domains: gross motor, fine motor activity, personal-social and language.[35] It has four age sets applicable for children aged 0 to 6 years: 0 to 9 months, 9 to 24 months, 2 to 4 years and 4 to

6 years. Each questionnaire contained 25 items. To score a child, the responding person had to keep answering the questions until there were three negative responses under a specific domain. In the study by Awasthi et al., 1997; the 2 to 4 years questionnaire of R-PDQ was validated against the Denver Developmental Screening Test. The study participants were randomly selected 126 children living in urban slums of Lucknow, India. To validate the tool, when a delay in more than one domain was considered as the cut-off, the tool was revealed to be 100% sensitive and 7.8% specific. Similarly, when a delay in more than two domains was considered as the cut-off, the sensitivity and specificity were found to be 18.2% and 42.6%, respectively.[35] Inconvenient validity and high referral rate compared to US children were explained by the presence of various "difficult to interpret" questions and Denver Developmental Screening Test being an unsuitable reference standard for R-PDQ.

Road to Health Booklet Developmental Checklist (RTHB-DC)

The RTHB-DC was prepared as an integrated part of The Road to Health Booklet, the revised version of which was introduced in October 2010. RTHB-DC is the only developmental surveillance and screening tool, currently implemented nationally in South Africa. The tool consists of 21 questions covering gross motor, fine motor, communication, vision, and hearing domains. The checklist is applicable for children aged 14 weeks to 6 years.[53] In the study by Linde et al., 2015; RTHB-DC was validated against PEDS and Parent Evaluation of Developmental Status: Developmental Milestones tools. The sample size was 201, consisting of children aged 6 to 12 months old. In a primary health care clinic setting in South Africa, the sensitivity of the tool was found to be very low, i.e. 25% compared to reasonably high specificity of 91%.[46] Further development of the tool has been suggested by the authors incorporating consistent age gaps and inclusion of all developmental domains.

Ten Questions (TQ)

The TQ Screening Instrument was developed in 1984 as part of a pilot study conducted by the University of Columbia, USA, for use in resource-poor countries.[54, 55] TQ is a parent reported tool comprising of ten questions addressing motor, cognitive, vision, hearing, and seizure status. A child is considered screen positive if any of the questions are found to be positive. The tool is appropriate for children aged 2 to 9 years. In a study by Koura et al., 2013; the TQ was validated against the Mullen Scales of Early Learning in a sample of 357 children aged 12 months.[45] The participants were the offspring of the mothers who were enrolled in the "Malaria in Pregnancy Preventive Alternative Drugs" trial. To adjust the tool for that age group, researchers had excluded the language domain which is applicable for children above 2 years. In that study, screening was done in the community followed by a detailed assessment done in the health centre. It was found that the overall tool had reasonably high sensitivity (81%) but poor specificity (31%) for children of Benin. This is compared to the 76.5% sensitivity and 75.7% specificity where only the motor domain was considered.[45] Mullen Scales of Early Learning was used due to lack of a reference standard assessment tool for the Beninese population. The result suggests that the TQ tool might be useful for resource-poor settings to screen out moderate to severe delay in motor function.

The major findings of this systematic review are presented in Table 3.

Table 3: Major findings from the selected studies used in this review

General Screening Tools							
Ref.	**Country**	**Screening Tool**	**Reference Standard**	**Study**	**Participants**	**Key Findings**	
Suitable for non-medical settings							
[35]	**India** Lower-Middle- Income	Revised Prescreening Denver Questionnaire (R-PDQ)	Denver Developmental Screening Test	**Design** Cross-Sectional **Setting** Community	**Sample** - 126 **Age** – 2-4 years **Cluster random sample**	Delay in ≥ 1 domain	Sensitivity 100% Specificity 7.8%
						Delay in ≥ 2 domains	Sensitivity 18.2% Specificity 42.6%
[44]	**Bangladesh** Lower-Middle- Income	Development Screening Questionnaire (DSQ)	Rapid Neurodevelopmental Assessment	**Design** Cross-Sectional **Setting** Screening- Household Assessment- Hospital	**Sample** – 197 **Age** - 0-2 years **Random sample**	Overall	Sensitivity 47.1% Specificity 97.2%
[45]	**Benin** Low-Income	Ten Questions (TQ)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting** Screening- Household Assessment- Health Centre	**Sample** - 357 **Age** – 12 months **Random sample**	Motor	Sensitivity 76.5% Specificity 75.7%
						Overall	Sensitivity 81% Specificity 31%
Suitable for primary care							
[46]	**South Africa** Upper-Middle- Income	Road to Health Booklet Developmental Checklist (RTHB-DC)	Parent Evaluation of Developmental Status (PEDS) Parent Evaluation of Developmental Status: Developmental Milestones	**Design** Comparative Cross-sectional within-subject **Setting** PHC clinics	**Sample** - 201 **Age** – 6-12 months **Convenience sample**	Overall	Sensitivity 25% Specificity 91%
Suitable for a tertiary hospital							
[36]	**India** Lower-Middle- Income	Lucknow Development Screen (LDS)	Developmental Assessment Scales for Indian Infants (DASII) Vineland Social Maturity Scale	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 142 **Age** - 6-24 months **Convenience sample**	Overall	Sensitivity 95.9% Specificity 73.1%
[39]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS- Thai)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 137 **Age** – 18-30 months **Convenience sample**	Overall	Sensitivity 92.8% Specificity 49.2%
[40]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS)	Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 266 **Age** – 9, 18 and 30 months	≥ 1 significant concern	Sensitivity 67.7% Specificity 60.7%
						≥ 2 significant	Sensitivity 27.7%

					Convenience sample	concerns	Specificity 93.0%
[41]	**Mongolia** Lower-Middle- Income	Mongolian Rapid Baby Scale (MORBAS)	Bayley Scales of Infant and Toddler Development-III	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 150 **Age** – 0 month 16 days – 42 months 15 days **Convenience sample**	Overall	Sensitivity 81.8% Specificity 52.3%
[42]	**India** Lower-Middle- Income	New Delhi – Development Screening Questionnaire (ND-DSQ)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 9 and 18 months **Convenience sample**	9-months	Sensitivity 100% Specificity 87.2%
						18-months	Sensitivity 91.4% Specificity 88.7%
[43]	**India** Lower-Middle- Income	Ages and Stages Questionnaire (ASQ-II)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 4, 10, 18 and 24 months **Convenience sample**	Overall	Sensitivity 83.3% Specificity 75.4%
Motor Screening Tools							
Ref.	**Country**	**Screening Tool**	**Reference Standard**	**Study**	**Participants**	**Key Findings**	
Suitable for non-medical settings							
[38]	**South Africa** Upper-Middle- Income	Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Movement Assessment Battery for Children -2	**Design –** Cross-sectional **Setting** – nursery schools	**Sample** – 53 **Age** – 3-5 years **Convenience sample**	Overall	Sensitivity 57.14% Specificity 81.25%
Suitable for tertiary hospital							
[37]	**Iran** Upper-Middle- Income	Infant Neurological International Battery (INFANIB)	Developmental Assessment by Pediatric Neurologist	**Design** – Cross-Sectional **Setting** Hospital	**Sample** – 153 **Age** – 4-18 months **Random sample**	Overall	Sensitivity 90% Specificity 83%
Language Screening Tool							
Ref.	**Country**	**Screening Tool**	**Reference Standard**	**Study**	**Participants**	**Key Findings**	
Suitable for non-medical settings							
[47]	**India** Lower-Middle- Income	Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	Receptive Expressive Emergent Language Scale	**Design** Cross-Sectional **Setting** - Community	**Sample** – 643 **Age** – 0-3 years **Cluster random sample**	One item delay	Sensitivity 95.8% Specificity 77.5%
						Two item delay	Sensitivity 66.7% Specificity 94.8%

DISCUSSION

To the best of our knowledge, this is the first systematic review which attempts to find the available screening tools for early identification of children with developmental delay in LMICs. Although some systematic reviews were found who considered developmental assessment tools requiring professional experts with a special office setup,[56] screening neurodevelopmental disability irrespective of age limit and diagnosis (e.g. developmental delay, global developmental delay, cerebral palsy, autism spectrum disorder, attention deficit hyperactivity disorder, epilepsy, etc.),[57] or reflected high-income country context.[8] We have also observed a study in which both screening and assessment tools have been systematically rated for accuracy and feasibility to use in LMICs.[58] Where, information was significantly dependent to World Bank's toolkit and inventory on early child development tools,[59] rather than being obtained from systematic search through databases. In contrast, the purpose of this review was to systematically look for the available studies where screening tools were used exclusively for early identification (limited to children under 5 years of age) of developmental delay in the LMICs region where all types of study settings (i.e. from household to health facilities) were addressed in order to go for early intervention and rehabilitation of the screened cases. Therefore, the unique contribution of this review is to be able to report those screening tools exclusively designed for screening of developmental delay at the earliest possible time in both single and multiple domains. The review also provides a comparative analysis of available studies reporting the eligible tools.

Research gaps and future directions

Several research gaps have been identified in the reported studies. Primarily, there was a lack of standard terminologies to indicate the developmental domains. The examples of synonymous domain names are as follows: (i) **cognitive**: cognition, cognitive, global, mental,

problem solving, etc.;[36, 39-41, 43-45] (ii) **language**: communication, expressive communication, expressive language, language, receptive communication, receptive language, speech, speech and language, etc.;[35, 36, 39-41, 43, 44, 46, 47] (iii) **psycho-social**: adaptive behaviour, behaviour, personal-social, self-help, social, social-emotional, socialization, etc.[35, 36, 39-41, 43, 44] Apart from those, few researchers incorporated unconventional developmental domains in their tools, such as: hearing, school, seizure, vision, etc.[39, 40, 45, 46] Secondarily, there was a lack of standard proxy measures to define the screen-positive cases. Common examples are as follows: overall scores,[43] number of items,[47] number of functional domains,[35] number of significant concerns[40] etc. These two factors together, often make the screening results incomprehensible to health professionals who are not familiar with the tool in question. Moreover, it is neither possible to convert nor compare the test scores between separate screening tools, for better understanding. Many of the tools developed in English speaking countries might not be suitable for non-English speaking countries due to different socio-cultural backgrounds and problematic translation.[60-62] These issues might become a barrier for early identification and rehabilitation of developmental delay from the service providers' end. Lastly, several studies reported that the expected sensitivity-specificity was not achieved due to the lack of validated reference standard assessment tool for the particular culture in question.[35, 45, 47] To the best of our knowledge, there is a lack of WHO's centralized initiatives, as well as no Global regulatory body is currently working in this regard.

In this systematic review, we observed both Asian and African cultural contexts among the eligible studies. Although, the number of countries engaged in similar studies are alarmingly low compared to the number of LMICs, in total.[31] This reveals the urgent need for valid and culturally sensitive screening tools for the rest of the LMICs. Among the twelve eligible screening tools, half of them were developed in LMICs (DSQ, LEST 0-3, LDS,

MORBAS, ND-DSQ and RTHB-DC) and another half were developed in high-income countries (ASQ, INFANIB, Little DCDQ, PEDS, R-PDQ and TQ). We have found the majority of the culturally sensitive tools translated in their native language. Still, for multilingual countries like Benin, Ethiopia, India, etc. the necessity of translating the tools in regional languages remains high. None of the LMICs has been found to be engaged in collecting nationally representative longitudinal data on the prevalence of developmental delay, which is vital for disease projection. The gathering of nationally representative prevalence data in linguistic, social, ethnic and cultural subgroups would allow the validation of customized developmental screening tools according to disease burden. Greater customization to respect the diverse cultural norms[63] of a particular community, will also most likely result in greater acceptance[64, 65] of the screening process, which is crucial for the success of a large-scale surveillance program.

Limitations

Despite our best efforts, there were several limitations to this study. This study was limited to articles published in the English language only due to constraints in resources and time. In this study, we could neither address developmentally delayed children due to HIV exposure nor due to autism spectrum disorder or other behavioural disorders. Though these two groups of children also suffer from varying degree of developmental delay, the pathogenesis behind those delays is closely related to the diseases themselves.[66, 67] Moreover, conventionally it takes more than two years of age to diagnose a child with autism spectrum disorder and hence the age range of currently available autism screening tools start later than general developmental screening tools (e.g. Modified Checklist for Autism in Toddlers: 16-30 months; where ASQ-3: 1-66 months). This conflicts with the objectives of our study to ensure early diagnosis of developmental delay. So, with respect to other neurodevelopmental

disorders, we preferred to focus exclusively on developmental delay in our study. Moreover, we were unable to critically appraise the available screening tools in terms of diagnostic accuracy due to the unavailability of the necessary information. Which is quite reasonable as Boggs and her colleagues also reported that authors tend to provide validity information very briefly and evidence on accuracy are most difficult to obtain.[58] We are hopeful to conduct subsequent systematic review and meta-analysis on geographical region/ country/ domain specific screening tools and their psychometric properties based on the information obtained from this study.

Recommendations

(1) A global regulatory body should be formed to standardize the terminologies and cut-off scores of available and future screening tools to improve comprehensiveness and interpretation of test results, simultaneously ensuring better correlation between results obtained from different screening tools.

(2) Future research work should focus on revising existing screening tools in different ethnic and cultural perspectives and validate them in the respective normative sample as well as conducting systematic reviews based on individual screening tools in different cultural settings.

(3) We also recommend ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools to identify and treat developmental delay as early as possible. Developmental screening at the time of routine immunization schedule could be a possible way to integrate this with an existing successful public health program in LMICs. This timing would be both cost-effective and maximize response rates.

CONCLUSION

Developmental screening is required for early diagnosis of developmental delays in infants and young children in LMICs to enable early intervention and rehabilitation. In order to do this, culturally-sensitive, easy to administer screening tools with good psychometric properties are needed. We observed that there is a lack of culturally sensitive developmental screening tools validated among under 5 children in LMICs. However, we have found five screening tools with relatively high sensitivity and specificity. We also identified key research gaps and consequently proposed a few recommendations for overcoming those gaps. These include (but not limited to) global standardization of terminologies and cut-off scores for screening tools, revising existing tools according to diverse cultural norms and validating them in the respective normative sample and finally ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools. Therefore, future research should focus on enabling the caregivers, health workers, and therapists to assist in children with developmental delays in LMICs to reach their full developmental potential.

Declaration of interest

This manuscript is new and entirely original, has not been copyrighted, published, submitted, or accepted for publication elsewhere. All authors have given their consent and agreed to submit to your journal. The authors have no conflict of interest.

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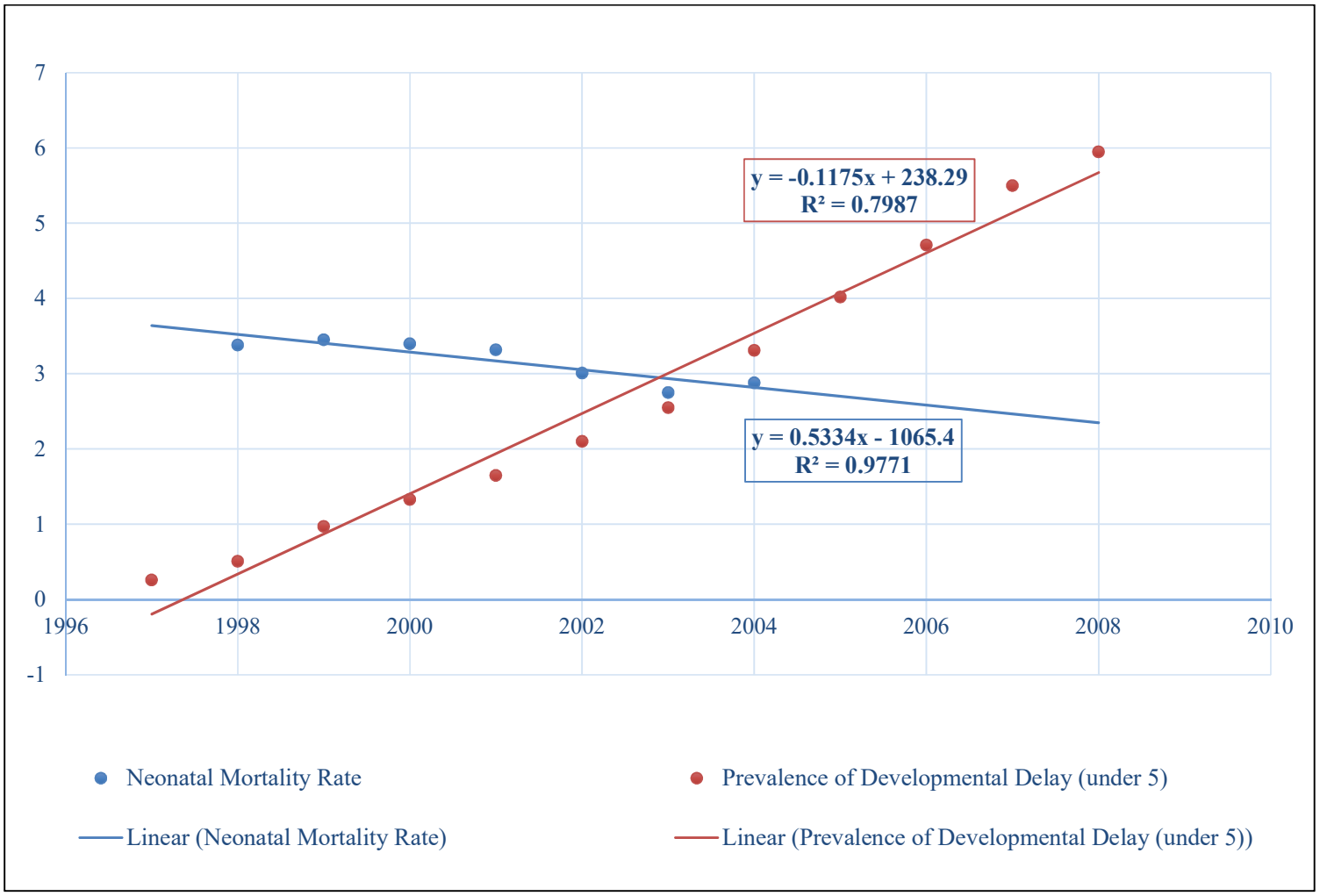
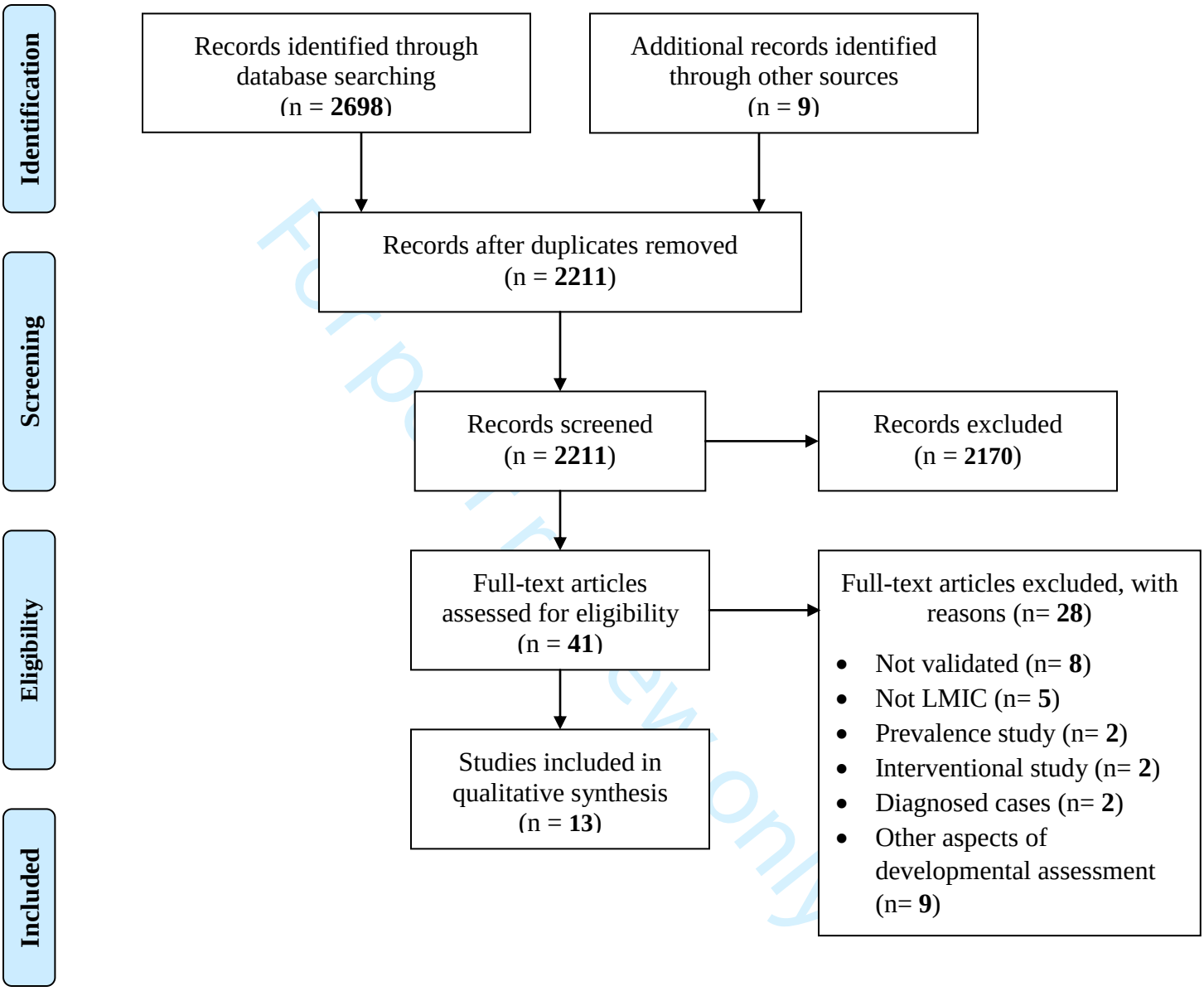
Figure 1: Correlation between neonatal mortality rate and prevalence of developmental delay (Taiwan 1997-2008)

Footnote: We have used prevalence of developmental delay among under 5 children (1997-2008) from a nation-wide population based retrospective study [16] and neonatal mortality rate (1998-2004) from another study [17]. It was revealed that the prevalence of developmental delay is positively associated with time and negatively associated with NMR. So, it can be said that, with time, while neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing.

