BMJ Paediatrics Open

Antenatal dexamethasone for preterm birth and long-term health outcomes in children: a pilot follow-up cohort study of ACTION-I trial participants in Sylhet, Bangladesh

Saima Sultana ,[1,2] Iffat A Jaben,[3] Tamsasul Farha,[3] Shouvik Roy,[3] Salahuddin Ahmed,[3] Caroline S E Homer,[1,2] Abdullah H Baqui,[4] Joshua P Vogel[1,2]

To cite: Sultana S, Jaben IA, Farha T, *et al*. Antenatal dexamethasone for preterm birth and long-term health outcomes in children: a pilot follow-up cohort study of ACTION-I trial participants in Sylhet, Bangladesh. *BMJ Paediatrics Open* 2025;**9**:e003983. doi:10.1136/bmjpo-2025-003983

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjpo-2025-003983).

Received 16 August 2025
Accepted 9 November 2025

For numbered affiliations see end of article.

Correspondence to
Dr Saima Sultana; saima.sultana@monash.edu

ABSTRACT

Background The WHO ACTION-I trial in 2020 demonstrated the short-term efficacy and safety of antenatal dexamethasone for women at risk of early preterm birth in low-resource settings. However, the long-term effects of antenatal corticosteroids remain unclear, and no long-term follow-up studies have been conducted in low-resource settings. This pilot study aimed to evaluate the feasibility of participant follow-up from the ACTION-I trial and generate preliminary data on child health outcomes to inform the design of a larger follow-up cohort study within the trial population.

Methods A follow-up cohort study was conducted in Sylhet, Bangladesh, among children born to women enrolled in the ACTION-I trial at three hospitals. Eligible participants were 181 infants who had survived to 28 completed days after birth. The primary outcomes were participant follow-up rate and neurodevelopmental outcomes at 5 years' corrected age.

Results Of the 181 eligible children, 160 (88%) were found and enrolled in this follow-up—78 from the dexamethasone group and 82 from the placebo group. Median Ages and Stages Questionnaire-Third Edition scores were similar between groups, except for a modest yet significant reduction in gross motor scores in the dexamethasone group (adjusted median difference: −5; 95% CI −8.7 to −1.3). Neurodevelopmental difficulties, particularly in fine motor and problem-solving domains, were the most common, affecting 39% and 34% of children in the dexamethasone group, and 33% and 36% in the placebo group, respectively. Behavioural and emotional problems were less common, with no significant differences between groups.

Conclusions Long-term follow-up of preterm infants in a low-resource setting is feasible. High retention rates, along with preliminary outcome estimates, provide a critical foundation for planning larger, more definitive cohort studies in similar settings. Furthermore, the high prevalence of neurodevelopmental difficulties in this population highlights the need for early childhood interventions and continued developmental surveillance.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Antenatal corticosteroids (ACS) are among the critical interventions to reduce neonatal mortality and short-term morbidities in preterm infants, including in low-resource settings.

⇒ Evidence on the long-term outcomes of ACS, especially in low- and middle-income countries, is limited; most data to date are from high-income countries.

WHAT THIS STUDY ADDS

⇒ This is the first follow-up of the WHO ACTION-I trial participants, demonstrating that long-term follow-up of children exposed to antenatal dexamethasone in a low-resource setting is feasible.

⇒ A high prevalence of neurodevelopmental difficulties was observed in both groups, particularly in the fine motor and problem-solving domains. However, no significant differences were found between treatment groups for most outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results demonstrate both the feasibility and importance of establishing long-term cohorts in low-resource settings to assess the long-term effects of ACS and inform global and national policy, while also emphasising the urgent need for early childhood interventions and continuous developmental monitoring among preterm survivors in similar settings.

INTRODUCTION

Preterm birth remains the leading cause of neonatal mortality and is a major contributor to deaths among children under 5 years of age.[1] Beyond the immediate concerns of survival and short-term morbidities, preterm birth is associated with a broad range of long-term sequelae across multiple developmental domains. Children born preterm have an increased risk of neurodevelopmental

morbidities such as cerebral palsy, cognitive deficits, visual and hearing impairments, developmental delays, behavioural problems and learning difficulties.[2 3] They also experience higher rates of hospitalisation, growth impairment and impaired lung function compared with term-born peers.[4 5]

Antenatal corticosteroids (ACS), typically a single course of dexamethasone or betamethasone, are a key perinatal intervention for improving survival and short-term morbidities in preterm newborns.[6] When administered to pregnant women at high risk of preterm birth, ACS cross the placenta and accelerate fetal lung maturation, increase surfactant production and affect the maturation of other organ systems.[7] The 2020 Cochrane review on ACS efficacy included 27 trials of 11 272 women and 11 925 neonates from 20 countries, including 10 trials from low- and middle-income countries.[8] The results indicate that a single course of ACS significantly reduces the risk of perinatal death and neonatal death, respiratory distress syndrome and intraventricular haemorrhage. This evidence base includes efficacy trials across high-, middle- and low-income countries. Notably, the 2020 WHO ACTION-I trial in five low-resource countries reported a 16% reduction in the relative risk of neonatal mortality following ACS administration to women at risk of imminent preterm birth prior to 34 weeks' gestation.[9]

Despite robust evidence of the short-term benefits of ACS, knowledge regarding the long-term effects remains limited. Few trials and observational studies from high-income countries suggest that ACS exposure may reduce the risk of developmental delays or cerebral palsy in infants born before 34 weeks' gestation.[8 10] However, for those born after 34 weeks, emerging evidence indicates the potential for adverse long-term health outcomes. Furthermore, evidence on the effects of ACS on long-term survival and growth remains insufficient, and there are no data on these longer-term outcomes from low-resource settings.[11] Most ACS efficacy trials in early preterm birth—aside from the WHO ACTION-I trial—were conducted many decades ago, limiting opportunities for follow-up into childhood.