Figure 2: PRISMA flow diagram


7
6
5
4
3
2
1
0
-1
1996
1998
2000
2002
2004
2006
2008
2010
y = -0.1175x + 238.29
R² = 0.7987
y = 0.5334x - 1065.4
R² = 0.9771
Neonatal Mortality Rate
Prevalence of Developmental Delay (under 5)
Linear (Neonatal Mortality Rate)
Linear (Prevalence of Developmental Delay (under 5))



Supplementary Table S1: Medline search strategy

MEDLINE: Systematic review - screening for disorders in children in LMIC (as at 05.03.18)

Notes: No date or language limits applied.

Database: Ovid MEDLINE <1946 to 2018 February 28>
Search Strategy:
---

1 exp Mass Screening/ (114856)
2 screen$.tw. (543259)
3 exp DIAGNOSIS/ (7780076)
4 (early adj5 (diagnos$ or identif$ or detect$ or discover$)).tw. (179324)
5 1 or 2 or 3 or 4 (8132793)
6 exp "Surveys and Questionnaires"/ (881308)
7 (survey$ or questionnaire$).tw. (745680)
8 (instrument$ or tool$).tw. (665937)
9 6 or 7 or 8 (1849661)
10 5 and 9 (774120)
11 exp Neurodevelopmental Disorders/ (162135)
12 exp Motor Disorders/ (197)
13 exp Cerebral Palsy/ (18455)
14 (cerebral adj pals$).tw. (17316)
15 CP.tw. (36947)
16 exp Cognitive Dysfunction/ (7530)
17 exp Communication Disorders/ (59072)
18 ((development$ or motor$ or speech$ or cogniti$ or behav$) adj5 (disorder$ or disabilit$ or condition$ or impair$ or deficit$)).tw. (200268)
19 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (415783)
20 10 and 19 (27683)
21 exp Developing Countries/ (69408)
22 exp ASIA/ (698877)
23 exp AFRICA/ (230576)
24 exp South America/ (134532)
25 asia$.tw. (100200)
26 africa$.tw. (169185)
27 (south adj1 america$).tw. (14876)
28 (low adj2 income adj2 countr$).tw. (4196)
29 (middle adj2 income adj2 countr$).tw. (7713)
30 LMIC.tw. (649)
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (1214625)
32 20 and 31 (2207)
33 limit 32 to humans (2185)
34 remove duplicates from 33 (2183)
35 limit 34 to "all child (0 to 18 years)" (1270)
36 exp INFANT/ (1056001)
37 exp CHILD/ (1753019)
38 exp ADOLESCENT/ (1842871)
39 (paediatric$ or pediatric$ or child$ or adolescen$ or teen$ or infant$ or baby or babies).tw. (1586099)
40 36 or 37 or 38 or 39 (3520016)
41 34 and 40 (1313)
42 35 or 41 (1313)
****

Supplementary Table S2: Quality Assessment Tool for Diagnostic Accuracy Studies-2 rating of the selected studies

	[35]	[36]	[37]	[38]	[39]	[40]	[41]	[42]	[43]	[44]	[45]	[46]	[47]
DOMAIN 1: PATIENT SELECTION													
A. Risk of Bias													
Was a consecutive or random sample of patients enrolled?	Yes	No	Yes	No	No	No	No	No	No	Yes	Yes	No	Yes
Was a case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did the study avoid inappropriate exclusions?	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes
Could the selection of patients have introduced bias?	Low	High	Unclear	High	High	High	High	High	High	Unclear	Unclear	Unclear	Low
B. Concerns regarding applicability													
Is there concern that the included patients do not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 2: INDEX TEST(S)													
A. Risk of Bias													
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If a threshold was used, was it pre-specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
B. Concerns regarding applicability													
Is there concern that the index test, its conduct, or interpretation differ from the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 3: REFERENCE STANDARD													
A. Risk of Bias													
Is the reference standard likely to correctly classify the target condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	Yes	Unclear	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	Low	Unclear	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear	Unclear	Low
B. Concerns regarding applicability													
Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 4: FLOW AND TIMING													
A. Risk of Bias													
Was there an appropriate interval between index test(s) and reference standard?	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	No	Yes	Yes	Unclear	Unclear
Did all patients receive a reference standard?	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
Did patients receive the same reference standard?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all patients included in the analysis?	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Could the patient flow have introduced bias?	High	Low	High	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Unclear

Supplementary Table S3: Newcastle-Ottawa Scale scores of the selected studies

	[35]	[36]	[37]	[38]	[39]	[40]	[41]	[42]	[43]	[44]	[45]	[46]	[47]
Selection: (Maximum 5 stars)													
Representativeness of the sample	*	*	*	*	*	*	*	*	*	*	*	*	*
Sample size	*	*							*	*			*
Non-respondents													
Ascertainment of the exposure	**	**	**	**	**	**	**	**	**	**	**	**	**
Comparability: (Maximum 2 stars)													
The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled	Not Applicable												
Outcome: (Maximum 3 stars)													
Assessment of the outcome	**	**	**	**	**	**	**	**	**	**	**	**	**
Statistical test	*		*	*	*	*	*	*	*	*	*	*	*

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8-9

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8-9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Sensitivity, Specificity
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig 2 (Prisma)
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table S2-3

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	14-23
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23-24
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	25-26
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	28
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A (29)

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Title: Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

Running head: Screening Tools for Developmental Delay

Article category: Review Article

Abstract

Objective: To systematically review, identify and report the screening tools used for early identification of developmental delay in Low-and Middle-Income Countries.

Design: Systematic review

Data sources: Four bibliographic databases: Medline (1946 to July 13, 2020), Embase (1974 to July 13, 2020), Scopus (1823 to July 11, 2020), and PsycINFO (1987 to July Week 1 2020).

Eligibility criteria: Peer-reviewed original articles published in English addressing validated culturally sensitive developmental screening tools among children aged < 5 years were included in this review.

Data extraction and synthesis: One author (CK, medical librarian) developed the search strategy. Three authors conducted the database search (phase 1: CK; phase 2: IJ and MKI). Two authors (TF and IJ) independently screened the title and abstracts. TF, MKI and GK independently performed the full-text review of the screened articles. During each step of the study selection process, disagreements were resolved through discussion. PRISMA statement was used to guide the systematic review. Data extraction and analysis were performed using MS Excel. Meta-analysis was not possible due to heterogeneity of the study findings.

Results: We identified 3349 articles, of which eighteen studies from ten countries, reporting sixteen screening tools, were selected for qualitative synthesis. Six cultural contexts were explored. Twelve general, two motor and two speech-language tools were identified. Seven of them found to be parent-completed ones. Five screening tools (American Speech-Language and Hearing Association, Guide for Monitoring Child Development, Infant Neurological International Battery, New Delhi – Development Screening Questionnaire and Woodside Screening Technique) reported relatively higher sensitivity (82.5-100)% and specificity (83-98.93)%.

Conclusions: Limited number of culturally sensitive developmental screening tools were validated for children aged <5 year in Low-and Middle-Income Countries. Revising existing screening tools in different ethnic and cultural settings and subsequent validation with normative value should be a research priority.

PROSPERO registration number CRD42018095232

Key words: Developmental delay, Disability, Screening, Early diagnosis, Rehabilitation, Low and Middle-Income Countries

Strengths and limitations of this study

- This review puts together extensive literature searches on original studies (both observational and experimental) conducted among under-5 children from LMICs reporting standardization, validity (in terms of sensitivity and specificity) of developmental screening tools in early diagnosis of developmental delay.
- Meta-analysis was not possible due to the heterogeneity of the study setting and findings.
- Critical evaluation of the available screening tools in terms of diagnostic accuracy was not possible to perform due to the unavailability of the necessary information.

Introduction

Developmental delay is a condition where children exhibit significant variation in achieving developmental milestones as expected for their actual or adjusted age.[1-3] Complications at birth including premature birth; brain trauma and encephalitis; severe medical problems after birth; inborn metabolic errors; genetic or chromosomal abnormalities; inadequate stimulation; malnutrition; iron deficiency anaemia; chronic illness; adverse environmental, familiar and psychological states may lead to developmental delay.[4-6] Although the condition itself may not be permanent, it can provide a foundation for recognizing children who might have more severe and permanent health conditions i.e. developmental disabilities. Apart from developmental delay, developmental disability is considered as a severe, chronic disability originating at birth or during childhood, expected to continue indefinitely, and substantially restricts the individual's functioning in several major life activities.[2, 7] Examples of developmental disabilities include Autism Spectrum Disorder, Behavioural Disorders, Cerebral Palsy, Down Syndrome, Fetal Alcohol Syndrome, Intellectual Disability, etc. As a predictive of above-mentioned learning, movement and behavioral disorders, it is possible to identify developmental delay to a great extend during the preschool period (i.e. before the age of 5 years) with the help of well validated screening tools.[8, 9] There is a long-term financial impact on society in terms of healthcare, educational support and other special services related to developmental delay and/ disability. This is because the affected children require substantial resources and increased cost over their lifespan compared to those without such conditions.[10] This further accentuates the significance of early identification to initiate appropriate interventions and/ rehabilitations with the intention of preventing further delays, stimulating emerging skills and creating a more encouraging and protective surroundings.[5]

In the last few decades, successful implementation of World Health Organization's (WHO's) key health services[11] regarding "The Countdown to 2015 Initiatives" resulted in the reduction of the neonatal mortality rate from 37 deaths per 1000 live births in 1990 to 19 per 1000 live births in 2016, worldwide with a projection of further future reductions.[12, 13] Among the survivors, more than 250 million under-5 children from Low-and Middle-Income Countries (LMICs) are not fulfilling their developmental potential in cognitive, motor, and social-emotional domains due to poor nutrition, poverty and conflicts.[4, 14-16] In addition to them, there is an undetected number of surviving children suffering from various forms of developmental delay presumably due to brain injury during the fetal, perinatal and post-neonatal period.[17] We have discovered that, with time, while the neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing (by analysing the data generated from two nation-wide population-based retrospective studies conducted in Taiwan) (Supplementary Figure S1).[18, 19]

Developmental screening is the first step of the comprehensive diagnostic procedure for secondary prevention and early identification of developmental delay.[16, 20, 21] Thus a well validated developmental screening tool is very important. The standardized tools available from western countries provide well-validated assessment in their own settings. However, the transfer of such western-based tools to non-western countries is linked with substantial limitations in terms of score interpretation and feasibility of their use in resource-constrained settings such as in LMICs.[22] In the developed countries, early identification of developmental delay is considered as mandatory part of good healthcare practice which is recommended by the American Academy of Pediatrics.[16] In contrast, in LMICs, most teaching and training programs of health professionals are still concentrated on acute illness and growth aspects of children rather than a developmental perspective, resulting in limited

attention in developmental delay.[16] Also, in these geographical areas, parents and caregivers with strong cultural beliefs and superstitions regarding health not only remain ignorant of the child's developmental deficit but also about the future impact of the condition.[23] The combined effect of these two factors often results in overlooking or delayed the diagnosis of developmental concerns.

The perspective on developmental disability varies from one culture to another. Along with economic, geographical, social factors, it often becomes a barrier to healthcare accessibility for children with disability.[24] In Chinese culture, having children with disability is often considered shameful for the family. In Southeast Asian cultures, parents often face social deprivation due to the stigma related to developmental disability.[25] Moreover, cultural believe often holds control over treatment approaches for developmental delay or disabilities, including: (1) whether to seek help or not; (2) which treatment option to choose; (3) parental expectations for their child; (4) interpersonal relationship between caregiver and healthcare professionals, etc.[26] One of the biggest challenges in early identification of developmental delay or disability is providing culturally sensitive screening tools, which not only include cultural perception of delay and/or disability but also easily adaptable across the various cultural/ nation.[22] Among the developmental domains, social development is culturally specific and difficult to adapt, whereas the gross motor domain is easier to adapt culturally.[27]

The purpose of this study was to look for the screening tools which have been used and validated for early identification of developmental delay in LMICs, to report how effective they are for early identification of developmental delay in terms of validity, and to identify areas for future research.

Materials and methods

Data sources and search strategy

To locate items on screening tools for early identification of developmental delay among children in low and middle-income countries, the search strategy was developed by an experienced medical librarian (Dr. Catherine King). Literature search was conducted in two phases (phase 1 up to March 2018: CK; phase 2 up to July 2020: IJ and MKI) in four bibliographic databases. The databases searched were: OVID Medline (1946 to July 13, 2020), OVID Embase (1974 to July 13, 2020), SCOPUS (1823 to July 11, 2020), and PsycINFO (1987 to July Week 1 2020). Search terms included database-specific thesaurus terms where available such as 'Mass Screening', 'Diagnosis', 'Surveys and Questionnaires', 'Neurodevelopmental Disorders', 'Motor Disorders', 'Cerebral Palsy', 'Cognitive Dysfunction', and 'Communication Disorders' as well as relevant associated text word terms. These were combined with low and middle-income country terms and infant, child and adolescent terms. To minimize the introduction of bias, no publication date and language limits were used. The date of the latest search was 13.07.2020. The Medline search strategy could be found online as Supplementary Table S1.

In addition to bibliographic database searches, we manually checked the reference lists of recent systematic reviews [28, 29] as well as articles included in the full-text review. We also contacted experts in the field to identify any additional studies or information.

Selection criteria

Study inclusion criteria were: (1) Children aged less than 5 years who were at risk of developmental delay; (2) Original studies (both observational and experimental); (3) Study where single, as well as multiple developmental domains, were examined; (4) Studies

conducted only in LMICs. The exclusion criteria were: (1) Studies conducted on diagnosed cases of developmental delay; (2) Studies focusing on autism spectrum disorder and other behavioural disorders; (3) Studies conducted among HIV exposed children; (4) Studies on developmental delay among children aged more than 5 years; (5) Interventional studies on developmental delay; (6) Studies on developmental delay published before 1946; (7) Article published in languages other than English; (8) Conference papers, letter to the editor, protocols, systematic reviews and ongoing studies; (9) Study conducted among children of eligible ethnic origin but in different country settings (i.e. children adopted from LMICs but study conducted in higher income countries). List of key definitions regarding study selection are available in Supplementary Table S2.

All the under-5 children who weren't previously diagnosed with any neurodevelopmental delay or disability, were considered as "at risk of developmental delay". Studies where overall or categorised (based on different age group/ cut off score) sensitivity-specificity of screening tools were examined and clearly reported, were considered as validated. We did not discriminate among screening, monitoring and surveillance tools. If any of those tools were validated for screening developmental delay among under-5 children, considered eligible for inclusion. Tools which were declared as assessment tools by the developer themselves as well as studies where a tool was utilized for developmental assessment by the researchers, were excluded from the review.

When we had searched the keywords "Autism Spectrum Disorder" and "Developmental Delay" in the medical databases, the number of search items were as follows- i) OVID Medline- 9320: 12402; ii) OVID Embase- 21750: 7506; iii) Scopus- 20675: 7530 and iv) PsycINFO- 17130: 3067, respectively. Which is a bit alarming. We have excluded autism

and other behavioural disorders from the study to provide undivided attention to developmental delay. Apart from scientific community, parents, and caregivers of LMICs are more familiar with the term ASD compared to Developmental Delay. Which is evident from growing concerns regarding speech-language and behavioural domains of child development compared to rest of the domains.[30] We believe, to ensure successful developmental screening/ surveillance program in LMICs in the long run, and more importantly, to raise public awareness about developmental delay; we need to work more in this area than we used to.

LMICs consist of countries belonging to three World Bank income groups (low, lower-middle, upper-middle, and high) of WHO's Member States. The classification is based on the estimated per capita gross national income. We have used the World Bank's country classifications by income level (2020-2021) in this review.[31, 32]

Study selection, data extraction and quality appraisal

We carried out the following steps to decide on the studies: (1) Searching the above-mentioned databases using similar search strategy (CK, IJ, MKI); (2) Deduplicating and merging search results using the EndNote bibliographic software (TF); (3) Examining titles and abstracts to remove obviously irrelevant reports (TF, IJ); (4) Retrieving and examining the full text reports of eligible studies (TF, MKI, GK); (5) Applying the selection criteria on the shortlisted articles (TF, GK); (6) Making final decisions on study inclusion and proceeding for data collection. Extracted information included: publication year, the country where the study was conducted, the name of the screening tool, the gold standard tool(s) against which the screening tool was validated, study design, study setting, sample size, sampling technique, the age of the participants, selection criteria and sensitivity-specificity of the screening tools. During each step of the study selection process, disagreements were resolved through discussion. We used

the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, including 27- item PRISMA checklist to guide the systematic review.[33] The included studies has been screened and assessed for risk of bias according to PRISMA checklist. The following domains has been evaluated to ensure the quality of the studies: study design, data collection method and selection bias.

Data analysis

Individual study findings were reported including the country, study design, study setting, sample size, sampling technique, proportions and age range of participants, sensitivity-specificity of the developmental screening tools etc. Data extraction and analysis were performed using MS Excel. We were unable to perform a meta-analysis due to the heterogeneity of the study setting and findings.

Protocol registration and ethical approval

The protocol of this systematic review has been registered in PROSPERO (registration number CRD42018095232). As this systematic review did not directly involve human or animal subjects, or access to medical records; ethical approval was not required.

Results

Search results

The initial search retrieved 3349 records. We have found 3320 records from four bibliographic databases (1555 from OVID Medline, 1317 from OVID Embase, 348 from Scopus and 100 from PsycINFO). 29 records were located by reviewing the reference lists of recent systematic

reviews, fully extracted articles and consulting expert researchers in this area. There were 2838 unique records once duplicates were removed. Following the screening of title and abstracts for articles, which described the validation of tools to screen out developmentally delayed children, 99 articles were selected for further evaluation. After further review and application of selection criteria, 18 articles were selected for inclusion in study.[34-51] A PRISMA flow diagram has been prepared to illustrate the study selection process (as shown in Fig. 1).

Summary of the included studies

All of the eighteen studies included for qualitative synthesis were original articles published in English, with a publication date range from 1991 to 2020 inclusive. Eight studies originated in "South Asia",[34, 37, 40, 42, 44, 47, 50, 51] four studies from "East Asia and Pacific",[35, 43, 45, 46] three studies from "Sub-Saharan Africa",[41, 48, 49] one study each from the "Middle East and North Africa",[39] "Latin America and Caribbean",[36] and "Europe and Central Asia"[38] region of the World Bank. region. In total, sixteen developmental screening tools were used in ten countries. Among the sixteen screening tools, American Speech-Language and Hearing Association (ASHA), Language Evaluation Scale Trivandrum for 0-3 years LEST (LEST 0-3) focus on language domain; Infant Neurological International Battery (INFANIB) and Little Developmental Coordination Disorder Questionnaire (Little DCDQ) work on motor domains. The remaining tools are general developmental screening tools. A brief description of the selected screening tools is provided in Table 1.

Table 1: Brief description of the selected screening tools

Screening Tool	Country of Origin	Study Country	Concerned Age	Parent-Reported Version	Questionnaire Type	Number of Questionnaires	Number of items	Developmental Domain	Validated Against
Ages and Stages Questionnaire (ASQ)	USA	India, China	1–66 months	Yes	Q & A	21 age sets	30 items per set	Communication, gross motor, fine motor, problem solving, personal-social	Developmental Assessment Scales for Indian Infants (DASII) **[34]** Bayley Scales of Infant Development (BSID-III) **[35]**
American Speech-Language and Hearing Association (ASHA)	USA	Brazil	0-5 years	No	Q & A	7 age sets	6-13 items	Language reception and expression	ABFW test **[36]**
Development Screening Questionnaire (DSQ)	Bangladesh	Bangladesh	birth to 24 months	No	Q & A	24 age sets	8 questions per set	Gross motor, fine motor, vision; hearing, cognition, socialization, behavior, and speech	Rapid Neurodevelopmental Assessment (RNDA) **[37]**
Guide for Monitoring Child Development (GMCD)	Turkey	Turkey	0-3.5 years	Yes	Q & A	Single	7 items	Expressive language and communication, Receptive language, Fine and gross motor, Social-emotional, Self-help	Bayley Scales of Infant Development (Bayley-II) **[38]**
Infant Neurological International Battery (INFANIB)	USA	Iran	0 to 18 months	No	Not found	Single	20-items	Gross motor	Developmental Assessment by Pediatric Neurologist **[39]**
Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	India	India	0 to 3 years	No	Chart	Single	33 items	Speech and language	Receptive Expressive Emergent Language Scale **[40]**
Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Canada	South Africa	3-5 years	Yes	Q & A	Single	15 items	Gross motor, fine motor	Movement Assessment Battery for Children -2 **[41]**
Lucknow Developmental Screen (LDS)	India	India	birth to 24 months	Yes	Chart	Single	27 item	Motor, mental, language, social	Developmental Assessment Scales for Indian Infants (DASII) **[42]** Vineland Social Maturity Scale **[42]**
Mongolian Rapid Baby Scale (MORBAS)	Mongolia	Mongolia	0 to 42 months	No	Written	Single	161 item	Cognitive, receptive communication, expressive communication, fine	Bayley Scales of Infant and Toddler Development (BSID-III) **[43]**

								motor, gross motor, social-emotional, adaptive behavior	
New Delhi – Development Screening Questionnaire (ND-DSQ)	India	India	9 to 18 months	Yes	Q & A	2 age sets	20 items	General screening tool (domains not explicitly mentioned)	Developmental Assessment Scales for Indian Infants (DASII) **[44]**
Parent Evaluation of Developmental Status (PEDS)	USA	Thailand	birth to 8 years	Yes	Q & A	Single	10 items	Global /cognitive, speech / expressive language, receptive language, behavior, social-emotional, school, self-help, fine motor, gross motor, other	Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level **[45]** Mullen Scales of Early Learning **[46]**
Rapid Prescreening Denver Questionnaire (R-PDQ)	USA	India	0-6 years	No	Q & A	4 age sets	25 items	Gross motor, fine motor activity, personal-social, language	Denver Developmental Screening Test (DDST) **[47]**
Road to Health Booklet Developmental Checklist (RTHB-DC)	South Africa	South Africa	14 weeks to 6 years	No	Checklist	Single	21 items	Gross motor, fine motor, communication, vision, hearing	Parent Evaluation of Developmental Status (PEDS) **[48]** Parent Evaluation of Developmental Status: Developmental Milestones **[48]**
Ten Questions Screening Instrument (TQSI)	Multiple	Benin	2 to 9 years	Yes	Q & A	Single	10 items	Vision, hearing, seizure, cognition, motor	Mullen Scales of Early Learning **[49]**
Trivandrum Developmental Screening Chart (TDSC)	India	India	0 to 2 years	No	Chart	Single	17 items	Mental, motor, vision, hearing	Denver Developmental Screening Test (DDST) **[50]**
Woodside System Screening Technique (WSST)	Scotland	India	0 to 4 years	No	Chart	Single	70 items	'Social', 'Hearing and language', 'Vision and fine motor', and 'Gross motor	Gesell's Developmental Schedules (GDS) **[51]**

Participant characteristics

All the studies involved males and females, age range 0 to 5 years. The smallest sample size was 53 and the largest was 1945. The studies explored the following cultural contexts: East Asia and Pacific (China, Mongolia, Thailand), Europe and Central Asia (Turkey), Latin America and the Caribbean (Brazil), Middle East and North Africa (Iran) South Asia (Bangladesh, India) Sub-Saharan Africa (Benin, South Africa). Selection criteria used for participation in those studies are stated in Supplementary Table S3.