The WHO ACTION-I trial established the short-term efficacy and safety of antenatal dexamethasone for early preterm birth in low-resource countries. This trial also offers a unique opportunity to address the knowledge gap on longer-term outcomes through follow-up studies of trial participants. Participants from the ACTION-I trial have not previously been contacted for follow-up, and their availability, accessibility and willingness to participate are unknown. In addition, the prevalence of long-term child health outcomes and the expected effect sizes required to inform sample size calculations for future definitive cohort studies are unclear due to a lack of available evidence. Therefore, this pilot study aimed to evaluate the feasibility of participant follow-up from the ACTION-I trial and generate preliminary data to inform the design of a larger follow-up cohort study within the trial population.

METHODS

This was a pilot follow-up cohort study of participants who were enrolled in the double-blind, individually randomised WHO ACTION-I trial in Sylhet, Bangladesh.

Initial study—the WHO ACTION-I trial

The WHO ACTION-I trial methods have been published previously.[12] The trial evaluated the efficacy and safety of dexamethasone in women in low-resource countries who were at risk of early preterm birth. Eligible women were those identified to be at risk of imminent preterm birth at 26 weeks to <34 weeks of gestation. Eligible women were randomised to a regimen of intramuscular injections of either 6 mg dexamethasone or an identical placebo administered every 12 hours, to a maximum of four doses. A repeat course could also be used if the woman had not given birth after 7 completed days and she remained at risk of imminent preterm birth prior to 34 weeks of gestation. The trial was conducted in 29 secondary and tertiary hospitals across five low-resource countries (Bangladesh, India, Kenya, Nigeria and Pakistan), and recruited 2852 women and their 3070 babies between December 2017 and November 2019.

Present study—follow-up at 5 years

Study site

The WHO ACTION-I trial was conducted in six hospitals in Bangladesh—three in Dhaka and three in Sylhet. These hospitals (five tertiary and one secondary level) were included following a standardised assessment of their maternal and neonatal care services, ensuring they can meet WHO's ACS recommendations.[13] This follow-up study was conducted in Sylhet, Bangladesh, for its pragmatic and logistical feasibility, including the availability of research infrastructure to support long-term child assessments. Sylhet is located in the north-eastern region of Bangladesh, comprising four districts—Sylhet, Sunamganj, Moulvibazar and Habiganj (see online supplemental figure 1). The three participating hospitals were located in the metropolitan area of Sylhet district, though study participants were referred from all four districts to access tertiary-level care for preterm birth.

Study population and sample size

The population of interest for this follow-up study was children whose mothers were enrolled in ACTION-I at the three hospitals in Sylhet. There were 259 live births among 259 randomised women, of which 181 infants survived to 28 completed days after birth (89 in the dexamethasone group and 92 in the placebo group). All surviving children who were alive at 28 days of life were eligible for this 5-year follow-up study, if their parents agreed to participate.

Participant recruitment

At the time of recruitment to ACTION-I, all participants provided their contact details (home address, and at least two phone/mobile numbers). We used a multimodal approach to locate the participants. First, we tried to

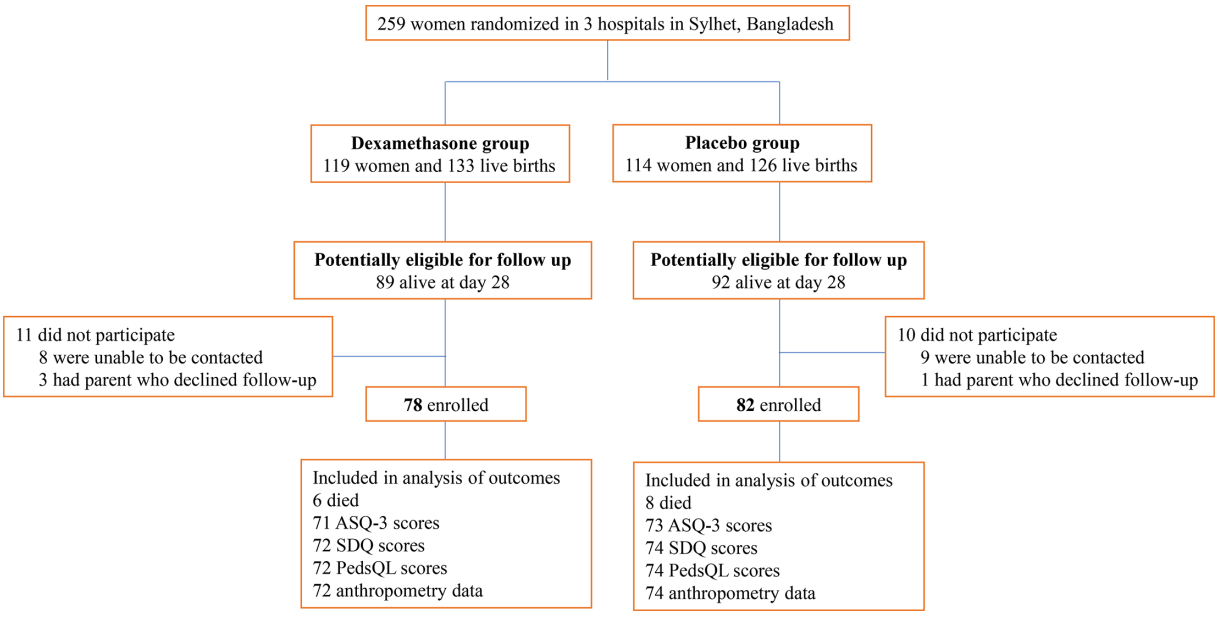

Figure 1 Participant flow diagram. ASQ-3, Ages and Stages Questionnaire-Third Edition; PedsQL, Pediatric Quality of Life Inventory; SDQ, Strengths and Difficulties Questionnaire.

contact ACTION-I parents via phone/mobile numbers. If they were unable to contact via phone/mobile numbers, we arranged home visits to the given addresses and also sought assistance from neighbours and local contacts to locate the participants. For those willing to participate, a home visit was arranged for the follow-up assessment. Parents were asked to provide written informed consent for their child to participate. Follow-up visits took place from May 2024 to November 2024.