Study characteristics

All the included studies were cross-sectional in nature. Among the eighteen studies, one study was conducted in the community and tertiary hospital simultaneously,[50] eight were conducted in the tertiary hospital,[34, 38, 39, 42-46] five were conducted in the community,[35, 36, 40, 47, 51] and one study each was conducted in a nursery school setting[41] and primary health care clinic setting.[48] In the remaining two studies, screening was done in the community followed by a hospital-based detailed assessment in one[37] and primary health care clinic-based assessment in another.[49]

Validated screening tools

The Ages and Stages Questionnaire (ASQ)

This is a parent-completed questionnaire that could be used as a general developmental screening tool. The ASQ was designed and developed by J. Squires and D. Bricker, at the University of Oregon and can be completed in 12-18 minutes.[52] The questionnaire has 30 items focusing on five domains of child development, named gross motor, fine motor, problem-solving, communication, and personal-social. Obtaining lower scores than the cut off in any domain is considered as “screen positive”. The latest version of ASQ, ASQ-3, has 21 sets of questionnaires, appropriate for children aged 1–66 months.[53] In the study by Juneja et al.,

2012; a Hindi adaptation of an older version of ASQ, (ASQ-2, which had 19 sets of questionnaires for 4 to 60 months aged children) was used in a convenience sample of 200 children divided into 4 age groups: 4, 10, 18 and 24 months, in a tertiary hospital setting.[34] Each age group consisted of 30 low risk and 20 high-risk children. High-risk status was determined by the presence of any of the following risk factors: prematurity, low birth weight, history of neonatal hospitalization, history of central nervous system infection, history of afebrile seizure, diagnosed cases of developmental disorder and chromosomal abnormalities. Children without these risk factors were treated as being in the low-risk group. Eventually, 4, 10, 18 and 24 months questionnaires of ASQ-2 were validated against "Developmental Assessment Scales for Indian Infants (DASII)", considered as a gold standard for developmental assessment tool among Indian children.[34] The overall sensitivity and specificity of ASQ-2 for Indian children were found to be 83.3% and 75.4% respectively.

In the study by Yue et al., 2019; Chinese adaptation of ASQ-3 was used among 1831 children aged 5 to 24 months in a cluster random sample from rural China. Eventually the tool was validated against the Bayley Scales of Infant and Toddler Development-III. Overall sensitivity and specificity of ASQ-3 found to be 76.52% and 40.97%, respectively. The authors suggested to avoid using ASQ-3 for children lower than 13 months of age as well as children whose primary caregiver aren't their mother, due to poor performance in those group of children.[35]

American Speech-Language and Hearing Association Screening Tool (ASHA)

The ASHA was designed and developed by the American Speech-Language and Hearing Association to screen out under-5 children for language delay in receptive and expressive language domain. There are 7 age sets consisting of 6-13 questions per age set. Cut-off score

for screen positive result varies from one age set to another. In general, if a child gets more than two negative answers in any domain will be considered as "screen positive". In the study conducted by Dias et. al, 2020; 1000 under-5 children were screened for language delay during a polio vaccination campaign in Sao Paulo, Brazil by utilizing the tool. Later detailed assessment was conducted using ABFW Child Language Test. ASHA found to have excellent sensitivity and specificity (82.5% and 98.93%, respectively) against ABFW Child Language Test.[36] The authors recommended to adapt the instrument for bilingual children as well as validating it in larger sample size.

Development Screening Questionnaire (DSQ)

The DSQ was designed and developed in Bangladesh, to be administered to mothers of children from birth to 24 months of age to screen their child's neurodevelopmental status. The DSQ has 24 age sets with 8 questions per set related to eight functional domains, named: gross motor, fine motor, vision; hearing, cognition, socialization, behaviour and speech.[37] Any child found to be positive on one or more functional domain is considered "screen positive". In a study conducted in urban Bangladesh, a random sample of 197 children aged 0-24 months was screened in the community with DSQ, and then a detailed developmental assessment was done in a tertiary hospital with the help of the "Rapid Neurodevelopmental Assessment" tool as the gold standard. Overall sensitivity and specificity of DSQ for under 2-year-old Bangladeshi children was found to be 47.1% and 97.2% respectively.[37] Despite moderate sensitivity, the DSQ might be advantageous for resource-poor settings due to its high specificity.

Guide for Monitoring Child Development (GMCD)

The GMCD was designed and developed in Turkey to monitor development of 0-3.5 years old children in LMICs. The tool consists of 7 open ended questions focusing on the following

domains- Expressive language and communication, Receptive language, Fine and gross motor, Social-emotional, Self-help. Children declared screened positive if they failed to demonstrate one or more age appropriate milestones. In a study conducted by Ertem et. al. 2008; GMCD was validated against Bayley Scales of Infant Development (Bayley-II) in a random sample 79 Turkish children of 1-24 months of age. The overall sensitivity and specificity of GMCD were found to be 88% and 93% respectively.[38]

Infant Neurological International Battery (INFANIB)

The INFANIB was established by Ellison and Browning in 1985 to assess the gross motor function of children aged 0 to 18 months. The tool contains 20-items focusing on spasticity, vestibular function, head and trunk, French angles and legs.[54] In the study by Soleimani and Dadkhah, 2006; a consecutive sample of 6150 children were screened using INFANIB and classified as normal, transiently abnormal and abnormal. To validate the tool a random sample of 153 children from the above-mentioned groups were assessed by pediatric neurologists. It was found that overall sensitivity and specificity of INFANIB for Iranian children were 90% and 83% respectively.[39]

Language Evaluation Scale Trivandrum (LEST 0-3)

Designed and developed at the Child Development Centre of the Trivandrum Government Medical College, India, LEST (0-3) is a 33 items screening tool to screen out language delay among 0 to 3 years old children.[40] The LEST (0-3) was validated against the "Receptive-Expressive Emergent Language Scale" tool as a gold standard in a community sample of 643 Indian children aged 0 to 36 months. To decide on the best possible combination, researchers considered both "one item delay" and "two items delay" as screen positive. When one item delay considered as screen positive, sensitivity and specificity of LEST (0-3) found to be 95.8% and 77.5% respectively. Similarly, when two items delay measured as screen positive, the

sensitivity and specificity obtained as 66.7% and 94.8% respectively.[40] It should be noted that the original version of Receptive-Expressive Emergent Language Scale (1971) was used in this study for validation due to the lack of age-appropriate language assessment tool for language delay.

Little Developmental Coordination Disorder Questionnaire (Little DCDQ)

The Little DCDQ was developed by Rithman and colleagues in Canada to assess gross motor and fine motor function of children between 3 to 5 years of age. It is a parent-reported questionnaire with 15 items under three main components, control during execution, fine motor execution and overall coordination.[41] The Little DCDQ was validated against the Movement Assessment Battery for Children-2 as a gold standard in a group of 53 South African preschoolers between 3 to 5 years of age, with Afrikaans, Tswana or English speaking parents.[41] With 57.14% sensitivity and 81.25% specificity, Little DCDQ had the potential to be used in South African culture, however, some adjustments would be required.

Lucknow Development Screen (LDS)

The LDS was developed in CSM Medical University, Lucknow, India, using selected milestones from Baroda Development Screening Test. It is a 27 items chart format tool, covering four domains namely motor, mental, language and social. Suitable for children aged 0 to 24 months. The LDS is said to be easily administrable by interviewing parents or caregiver.[42] In a study conducted in India, the LDS tool was validated against the DASII and the Vineland Social Maturity Scale. They administered the tool to mothers of a sample of 142 children, aged between 6 to 24 months, attending Pediatric Outpatients or Neurology Clinic of CSM Medical University, Lucknow, India. The screening tool was translated into Hindi for easy understanding and administration. For 3 children among the sample size of 142, Vineland Social Maturity scale was used as a gold standard, as DASII couldn't be applied to them. It is

claimed that the LDS has a great potential to be used as a community screening tool among Indian children, with an overall sensitivity of 95.9% and specificity 73.1%.[42]

Mongolian Rapid Baby Scale (MORBAS)

The MORBAS is a written developmental screening test, designed and developed in Mongolia. It has 161 items arranged under seven developmental domains, namely gross motor, fine motor, cognitive, expressive language, receptive language, social-emotional and adaptive behaviour. The tool is suitable for children aged 0 to 42 months.[43] In a study conducted in Mongolia, MORBAS was administered in a convenience sample of 150 Mongolian children aged 0 to 42 months and thus validated against the Bayley Scales of Infant and Toddler Development-III. With sensitivity 81.8% and specificity 52.3%,[43] MORBAS could be useful in the long run to screen out children for early intervention and rehabilitation.

New Delhi – Development Screening Questionnaire (ND-DSQ)

The ND-DSQ was developed by Jain and colleagues, at Chacha Nehru Bal Chikitsalaya, a tertiary hospital of northern India. ND-DSQ has 20 items, two age sets (9 months and 18 months) and applicable for children aged 9 to 18 months.[44] The items mentioned were milestone specific. Thus, no explicit mention of the developmental domains was found. In the study by Jain et al., 2017; ND-DSQ was validated against DASII in a convenience sample of 200 children aged 9 and 18 months (with 100 children per age group). It was established that the 9-month questionnaire was 100% sensitive and 87.2% specific for Indian children. Correspondingly, the 18 months questionnaire was validated with 91.4% sensitivity and 88.7% specificity.[44] As a newly developed tool, the ND-DSQ is promising to be useful for Indian and similar cultural settings.

Parent Evaluation of Developmental Status (PEDS)

This tool was developed in 1997 by F. P. Glascoe at Tennessee, USA.[55] It is the only screening tool available to date that addresses parent's concern about children's development in the following domains: gross motor, fine motor, cognitive, expressive language, receptive language, behaviour, social-emotional, self-help, school and other.[56] It has ten open-ended questions under ten areas of parental concerns, applicable for children aged 0 to 8 years. The other category allows parents to express concerns not already addressed under previous categories. This unique property makes PEDS unique as a developmental screening tool. In PEDS, parental concerns are labelled as "predictive" (significant) and "non-predictive" (non-significant). Thus, children are screened as low risk, moderate risk and high-risk group if they have no or non-predictive concerns, one predictive concern and two predictive concerns, respectively.[45]

In the study by Chunusuwan et al., 2016; the PEDS- Thai was validated against the "Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level" in a tertiary hospital. A convenience sample of 266 children of 9, 18 and 30 months of age was selected. Screen positive children were assembled as "high risk" (≥ 2 significant concerns) and "moderate or high risk" (≥ 1 significant concern) group. Sensitivity and specificity of PEDS against Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level for the high-risk group was established as 27.7% and 93.0%, respectively. For moderate or high-risk group, the tool was 67.7% sensitive and 60.7% specific.[45] In order to avoid unnecessary/over-referral, the authors suggested to practice second stage evaluation (using Parent Evaluation of Developmental Status: Developmental Milestones, ASQ, Denver-II etc. tools) alongside/after PEDS screening.

In another study by Wantanakorn et al., 2016; they validated the PEDS- Thai against the Mullen Scales of Early Learning tool as a gold standard in a convenience sample of 137

children aged 18 to 36 months in another tertiary hospital. It was found that the PEDS-Thai is a promising tool for Thai cultural backgrounds with overall sensitivity of 92.8% and specificity 49.2%.[46] According to the authors, "the relatively low specificity of PEDS seen here may be because of the excessive concern of parents regarding their child's development, especially who are in relatively high socioeconomic status". The selection bias of participants was mentioned as the major limitation of the study. Thus, they advised further evaluation of the diagnostic performances of the tool using a representative sample of the population.

Rapid Pre-screening Denver Questionnaire (R-PDQ)

The R-PDQ is a general developmental screening tool covering four developmental domains: gross motor, fine motor activity, personal-social and language.[47] It has four age sets applicable for children aged 0 to 6 years: 0 to 9 months, 9 to 24 months, 2 to 4 years and 4 to 6 years. Each questionnaire contained 25 items. To score a child, the responding person had to keep answering the questions until there were three negative responses under a specific domain. In the study by Awasthi et al., 1997; the 2 to 4 years questionnaire of R-PDQ was validated against the Denver Developmental Screening Test. The study participants were randomly selected 126 children living in urban slums of Lucknow, India. To validate the tool, when a delay in more than one domain was considered as the cut-off, the tool was revealed to be 100% sensitive and 7.8% specific. Similarly, when a delay in more than two domains was considered as the cut-off, the sensitivity and specificity were found to be 18.2% and 42.6%, respectively.[47] Inconvenient validity and high referral rate compared to US children were explained by the presence of various "difficult to interpret" questions and Denver Developmental Screening Test being an unsuitable gold standard for R-PDQ.

Road to Health Booklet Developmental Checklist (RTHB-DC)

The RTHB-DC was prepared as an integrated part of The Road to Health Booklet, the revised version of which was introduced in October 2010. RTHB-DC is the only developmental surveillance and screening tool, currently implemented nationally in South Africa. The tool consists of 21 questions covering gross motor, fine motor, communication, vision, and hearing domains. The checklist is applicable for children aged 14 weeks to 6 years.[57] In the study by Linde et al., 2015; RTHB-DC was validated against PEDS and Parent Evaluation of Developmental Status: Developmental Milestones tools. The sample size was 201, consisting of children aged 6 to 12 months old. In a primary health care clinic setting in South Africa, the sensitivity of the tool was found to be very low, i.e. 25% compared to reasonably high specificity of 91%.[48] Further development of the tool has been suggested by the authors incorporating consistent age gaps and inclusion of all developmental domains.

Ten Questions Screening Instrument (TQSI)

The TQSI Screening Instrument was developed in 1984 as part of a pilot study conducted by the University of Columbia, USA, for use in resource-poor countries.[58, 59] TQSI is a parent reported tool comprising of ten questions addressing motor, cognitive, vision, hearing, and seizure status. A child is considered screen positive if any of the questions are found to be positive. The tool is appropriate for children aged 2 to 9 years. In a study by Koura et al., 2013; the TQSI was validated against the Mullen Scales of Early Learning in a sample of 357 children aged 12 months.[49] The participants were the offspring of the mothers who were enrolled in the "Malaria in Pregnancy Preventive Alternative Drugs" trial. To adjust the tool for that age group, researchers had excluded the language domain which is applicable for children above 2 years. In that study, screening was done in the community followed by a detailed assessment done in the health centre. It was found that the overall tool had reasonably high sensitivity (81%) but poor specificity (31%) for children of Benin. This is compared to the 76.5% sensitivity and 75.7% specificity where only the motor domain was considered.[49] Mullen

Scales of Early Learning was used due to lack of a gold standard assessment tool for the Beninese population. The result suggests that the TQSI tool might be useful for resource-poor settings to screen out moderate to severe delay in motor function.

Trivandrum Developmental Screening Chart (TDSC)

The TDSC was designed and developed by Nair and colleagues in 1991 in Child Development Center, Kerala, India. The chart contains 17 items under four developmental domains- mental, motor, vision and hearing; applicable for children under two years od age.[50] If a child fails to achieve any item appropriate for his chronological age, considered as screened positive. In a study conducted by Nair et al. 1991; TDSC was validated against Denver Developmental Screening Test (DDST) simultaneously in community as well as hospital settings in a cluster random sample of 1945 Indian children aged less than two years. Overall sensitivity and specificity of TDSC found to be 66.7% and 78.8%, respectively.[50] The authors recommended to utilize the chart for mass screening of developmental delay among under-2 children in resource poor settings.

Woodside Screening Technique (WSST)

The WSST was designed and developed in Glasgow, Scotland in the year 1976. The tool consists of 70 items covering social, hearing and language, vision and fine motor, and gross motor domains, suitable for children under 4 years of age.[51] In a study conducted by Gupta and Patel, 1991; WSST was validated against Gesell's Developmental Schedules (GDS) in a random sample of 619 children aged 6 weeks-2 years from Jabalpur, India. Overall sensitivity and specificity of WSST found to be 83% and 88%, respectively.[51]

The major findings of this systematic review are presented in Table 2. We have classified the eligible tools into two broad categories- "Parents/ Caregiver Reported Tools" and "Direct Child

Testing/ Observation Tools". The tools/ studies which were not included in this review as they failed to meet the selection criteria were enlisted along with the reasons for rejection in Supplementary Table S4.

Table 2: Major findings from the selected studies used in this review

Parents/ Caregiver Reported Tools							
General Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[34]	**India** Lower-Middle- Income	Ages and Stages Questionnaire (ASQ-II)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 4, 10, 18 and 24 months **Convenience sample**	Overall	Sensitivity 83.3% Specificity 75.4%
[35]	**China** Upper-Middle- Income	Ages and Stages Questionnaire (ASQ-III)	Bayley Scales of Infant Development (BSID-III)	**Design** Cross-Sectional **Setting** Community	**Sample** – 1831 **Age** – 5-24 months **Cluster random sample**	Overall	Sensitivity 76.52% Specificity 40.97%
[38]	**Turkey** Upper-Middle- Income	Guide for Monitoring Child Development (GMCD)	Bayley Scales of Infant Development (Bayley-II)	**Design** Cross-Sectional **Setting** - Hospital	**Sample** – 79 **Age** – 1-24 months **Random sample**	Overall	Sensitivity 88% Specificity 93%
[42]	**India** Lower-Middle- Income	Lucknow Development Screen (LDS)	Developmental Assessment Scales for Indian Infants (DASII) Vineland Social Maturity Scale	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 142 **Age** - 6-24 months **Convenience sample**	Overall	Sensitivity 95.9% Specificity 73.1%
[44]	**India** Lower-Middle- Income	New Delhi – Development Screening Questionnaire (ND-DSQ)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 9 and 18 months **Convenience sample**	9-months	Sensitivity 100% Specificity 87.2%
						18-months	Sensitivity 91.4% Specificity 88.7%
[45]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS)	Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 266 **Age** – 9, 18 and 30 months **Convenience sample**	≥ 1 significant concern	Sensitivity 67.7% Specificity 60.7%
						≥ 2 significant concerns	Sensitivity 27.7% Specificity 93.0%
[46]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS- Thai)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 137 **Age** – 18-30 months **Convenience sample**	Overall	Sensitivity 92.8% Specificity 49.2%
[49]	**Benin** Lower-Middle- Income	Ten Questions Screening Instrument (TQSI)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting**	**Sample** - 357 **Age** – 12 months	Motor	Sensitivity 76.5% Specificity 75.7%
						Overall	Sensitivity 81%

				Screening- Household Assessment- Health Centre	**Random sample**		Specificity 31%
Motor Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[41]	**South Africa** Upper-Middle- Income	Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Movement Assessment Battery for Children -2	**Design –** Cross-sectional **Setting** – nursery schools	**Sample** – 53 **Age** – 3-5 years **Convenience sample**	Overall	Sensitivity 57.14% Specificity 81.25%
Direct Child Testing/ Observation Tools							
General Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[37]	**Bangladesh** Lower-Middle- Income	Development Screening Questionnaire (DSQ)	Rapid Neurodevelopmental Assessment (RNDA)	**Design** Cross-Sectional **Setting** Screening- Household Assessment- Hospital	**Sample** – 197 **Age** - 0-2 years **Random sample**	Overall	Sensitivity 47.1% Specificity 97.2%
[43]	**Mongolia** Lower-Middle- Income	Mongolian Rapid Baby Scale (MORBAS)	Bayley Scales of Infant and Toddler Development-III	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 150 **Age** – 0 month 16 days – 42 months 15 days **Convenience sample**	Overall	Sensitivity 81.8% Specificity 52.3%
[47]	**India** Lower-Middle- Income	Revised Prescreening Denver Questionnaire (R-PDQ)	Denver Developmental Screening Test (DDST)	**Design** Cross-Sectional **Setting** Community	**Sample** - 126 **Age** – 2-4 years **Cluster random sample**	Delay in ≥ 1 domain	Sensitivity 100% Specificity 7.8%
						Delay in ≥ 2 domains	Sensitivity 18.2% Specificity 42.6%
[48]	**South Africa** Upper-Middle- Income	Road to Health Booklet Developmental Checklist (RTHB-DC)	Parent Evaluation of Developmental Status (PEDS) Parent Evaluation of Developmental Status: Developmental Milestones	**Design** Comparative Cross-sectional within-subject **Setting** PHC clinics	**Sample** - 201 **Age** – 6-12 months **Convenience sample**	Overall	Sensitivity 25% Specificity 91%
[50]	**India** Lower-Middle- Income	Trivandrum Developmental Screening Chart (TDSC)	Denver Developmental Screening Test (DDST)	**Design** Cross-Sectional **Setting** – Hospital + Community	**Sample** – 1945 **Age** – 0-2 years **Cluster random sample**	Overall	Sensitivity 66.7% Specificity 78.8%
[51]	**India**	Woodside Screening Technique (WSST)	Gesell's Developmental Schedules (GDS)	**Design** Cross-Sectional	**Sample** – 619	Overall	Sensitivity 83% Specificity 88%

	Lower-Middle- Income			**Setting** – Community	**Age** – 6 weeks-2 years **Random sample**		
Motor Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[39]	**Iran** Upper-Middle- Income	Infant Neurological International Battery (INFANIB)	Developmental Assessment by Pediatric Neurologist	**Design** – Cross-Sectional **Setting** Hospital	**Sample** – 153 **Age** – 4-18 months **Random sample**	Overall	Sensitivity 90% Specificity 83%
Language Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[36]	**Brazil** Upper-Middle- Income	American Speech-Language and Hearing Association (ASHA)	ABFW test	**Design** Cross-Sectional **Setting** - Community	**Sample** – 1000 **Age** – 0-5 years **Random sample**	Overall	Sensitivity 82.5% Specificity 98.93%
[40]	**India** Lower-Middle- Income	Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	Receptive Expressive Emergent Language Scale	**Design** Cross-Sectional **Setting** - Community	**Sample** – 643 **Age** – 0-3 years **Cluster random sample**	One item delay	Sensitivity 95.8% Specificity 77.5%
						Two item delay	Sensitivity 66.7% Specificity 94.8%

Discussion

To the best of our knowledge, this is the first systematic review which attempts to find the available screening tools for early identification of children with developmental delay in LMICs. Although some systematic reviews were found who considered developmental assessment tools requiring professional experts with a special office setup,[60] screening neurodevelopmental disability irrespective of age limit and diagnosis (e.g. Developmental Delay, Global Developmental Delay, Cerebral Palsy, Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, Epilepsy, etc.),[61] or reflected high-income country context.[8] We have also observed a study in which both screening and assessment tools have been systematically rated for accuracy and feasibility to use in LMICs.[28] Where, information was significantly dependent to World Bank's toolkit and inventory on early child development tools,[62] rather than being obtained from systematic search through databases. In contrast, the purpose of this review was to systematically look for the available studies where screening tools were used exclusively for early identification (limited to children under 5 years of age) of developmental delay in the LMICs region where all types of study settings (i.e. from household to health facilities) were addressed in order to go for early intervention and rehabilitation of the screened cases. Therefore, the unique contribution of this review is to be able to report those screening tools exclusively designed for screening of developmental delay at the earliest possible time in both single and multiple domains.