Outcomes and measures

Primary outcomes for this study were the participant follow-up rate and the prevalence of neurodevelopmental outcomes (neurodevelopmental difficulties, and behavioural and emotional problems). Secondary outcomes included death, growth measurements (weight, height and head circumference) and health-related quality of life. Children underwent the 5-year follow-up assessment (ages between 4.75 and 5.5 years corrected age), performed by trained research assistants who were blinded to group allocation. Developmental assessments for preterm populations differ significantly depending on whether chronological or corrected age is used, especially in early childhood. Although correction is mainly critical for clinical purposes in the first 2–3 years of life, its continued use in research contexts is important to minimise residual bias associated with preterm birth.[14] Therefore, we applied the corrected age for all participants to ensure accurate developmental assessment.

Neurodevelopmental difficulties were assessed using the Ages and Stages Questionnaire-Third Edition (ASQ-3).[15] ASQ is a widely used tool and has previously been used in studies in many low- and middle-income countries, including in Bangladesh.[16–19] ASQ-3 contains 30 age-specific items that evaluate the child's development in five domains—communication, gross motor, fine motor, problem solving and personal-social. Each domain has a set of six items assessed to a possible 60 points. Items were rated to the most appropriate answer for the presence of each skill: yes (10 points), sometimes (5 points) or not yet (0 points). Higher scores indicate more developmental milestones reached. A score less than 2 SD below the mean score in each domain is considered 'abnormal' and indicative of potential neurodevelopmental difficulties.[20] We used the Bengali translated version, obtained from Brookes Publishing's Rights, Licensing and Permissions department. Given the potential inexperience of the parents in completing questionnaires, as well as possible limitations in literacy, we employed the 'home-procedure' outlined in the ASQ-3 manual. Within this approach, research assistants supported the child in demonstrating the intended developmental skills during the assessment session by using the materials that were part of the assessment. Using Item responses and scoring were based on the direct observations of the research assistants, who were supported by parental engagement in encouraging the child's behaviours.

Behavioural and emotional outcomes were assessed using the Bengali version of the parent-reported Strengths and Difficulties Questionnaire (SDQ).[21 22] SDQ is one of the widely used validated tools to screen psychosocial difficulties/disorders in children and youths and has been validated in Bangladesh.[23] The SDQ contains 25 items (on a 3-point scale with 0=not true, 1=somewhat true and 2=certainly true) divided across five subscales to assess emotional symptoms, conduct problems, hyperactivity/inattention, peer problems and prosocial behaviour. A higher score on the SDQ total difficulties scale, including the subscales for emotional symptoms, conduct problems, hyperactivity/attention

Table 1 Baseline characteristics of the participants

Characteristics	Dexamethasone	Placebo
Original trial		
Maternal characteristics		
No. of mothers	70	74
Age, median (IQR), years	25 (20–27)	23.5 (20–27)
Gestational age at trial entry, median (IQR), weeks	32.5 (31.4–33.3)	32.7 (31.5–33.3)
Secondary/tertiary education, n (%)	23 (32.9)	23 (31.1)
Nulliparous, n (%)	35 (50.0)	30 (40.5)
Singleton birth, n (%)	60 (85.7)	66 (89.2)
Vaginal birth, n (%)	40 (57.1)	34 (46.0)
No. of doses of trial treatments, n (%)		
1	27 (38.6)	38 (51.3)
2–3	12 (17.1)	11 (14.9)
≥4*	31 (44.3)	25 (33.8)
Use of tocolytic agent, n (%)	3 (4.3)	4 (5.4)
Use of MgSo4 for fetal neuroprotection, n (%)	2 (2.9)	3 (4.1)
Obstetrical conditions, n (%)		
Preterm prelabour rupture of membranes	27 (38.6)	23 (31.1)
Pre-eclampsia or eclampsia	4 (5.7)	10 (13.5)
Gestational hypertension	4 (5.7)	3 (4.1)
Oligohydramnios	14 (20.0)	17 (23.0)
Polyhydramnios	1 (1.4)	1 (1.4)
Antepartum haemorrhage	12 (19.4)	16 (21.6)
Gestational diabetes	1 (1.4)	0 (0)
Intrauterine growth restriction	1 (1.4)	2 (2.7)
Neonatal characteristics		
No. of infants	78	82
Birth weight, median (IQR), g	2000 (1800–2400)	2000 (1800–2400)
Gestational age at birth, median (IQR), weeks	32.4 (31.4–33.6)	32.7 (31.6–33.3)
Birth <37 weeks, n (%)	65 (90.3)	66 (89.2)
Male sex, n (%)	35 (44.9)	48 (58.5)
Apgar score <7 at 5 min after birth, n (%)	11 (14.1)	12 (14.6)
Major resuscitation at birth, n (%)	3 (3.9)	2 (2.4)
Sepsis, n (%)	10 (12.8)	19 (23.2)
Hypoglycaemia, n (%)	1 (1.3)	4 (4.9)
Admission to a special care unit, n (%)	25 (32.1)	28 (34.2)
Use of oxygen therapy, n (%)	28 (35.9)	32 (39.0)
Follow-up study		
Child characteristics†		
Corrected age at the time of follow-up assessment, mean (SD), years	5.1 (0.2)	5.1 (0.2)
Attending preschool/full-time schooling, n (%)	50 (69.4)	48 (64.9)

*Includes initial and repeat course of trial treatment.
†Includes 72 children in the dexamethasone group and 74 children in the placebo group who were alive at the time of follow-up assessment.

difficulties and peer problems, indicates greater difficulties for children, while a lower score on the prosocial behaviour subscale indicates poorer performance. The scores are categorised as 'normal', 'borderline' and 'abnormal'.