Research gaps and future directions

Several research gaps have been identified in the reported studies. Primarily, there was a lack of standard terminologies to indicate the developmental domains. The examples of synonymous domain names are as follows: (i) **cognitive**: cognition, cognitive, global, mental, problem solving, etc.;[34, 35, 37, 42, 43, 45, 46, 49, 50] (ii) **language**: communication,

expressive communication, expressive language, language, receptive communication, receptive language, speech, speech and language, etc.;[34- 38, 40, 42, 43, 45-48] (iii) **psycho-social**: adaptive behavior, behavior, personal-social, self-help, social, social-emotional, socialization, etc.[34, 35, 37, 38, 42, 43, 45-47, 51] Apart from those, few researchers incorporated unconventional developmental domains in their tools, such as: hearing, school, seizure, vision, etc.[45, 46, 48-51] Secondarily, there was a lack of standard proxy measures to define the screen-positive cases. Currently available examples of proxy measures are as follows: overall scores,[34, 35], number of negative answers,[36] number of milestones,[38] number of items,[40, 50] number of functional domains,[47] number of significant concerns[45, 46] etc. These two factors together, often make the screening results incomprehensible to health professionals who are not familiar with the tool in question. Moreover, it is neither possible to convert nor compare the test scores between separate screening tools, for better understanding. Many of the tools developed in English speaking countries might not be suitable for non-English speaking countries due to different socio-cultural backgrounds and problematic translation.[63-65] These issues might become a barrier for early identification and rehabilitation of developmental delay from the service providers' end. Lastly, several studies reported that the expected sensitivity-specificity was not achieved due to the lack of validated gold standard assessment tool for the particular culture in question.[40, 47, 49] To the best of our knowledge, there is a lack of WHO's centralized initiatives, as well as no Global regulatory body is currently working in this regard. Majority of the developmental assessment tools found in this review were established for high income countries (BSID, DDST, REELS, GDS, MABC-2, etc). Only three of them were designed and developed in LMICs (ABFW, DAASII and RNDA). None of the studies using assessment tools designed for high income counties, provided information on cultural adaptation. However, in a study conducted by Parveen et al., 2014, took the initiative to culturally adapt Bayley Scales

of Infant Development- Second Edition (BSID-II) items for Bangladeshi infants.[66] Example of culture-sensitive BSID-II items for Bangladeshi infants are presented in Supplementary Table S5. Future research work should focus on developing or adapting developmental assessment tools to be efficiently used as gold standard for LMICs.

In this systematic review, we had observed East Asian and Pacific, European and Central Asian, Latin American and the Caribbean, Middle East and North African, South Asian and Sub-Saharan cultural contexts among the eligible studies. Although, the number of countries engaged in similar studies are alarmingly low compared to the number of LMICs, in total.[32] This reveals the urgent need for valid and culturally sensitive screening tools for the rest of the LMICs. Among the sixteen eligible screening tools, half of them were developed in LMICs (DSQ, GMCD, LEST 0-3, LDS, MORBAS, ND-DSQ. RTHB-DC and TDSC) and another half were developed in high-income countries (ASHA, ASQ, INFANIB, Little DCDQ, PEDS, R-PDQ, TQSI and WSST). We have found the majority of the culturally sensitive tools translated in their native language. Still, for multilingual countries like Benin, Ethiopia, India, etc. the necessity of translating the tools in regional languages, remains high. None of the LMICs has been found to be engaged in collecting nationally representative longitudinal data on the prevalence of developmental delay, which is vital for disease projection. The gathering of nationally representative prevalence data in linguistic, social, ethnic and cultural subgroups would allow the validation of customized developmental screening tools according to disease burden. Greater customization to respect the diverse cultural norms[67] of a particular community, will also most likely result in greater acceptance[68, 69] of the screening process, which is crucial for the success of a large-scale surveillance program.

While planning surveillance program for resource-poor settings, additional factors should be kept in mind. According to Gupta et al 1991, lack of furniture as well as staircase at home often results in exhibition of delayed gross motor skills due to lack of practice. Similarly, being heavily dependant on recall method is also problematic, as it is burdensome for parents with no or minimal education.[51] To overcome these issues, Ertem et al 2008 suggested to target very young children for developmental screening/ surveillance. As, earlier we can screen the children, higher the chances of attaining similar milestones at similar ages despite of cultural differences.[38]

Promising quasi-validated tool

We have found quite a few promising screening tools suitable for early identification of developmental delay. Unfortunately, could not include them as the studies didn't fulfil our selection criteria. One of the quasi-validated tools is Neonatal Oral Motor Assessment Scale (NOMAS). NOMAS is a commonly used neonatal feeding evaluation which is developed by Marjorie Meyer Palmer in 1985. The NOMAS is the only available neonatal feeding evaluation that can be used for the term or preterm infants and for breast or bottle-fed infants. This is a 28-items observational checklist for tongue and jaw movement. Following the observation of non-nutritive sucking, oral feeding for the first 2 minutes are evaluated.[70] In a study conducted in Taiwan by Tsai et al., 2010, the predictive validity of NOMAS was assessed against BSID- II in a group of 27 preterm infants without brain lesion to demonstrate neurodevelopmental outcome at 6 months and 12 months of corrected age.[71]

Suitable screening tools for primary health care setting

Out of the ten screening tools, we would recommend two screening tools feasible enough to be used for developmental surveillance at the primary health care setting. They are ASQ and

PEDS. Both are parent-completed screening tools. Their strong points are: PEDS requires bare minimum additional materials and for ASQ, it provides 21 sets of questionnaires for 21 age groups. Besides, both are very easy to administer. We can easily build up a surveillance system using these tools. Where health workers can carry out screening at households using single PEDS questionnaire for all, then screened positive cases can be referred to the primary health care centres to conduct secondary screening with age specific ASQ questionnaire. Basic properties of ASQ and PEDS are stated in the Supplementary Table S6. (adopted from [72])

Limitations

Despite our best efforts, there were several limitations to this study. This study was limited to articles published in the English language only due to constraints in resources and time. In this study, we could neither address developmentally delayed children due to HIV exposure nor due to autism spectrum disorder or other behavioural disorders. Though these two groups of children also suffer from varying degree of developmental delay, the pathogenesis behind those delays is closely related to the diseases themselves.[73, 74] Moreover, conventionally it takes more than two years of age to diagnose a child with autism spectrum disorder and hence the age range of currently available autism screening tools starts later than general developmental screening tools (e.g. Modified Checklist for Autism in Toddlers: 16-30 months; where ASQ-3: 1-66 months). This conflicts with the objectives of our study to ensure early diagnosis of developmental delay. So, with respect to other neurodevelopmental disorders, we preferred to focus exclusively on developmental delay in our study. Though it is very difficult to rule out the possibility of undiagnosed cases of autism being included among all the developmentally delayed children, as none of the studies reported so. Moreover, we were unable to critically appraise the available screening tools in terms of diagnostic accuracy due to the unavailability of the necessary information. Which is quite reasonable as Boggs and her colleagues also

reported that authors tend to provide validity information very briefly and evidence on accuracy are most difficult to obtain.[28] We are hopeful to conduct subsequent systematic review and meta-analysis on geographical region/ country/ domain specific screening tools and their psychometric properties based on the information obtained from this study.

Recommendations

(1) A global regulatory body should be formed to standardize the terminologies and cut-off scores of available and future screening tools to improve comprehensiveness and interpretation of test results, simultaneously ensuring better correlation between results obtained from different screening tools.

(2) Future research work should focus on revising existing screening as well as assessment tools in different ethnic and cultural perspectives and validate them in the respective normative sample as well as conducting systematic reviews based on individual screening tools in different cultural settings.

(3) We also recommend ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools to identify and treat developmental delay as early as possible. Developmental screening at the time of routine immunization schedule could be a possible way to integrate this with an existing successful public health program in LMICs. This timing would be both cost-effective and maximize response rates.

Conclusions

Developmental screening is required for early diagnosis of developmental delays in infants and young children in LMICs to enable early intervention and rehabilitation. In order to do this, culturally-sensitive, easy to administer screening tools with good psychometric properties are

needed. We observed that there is a lack of culturally sensitive developmental screening tools validated among under 5 children in LMICs. However, we have found eight screening tools with relatively high sensitivity and specificity. We also identified key research gaps and consequently proposed a few recommendations for overcoming those gaps. These include (but not limited to) global standardization of terminologies and cut-off scores for screening tools, revising existing tools according to diverse cultural norms and validating them in the respective normative sample and finally ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools. To execute so, we have suggested a health worker centred screening system consisting ASQ and PEDS. Therefore, future research should focus on enabling the caregivers, health workers, and therapists to assist in children with developmental delays in LMICs to reach their full developmental potential.

Declaration of interest: This manuscript is new and entirely original, has not been copyrighted, published, submitted, or accepted for publication elsewhere. All authors have given their consent and agreed to submit to your journal. The authors have no conflict of interest.

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Author Statement: This study was conceived and designed by GK and TF. CK developed the search strategy. Three authors conducted the database search (phase 1 up to March 2018: CK; phase 2 up to July 2020: IJ and MKI). Two authors (TF and IJ) independently screened the title and abstracts. TF, MKI and GK independently performed the full-text review of the screened articles. During each step of the study selection process, disagreements were resolved through discussion. TF and MKI wrote the first draft with input from GK and KB. All authors reviewed all drafts and approved the final submitted manuscript.

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Patient consent for publication: Not required.

Ethics approval: As this systematic review did not directly involve human or animal subjects, or access to medical records; ethical approval was not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: No original data were generated for this study.

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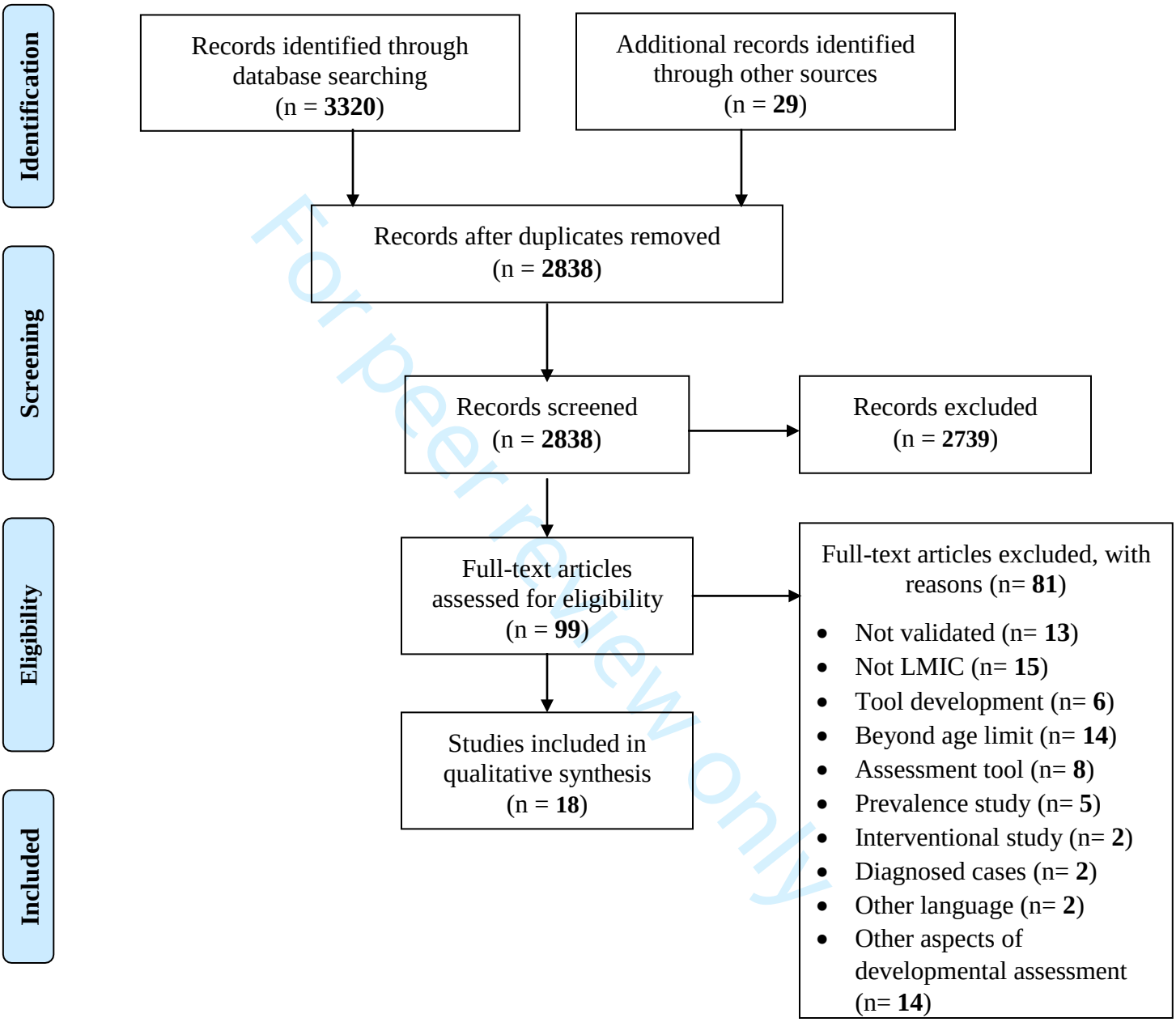
Figure 1: PRISMA flow diagram



Supplementary Figure S1: Correlation between NMR and Prevalence of DD (Taiwan 1997-2008)

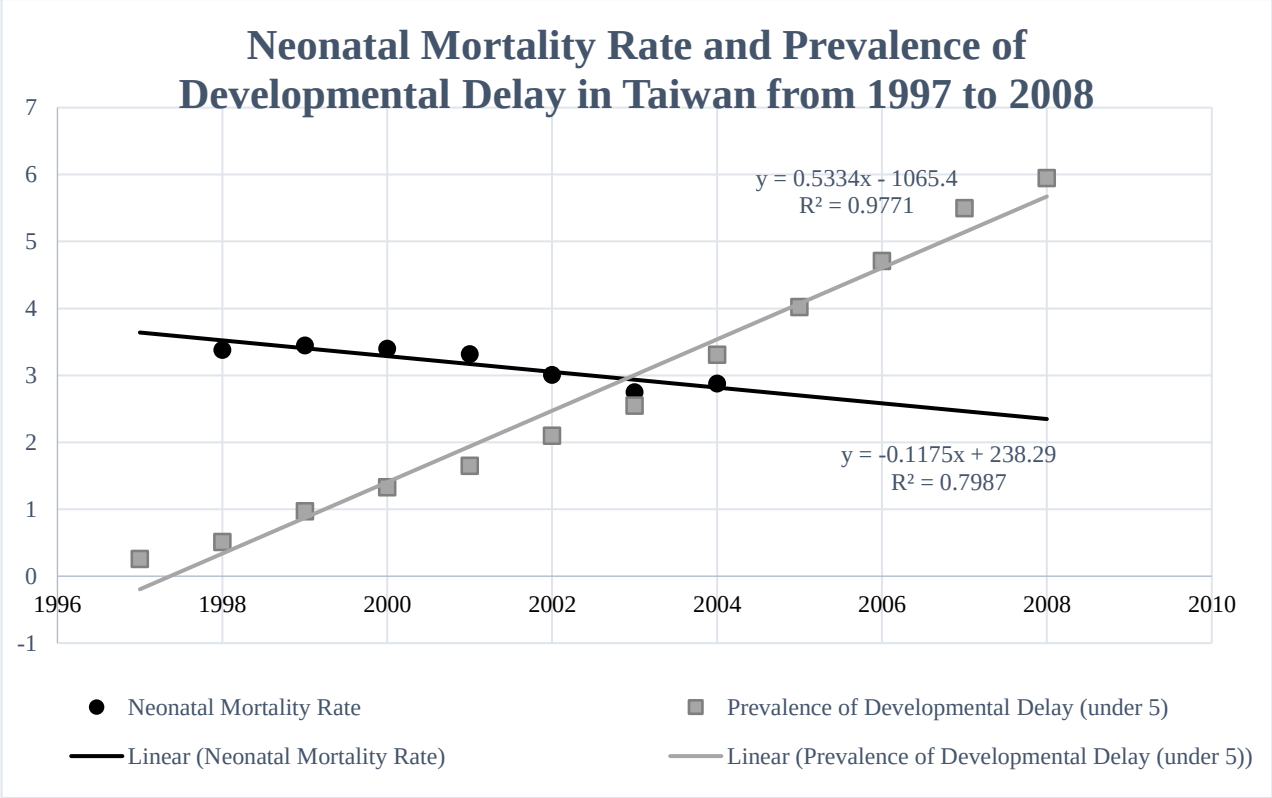


Figure S1: Correlation between neonatal mortality rate and prevalence of developmental delay (Taiwan 1997-2008)

Footnote: We have used prevalence of developmental delay among under 5 children (1997-2008) from a nation-wide population based retrospective study [18] and neonatal mortality rate (1998-2004) from another study [19]. It was revealed that the prevalence of developmental delay is positively associated with time and negatively associated with NMR. So, it can be said that, with time, while neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing.

Supplementary Table S1: Medline search strategy

MEDLINE: Systematic review - screening for disorders in children in LMIC (as at 05.03.18) Notes: No date or language limits applied.