Table 2 Primary neurodevelopmental outcomes at 5 years' corrected age

Primary outcome	Dexamethasone	Placebo	Effect size (95% CI)	
			Unadjusted	Adjusted*
ASQ-3 scores, median (IQR)†				
n	71	73		
Communication	50 (45–60)	50 (45–60)	0 (–1.7 to 1.7)	0.9 (–3.1 to 4.9)
Gross motor	45 (45–50)	50 (45–50)	–5 (–9.2 to –0.8)	–5 (–8.7 to –1.3)
Fine motor	35 (20–45)	35 (25–45)	0 (–7.8 to 7.8)	–2.0 (–10.5 to 6.5)
Problem solving	30 (20–45)	30 (20–40)	0 (–10.2 to 10.2)	–1.1 (–7.7 to 5.6)
Personal-social	50 (40–60)	55 (50–60)	–5 (–16.9 to 6.9)	–3.3 (–9.2 to 2.7)
Children with abnormal ASQ-3 scores, n (%)				
Communication	3 (4.2)	3 (4.1)	1.0 (0.2 to 6.3)	1.3 (0.2 to 7.1)
Gross motor	0 (0)	1 (1.4)	‡	
Fine motor	28 (39.4)	24 (32.9)	1.2 (0.7 to 1.9)	1.3 (0.9 to 2.0)
Problem solving	24 (33.8)	26 (35.6)	1.0 (0.6 to 1.5)	1.0 (0.6 to 1.6)
Personal-social	8 (11.3)	11 (15.1)	0.7 (0.3 to 1.8)	0.8 (0.4 to 1.9)
Behavioural and emotional outcomes by SDQ category				
Behavioural and emotional problems, n (%)				
n	72	74		
Total difficulties	1 (1.4)	1 (1.4)	‡	
Emotional symptoms	2 (2.8)	2 (2.7)	‡	
Conduct problems	3 (4.2)	6 (8.1)	0.5 (0.1 to 2.0)	0.6 (0.2 to 2.3)
Hyperactivity/inattention	0 (0)	2 (2.7)	‡	
Peer relationship problems	1 (1.4)	1 (1.4)	‡	
Prosocial behaviour	1 (1.4)	0		
Any behavioural or emotional problems	4 (5.6)	9 (12.2)	0.5 (0.1 to 1.4)	0.5 (0.2 to 1.8)

*Adjusted effect is median difference from the quantile regression model, or risk ratio from the Poisson regression model and adjusted for maternal age, gestational age at birth, maternal education level, child sex, child age at follow-up, and current child educational enrolment status.
†ASQ could not be administered to two children due to severe neurological deficits.
‡Analyses not performed owing to small number of events.
ASQ-3, Ages and Stages Questionnaire-Third Edition; SDQ, Strengths and Difficulties Questionnaire.

Health-related quality of life was measured using the parent-reported version of the Bengali Pediatric Quality of Life Inventory (PedsQL) form[24] which has 23 items across four generic core scales—physical functioning, emotional functioning, social functioning and school functioning. PedsQL scale scores range from 0 to 100, with higher scores indicating better health-related quality of life.

All children were assessed for growth (height, weight and head circumference). Height was measured using the seca 213 portable stadiometer, weight was measured using the TANITA HD-661 digital scale and the seca 212 measuring tape was used to measure the head circumference.

Parents were asked whether their children had been diagnosed with any physical disability, hearing problems, vision problems or other medical conditions by a health professional. To verify these diagnoses, medical records available to the parents were reviewed if they reported any such conditions.

Training and supervision

Two research assistants, each with at least a graduate-level education and prior experience in study data collection, were recruited for the study. Prior to data collection, they underwent a 6-day training programme led by the study investigators, including a physician trained in child developmental assessments. The training included both didactic and practical sessions covering study protocols, data collection procedures and administration of outcome measures, including standardisation exercises on ASQ-3 in five children. During the study, 30% (n=42) of ASQ assessments were double-scored for quality assurance. During this process, research assistants performed the assessments in the presence of a physician. Both the physician and the research assistants scored

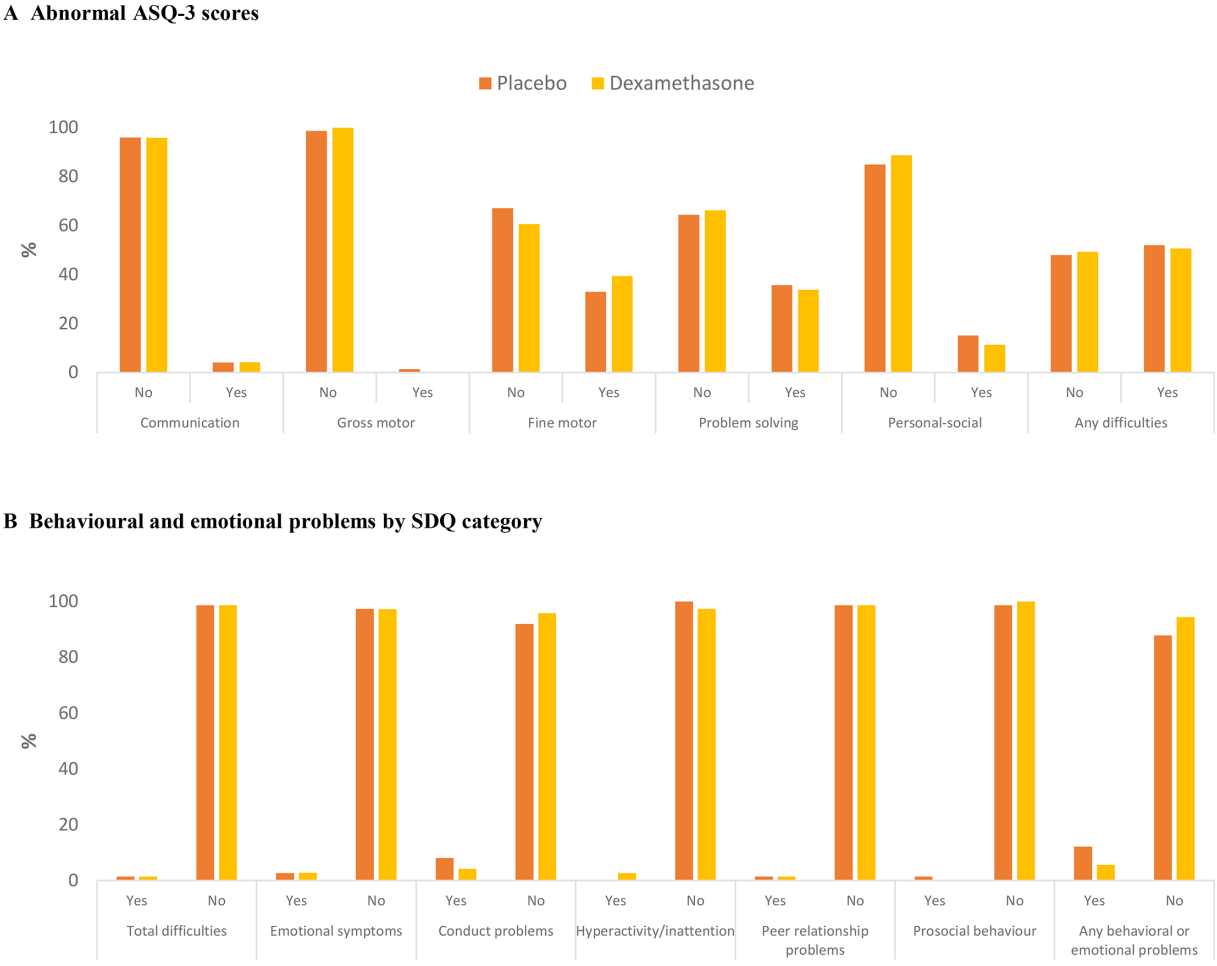

Figure 2 Prevalence of neurodevelopmental outcomes in the dexamethasone and placebo groups. ASQ-3, Ages and Stages Questionnaire-Third Edition; SDQ, Strengths and Difficulties Questionnaire.

independently and were blinded to each other's scores, achieving intraclass correlations >0.95 across all domains.

Sample characteristics

Baseline characteristics were derived both from the original ACTION-I trial and the 5-year follow-up study.

Statistical analyses

Data were analysed using STATA SE 18.0.[25] Baseline characteristics were summarised using descriptive statistics—continuous variables as means with SD or medians with IQRs based on distribution, and categorical variables as frequencies and percentages. All analyses followed intention-to-treat principles, including all participants with available outcome data. Outcomes were compared between the dexamethasone and placebo groups using modified Poisson regression for binary outcomes and quantile regression for continuous outcomes with non-normal distributions. All models accounted for clustering due to multiple births. Both unadjusted and adjusted analyses were performed. Analyses were adjusted for baseline characteristics associated with study outcomes that we identified in published literature, namely maternal age, gestational age at birth, maternal education level, child sex, child age at follow-up and current child educational enrolment status.

Patient and public involvement

Patients and/or the public were not involved.

RESULTS

Primary outcomes

Of the 181 potentially eligible participants, 164 were successfully located. Four parents (2%) declined participation, resulting in 160 children enrolled in this follow-up study—78 from the dexamethasone group and 82 from the placebo group (figure 1). This equates to a follow-up rate of 88% overall—88% in the dexamethasone group and 89% in the placebo group. For these 160 children, baseline maternal and newborn characteristics were generally comparable between groups. However, some differences were observed, including rates of nulliparity, vaginal birth, pre-eclampsia and the number of trial treatment doses received. Notably, neonatal sepsis was more common in the placebo group. For the follow-up study, the mean corrected age at follow-up was 5.1 (SD 0.2) years in both groups, and 69% children in the dexamethasone

Table 3 Secondary outcomes at 5 years' corrected age

Outcome	Dexamethasone	Placebo	Effect size (95% CI)	
			Unadjusted	Adjusted*
n	78	84		
Death, n (%)†	6 (7.7)	8 (9.8)	0.8 (0.3 to 2.1)	0.8 (0.3 to 2.2)
Growth outcomes, median (IQR)				
n	72	74		
Weight, kg	14.4 (13.2–15.8)	14.3 (13.4–15.7)	0.1 (–0.5 to 0.7)	0.1 (–0.7 to 0.6)
Height, cm	103.2 (100.1–106.3)	103.4 (101–106.1)	–0.2 (–1.8 to 1.4)	–0.5 (–2.2 to 1.1)
Head circumference, cm	48.1 (46.7–49.2)	48.3 (47–48.8)	–0.2 (–0.9 to 0.5)	–0.2 (–0.9 to 0.5)
Quality of life (PedsQL), median (IQR)				
n	72	74		
Total score	100 (96.7–100)	97.8 (95.7–100)	2.2 (–0.1 to 4.4)	0.6 (–0.5 to 1.8)