Database: Ovid MEDLINE <1946 to 2018 February 28> (Phase 1)

Search Strategy:

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1 exp Mass Screening/ (114856)
2 screen$.tw. (543259)
3 exp DIAGNOSIS/ (7780076)
4 (early adj5 (diagnos$ or identif$ or detect$ or discover$)).tw. (179324)
5 1 or 2 or 3 or 4 (8132793)
6 exp "Surveys and Questionnaires"/ (881308)
7 (survey$ or questionnaire$).tw. (745680)
8 (instrument$ or tool$).tw. (665937)
9 6 or 7 or 8 (1849661)
10 5 and 9 (774120)
11 exp Neurodevelopmental Disorders/ (162135)
12 exp Motor Disorders/ (197)
13 exp Cerebral Palsy/ (18455)
14 (cerebral adj pals$).tw. (17316)
15 CP.tw. (36947)
16 exp Cognitive Dysfunction/ (7530)
17 exp Communication Disorders/ (59072)
18 ((development$ or motor$ or speech$ or cogniti$ or behav$) adj5 (disorder$ or disabilit$ or condition$ or impair$ or deficit$)).tw. (200268)
19 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (415783)
20 10 and 19 (27683)
21 exp Developing Countries/ (69408)
22 exp ASIA/ (698877)
23 exp AFRICA/ (230576)
24 exp South America/ (134532)
25 asia$.tw. (100200)
26 africa$.tw. (169185)
27 (south adj1 america$).tw. (14876)
28 (low adj2 income adj2 countr$).tw. (4196)
29 (middle adj2 income adj2 countr$).tw. (7713)
30 LMIC.tw. (649)
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (1214625)
32 20 and 31 (2207)
33 limit 32 to humans (2185)
34 remove duplicates from 33 (2183)
35 limit 34 to "all child (0 to 18 years)" (1270)
36 exp INFANT/ (1056001)
37 exp CHILD/ (1753019)
38 exp ADOLESCENT/ (1842871)
39 (paediatric$ or pediatric$ or child$ or adolescen$ or teen$ or infant$ or baby or babies).tw. (1586099)
40 36 or 37 or 38 or 39 (3520016)
41 34 and 40 (1313)
42 35 or 41 (1313)

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Database: Ovid MEDLINE(R) ALL <1946 to July 13, 2020> (Phase 2)
Search Strategy:
---

1 exp Mass Screening/ (127799)
2 screen$.tw. (748410)
3 exp DIAGNOSIS/ (8521264)
4 (early adj5 (diagnos$ or identif$ or detect$ or discover$)).tw. (247525)
5 1 or 2 or 3 or 4 (9082816)
6 exp "Surveys and Questionnaires"/ (1030942)
7 (survey$ or questionnaire$).tw. (1039336)
8 (instrument$ or tool$).tw. (981681)
9 6 or 7 or 8 (2492583)
10 5 and 9 (930528)
11 exp Neurodevelopmental Disorders/ (180714)
12 exp Motor Disorders/ (480)
13 exp Cerebral Palsy/ (20558)
14 (cerebral adj pals$).tw. (22436)
15 CP.tw. (54326)
16 exp Cognitive Dysfunction/ (17245)
17 exp Communication Disorders/ (63349)
18 ((development$ or motor$ or speech$ or cogniti$ or behav$) adj5 (disorder$ or disabilit$ or condition$ or impair$ or deficit$)).tw. (283402)
19 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (537248)
20 10 and 19 (34449)
21 exp Developing Countries/ (74723)
22 exp ASIA/ (832820)
23 exp AFRICA/ (265707)
24 exp South America/ (161136)
25 asia$.tw. (146545)
26 africa$.tw. (228897)
27 (south adj1 america$).tw. (21374)
28 (low adj2 income adj2 countr$).tw. (7421)
29 (middle adj2 income adj2 countr$).tw. (18310)
30 LMIC.tw. (1795)
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (1497552)
32 20 and 31 (2846)
33 limit 32 to humans (2778)
34 limit 33 to "all child (0 to 18 years)" (1553)
35 exp INFANT/ (1136560)
36 exp CHILD/ (1905000)
37 exp ADOLESCENT/ (2022225)
38 (paediatric$ or pediatric$ or child$ or adolescen$ or teen$ or infant$ or baby or babies).tw. (1999177)
39 35 or 36 or 37 or 38 (4073700)
40 33 and 39 (1614)
41 34 or 40 (1614)
42 limit 41 to yr="2018 -Current" (242)

****

Supplementary Table S2: List of key definitions regarding study selection

Key words	Definitions
Assessment	Assessment is a process for defining the nature of that problem, determining a diagnosis, and developing specific treatment recommendations for addressing the problem or diagnosis.
Developmental Assessment	In-depth examination of child's development conducted by developmental pediatrician/ child psychologist
Developmental Delay	A condition where a child does not reach it's developmental milestones at the expected times
Developmental Disability	The severe and chronic form of developmental delay which is expected to continue indefinitely and substantially restricts the individual's daily living activities
Developmental Domain	A collective term used to describe different aspects of brain growth and development
Developmental Monitoring	Observing child's developmental progress by parents/ caregivers
Developmental Screening	Looking for specific developmental concern by doctors/ healthcare professionals using brief questionnaire/ checklist
Disability	any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being.
Gray Literature	Research that is either unpublished or has been published in non-commercial form. Example: government reports, conference proceedings, pre-prints and post-prints of articles, theses and dissertations, etc.
Hand Searching	The page-by-page examination of journal issues, conference proceedings, reference lists of journal articles and other publications for relevant studies
Impairment	any loss or abnormality of psychological, physiological or anatomical structure or function.
Item	List of activities under a screening tool or questionnaire
Monitoring	monitoring involves routine evaluation of changes to health or health risks
Original Article	It is the report of a study written by the researchers who conducted the study
Psychometric Properties	Psychometric properties refer to the reliability and validity of a test
Reliability	Reliability refers to the extent to which an assessment/ screening tool produces stable and consistent results
Review Article	Critical and constructive analysis of existing published literature in a field, considered as secondary literature.
Screening	Screening is a process for evaluating the possible presence of a particular problem. The outcome is normally a simple yes or no
Sensitivity	The ability of a test to correctly identify those who have the disease
specificity	The ability of a test to correctly identify those who do not have the disease
Surveillance	Ongoing systematic collection of health data essential to the planning, implementation and evaluation of the public health practice closely integrated with the timely dissemination of these data to those who need to know
Validity	The ability of a test to distinguish between who has a disease and who does not

Supplementary Table S3: Selection criteria used for participation in the studies

Ref.	Inclusion Criteria	Exclusion Criteria
[34]	Children attending the study hospital	Children without a proper birth record Children not accompanied by a caregiver at the time of evaluation
[35]	Children living in the study area	Not applicable
[36]	Parents willing to participate	Not applicable
[37]	Children living in the study area	Not applicable
[38]	Very Low Birth Wight Children treated in NICU of the study hospital	Not applicable
[39]	Children living in the study area	Not applicable
[40]	Children whose parents/ primary caregiver gave consent	Ill children Children uncooperative for testing
[41]	Afrikaans, Tswana or English speaking parents or guardian	Children suspected or diagnosed with mental retardation, autism or neuromotor delay
[42]	Children attending the study hospital	Children with acute illness Children not accompanied by parents Children whose parents did not give consent to participate
[43]	Children with apparently normal development	Children with acute and chronic disease Children not accompanied by a caregiver Children with illiterate caregiver
[44]	Parents completed primary education Parents able to read Hindi Parents living with the child	Premature children Children with acute severe illness Previous diagnosis of developmental disorder
[45]	Children attending the study hospital	Premature children Previous diagnosis of developmental delay Children with a visual/hearing problem The accompanying parent does not understand the Thai language
[46]	Parents willing to participate	Chronically ill children Previous diagnosis of developmental delay
[47]	Children living in the study area	Children whose parents did not give consent to participate
[48]	Afrikaans or English speaking parents Parents visiting the primary health care clinics Parents asked to participate	Not applicable
[49]	Children born to mothers enrolled in "Malaria in Pregnancy Preventive Alternative Drugs" trial	Non-singleton births
[50]	**Community:** Children living in the study area **Hospital:** Children attending the study hospital	Not applicable
[51]	Not applicable	Children with congenital malformation, acute illness and mental retardation

Supplementary Table S4: List of Rejected Studies and Tools

	Ref	Tool	Reason of Rejection
1.	Biasini et al. 2015	12 month Screener	Tool Development Intervention study
2.	Wirz et al. 2005	ACCESS Portfolio	Disability Screening tool Sensitivity-Specificity not measured
3.	Ngoun et al. 2012	AHC DMAT	Tool development 1-6 years Sensitivity-Specificity not measured
4.	Kwun et al. 2014	ASQ	Validated in non LIMC country
5.	Salomonsson et al. 2010	ASQ:SE	Validated in non LIMC country
6.	Bian et al. 2017	ASQ:SE	Translation and adaptation Sensitivity-Specificity not measured
7.	Parveen et al. 2014	BSID-II	Assessment tool Tool adaptation
8.	Ranjitkar et al. 2018	Bayley III	Efficacy of vitamin B12 supplementation on growth and neurodevelopment
9.	Rizzoli-Córdoba et el. 2015	BDI-2 ST	Prevalence study English translation is not available
10.	Kishore et al. 2018	BDST	Correlation Study Sensitivity-Specificity not measured
11.	Pathak et al. 1991	BDST	Preparing developmental curve Sensitivity-Specificity not measured
12.	Guedes et al. 2011	BINS	Sensitivity-Specificity not clearly documented
13.	Sheldrick et al. 2013	BPSC	Validated in non LIMC country
14.	Glascoe et al. 2005	Brigance-II	Validated in non LIMC country
15.	Ireton et al.1996	CDR-PQ	Validated in non LIMC country
16.	Liao et al. 2008	CDIIT	Validated in non LIMC country
17.	McCoy et al. 2017	CREDI	Tool development, Correlation study
18.	Altafim et al. 2018	CREDI	Sensitivity-Specificity not measured
19.	Wetherby et al. 2003	CSBS-DP	Validated in non LIMC country
20.	Nair et al. 2009	DATA	Tool development and standardization Sensitivity-Specificity not measured
21.	Nair et al. 2012	DATA II	Tool development
22.	Luiz et al. 2004	DDST II	3-6 years Correlation study
23.	Wijedasa et al. 2011	DDST II	Adaptation and standardization
24.	Shahshahani et al. 2010	DDST II	0-6 years
25.	Scherzer et al 2009	DMChart	0-8 years Sensitivity-Specificity not measured
26.	Abubakar et al. 2009	DMChecklist	Correlation study Sensitivity-Specificity not measured
27.	Prado et al. 2014	DMCchecklist II	Correlation study Sensitivity-Specificity not measured
28.	Chopra et al. 1999	DSS	Disability Screening tool 0-6 years
29.	Velez et al. 2007	EAD 1	Prevalence Study
30.	Rao et al. 2014	EAP ECDS	Assessment tool 36-71 months
31.	Janus et al. 2007	EDI	4-6 years Validated in non LIMC country
32.	Verdisco et al. 2015	Engle	Correlation study Sensitivity-Specificity not measured
33.	Schafer et al. 2014	ERIC	Validated in non LIMC country
34.	Meisels etal. 1993	ESI-R	3-6 years

			Validated in non LIMC country
35.	Lenkarski et al. 2001	ESP	Validated in non LIMC country
36.	Hatakenaka et al. 2016	ESSENCE-Q	0-6 years Validated in non LIMC country
37.	Munir et al. 1999	IBAS	Assessment tool 1-10 years
38.	Gulati et al. 2014	INCLEN-NDST	2-9 years
39.	Fernandes et al. 2014 Murray et al. 2018	Intergrowth-21	Assessment tool
40.	Abubakar et al. 2008	KDI	Assessment tool Part of sample consists of children with NDD
41.	Gladstone et al. 2008 Gladstone et al. 2010	MDAT	Assessment tool 0-6 years
42.	Hwang et al. 2015	MuSiC	Validated in non LIMC country
43.	Arya et al. 1991	NIMH-DSS	0-6 years
44.	Schroeder et al. 2014	PCQ	Sensitivity-Specificity not clearly documented
45.	Malik et al. 2007	PDST	Sensitivity-Specificity not measured
46.	Sheldrick et al. 2012	PPSC	1.5-5.5 years Tool development Validated in non LIMC country
47.	Simonian and Tarnowski 2001	PSC	4-16 years
48.	Boyede et al.2016	Red Cross	Validated among HIV infected children
49.	Islam et al. 2016	RNDA	Assessment tool Prediction
50.	Ara et al. 2015	RNDA	Prevalence of NDI
51.	Khan et al. 2014	RNDA	Assessment 2-9 years
52.	Haataja et al. 2002	Shoklo	Assessment tool Validated in non LIMC cohort
53.	Sheldrick and Perrin 2013	SWYC	Tool development
54.	Wu et al. 2012	TQP	Association study
55.	Pérez-Escamilla 2017		Spanish

Supplementary Table S5: Example of culture-sensitive BSID-II items for Bangladeshi infants (adopted from [66])

	Original	Culture Sensitive
Picture	Pomfret	Ilish
	Star	National Flag
	House with chimney	Tin-shed house
Material	Sugar pellet	Iron tablets
	Small toy (rabbit)	Small doll (boy or girl)
	Thomas The Tank Engine Visits a Farm	Shishur Jotno' from 'Meena Raju Series'
	Sugar pellet	Iron tablets
Word	Auto	Vo
	Leaf	Pata/ Shak

Supplementary Table S6: Basic properties of ASQ and PEDS (adopted from [72])

Characteristic	PEDS	ASQ
Screening approach	Parents' developmental concerns	Parents provide information about child's skills
Age Range	0 to 96 months	1 to 66 months
Questionnaire	One	21 sets of questionnaire for 21 age groups
Developmental domains	Gross motor, Fine motor, Cognitive, Expressive language, Receptive language, Self-help, Social-emotional, Behavior, School, Other	Gross motor, Fine motor, Problem solving, Communication, Personal-social
Format	10 questions covering 9 developmental concerns Response options: no/yes/a little	30 questions covering 5 developmental domains Response options: yes/sometimes/not yet
Example of item	Expressive language: "Do you have any concerns about how your child talks and makes speech sounds?"	Communication skill at 18 months: "Does your child say 8 or more words in addition to 'Mama' and 'Dada'?"
Time to screen	5 min of parent time 1–2 min for provider/staff to score	10–15 min of parent time 1–2 min for provider/staff to score

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title file
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	10
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-10

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-9 Table S2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9-10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Sensitivity, Specificity
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A (eliminated in revised

			manuscript)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	14-27
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	28-32
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	32-33
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	33-34
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Title: Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

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Screening Tools for Early Identification of Children with Developmental Delay in Low- and Middle-income Countries: A Systematic Review

Running head: Screening Tools for Developmental Delay

Article category: Review Article

Abstract

Objective: To systematically review, identify and report the screening tools used for early identification of developmental delay in Low-and Middle-Income Countries.

Design: Systematic review

Data sources: Four bibliographic databases: Medline (1946 to July 13, 2020), Embase (1974 to July 13, 2020), Scopus (1823 to July 11, 2020), and PsycINFO (1987 to July Week 1 2020).

Eligibility criteria: Peer-reviewed original articles published in English addressing validated culturally sensitive developmental screening tools among children aged < 5 years were included in this review.

Data extraction and synthesis: One author (CK, medical librarian) developed the search strategy. Three authors conducted the database search (phase 1: CK; phase 2: IJ and MKI). Two authors (TF and IJ) independently screened the title and abstracts. TF, MKI and GK independently performed the full-text review of the screened articles. During each step of the study selection process, disagreements were resolved through discussion. PRISMA statement was used to guide the systematic review. Data extraction and analysis were performed using MS Excel. Meta-analysis was not possible due to heterogeneity of the study findings.

Results: We identified 3349 articles, of which eighteen studies from ten countries, reporting sixteen screening tools, were selected for qualitative synthesis. Six cultural contexts were explored. Twelve general, two motor and two speech-language tools were identified. Seven of them found to be parent-completed ones. Five screening tools (American Speech-Language and Hearing Association, Guide for Monitoring Child Development, Infant Neurological International Battery, New Delhi – Development Screening Questionnaire and Woodside Screening Technique) reported relatively higher sensitivity (82.5-100)% and specificity (83-98.93)%.

Conclusions: Limited number of culturally sensitive developmental screening tools were validated for children aged <5 year in Low-and Middle-Income Countries. Revising existing screening tools in different ethnic and cultural settings and subsequent validation with normative value should be a research priority.

PROSPERO registration number CRD42018095232

Key words: Developmental delay, Disability, Screening, Early diagnosis, Rehabilitation, Low and Middle-Income Countries

Strengths and limitations of this study

- This review puts together extensive literature searches on original studies (both observational and experimental) conducted among under-5 children from LMICs reporting standardization, validity (in terms of sensitivity and specificity) of developmental screening tools in early diagnosis of developmental delay.
- Meta-analysis was not possible due to the heterogeneity of the study setting and findings.

- Critical evaluation of the available screening tools in terms of diagnostic accuracy was not possible to perform due to the unavailability of the necessary information.

Introduction

Developmental delay is a condition where children exhibit significant variation in achieving developmental milestones as expected for their actual or adjusted age.[1-3] Complications at birth including premature birth; brain trauma and encephalitis; severe medical problems after birth; inborn metabolic errors; genetic or chromosomal abnormalities; inadequate stimulation; malnutrition; iron deficiency anaemia; chronic illness; adverse environmental, familiar and psychological states may lead to developmental delay.[4-6] Although the condition itself may not be permanent, it can provide a foundation for recognizing children who might have more severe and permanent health conditions i.e. developmental disabilities. Apart from developmental delay, developmental disability is considered as a severe, chronic disability originating at birth or during childhood, expected to continue indefinitely, and substantially restricts the individual's functioning in several major life activities.[2, 7] Examples of developmental disabilities include Autism Spectrum Disorder, Behavioural Disorders, Cerebral Palsy, Down Syndrome, Fetal Alcohol Syndrome, Intellectual Disability, etc. As a predictive of above-mentioned learning, movement and behavioral disorders, it is possible to identify developmental delay to a great extend during the preschool period (i.e. before the age of 5 years) with the help of well validated screening tools.[8, 9] There is a long-term financial impact on society in terms of healthcare, educational support and other special services related to developmental delay and/ disability. This is because the affected children require substantial resources and increased cost over their lifespan compared to those without such conditions.[10] This further accentuates the significance of early identification to initiate appropriate

interventions and/ rehabilitations with the intention of preventing further delays, stimulating emerging skills and creating a more encouraging and protective surroundings.[5]

In the last few decades, successful implementation of World Health Organization's (WHO's) key health services[11] regarding "The Countdown to 2015 Initiatives" resulted in the reduction of the neonatal mortality rate from 37 deaths per 1000 live births in 1990 to 19 per 1000 live births in 2016, worldwide with a projection of further future reductions.[12, 13] Among the survivors, more than 250 million under-5 children from Low-and Middle-Income Countries (LMICs) are not fulfilling their developmental potential in cognitive, motor, and social-emotional domains due to poor nutrition, poverty and conflicts.[4, 14-16] In addition to them, there is an undetected number of surviving children suffering from various forms of developmental delay presumably due to brain injury during the fetal, perinatal and post-neonatal period.[17] We have discovered that, with time, while the neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing (by analysing the data generated from two nation-wide population-based retrospective studies conducted in Taiwan) (Supplementary Figure S1).[18, 19]

Monitoring, screening, and surveillance have been found effective to track a child's developmental progress. As a means of tracking a child's developmental progress, developmental monitoring is the ordinary observation of child's developmental advancement performed by parents/ caregivers. On the contrary, developmental screening aims to identify specific developmental concern by doctors/ healthcare professionals using brief questionnaire/ checklist. When such activity is performed on a regular basis during routine health check-ups, it is termed as developmental surveillance.[20, 21] Among them, developmental screening is the first step of the comprehensive diagnostic procedure for secondary prevention and early

identification of developmental delay.[16, 22, 23] Thus a well validated developmental screening tool is very important. The standardized tools available from western countries provide well-validated assessment in their own settings. However, the transfer of such western-based tools to non-western countries is linked with substantial limitations in terms of score interpretation and feasibility of their use in resource-constrained settings such as in LMICs.[24] In the developed countries, early identification of developmental delay is considered as mandatory part of good healthcare practice which is recommended by the American Academy of Paediatrics.[16] In contrast, in LMICs, most teaching and training programs of health professionals are still concentrated on acute illness and growth aspects of children rather than a developmental perspective, resulting in limited attention in developmental delay.[16] Also, in these geographical areas, parents and caregivers with strong cultural beliefs and superstitions regarding health not only remain ignorant of the child's developmental deficit but also about the future impact of the condition.[25] The combined effect of these two factors often results in overlooking or delayed the diagnosis of developmental concerns.

The perspective on developmental disability varies from one culture to another. Along with economic, geographical, social factors, it often becomes a barrier to healthcare accessibility for children with disability.[26] In Chinese culture, having children with disability is often considered shameful for the family. In Southeast Asian cultures, parents often face social deprivation due to the stigma related to developmental disability.[27] Moreover, cultural believe often holds control over treatment approaches for developmental delay or disabilities, including: (1) whether to seek help or not; (2) which treatment option to choose; (3) parental expectations for their child; (4) interpersonal relationship between caregiver and healthcare professionals, etc.[28] One of the biggest challenges in early identification of developmental delay or disability is providing culturally sensitive screening tools, which not only include

cultural perception of delay and/or disability but also easily adaptable across the various cultural/ nation.[24] Among the developmental domains, social development is culturally specific and difficult to adapt, whereas the gross motor domain is easier to adapt culturally.[29]

The purpose of this study was to look for the screening tools which have been used and validated for early identification of developmental delay in LMICs, to report how effective they are for early identification of developmental delay in terms of validity, and to identify areas for future research.

Materials and methods

Data sources and search strategy

To locate items on screening tools for early identification of developmental delay among children in low and middle-income countries, the search strategy was developed by an experienced medical librarian {Dr. Catherine King (CK)}. Literature search was conducted in two phases (phase 1 up to March 2018: CK; phase 2 up to July 2020: IJ and MKI) in four bibliographic databases. The databases searched were: OVID Medline (1946 to July 13, 2020), OVID Embase (1974 to July 13, 2020), SCOPUS (1823 to July 11, 2020), and PsycINFO (1987 to July Week 1 2020). Search terms included database-specific thesaurus terms where available such as 'Mass Screening', 'Diagnosis', 'Surveys and Questionnaires', 'Neurodevelopmental Disorders', 'Motor Disorders', 'Cerebral Palsy', 'Cognitive Dysfunction', and 'Communication Disorders' as well as relevant associated text word terms. These were combined with low and middle-income country terms and infant, child and adolescent terms. To minimize the introduction of bias, no publication date and language limits were used. The date of the latest search was 13.07.2020. The Medline search strategy could be found online as Supplementary Table S1.

In addition to bibliographic database searches, we manually checked the reference lists of recent systematic reviews [30, 31] as well as articles included in the full-text review. We also contacted experts in the relevant field to identify any additional studies or information.

Selection criteria

Study inclusion criteria were: (1) Children aged less than 5 years who were at risk of developmental delay; (2) Original studies (both observational and experimental); (3) Study where single, as well as multiple developmental domains, were examined; (4) Studies conducted only in LMICs. The exclusion criteria were: (1) Studies conducted on diagnosed cases of developmental delay; (2) Studies focusing on autism spectrum disorder and other behavioural disorders; (3) Studies conducted among HIV exposed children; (4) Studies on developmental delay among children aged more than 5 years; (5) Interventional studies on developmental delay; (6) Studies on developmental delay published before 1946; (7) Article published in languages other than English; (8) Conference papers, letter to the editor, protocols, systematic reviews and ongoing studies; (9) Study conducted among children of eligible ethnic origin but in different country settings (i.e. children adopted from LMICs but study conducted in higher income countries). List of key definitions regarding study selection are available in Supplementary Table S2.

All the under-5 children who weren't previously diagnosed with any neurodevelopmental delay or disability, were considered as "at risk of developmental delay". Studies where overall or categorised (based on different age group/ cut off score) sensitivity-specificity of screening tools were examined and clearly reported, were considered as validated. We did not discriminate among screening, monitoring and surveillance tools. If any

of those tools were validated for screening developmental delay among under-5 children, considered eligible for inclusion. Tools which were declared as assessment tools by the developer themselves as well as studies where a tool was utilized for developmental assessment by the researchers, were excluded from the review.

When we had searched the keywords "Autism Spectrum Disorder" and "Developmental Delay" in the medical databases, the number of search items were as follows- i) OVID Medline- 9320: 12402; ii) OVID Embase- 21750: 7506; iii) Scopus- 20675: 7530 and iv) PsycINFO- 17130: 3067, respectively. Which is a bit alarming. We have excluded autism and other behavioural disorders from the study to provide undivided attention to developmental delay. Apart from scientific community, parents, and caregivers of LMICs are more familiar with the term ASD compared to Developmental Delay. Which is evident from growing concerns regarding speech-language and behavioural domains of child development compared to rest of the domains.[32] We believe, to ensure successful developmental screening/ surveillance program in LMICs in the long run, and more importantly, to raise public awareness about developmental delay; we need to work more in this area than we used to.