*Adjusted effect is median difference from the quantile regression model, or risk ratio from the Poisson regression model and adjusted for maternal age, gestational age at birth, maternal education level, child sex, child age at follow-up and current child educational enrolment status, unless otherwise indicated.
†Included all participants who were located for follow-up study (n=160); adjusted for maternal age, gestational age at birth, maternal education level and child sex.
PedsQL, Pediatric Quality of Life Inventory.

group and 65% in the placebo group had initiated preschool or formal schooling (table 1). Characteristics of participants lost to follow-up are summarised in online supplemental table 1.

The median ASQ-3 scores were similar between groups across most developmental domains, including communication, fine motor, problem solving and personal-social skills. However, a modest but statistically significant reduction in gross motor scores was observed in the dexamethasone group compared with placebo (adjusted median difference: −5; 95% CI −8.7 to −1.3) (table 2).

The proportion of children with abnormal ASQ-3 scores was similar between the groups. Difficulties in fine motor and problem-solving domains were most prevalent, affecting 39.4% and 33.8% of children in the dexamethasone group, and 32.9% and 35.6% in the placebo group, respectively (figure 2). No statistically significant differences were found between groups across any of the five ASQ-3 domains (table 2). Higher maternal education and current child educational enrolment were associated with better fine motor and problem-solving skills. Subgroup analyses were conducted by maternal education level and the child's current educational status. These analyses did not reveal any significant differences in neurodevelopmental difficulties between the groups (see online supplemental tables 2 and 3).

Behavioural and emotional difficulties were less common (figure 2). 'Conduct' problems were most prevalent—4.2% of children in the dexamethasone group and 8.1% in the placebo group (adjusted Risk Ratio (RR) 0.6; 95% CI 0.2 to 2.3). Overall, 5.6% of children in the dexamethasone group compared with 12.2% in the placebo group were identified with any behavioural or emotional problems (adjusted RR 0.5; 95% CI 0.2 to 1.8). There were no statistically significant differences between the groups across any of the SDQ behavioural subscales (table 2).

Secondary outcomes

By 5 years of age, six children (7.7%) in the dexamethasone group and eight (9.8%) in the placebo group had died. Growth outcomes, including weight, height and head circumference, were similar between groups. Health-related quality of life, assessed using PedsQL total score, was generally high in both groups. The dexamethasone group had a slightly higher median total score, though this was not statistically significant (adjusted median difference: 0.6; 95% CI −0.5 to 1.8) (table 3).

Other health outcomes

Three children had formal neurological or sensory impairment diagnoses. In the dexamethasone group, one child was diagnosed with both cerebral palsy and seizures/epilepsy. In the placebo group, one child had a hearing impairment requiring hearing aids, and another was diagnosed with severe visual impairment (see online supplemental table 4).

DISCUSSION

This pilot follow-up study provides important evidence on the feasibility of measuring long-term effects of antenatal dexamethasone in a low-resource setting. One of the key accomplishments of this study is the high follow-up rate (88%), which is particularly notable in low-resource countries like Bangladesh, where participant retention can be challenging due to migration, lack of formal health records and healthcare system limitations.

This high retention rate demonstrates the feasibility of establishing and sustaining long-term cohorts in such settings and provides a foundation for future longitudinal research on child health and development. Rather than evaluating the efficacy or potential harm of dexamethasone, the study's main contribution lies in its demonstration of operational feasibility—specifically, the ability to successfully trace participants and collect developmental outcomes 5 years post-exposure. The preliminary data on developmental outcomes and effect size estimates offer valuable guidance for the design and implementation of future large-scale cohort studies, including sample size calculations and logistical planning. Moreover, key operational strategies and lessons learnt from this pilot provide a critical framework for conducting definitive cohort studies in other participating countries.

Our findings showed no significant differences between the dexamethasone and placebo groups across most developmental, behavioural and growth outcomes at 5 years. Although we observed a modest yet statistically significant reduction in gross motor scores among children exposed to dexamethasone, the median scores in both groups remained above the ASQ-3 cut-off for abnormal development. This indicates that most children in both groups demonstrated age-appropriate gross motor skills. Given that the ASQ-3 is a screening tool rather than a diagnostic test, and in the absence of consistent differences in other developmental domains or a higher prevalence of abnormal gross motor scores, the functional implications of this finding remain uncertain. As no direct measures of motor functioning were included in this study, this further limits the interpretation of the observed gross motor score difference, as certain motor abilities may not be fully captured by the ASQ-3 alone. Larger-scale studies with more detailed motor assessments and extended follow-up are warranted to determine whether these differences persist over time and whether they represent any clinically meaningful effects.

The 2020 Cochrane review findings suggest that ACS likely reduce the risk of developmental delay in childhood.[8] In contrast, a 2015 systematic review by Sotiriadis *et al* reported no significant associations between a single course of dexamethasone and adverse neurodevelopmental outcomes.[26] Notably, the majority of studies included in both reviews were conducted in high-income countries, where health system capacities, early intervention services and developmental supports differ substantially from low-resource settings. These mixed findings underscore the limited and inconsistent evidence on long-term effects of ACS and emphasise the critical need for data from low-resource settings (like those generated from following up the ACTION-I trial cohort)—where the developmental trajectory of children may be influenced by vastly different social and environmental factors.