LMICs consist of countries belonging to three World Bank income groups (low, lower-middle, and upper-middle) of WHO's Member States. The classification is based on the estimated per capita gross national income. We have used the World Bank's country classifications by income level (2020-2021) in this review.[33, 34]

Study selection, data extraction and quality appraisal

We carried out the following steps to decide on the studies: (1) Searching the above-mentioned databases using similar search strategy (CK, IJ, MKI); (2) Deduplicating and merging search

results using the EndNote bibliographic software (TF); (3) Examining titles and abstracts to remove obviously irrelevant reports (TF, IJ, MKI); (4) Retrieving and examining the full text reports of eligible studies (TF, MKI, GK); (5) Applying the selection criteria on the shortlisted articles (TF, GK); (6) Making final decisions on study inclusion and proceeding for data collection. Extracted information included: publication year, the country where the study was conducted, the name of the screening tool, the gold standard tool(s) against which the screening tool was validated, study design, study setting, sample size, sampling technique, the age of the participants, selection criteria and sensitivity-specificity of the screening tools. During each step of the study selection process, disagreements were resolved through discussion. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, including 27- item PRISMA checklist to guide the systematic review.[35] The quality of the selected studies was assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies-2 [36] (Supplementary Table S3) and Newcastle-Ottawa Scale for cross-sectional studies [37] (Supplementary Table S4).

Data analysis

Individual study findings were reported including the country, study design, study setting, sample size, sampling technique, proportions and age range of participants, sensitivity-specificity of the developmental screening tools etc. Data extraction and analysis were performed using MS Excel. We were unable to perform a meta-analysis due to the heterogeneity of the study setting and findings.

Protocol registration and ethical approval

The protocol of this systematic review has been registered in PROSPERO (registration number CRD42018095232). As this systematic review did not directly involve human or animal subjects, or access to medical records; ethical approval was not required.

Patient and public involvement

No patient involved

Results

Search results

The initial search retrieved 3349 records. We have found 3320 records from four bibliographic databases (1555 from OVID Medline, 1317 from OVID Embase, 348 from Scopus and 100 from PsycINFO). 29 records were located by reviewing the reference lists of recent systematic reviews, fully extracted articles and consulting expert researchers in this area. There were 2838 records once duplicates were removed. Following the screening of title and abstracts for articles, which described the validation of tools to screen developmental delay among children, 99 articles were selected for further evaluation. After further review and application of selection criteria, 18 articles were selected for inclusion in study.[38-55] A PRISMA flow diagram has been prepared to illustrate the study selection process (as shown in Fig. 1).

Summary of the included studies

All of the eighteen studies included for qualitative synthesis were original articles published in English, with a publication date range from 1991 to 2020 inclusive. Eight studies originated in "South Asia",[38, 41, 44, 46, 48, 51, 54, 55] four from "East Asia and Pacific",[39, 47, 49, 50] three from "Sub-Saharan Africa",[45, 52, 53] one study each from the "Middle East and North Africa",[43] "Latin America and Caribbean",[40] and "Europe and Central Asia"[42] region

of the World Bank. In total, sixteen developmental screening tools were used in ten countries. Among the sixteen screening tools, American Speech-Language and Hearing Association (ASHA), Language Evaluation Scale Trivandrum for 0-3 years LEST (LEST 0-3) focus on language domain; Infant Neurological International Battery (INFANIB) and Little Developmental Coordination Disorder Questionnaire (Little DCDQ) work on motor domains. The remaining tools are for general developmental screening. A brief description of the selected screening tools has been provided in Table 1.

Participant characteristics

All the studies involved males and females; age ranged between 0-5 years. The smallest sample size was 53 and the largest was 1945. The studies explored the following cultural contexts: East Asia and Pacific (China, Mongolia, and Thailand), Europe and Central Asia (Turkey), Latin America and the Caribbean (Brazil), Middle East and North Africa (Iran) South Asia (Bangladesh, India) Sub-Saharan Africa (Benin, South Africa). Selection criteria used for participation in those studies are stated in Supplementary Table S5.

Study characteristics

All the included studies were cross-sectional in nature. Among the eighteen studies, one study was conducted in the community and tertiary hospital simultaneously,[54] eight were conducted in the tertiary hospital,[38, 42, 43, 46-50] five were conducted in the community,[39, 40, 44, 51, 55] and one study each was conducted in a nursery school setting[45] and primary health care clinic setting.[52] In the remaining two studies, screening was done in the community followed by a hospital-based detailed assessment in one[41] and primary health care clinic-based assessment in another.[53]

Validated screening tools

The Ages and Stages Questionnaire (ASQ)

This is a parent-completed questionnaire that could be used as a general developmental screening tool. The ASQ was designed and developed by J. Squires and D. Bricker, at the University of Oregon and can be completed in 12-18 minutes.[56] The questionnaire has 30 items focusing on five domains of child development, named gross motor, fine motor, problem-solving, communication, and personal-social. Obtaining lower scores than the cut off in any domain is considered as "screen positive". The latest version of ASQ, ASQ-3, has 21 sets of questionnaires, appropriate for children aged 1–66 months.[57] In the study by Juneja et al., 2012; a Hindi adaptation of an older version of ASQ, (ASQ-2, which had 19 sets of questionnaires for 4 to 60 months aged children) was used in a convenience sample of 200 children divided into 4 age groups: 4, 10, 18 and 24 months, in a tertiary hospital setting.[38] Each age group consisted of 30 low risk and 20 high-risk children. High-risk status was determined by the presence of any of the following risk factors: prematurity, low birth weight, history of neonatal hospitalization, history of central nervous system infection, history of afebrile seizure, diagnosed cases of developmental disorder and chromosomal abnormalities. Children without these risk factors were treated as being in the low-risk group. Eventually, 4, 10, 18 and 24 months questionnaires of ASQ-2 were validated against "Developmental Assessment Scales for Indian Infants (DASII)", considered as a gold standard for developmental assessment tool among Indian children.[38] The overall sensitivity and specificity of ASQ-2 for Indian children were found to be 83.3% and 75.4% respectively.

In the study by Yue et al., 2019; Chinese adaptation of ASQ-3 was used among 1831 children aged 5 to 24 months in a cluster random sample from rural China. Eventually the tool was validated against the Bayley Scales of Infant and Toddler Development-III. Overall sensitivity and specificity of ASQ-3 found to be 76.52% and 40.97%, respectively. The authors

suggested to avoid using ASQ-3 for children lower than 13 months of age as well as children whose primary caregiver aren't their mother, due to poor performance in those group of children.[39]

American Speech-Language and Hearing Association Screening Tool (ASHA)

The ASHA was designed and developed by the American Speech-Language and Hearing Association to screen out under-5 children for language delay in receptive and expressive language domain. There are 7 age sets consisting of 6-13 questions per age set. Cut-off score for screen positive result varies from one age set to another. In general, if a child gets more than two negative answers in any domain will be considered as "screen positive". In the study conducted by Dias et. al, 2020; 1000 under-5 children were screened for language delay during a polio vaccination campaign in Sao Paulo, Brazil by utilizing the tool. Later detailed assessment was conducted using ABFW Child Language Test. ASHA found to have excellent sensitivity and specificity (82.5% and 98.93%, respectively) against ABFW Child Language Test.[40] The authors recommended to adapt the instrument for bilingual children as well as validating it in larger sample size.

Development Screening Questionnaire (DSQ)

The DSQ was designed and developed in Bangladesh, to be administered to mothers of children from birth to 24 months of age to screen their child's neurodevelopmental status. The DSQ has 24 age sets with 8 questions per set related to eight functional domains, named: gross motor, fine motor, vision; hearing, cognition, socialization, behaviour and speech.[41] Any child found to be positive on one or more functional domain is considered "screen positive". In a study conducted in urban Bangladesh, a random sample of 197 children aged 0-24 months was screened in the community with DSQ, and then a detailed developmental assessment was done

in a tertiary hospital with the help of the "Rapid Neurodevelopmental Assessment" tool as the gold standard. Overall sensitivity and specificity of DSQ for under 2-year-old Bangladeshi children was found to be 47.1% and 97.2% respectively.[41] Despite moderate sensitivity, the DSQ might be advantageous for resource-poor settings due to its high specificity.

Guide for Monitoring Child Development (GMCD)

The GMCD was designed and developed in Turkey to monitor development of 0-3.5 years old children in LMICs. The tool consists of 7 open ended questions focusing on the following domains- Expressive language and communication, Receptive language, Fine and gross motor, Social-emotional, Self-help. Children declared screened positive if they failed to demonstrate one or more age appropriate milestones. In a study conducted by Ertem et al. 2008; GMCD was validated against Bayley Scales of Infant Development (Bayley-II) in a random sample 79 Turkish children of 1-24 months of age. The overall sensitivity and specificity of GMCD were found to be 88% and 93% respectively.[42]

Infant Neurological International Battery (INFANIB)

The INFANIB was established by Ellison and Browning in 1985 to assess the gross motor function of children aged 0 to 18 months. The tool contains 20-items focusing on spasticity, vestibular function, head and trunk, French angles and legs.[58] In the study by Soleimani and Dadkhah, 2006; a consecutive sample of 6150 children were screened using INFANIB and classified as normal, transiently abnormal and abnormal. To validate the tool a random sample of 153 children from the above-mentioned groups were assessed by paediatric neurologists. It was found that overall sensitivity and specificity of INFANIB for Iranian children were 90% and 83% respectively.[43]

Language Evaluation Scale Trivandrum (LEST 0-3)

Designed and developed at the Child Development Centre of the Trivandrum Government Medical College, India, LEST (0-3) is a 33 items screening tool to screen out language delay among 0 to 3 years old children.[44] The LEST (0-3) was validated against the "Receptive-Expressive Emergent Language Scale" tool as a gold standard in a community sample of 643 Indian children aged 0 to 36 months. To decide on the best possible combination, researchers considered both "one item delay" and "two items delay" as screen positive. When one item delay considered as screen positive, sensitivity and specificity of LEST (0-3) found to be 95.8% and 77.5% respectively. Similarly, when two items delay measured as screen positive, the sensitivity and specificity obtained as 66.7% and 94.8% respectively.[44] It should be noted that the original version of Receptive-Expressive Emergent Language Scale (1971) was used in this study for validation due to the lack of age-appropriate language assessment tool for language delay.

Little Developmental Coordination Disorder Questionnaire (Little DCDQ)

The Little DCDQ was developed by Rithman and colleagues in Canada to assess gross motor and fine motor function of children between 3 to 5 years of age. It is a parent-reported questionnaire with 15 items under three main components, control during execution, fine motor execution and overall coordination.[45] The Little DCDQ was validated against the Movement Assessment Battery for Children-2 as a gold standard in a group of 53 South African pre-schoolers between 3 to 5 years of age, with Afrikaans, Tswana or English speaking parents.[45] With 57.14% sensitivity and 81.25% specificity, Little DCDQ had the potential to be used in South African culture, however, some adjustments would be required.

Lucknow Development Screen (LDS)

The LDS was developed in CSM Medical University, Lucknow, India, using selected milestones from Baroda Development Screening Test. It is a 27 items chart format tool,

covering four domains namely motor, mental, language and social. Suitable for children aged 0 to 24 months. The LDS is said to be easily administrable by interviewing parents or caregiver.[46] In a study conducted in India, the LDS tool was validated against the DASII and the Vineland Social Maturity Scale. They administered the tool to mothers of a sample of 142 children, aged between 6 to 24 months, attending Paediatric Outpatients or Neurology Clinic of CSM Medical University, Lucknow, India. The screening tool was translated into Hindi for easy understanding and administration. For 3 children among the sample size of 142, Vineland Social Maturity scale was used as a gold standard, as DASII couldn't be applied to them. It is claimed that the LDS has a great potential to be used as a community screening tool among Indian children, with an overall sensitivity of 95.9% and specificity 73.1%.[46]

Mongolian Rapid Baby Scale (MORBAS)

The MORBAS is a written developmental screening test, designed and developed in Mongolia. It has 161 items arranged under seven developmental domains, namely gross motor, fine motor, cognitive, expressive language, receptive language, social-emotional and adaptive behaviour. The tool is suitable for children aged 0 to 42 months.[47] In a study conducted in Mongolia, MORBAS was administered in a convenience sample of 150 Mongolian children aged 0 to 42 months and thus validated against the Bayley Scales of Infant and Toddler Development-III. With sensitivity 81.8% and specificity 52.3%,[47] MORBAS could be useful in the long run to screen out children for early intervention and rehabilitation.

New Delhi – Development Screening Questionnaire (ND-DSQ)

The ND-DSQ was developed by Jain and colleagues, at Chacha Nehru Bal Chikitsalaya, a tertiary hospital of northern India. ND-DSQ has 20 items, two age sets (9 months and 18 months) and applicable for children aged 9 to 18 months.[48] The items mentioned were milestone specific. Thus, no explicit mention of the developmental domains was found. In the

study by Jain et al., 2017; ND-DSQ was validated against DASII in a convenience sample of 200 children aged 9 and 18 months (with 100 children per age group). It was established that the 9-month questionnaire was 100% sensitive and 87.2% specific for Indian children. Correspondingly, the 18 months questionnaire was validated with 91.4% sensitivity and 88.7% specificity.[48] As a newly developed tool, the ND-DSQ is promising to be useful for Indian and similar cultural settings.

Parent Evaluation of Developmental Status (PEDS)

This tool was developed in 1997 by F. P. Glascoe at Tennessee, USA.[59] It is the only screening tool available to date that addresses parent's concern about children's development in the following domains: gross motor, fine motor, cognitive, expressive language, receptive language, behaviour, social-emotional, self-help, school and other.[60] It has ten open-ended questions under ten areas of parental concerns, applicable for children aged 0 to 8 years. The other category allows parents to express concerns not already addressed under previous categories. This unique property makes PEDS unique as a developmental screening tool. In PEDS, parental concerns are labelled as "predictive" (significant) and "non-predictive" (non-significant). Thus, children are screened as low risk, moderate risk and high-risk group if they have no or non-predictive concerns, one predictive concern and two predictive concerns, respectively.[49]

In the study by Chunusuwan et al., 2016; the PEDS- Thai was validated against the "Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level" in a tertiary hospital. A convenience sample of 266 children of 9, 18 and 30 months of age was selected. Screen positive children were assembled as "high risk" (≥ 2 significant concerns) and "moderate or high risk" (≥ 1 significant concern) group. Sensitivity and specificity of PEDS against Parent Evaluation of Developmental Status: Developmental Milestones, Assessment

Level for the high-risk group was established as 27.7% and 93.0%, respectively. For moderate or high-risk group, the tool was 67.7% sensitive and 60.7% specific.[49] In order to avoid unnecessary/over-referral, the authors suggested to practice second stage evaluation (using Parent Evaluation of Developmental Status: Developmental Milestones, ASQ, Denver-II etc. tools) alongside/after PEDS screening.

In another study by Wantanakorn et al., 2016; they validated the PEDS- Thai against the Mullen Scales of Early Learning tool as a gold standard in a convenience sample of 137 children aged 18 to 36 months in another tertiary hospital. It was found that the PEDS-Thai is a promising tool for Thai cultural backgrounds with overall sensitivity of 92.8% and specificity 49.2%.[50] According to the authors, "the relatively low specificity of PEDS seen here may be because of the excessive concern of parents regarding their child's development, especially who are in relatively high socioeconomic status". The selection bias of participants was mentioned as the major limitation of the study. Thus, they advised further evaluation of the diagnostic performances of the tool using a representative sample of the population.

Rapid Pre-screening Denver Questionnaire (R-PDQ)

The R-PDQ is a general developmental screening tool covering four developmental domains: gross motor, fine motor activity, personal-social and language.[51] It has four age sets applicable for children aged 0 to 6 years: 0 to 9 months, 9 to 24 months, 2 to 4 years and 4 to 6 years. Each questionnaire contained 25 items. To score a child, the responding person had to keep answering the questions until there were three negative responses under a specific domain. In the study by Awasthi et al., 1997; the 2 to 4 years questionnaire of R-PDQ was validated against the Denver Developmental Screening Test. The study participants were randomly selected 126 children living in urban slums of Lucknow, India. To validate the tool, when a delay in more than one domain was considered as the cut-off, the tool was revealed to

be 100% sensitive and 7.8% specific. Similarly, when a delay in more than two domains was considered as the cut-off, the sensitivity and specificity were found to be 18.2% and 42.6%, respectively.[51] Inconvenient validity and high referral rate compared to US children were explained by the presence of various "difficult to interpret" questions and Denver Developmental Screening Test being an unsuitable gold standard for R-PDQ.

Road to Health Booklet Developmental Checklist (RTHB-DC)

The RTHB-DC was prepared as an integrated part of The Road to Health Booklet, the revised version of which was introduced in October 2010. RTHB-DC is the only developmental surveillance and screening tool, currently implemented nationally in South Africa. The tool consists of 21 questions covering gross motor, fine motor, communication, vision, and hearing domains. The checklist is applicable for children aged 14 weeks to 6 years.[61] In the study by Linde et al., 2015; RTHB-DC was validated against PEDS and Parent Evaluation of Developmental Status: Developmental Milestones tools. The sample size was 201, consisting of children aged 6 to 12 months old. In a primary health care clinic setting in South Africa, the sensitivity of the tool was found to be very low, i.e. 25% compared to reasonably high specificity of 91%.[52] Further development of the tool has been suggested by the authors incorporating consistent age gaps and inclusion of all developmental domains.

Ten Questions Screening Instrument (TQSI)

The TQSI Screening Instrument was developed in 1984 as part of a pilot study conducted by the University of Columbia, USA, for use in resource-poor countries.[62, 63] TQSI is a parent reported tool comprising of ten questions addressing motor, cognitive, vision, hearing, and seizure status. A child is considered screen positive if any of the questions are found to be positive. The tool is appropriate for children aged 2 to 9 years. In a study by Koura et al., 2013; the TQSI was validated against the Mullen Scales of Early Learning in a sample of 357 children

aged 12 months.[53] The participants were the offspring of the mothers who were enrolled in the "Malaria in Pregnancy Preventive Alternative Drugs" trial. To adjust the tool for that age group, researchers had excluded the language domain which is applicable for children above 2 years. In that study, screening was done in the community followed by a detailed assessment done in the health centre. It was found that the overall tool had reasonably high sensitivity (81%) but poor specificity (31%) for children of Benin. This is compared to the 76.5% sensitivity and 75.7% specificity where only the motor domain was considered.[53] Mullen Scales of Early Learning was used due to lack of a gold standard assessment tool for the Beninese population. The result suggests that the TQSI tool might be useful for resource-poor settings to screen out moderate to severe delay in motor function.

Trivandrum Developmental Screening Chart (TDSC)

The TDSC was designed and developed by Nair and colleagues in 1991 in Child Development Center, Kerala, India. The chart contains 17 items under four developmental domains- mental, motor, vision and hearing; applicable for children under two years od age.[54] If a child fails to achieve any item appropriate for his chronological age, considered as screened positive. In a study conducted by Nair et al. 1991; TDSC was validated against Denver Developmental Screening Test (DDST) simultaneously in community as well as hospital settings in a cluster random sample of 1945 Indian children aged less than two years. Overall sensitivity and specificity of TDSC found to be 66.7% and 78.8%, respectively.[54] The authors recommended to utilize the chart for mass screening of developmental delay among under-2 children in resource poor settings.

Woodside Screening Technique (WSST)

The WSST was designed and developed in Glasgow, Scotland in the year 1976. The tool consists of 70 items covering social, hearing and language, vision and fine motor, and gross

motor domains, suitable for children under 4 years of age.[55] In a study conducted by Gupta and Patel, 1991; WSST was validated against Gesell's Developmental Schedules (GDS) in a random sample of 619 children aged 6 weeks-2 years from Jabalpur, India. Overall sensitivity and specificity of WSST found to be 83% and 88%, respectively.[55]

The major findings of this systematic review are presented in Table 2. We have classified the eligible tools into two broad categories- "Parents/ Caregiver Reported Tools" and "Direct Child Testing/ Observation Tools". The tools/ studies which were not included in this review as they did not meet the selection criteria, were enlisted along with the reasons for rejection in Supplementary Table S6.

Discussion

To the best of our knowledge, this is the first systematic review which attempts to find the available screening tools for early identification of children with developmental delay in LMICs. Although some systematic reviews were found who considered developmental assessment tools requiring professional experts with a special office setup,[64] screening neurodevelopmental disability irrespective of age limit and diagnosis (e.g. Developmental Delay, Global Developmental Delay, Cerebral Palsy, Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, Epilepsy, etc.),[65] or reflected high-income country context.[8] We have also observed a study in which both screening and assessment tools have been systematically rated for accuracy and feasibility to use in LMICs.[30] Where, information was significantly dependent to World Bank's toolkit and inventory on early child development tools,[66] rather than being obtained from systematic search through databases. In contrast, the purpose of this review was to systematically look for the available studies where screening tools were used exclusively for early identification (limited to children under 5 years of age)

of developmental delay in the LMICs region where all types of study settings (i.e. from household to health facilities) were addressed in order to go for early intervention and rehabilitation of the screened cases. Therefore, the unique contribution of this review is to be able to report those screening tools exclusively designed for screening of developmental delay at the earliest possible time in both single and multiple domains.

Research gaps and future directions

Several research gaps have been identified in the reported studies. Primarily, there was a lack of standard terminologies to indicate the developmental domains. The examples of synonymous domain names are as follows: (i) **cognitive**: cognition, cognitive, global, mental, problem solving, etc.;[38, 39, 41, 46, 47, 49, 50, 53, 54] (ii) **language**: communication, expressive communication, expressive language, language, receptive communication, receptive language, speech, speech and language, etc.;[38- 42, 44, 46, 47, 49-51] (iii) **psycho-social**: adaptive behaviour, behaviour, personal-social, self-help, social, social-emotional, socialization, etc.[38, 39, 41, 42, 46, 47, 49-51, 55] Apart from those, few researchers incorporated unconventional developmental domains in their tools, such as: hearing, school, seizure, vision, etc.[49, 50, 52-55] Secondarily, there was a lack of standard proxy measures to define the screen-positive cases. Currently available examples of proxy measures are as follows: overall scores,[38, 39], number of negative answers,[40] number of milestones,[42] number of items,[44, 54] number of functional domains,[51] number of significant concerns[49, 50] etc. These two factors together, often make the screening results incomprehensible to health professionals who are not familiar with the tool in question. Moreover, it is neither possible to convert nor compare the test scores between separate screening tools, for better understanding. Many of the tools developed in English speaking countries might not be suitable for non-English speaking countries due to different socio-

cultural backgrounds and problematic translation.[67-69] These issues might become a barrier for early identification and rehabilitation of developmental delay from the service providers' end. Lastly, several studies reported that the expected sensitivity-specificity was not achieved due to the lack of validated gold standard assessment tool for the particular culture in question.[44, 51, 53] To the best of our knowledge, there is a lack of WHO's centralized initiatives, as well as no Global regulatory body is currently working in this regard. Majority of the developmental assessment tools found in this review were established for high income countries (BSID, DDST, REELS, GDS, MABC-2, etc). Only three of them were designed and developed in LMICs (ABFW, DAASII and RNDA). None of the studies using assessment tools designed for high income counties, provided information on cultural adaptation. However, in a study conducted by Parveen et al., 2014, took the initiative to culturally adapt Bayley Scales of Infant Development- Second Edition (BSID-II) items for Bangladeshi infants.[70] Example of culture-sensitive BSID-II items for Bangladeshi infants are presented in Supplementary Table S7. Future research work should focus on developing or adapting developmental assessment tools to be efficiently used as gold standard for LMICs.

In this systematic review, we had observed East Asian and Pacific, European and Central Asian, Latin American and the Caribbean, Middle East and North African, South Asian and Sub-Saharan cultural contexts among the eligible studies. Although, the number of countries engaged in similar studies are alarmingly low compared to the number of LMICs, in total.[34] This reveals the urgent need for valid and culturally sensitive screening tools for the rest of the LMICs. Among the sixteen eligible screening tools, half of them were developed in LMICs (DSQ, GMCD, LEST 0-3, LDS, MORBAS, ND-DSQ. RTHB-DC and TDSC) and another half were developed in high-income countries (ASHA, ASQ, INFANIB, Little DCDQ, PEDS, R-PDQ, TQSI and WSST). We have found the majority of the culturally sensitive tools

translated in their native language. Still, for multilingual countries like Benin, Ethiopia, India, etc. the necessity of translating the tools in regional languages, remains high. None of the LMICs has been found to be engaged in collecting nationally representative longitudinal data on the prevalence of developmental delay, which is vital for disease projection. The gathering of nationally representative prevalence data in linguistic, social, ethnic and cultural subgroups would allow the validation of customized developmental screening tools according to disease burden. Greater customization to respect the diverse cultural norms[71] of a particular community, will also most likely result in greater acceptance[72, 73] of the screening process, which is crucial for the success of a large-scale surveillance program.

While planning surveillance program for resource-poor settings, additional factors should be kept in mind. According to Gupta et al 1991, lack of furniture as well as staircase at home often results in exhibition of delayed gross motor skills due to lack of practice. Similarly, being heavily dependent on recall method is also problematic, as it is burdensome for parents with no or minimal education.[55] To overcome these issues, Ertem et al 2008 suggested to target very young children for developmental screening/ surveillance. As, earlier we can screen the children, higher the chances of attaining similar milestones at similar ages despite of cultural differences.[42]

Promising quasi-validated tool

We have found quite a few promising screening tools suitable for early identification of developmental delay. Unfortunately, could not include them as the studies did not fulfil our selection criteria. One of the quasi-validated tools is Neonatal Oral Motor Assessment Scale (NOMAS). NOMAS is a commonly used neonatal feeding evaluation which is developed by Marjorie Meyer Palmer in 1985. The NOMAS is the only available neonatal feeding evaluation

that can be used for the term or preterm infants and for breast or bottle-fed infants. This is a 28-items observational checklist for tongue and jaw movement. Following the observation of non-nutritive sucking, oral feeding for the first 2 minutes are evaluated.[74] In a study conducted in Taiwan by Tsai et al., 2010, the predictive validity of NOMAS was assessed against BSID- II in a group of 27 preterm infants without brain lesion to demonstrate neurodevelopmental outcome at 6 months and 12 months of corrected age.[75]

Suitable screening tools for primary health care setting

Out of the ten screening tools, we would recommend two screening tools feasible enough to be used for developmental surveillance at the primary health care setting. They are ASQ and PEDS. Both are parent-completed screening tools. Their strong points are: PEDS requires bare minimum additional materials and for ASQ, it provides 21 sets of questionnaires for 21 age groups. Besides, both are very easy to administer. We can easily build up a surveillance system using these tools. Where health workers can carry out screening at households using single PEDS questionnaire for all, then screened positive cases can be referred to the primary health care centres to conduct secondary screening with age specific ASQ questionnaire. Basic properties of ASQ and PEDS are stated in the Supplementary Table S8. (adopted from [76])

Limitations

Despite our best efforts, there were several limitations to this study. This study was limited to articles published in the English language only due to constraints in resources and time. In this study, we exclude children who had developmental delay due to HIV exposure or autism spectrum disorder or other behavioural disorders. Though these children also suffer from varying degrees of developmental delay, the pathogenesis behind those delays is closely related to the diseases.[77, 78] Moreover, conventionally it takes more than two years of age to

diagnose a child with autism spectrum disorder and hence the age range of currently available autism screening tools starts later than general developmental screening tools (e.g. Modified Checklist for Autism in Toddlers: 16-30 months; where ASQ-3: 1-66 months). This conflicts with the objectives of our study to ensure early diagnosis of developmental delay. So, with respect to other neurodevelopmental disorders, we preferred to focus exclusively on developmental delay in our study. Though it is very difficult to rule out the possibility of undiagnosed cases of autism being included among all the developmentally delayed children, as none of the studies reported so. Moreover, we were unable to critically appraise the available screening tools in terms of diagnostic accuracy due to the unavailability of the necessary information. Which is quite reasonable as Boggs and her colleagues also reported that authors tend to provide validity information very briefly and evidence on accuracy are most difficult to obtain.[30] We are hopeful to conduct subsequent systematic review and meta-analysis on geographical region/ country/ domain specific screening tools and their psychometric properties based on the information obtained from this study.

Recommendations

(1) A global regulatory body should be formed to standardize the terminologies and cut-off scores of available and future screening tools to improve comprehensiveness and interpretation of test results, simultaneously ensuring better correlation between results obtained from different screening tools.

(2) Future research work should focus on revising existing screening as well as assessment tools in different ethnic and cultural perspectives and validate them in the respective normative sample as well as conducting systematic reviews based on individual screening tools in different cultural settings.

(3) We also recommend ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools to identify and treat developmental delay as early as possible. Developmental screening at the time of routine immunization schedule could be a possible way to integrate this with an existing successful public health program in LMICs. This timing would be both cost-effective and maximize response rates.

Conclusions

Developmental screening is required for early diagnosis of developmental delays in infants and young children in LMICs to enable early intervention and rehabilitation. In order to do this, culturally-sensitive, easy to administer screening tools with good psychometric properties are needed. We observed that there is a lack of culturally sensitive developmental screening tools validated among under 5 children in LMICs. However, we have found eight screening tools with relatively high sensitivity and specificity. We also identified key research gaps and consequently proposed a few recommendations for overcoming those gaps. These include (but not limited to) global standardization of terminologies and cut-off scores for screening tools, revising existing tools according to diverse cultural norms and validating them in the respective normative sample and finally ensuring nationwide routine developmental surveillance programs in LMICs using culturally sensitive tools. To execute so, we have suggested a health worker centred screening system consisting ASQ and PEDS. Therefore, future research should focus on enabling the caregivers, health workers, and therapists to assist in children with developmental delays in LMICs to reach their full developmental potential.

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Table 1: Brief description of the selected screening tools

Screening Tool	Country of Origin	Study Country	Concerned Age	Parent-Reported Version	Questionnaire Type	Number of Questionnaires	Number of items	Developmental Domain	Validated Against
General Screening Tools									
Ages and Stages Questionnaire (ASQ)	USA	India, China	1–66 months	Yes	Q & A	21 age sets	30 items per set	Communication, gross motor, fine motor, problem solving, personal-social	Developmental Assessment Scales for Indian Infants (DASII) **[38]** Bayley Scales of Infant Development (BSID-III) **[39]**
Development Screening Questionnaire (DSQ)	Bangladesh	Bangladesh	birth to 24 months	No	Q & A	24 age sets	8 questions per set	Gross motor, fine motor, vision; hearing, cognition, socialization, behaviour, and speech	Rapid Neurodevelopmental Assessment (RNDA) **[41]**
Guide for Monitoring Child Development (GMCD)	Turkey	Turkey	0-3.5 years	Yes	Q & A	Single	7 items	Expressive language and communication, Receptive language, Fine and gross motor, Social-emotional, Self-help	Bayley Scales of Infant Development (Bayley-II) **[42]**
Lucknow Developmental Screen (LDS)	India	India	birth to 24 months	Yes	Chart	Single	27 item	Motor, mental, language, social	Developmental Assessment Scales for Indian Infants (DASII) **[46]** Vineland Social Maturity Scale **[46]**
Mongolian Rapid Baby Scale (MORBAS)	Mongolia	Mongolia	0 to 42 months	No	Written	Single	161 item	Cognitive, receptive communication, expressive communication, fine motor, gross motor, social-emotional, adaptive behavior	Bayley Scales of Infant and Toddler Development (BSID-III) **[47]**
New Delhi – Development Screening Questionnaire (ND-DSQ)	India	India	9 to 18 months	Yes	Q & A	2 age sets	20 items	General screening tool (domains not explicitly mentioned)	Developmental Assessment Scales for Indian Infants (DASII) **[48]**
Parent Evaluation of Developmental Status (PEDS)	USA	Thailand	birth to 8 years	Yes	Q & A	Single	10 items	Global /cognitive, speech / expressive language, receptive language, behaviour, social-emotional, school, self-help, fine motor, gross motor, other	Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level **[49]** Mullen Scales of Early Learning **[50]**

Rapid Prescreening Denver Questionnaire (R-PDQ)	USA	India	0-6 years	No	Q & A	4 age sets	25 items	Gross motor, fine motor activity, personal-social, language	Denver Developmental Screening Test (DDST) **[51]**
Road to Health Booklet Developmental Checklist (RTHB-DC)	South Africa	South Africa	14 weeks to 6 years	No	Checklist	Single	21 items	Gross motor, fine motor, communication, vision, hearing	Parent Evaluation of Developmental Status (PEDS) **[52]** Parent Evaluation of Developmental Status: Developmental Milestones **[52]**
Ten Questions Screening Instrument (TQSI)	Multiple	Benin	2 to 9 years	Yes	Q & A	Single	10 items	Vision, hearing, seizure, cognition, motor	Mullen Scales of Early Learning **[53]**
Trivandrum Developmental Screening Chart (TDSC)	India	India	0 to 2 years	No	Chart	Single	17 items	Mental, motor, vision, hearing	Denver Developmental Screening Test (DDST) **[54]**
Woodside System Screening Technique (WSST)	Scotland	India	0 to 4 years	No	Chart	Single	70 items	'Social', 'Hearing and language', 'Vision and fine motor', and 'Gross motor	Gesell's Developmental Schedules (GDS) **[55]**
Language Screening Tools									
American Speech-Language and Hearing Association (ASHA)	USA	Brazil	0-5 years	No	Q & A	7 age sets	6-13 items	Language reception and expression	ABFW test **[40]**
Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	India	India	0 to 3 years	No	Chart	Single	33 items	Speech and language	Receptive Expressive Emergent Language Scale **[44]**
Motor Screening Tools									
Infant Neurological International Battery (INFANIB)	USA	Iran	0 to 18 months	No	Not found	Single	20-items	Gross motor	Developmental Assessment by Pediatric Neurologist **[43]**
Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Canada	South Africa	3-5 years	Yes	Q & A	Single	15 items	Gross motor, fine motor	Movement Assessment Battery for Children -2 **[45]**

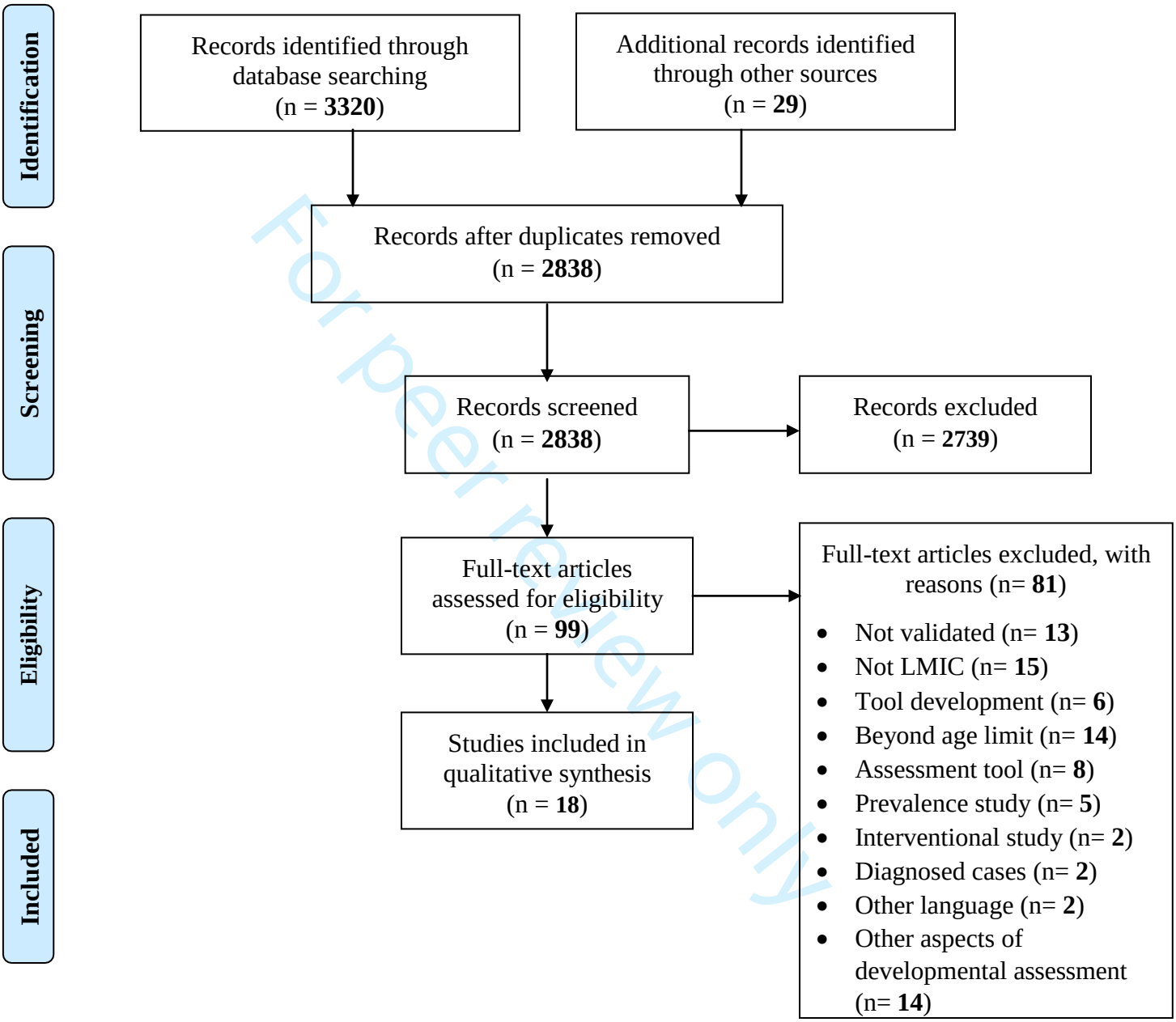
Table 2: Major findings from the selected studies used in this review

Parents/ Caregiver Reported Tools							
General Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[38]	**India** Lower-Middle- Income	Ages and Stages Questionnaire (ASQ-II)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 4, 10, 18 and 24 months **Convenience sample**	Overall	Sensitivity 83.3% Specificity 75.4%
[39]	**China** Upper-Middle- Income	Ages and Stages Questionnaire (ASQ-III)	Bayley Scales of Infant Development (BSID-III)	**Design** Cross-Sectional **Setting** Community	**Sample** – 1831 **Age** – 5-24 months **Cluster random sample**	Overall	Sensitivity 76.52% Specificity 40.97%
[42]	**Turkey** Upper-Middle- Income	Guide for Monitoring Child Development (GMCD)	Bayley Scales of Infant Development (Bayley-II)	**Design** Cross-Sectional **Setting** - Hospital	**Sample** – 79 **Age** – 1-24 months **Random sample**	Overall	Sensitivity 88% Specificity 93%
[46]	**India** Lower-Middle- Income	Lucknow Development Screen (LDS)	Developmental Assessment Scales for Indian Infants (DASII) Vineland Social Maturity Scale	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 142 **Age** - 6-24 months **Convenience sample**	Overall	Sensitivity 95.9% Specificity 73.1%
[48]	**India** Lower-Middle- Income	New Delhi – Development Screening Questionnaire (ND-DSQ)	Developmental Assessment Scales for Indian Infants (DASII)	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 200 **Age** – 9 and 18 months **Convenience sample**	9-months 18-months	Sensitivity 100% Specificity 87.2% Sensitivity 91.4% Specificity 88.7%
[49]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS)	Parent Evaluation of Developmental Status: Developmental Milestones, Assessment Level	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 266 **Age** – 9, 18 and 30 months **Convenience sample**	≥ 1 significant concern ≥ 2 significant concerns	Sensitivity 67.7% Specificity 60.7% Sensitivity 27.7% Specificity 93.0%
[50]	**Thailand** Upper-Middle- Income	Parent Evaluation of Developmental Status (PEDS- Thai)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 137 **Age** – 18-30 months **Convenience sample**	Overall	Sensitivity 92.8% Specificity 49.2%
[53]	**Benin** Lower-Middle- Income	Ten Questions Screening Instrument (TQSI)	Mullen Scales of Early Learning	**Design** Cross-Sectional **Setting** Screening- Household	**Sample** - 357 **Age** – 12 months **Random sample**	Motor Overall	Sensitivity 76.5% Specificity 75.7% Sensitivity 81% Specificity 31%

				Assessment- Health Centre			
Motor Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[45]	**South Africa** Upper-Middle- Income	Little Developmental Coordination Disorder Questionnaire (Little DCDQ)	Movement Assessment Battery for Children -2	**Design –** Cross-sectional **Setting** – nursery schools	**Sample** – 53 **Age** – 3-5 years **Convenience sample**	Overall	Sensitivity 57.14% Specificity 81.25%
Direct Child Testing/ Observation Tools							
General Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[41]	**Bangladesh** Lower-Middle- Income	Development Screening Questionnaire (DSQ)	Rapid Neurodevelopmental Assessment (RNDA)	**Design** Cross-Sectional **Setting** Screening- Household Assessment- Hospital	**Sample** – 197 **Age** - 0-2 years **Random sample**	Overall	Sensitivity 47.1% Specificity 97.2%
[47]	**Mongolia** Lower-Middle- Income	Mongolian Rapid Baby Scale (MORBAS)	Bayley Scales of Infant and Toddler Development-III	**Design** Cross-Sectional **Setting** Hospital	**Sample** - 150 **Age** – 0 month 16 days – 42 months 15 days **Convenience sample**	Overall	Sensitivity 81.8% Specificity 52.3%
[51]	**India** Lower-Middle- Income	Revised Prescreening Denver Questionnaire (R-PDQ)	Denver Developmental Screening Test (DDST)	**Design** Cross-Sectional **Setting** Community	**Sample** - 126 **Age** – 2-4 years **Cluster random sample**	Delay in ≥ 1 domain	Sensitivity 100% Specificity 7.8%
						Delay in ≥ 2 domains	Sensitivity 18.2% Specificity 42.6%
[52]	**South Africa** Upper-Middle- Income	Road to Health Booklet Developmental Checklist (RTHB-DC)	Parent Evaluation of Developmental Status (PEDS) Parent Evaluation of Developmental Status: Developmental Milestones	**Design** Comparative Cross-sectional within-subject **Setting** PHC clinics	**Sample** - 201 **Age** – 6-12 months **Convenience sample**	Overall	Sensitivity 25% Specificity 91%
[54]	**India** Lower-Middle- Income	Trivandrum Developmental Screening Chart (TDSC)	Denver Developmental Screening Test (DDST)	**Design** Cross-Sectional **Setting** – Hospital + Community	**Sample** – 1945 **Age** – 0-2 years **Cluster random sample**	Overall	Sensitivity 66.7% Specificity 78.8%
[55]	**India** Lower-Middle- Income	Woodside Screening Technique (WSST)	Gesell's Developmental Schedules (GDS)	**Design** Cross-Sectional **Setting** – Community	**Sample** – 619 **Age** – 6 weeks-2 years **Random sample**	Overall	Sensitivity 83% Specificity 88%
Language Screening Tools							

Ref.	Country	Screening Tool	Gold Standard	Study	Participants	Key Findings	
[40]	**Brazil** Upper-Middle- Income	American Speech-Language and Hearing Association (ASHA)	ABFW test	**Design** Cross-Sectional **Setting** - Community	**Sample** – 1000 **Age** – 0-5 years **Random sample**	Overall	Sensitivity 82.5% Specificity 98.93%
[44]	**India** Lower-Middle- Income	Language Evaluation Scale Trivandrum for 0-3 years (LEST 0-3)	Receptive Expressive Emergent Language Scale	**Design** Cross-Sectional **Setting** - Community	**Sample** – 643 **Age** – 0-3 years **Cluster random sample**	One item delay	Sensitivity 95.8% Specificity 77.5%
						Two item delay	Sensitivity 66.7% Specificity 94.8%
Motor Screening Tools							
Ref.	**Country**	**Screening Tool**	**Gold Standard**	**Study**	**Participants**	**Key Findings**	
[43]	**Iran** Upper-Middle- Income	Infant Neurological International Battery (INFANIB)	Developmental Assessment by Pediatric Neurologist	**Design** – Cross-Sectional **Setting** Hospital	**Sample** – 153 **Age** – 4-18 months **Random sample**	Overall	Sensitivity 90% Specificity 83%

Figure 1: PRISMA flow diagram



Supplementary Figure S1: Correlation between NMR and Prevalence of DD (Taiwan 1997-2008)