Although no between-group differences were observed in most outcomes, the overall burden of neurodevelopmental difficulties was substantial in this cohort, affecting 51% of children—49% in the dexamethasone group and 51% in the placebo group, particularly in the fine motor and problem-solving domains. These findings align with existing literature from Bangladesh, which consistently documents low developmental attainment among young children.[27–29] For instance, the 2019 Bangladesh Multiple Indicator Cluster Survey reported that approximately 25% of children aged 3–5 years exhibited developmental delays based on the Early Childhood Development Index, including over 70% with delays in literacy-numeracy, 27% in the social-emotional development and 9% in the learning, highlighting the scale of developmental challenges nationally. Importantly, regional data indicate that children in Sylhet, where our study was conducted, have among the lowest rates of developmental attainment in Bangladesh.[27] The somewhat higher prevalence observed in our study is not unexpected given that our cohort comprised preterm children, a population well recognised to be at elevated risk for developmental challenges compared with children born at term.[30] Our ASQ-3 assessment findings are consistent with prior research from southern African populations, which has highlighted persistent difficulties in these domains at older ages. Notably, at both 54 and 60 months, several items in the problem-solving domain exhibited low item difficulty indices, indicating that these tasks were particularly challenging for children in their setting.[31 32] A range of social and contextual factors likely contributed to these outcomes, including delayed school enrolment, limited parental education and absence/lack of home-based developmental activities (eg, limited opportunities to draw or write, hold a pencil, recognise letters and numbers, count or identify colours), which not only restricted children's developmental progress but also reduced their ability to engage with, and complete certain assessment tasks. A large proportion of mothers in our cohort had low educational attainment, which likely limited their capacity to provide cognitively stimulating environments essential for early neurodevelopment. Less-educated mothers are less likely to be aware of responsive caregiving practices and often face barriers to accessing information and resources that support child learning and stimulation at home. Moreover, in many rural and resource-limited families in Bangladesh, older children are often tasked with caring for younger siblings, which may further limit opportunities for cognitive stimulation typically provided by adults. Substantial evidence from Bangladesh and comparable settings demonstrates that children from families with greater socioeconomic resources, higher parental education and exposure to books, toys and formal early learning environments are significantly more likely to be developmentally on track.[27 28 31 33 34] Thus, the high prevalence of neurodevelopmental difficulties observed in our study reflects not just methodological limitations but also reflects broader socio-structural inequities that potentially deter children's developmental potential.[35]

Behavioural and emotional difficulties were less prevalent in this study, with no statistically significant differences observed between the dexamethasone and placebo groups. These outcomes were assessed using parent-reported measures, which can be influenced by parents' perceptions, cultural norms and expectations around child behaviour.[36] In many settings, including Bangladesh, certain emotional or behavioural concerns may be under-recognised or under-reported due to stigma, lack of awareness or normalisation of behaviours that would be considered atypical in other contexts.[37] These cultural factors may lead to masking or misclassification of symptoms and consequently hinder accurate identification of concerns. Although our findings do not indicate an adverse effect of antenatal dexamethasone on behavioural outcomes at 5 years, growing evidence from observational studies has raised concerns about potential long-term behavioural and emotional problems in children following ACS exposure.[10 38] However, findings from randomised controlled trials have been more reassuring. In particular, a recent follow-up of a randomised trial evaluating antenatal betamethasone in the late preterm period reported no significant differences in behavioural outcomes between treatment and placebo groups.[39]

While our findings suggest no clear adverse long-term effects of antenatal dexamethasone, they highlight the need for ongoing surveillance of this population. Establishing and maintaining this cohort will enable future follow-up to track outcomes in later childhood and adolescence, when cognitive, educational and psychosocial effects may become more apparent.

The main strength of this study is its high follow-up rate and the successful implementation of standardised, blinded outcome assessments in a low-resource setting. However, several limitations should be acknowledged. First, certain developmental assessments—particularly those related to fine motor or problem-solving tasks—may not fully capture the capabilities of children in this context, where exposure to early stimulation and formal education is limited. Second, behavioural assessments relied on parental reports, which may be biased by sociocultural factors. This may have led to underreporting or misclassification of symptoms. Future studies would benefit from incorporating direct observational measures and a more comprehensive diagnostic approach. Additionally, the relatively small sample size presents several statistical challenges. Most notably, the study is underpowered to detect rare outcomes (eg, cerebral palsy or specific behavioural problems) or to identify subtle differences between the groups. As such, the absence of statistically significant findings should not be interpreted as evidence of equivalence or lack of effect. All null results must be considered as preliminary and interpreted with caution. Similarly, subgroup analysis results should also be interpreted with particular caution and should not be considered definitive. Covariates included in regression models were restricted to variables with strong empirical support for their association with neurodevelopmental outcomes. While this approach aimed to minimise bias, adjusting for multiple covariates in a modest sample increases the risk of overfitting, and resulting estimates should be considered as exploratory and hypothesis-generating, rather than confirming any causal relationships. Taken together, these limitations underscore the need for future studies with larger, adequately powered sample sizes to validate these results and more robustly assess neurodevelopmental outcomes.

CONCLUSION

This study successfully demonstrated the feasibility of long-term follow-up of children exposed to antenatal dexamethasone for early preterm birth within the WHO ACTION-I trial. High follow-up rates, along with estimates of neurodevelopmental outcomes, provide a critical foundation for designing larger, more definitive cohort studies across similar settings. Although no significant differences were observed between treatment groups across most outcomes, the substantial burden of neurodevelopmental difficulties in both groups highlights the need for early childhood interventions to promote optimal development in resource-limited environments.