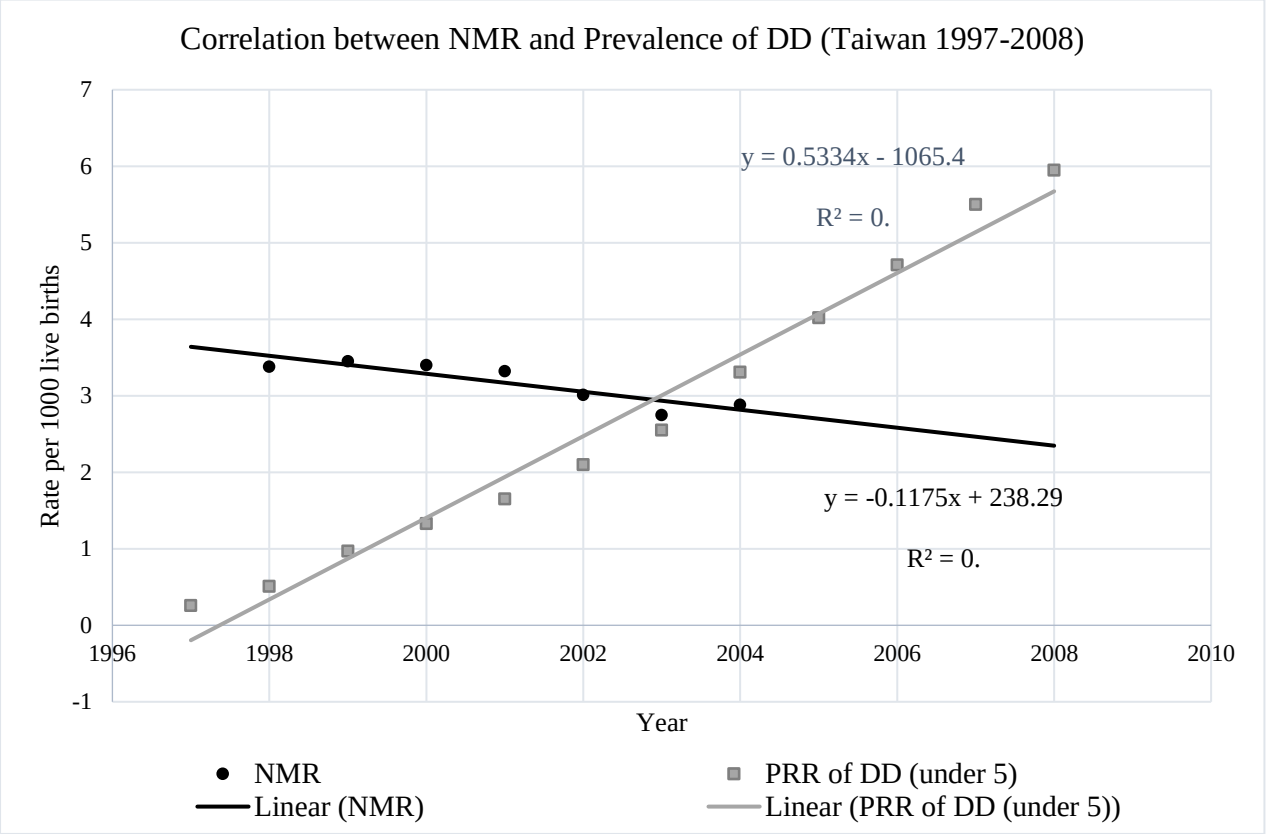


Figure S1: Correlation between neonatal mortality rate and prevalence of developmental delay (Taiwan 1997-2008)

Footnote: We have used prevalence of developmental delay among under 5 children (1997-2008) from a nation-wide population based retrospective study [18] and neonatal mortality rate (1998-2004) from another study [19]. It was revealed that the prevalence of developmental delay is positively associated with time and negatively associated with NMR. So, it can be said that, with time, while neonatal mortality rate is reducing, the prevalence of developmental delay is gradually increasing.

Supplementary Table S1: Medline search strategy

MEDLINE: Systematic review - screening for disorders in children in LMIC (as at 05.03.18)

Notes: No date or language limits applied.

Database: Ovid MEDLINE <1946 to 2018 February 28> (Phase 1)

Search Strategy:

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1 exp Mass Screening/ (114856)
2 screen$.tw. (543259)
3 exp DIAGNOSIS/ (7780076)
4 (early adj5 (diagnos$ or identif$ or detect$ or discover$)).tw. (179324)
5 1 or 2 or 3 or 4 (8132793)
6 exp "Surveys and Questionnaires"/ (881308)
7 (survey$ or questionnaire$).tw. (745680)
8 (instrument$ or tool$).tw. (665937)
9 6 or 7 or 8 (1849661)
10 5 and 9 (774120)
11 exp Neurodevelopmental Disorders/ (162135)
12 exp Motor Disorders/ (197)
13 exp Cerebral Palsy/ (18455)
14 (cerebral adj pals$).tw. (17316)
15 CP.tw. (36947)
16 exp Cognitive Dysfunction/ (7530)
17 exp Communication Disorders/ (59072)
18 ((development$ or motor$ or speech$ or cogniti$ or behav$) adj5 (disorder$ or disabilit$ or condition$ or impair$ or deficit$)).tw. (200268)
19 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (415783)
20 10 and 19 (27683)
21 exp Developing Countries/ (69408)
22 exp ASIA/ (698877)
23 exp AFRICA/ (230576)
24 exp South America/ (134532)
25 asia$.tw. (100200)
26 africa$.tw. (169185)
27 (south adj1 america$).tw. (14876)
28 (low adj2 income adj2 countr$).tw. (4196)
29 (middle adj2 income adj2 countr$).tw. (7713)
30 LMIC.tw. (649)
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (1214625)
32 20 and 31 (2207)
33 limit 32 to humans (2185)
34 remove duplicates from 33 (2183)
35 limit 34 to "all child (0 to 18 years)" (1270)
36 exp INFANT/ (1056001)
37 exp CHILD/ (1753019)
38 exp ADOLESCENT/ (1842871)
39 (paediatric$ or pediatric$ or child$ or adolescen$ or teen$ or infant$ or baby or babies).tw. (1586099)
40 36 or 37 or 38 or 39 (3520016)
41 34 and 40 (1313)
42 35 or 41 (1313)

****

Database: Ovid MEDLINE(R) ALL <1946 to July 13, 2020> (Phase 2)

Search Strategy:

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1 exp Mass Screening/ (127799)
2 screen$.tw. (748410)
3 exp DIAGNOSIS/ (8521264)
4 (early adj5 (diagnos$ or identif$ or detect$ or discover$)).tw. (247525)
5 1 or 2 or 3 or 4 (9082816)
6 exp "Surveys and Questionnaires"/ (1030942)
7 (survey$ or questionnaire$).tw. (1039336)
8 (instrument$ or tool$).tw. (981681)
9 6 or 7 or 8 (2492583)
10 5 and 9 (930528)
11 exp Neurodevelopmental Disorders/ (180714)
12 exp Motor Disorders/ (480)
13 exp Cerebral Palsy/ (20558)
14 (cerebral adj pals$).tw. (22436)
15 CP.tw. (54326)
16 exp Cognitive Dysfunction/ (17245)
17 exp Communication Disorders/ (63349)
18 ((development$ or motor$ or speech$ or cogniti$ or behav$) adj5 (disorder$ or disabilit$ or condition$ or impair$ or deficit$)).tw. (283402)
19 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (537248)
20 10 and 19 (34449)
21 exp Developing Countries/ (74723)
22 exp ASIA/ (832820)
23 exp AFRICA/ (265707)
24 exp South America/ (161136)
25 asia$.tw. (146545)
26 africa$.tw. (228897)
27 (south adj1 america$).tw. (21374)
28 (low adj2 income adj2 countr$).tw. (7421)
29 (middle adj2 income adj2 countr$).tw. (18310)
30 LMIC.tw. (1795)
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (1497552)
32 20 and 31 (2846)
33 limit 32 to humans (2778)
34 limit 33 to "all child (0 to 18 years)" (1553)
35 exp INFANT/ (1136560)
36 exp CHILD/ (1905000)
37 exp ADOLESCENT/ (2022225)
38 (paediatric$ or pediatric$ or child$ or adolescen$ or teen$ or infant$ or baby or babies).tw. (1999177)
39 35 or 36 or 37 or 38 (4073700)
40 33 and 39 (1614)
41 34 or 40 (1614)
42 limit 41 to yr="2018 -Current" (242)
****

Supplementary Table S2: List of key definitions regarding study selection

Key words	Definitions
Assessment	Assessment is a process for defining the nature of that problem, determining a diagnosis, and developing specific treatment recommendations for addressing the problem or diagnosis.
Developmental Assessment	In-depth examination of child's development conducted by developmental pediatrician/ child psychologist
Developmental Delay	A condition where a child does not reach it's developmental milestones at the expected times
Developmental Disability	The severe and chronic form of developmental delay which is expected to continue indefinitely and substantially restricts the individual's daily living activities
Developmental Domain	A collective term used to describe different aspects of brain growth and development
Developmental Monitoring	Observing child's developmental progress by parents/ caregivers
Developmental Screening	Looking for specific developmental concern by doctors/ healthcare professionals using brief questionnaire/ checklist
Disability	any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being.
Gray Literature	Research that is either unpublished or has been published in non-commercial form. Example: government reports, conference proceedings, pre-prints and post-prints of articles, theses and dissertations, etc.
Hand Searching	The page-by-page examination of journal issues, conference proceedings, reference lists of journal articles and other publications for relevant studies
Impairment	any loss or abnormality of psychological, physiological or anatomical structure or function.
Item	List of activities under a screening tool or questionnaire
Monitoring	monitoring involves routine evaluation of changes to health or health risks
Original Article	It is the report of a study written by the researchers who conducted the study
Psychometric Properties	Psychometric properties refer to the reliability and validity of a test
Reliability	Reliability refers to the extent to which an assessment/ screening tool produces stable and consistent results
Review Article	Critical and constructive analysis of existing published literature in a field, considered as secondary literature.
Screening	Screening is a process for evaluating the possible presence of a particular problem. The outcome is normally a simple yes or no
Sensitivity	The ability of a test to correctly identify those who have the disease
specificity	The ability of a test to correctly identify those who do not have the disease
Surveillance	Ongoing systematic collection of health data essential to the planning, implementation and evaluation of the public health practice closely integrated with the timely dissemination of these data to those who need to know
Validity	The ability of a test to distinguish between who has a disease and who does not

Supplementary Table S3: Quality Assessment Tool for Diagnostic Accuracy Studies-2 rating of the selected studies (Part 1)

	[38]	[39]	[40]	[41]	[42]	[43]	[44]	[45]	[46]
DOMAIN 1: PATIENT SELECTION									
A. Risk of Bias									
Was a consecutive or random sample of patients enrolled?	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Was a case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did the study avoid inappropriate exclusions?	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes
Could the selection of patients have introduced bias?	High	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High	High
B. Concerns regarding applicability									
Is there concern that the included patients do not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 2: INDEX TEST(S)									
A. Risk of Bias									
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If a threshold was used, was it pre-specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low	Low
B. Concerns regarding applicability									
Is there concern that the index test, its conduct, or interpretation differ from the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 3: REFERENCE STANDARD									
A. Risk of Bias									
Is the reference standard likely to correctly classify the target condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	Low	Low	Low	Low	Unclear	Low	Low	Low
B. Concerns regarding applicability									
Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 4: FLOW AND TIMING									
A. Risk of Bias									
Was there an appropriate interval between index test(s) and reference standard?	No	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear
Did all patients receive a reference standard?	Yes	Yes	Yes	No	Yes	No	No	No	Yes
Did patients receive the same reference standard?	Yes	Yea	Yea	Yes	Yea	Yes	Yes	Yes	No
Were all patients included in the analysis?	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
Could the patient flow have introduced bias?	Low	Low	Low	Low	Low	High	Unclear	Unclear	Low

Supplementary Table S3: Quality Assessment Tool for Diagnostic Accuracy Studies-2 rating of the selected studies (Part 2)

	[47]	[48]	[49]	[50]	[51]	[52]	[53]	[54]	[55]
DOMAIN 1: PATIENT SELECTION									
A. Risk of Bias									
Was a consecutive or random sample of patients enrolled?	No	No	No	No	Yes	No	Yes	Yes	Yes
Was a case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did the study avoid inappropriate exclusions?	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Could the selection of patients have introduced bias?	High	High	High	High	Low	Unclear	Unclear	Low	Low
B. Concerns regarding applicability									
Is there concern that the included patients do not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 2: INDEX TEST(S)									
A. Risk of Bias									
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If a threshold was used, was it pre-specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low	Low
B. Concerns regarding applicability									
Is there concern that the index test, its conduct, or interpretation differ from the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 3: REFERENCE STANDARD									
A. Risk of Bias									
Is the reference standard likely to correctly classify the target condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear	Yes	Yes	Unclear	Yes	Unclear	Unclear	Yes	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear	Low	Low	Unclear	Low	Unclear	Unclear	Low	Low
B. Concerns regarding applicability									
Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	Low	Low	Low	Low	Low	Low	Low	Low
DOMAIN 4: FLOW AND TIMING									
A. Risk of Bias									
Was there an appropriate interval between index test(s) and reference standard?	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Yes
Did all patients receive a reference standard?	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No
Did patients receive the same reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all patients included in the analysis?	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes
Could the patient flow have introduced bias?	Low	Low	Low	Low	High	Low	Low	High	Low

Supplementary Table S4: Newcastle-Ottawa Scale scores of the selected studies

	[38]	[39]	[40]	[41]	[42]	[43]	[44]	[45]	[46]	[47]	[48]	[49]	[50]	[51]	[52]	[53]	[54]	[55]
Selection: (Maximum 5 stars)																		
Representativeness of the sample	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Sample size		**	**				*										**	*
Non-respondents	Not Applicable																	
Ascertainment of the exposure	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
Comparability: (Maximum 2 stars)																		
The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled	Not Applicable																	
Outcome: (Maximum 3 stars)																		
Assessment of the outcome	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
Statistical test	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*

Supplementary Table S5: Selection criteria used for participation in the studies

Ref.	Inclusion Criteria	Exclusion Criteria
[38]	Children attending the study hospital	Children without a proper birth record Children not accompanied by a caregiver at the time of evaluation
[39]	Children living in the study area	Not applicable
[40]	Parents willing to participate	Not applicable
[41]	Children living in the study area	Not applicable
[42]	Very Low Birth Wight Children treated in NICU of the study hospital	Not applicable
[43]	Children living in the study area	Not applicable
[44]	Children whose parents/ primary caregiver gave consent	Ill children Children uncooperative for testing
[45]	Afrikaans, Tswana or English speaking parents or guardian	Children suspected or diagnosed with mental retardation, autism or neuromotor delay
[46]	Children attending the study hospital	Children with acute illness Children not accompanied by parents Children whose parents did not give consent to participate
[47]	Children with apparently normal development	Children with acute and chronic disease Children not accompanied by a caregiver Children with illiterate caregiver
[48]	Parents completed primary education Parents able to read Hindi Parents living with the child	Premature children Children with acute severe illness Previous diagnosis of developmental disorder
[49]	Children attending the study hospital	Premature children Previous diagnosis of developmental delay Children with a visual/hearing problem The accompanying parent does not understand the Thai language
[50]	Parents willing to participate	Chronically ill children Previous diagnosis of developmental delay
[51]	Children living in the study area	Children whose parents did not give consent to participate
[52]	Afrikaans or English speaking parents Parents visiting the primary health care clinics Parents asked to participate	Not applicable
[53]	Children born to mothers enrolled in "Malaria in Pregnancy Preventive Alternative Drugs" trial	Non-singleton births
[54]	**Community:** Children living in the study area **Hospital:** Children attending the study hospital	Not applicable
[55]	Not applicable	Children with congenital malformation, acute illness and mental retardation

Supplementary Table S6: List of Rejected Studies and Tools

	Ref	Tool	Reason of Rejection
1.	Biasini et al. 2015	12 month Screener	Tool Development Intervention study
2.	Wirz et al. 2005	ACCESS Portfolio	Disability Screening tool Sensitivity-Specificity not measured
3.	Ngoun et al. 2012	AHC DMAT	Tool development 1-6 years Sensitivity-Specificity not measured
4.	Kwun et al. 2014	ASQ	Validated in non LIMC country
5.	Salomonsson et al. 2010	ASQ:SE	Validated in non LIMC country
6.	Bian et al. 2017	ASQ:SE	Translation and adaptation Sensitivity-Specificity not measured
7.	Parveen et al. 2014	BSID-II	Assessment tool Tool adaptation
8.	Ranjitkar et al. 2018	Bayley III	Efficacy of vitamin B12 supplementation on growth and neurodevelopment
9.	Rizzoli-Córdoba et el. 2015	BDI-2 ST	Prevalence study English translation is not available
10.	Kishore et al. 2018	BDST	Correlation Study Sensitivity-Specificity not measured
11.	Pathak et al. 1991	BDST	Preparing developmental curve Sensitivity-Specificity not measured
12.	Guedes et al. 2011	BINS	Sensitivity-Specificity not clearly documented
13.	Sheldrick et al. 2013	BPSC	Validated in non LIMC country
14.	Glascoe et al. 2005	Brigance-II	Validated in non LIMC country
15.	Ireton et al.1996	CDR-PQ	Validated in non LIMC country
16.	Liao et al. 2008	CDIIT	Validated in non LIMC country
17.	McCoy et al. 2017	CREDI	Tool development, Correlation study
18.	Altafim et al. 2018	CREDI	Sensitivity-Specificity not measured
19.	Wetherby et al. 2003	CSBS-DP	Validated in non LIMC country
20.	Nair et al. 2009	DATA	Tool development and standardization Sensitivity-Specificity not measured
21.	Nair et al. 2012	DATA II	Tool development
22.	Luiz et al. 2004	DDST II	3-6 years Correlation study
23.	Wijedasa et al. 2011	DDST II	Adaptation and standardization
24.	Shahshahani et al. 2010	DDST II	0-6 years
25.	Scherzer et al 2009	DMChart	0-8 years Sensitivity-Specificity not measured
26.	Abubakar et al. 2009	DMChecklist	Correlation study Sensitivity-Specificity not measured
27.	Prado et al. 2014	DMCchecklist II	Correlation study Sensitivity-Specificity not measured
28.	Chopra et al. 1999	DSS	Disability Screening tool 0-6 years
29.	Velez et al. 2007	EAD 1	Prevalence Study
30.	Rao et al. 2014	EAP ECDS	Assessment tool 36-71 months
31.	Janus et al. 2007	EDI	4-6 years

			Validated in non LIMC country
32.	Verdisco et al. 2015	Engle	Correlation study Sensitivity-Specificity not measured
33.	Schafer et al. 2014	ERIC	Validated in non LIMC country
34.	Meisels etal. 1993	ESI-R	3-6 years Validated in non LIMC country
35.	Lenkarski et al. 2001	ESP	Validated in non LIMC country
36.	Hatakenaka et al. 2016	ESSENCE-Q	0-6 years Validated in non LIMC country
37.	Munir et al. 1999	IBAS	Assessment tool 1-10 years
38.	Gulati et al. 2014	INCLEN-NDST	2-9 years
39.	Fernandes et al. 2014 Murray et al. 2018	Intergrowth-21	Assessment tool
40.	Abubakar et al. 2008	KDI	Assessment tool Part of sample consists of children with NDD
41.	Gladstone et al. 2008 Gladstone et al. 2010	MDAT	Assessment tool 0-6 years
42.	Hwang et al. 2015	MuSiC	Validated in non LIMC country
43.	Arya et al. 1991	NIMH-DSS	0-6 years
44.	Schroeder et al. 2014	PCQ	Sensitivity-Specificity not clearly documented
45.	Malik et al. 2007	PDST	Sensitivity-Specificity not measured
46.	Sheldrick et al. 2012	PPSC	1.5-5.5 years Tool development Validated in non LIMC country
47.	Simonian and Tarnowski 2001	PSC	4-16 years
48.	Boyede et al.2016	Red Cross	Validated among HIV infected children
49.	Islam et al. 2016	RNDA	Assessment tool Prediction
50.	Ara et al. 2015	RNDA	Prevalence of NDI
51.	Khan et al. 2014	RNDA	Assessment 2-9 years
52.	Haataja et al. 2002	Shoklo	Assessment tool Validated in non LIMC cohort
53.	Sheldrick and Perrin 2013	SWYC	Tool development
54.	Wu et al. 2012	TQP	Association study
55.	Pérez-Escamilla 2017		Spanish

Supplementary Table S7: Example of culture-sensitive BSID-II items for Bangladeshi infants (adopted from [70])

	Original	Culture Sensitive
Picture	Pomfret	Ilish
	Star	National Flag
	House with chimney	Tin-shed house
Material	Sugar pellet	Iron tablets
	Small toy (rabbit)	Small doll (boy or girl)
	Thomas The Tank Engine Visits a Farm	Shishur Jotno' from 'Meena Raju Series'
	Sugar pellet	Iron tablets
Word	Auto	Vo
	Leaf	Pata/ Shak

Supplementary Table S8: Basic properties of ASQ and PEDS (adopted from [76])

Characteristic	PEDS	ASQ
Screening approach	Parents' developmental concerns	Parents provide information about child's skills
Age Range	0 to 96 months	1 to 66 months
Questionnaire	One	21 sets of questionnaire for 21 age groups
Developmental domains	Gross motor, Fine motor, Cognitive, Expressive language, Receptive language, Self-help, Social-emotional, Behavior, School, Other	Gross motor, Fine motor, Problem solving, Communication, Personal-social
Format	10 questions covering 9 developmental concerns Response options: no/yes/a little	30 questions covering 5 developmental domains Response options: yes/sometimes/not yet
Example of item	Expressive language: "Do you have any concerns about how your child talks and makes speech sounds?"	Communication skill at 18 months: "Does your child say 8 or more words in addition to 'Mama' and 'Dada'?"
Time to screen	5 min of parent time 1–2 min for provider/staff to score	10–15 min of parent time 1–2 min for provider/staff to score

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	10-11
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9-10

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9-10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9-10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Sensitivity, Specificity
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table S3, S4

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12-22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-26
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	26-27
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	28
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	29

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.