Author affiliations
[1]School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
[2]Women's, Children's and Adolescents' Health Program, Burnet Institute, Melbourne, Victoria, Australia
[3]Projahnmo Research Foundation, Dhaka, Bangladesh
[4]Department of International Health, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, USA

Contributors SS is the guarantor. SS was involved in conception, design, project administration, investigation, formal analysis and writing of the original draft. IAJ was involved in project administration, data curation, validation and reviewing and editing the manuscript. TF and SR were involved in data curation, validation and reviewing and editing the manuscript. SA was involved in project administration, and reviewing and editing the manuscript. AHB was involved in supervision, and reviewing and editing the manuscript. CSEH was involved in conception, design, supervision, investigation, and reviewing and editing the manuscript. JPV was involved in conception, design, funding acquisition, supervision, investigation, and reviewing and editing the manuscript.

Funding The study was funded by Burnet Institute, Melbourne, Australia. The funding body had no role in designing the study; collecting, analysing or interpreting the data; or writing the manuscript. SS is supported by Monash Graduate Scholarship and Monash International Tuition Scholarship. JPV is supported by a NHMRC Investigator Grant (GNT1194248) and CSEH is supported by a NHMRC Investigator Grant (APP 2016379).

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Competing interests None declared.

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

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. This study was approved by the Monash University Human Research Ethics Committee (ID#40253) and the National Research Ethics Committee of Bangladesh Medical Research Council (Reg

#56207112023, BMRC/NREC/2022-2025/02). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study are available from the corresponding author upon request.

ORCID iD

Saima Sultana https://orcid.org/0000-0001-6129-918X

REFERENCES

1 Perin J, Mulick A, Yeung D, *et al*. Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet Child Adolesc Health* 2022;6:106–15.
2 Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet* 2008;371:261–9.
3 Aylward GP. Neurodevelopmental outcomes of infants born prematurely. *J Dev Behav Pediatr* 2014;35:394–407.
4 Blondel B, Truffert P, Lamarche-Vadel A, *et al*. Use of medical services by very preterm children during the first year of life in the Epipage cohort. *Arch Pediatr* 2003;10:960–8.
5 Srinivasjois R, Slimings C, Einarsdóttir K, *et al*. Association of Gestational Age at Birth with Reasons for Subsequent Hospitalisation: 18 Years of Follow-Up in a Western Australian Population Study. *PLoS One* 2015;10:e0130535.
6 WHO. WHO recommendations on antenatal corticosteroids for improving preterm birth outcomes. Geneva: World Health Organization, 2022.
7 Ballard PL, Ballard RA. Scientific basis and therapeutic regimens for use of antenatal glucocorticoids. *Am J Obstet Gynecol* 1995;173:254–62.
8 McGoldrick E, Stewart F, Parker R, *et al*. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2020;12:CD004454.
9 Oladapo OT, Vogel JP, Piaggio G, *et al*. Antenatal Dexamethasone for Early Preterm Birth in Low-Resource Countries. *N Engl J Med* 2020;383:2514–25.
10 Ninan K, Liyanage SK, Murphy KE, *et al*. Evaluation of Long-term Outcomes Associated With Preterm Exposure to Antenatal Corticosteroids: A Systematic Review and Meta-analysis. *JAMA Pediatr* 2022;176:e220483.
11 Sultana S, Bruinsma F, Fisher Z, *et al*. Long-term outcomes of antenatal corticosteroids for preterm birth: An overview of systematic reviews. *PLOS Glob Public Health* 2025;5:e0004575.
12 Bahl R, Gülmezoglu AM, Nguyen MH. The World Health Organization ACTION-I (Antenatal CorTicosteroids for Improving Outcomes in preterm Newborns) Trial: a multi-country, multi-centre, two-arm, parallel, double-blind, placebo-controlled, individually randomized trial of antenatal corticosteroids for women at risk of imminent birth in the early preterm period in hospitals in low-resource countries. *Trials* 2019;20:507.
13 WHO. WHO recommendations on interventions to improve preterm birth outcomes. Geneva World Health Organization; 2015.
14 Gould JF, Fuss BG, Roberts RM, *et al*. Consequences of using chronological age versus corrected age when testing cognitive and motor development in infancy and intelligence quotient at school age for children born preterm. *PLoS One* 2021;16:e0256824.
15 Squires J, Bricker DD, Twombly E. Ages & stages questionnaires. Baltimore: Paul H. Brookes, 2009.
16 Small JW, Hix-Small H, Vargas-Baron E, *et al*. Comparative use of the Ages and Stages Questionnaires in low- and middle-income countries. *Dev Med Child Neurol* 2019;61:431–43.
17 Tofail F, Fernald LC, Das KK, *et al*. Effect of water quality, sanitation, hand washing, and nutritional interventions on child development in rural Bangladesh (WASH Benefits Bangladesh): a cluster-randomised controlled trial. *Lancet Child Adolesc Health* 2018;2:255–68.
18 Pitchik HO, Tofail F, Akter F, *et al*. Concurrent validity of the Ages and Stages Questionnaire Inventory and the Bayley Scales of Infant and Toddler Development in rural Bangladesh. *BMC Pediatr* 2023;23:93.
19 Shrestha M, Kvestad I, Hysing M, *et al*. The relationship between the ages and stages questionnaire, 3rd edition scores in early childhood and future cognitive abilities in young Nepalese children. *BMC Pediatr* 2024;24:642.
20 Squires J, Twombly E, Bricker DD. ASQ®-3 user's guide. Baltimore, Maryland: Paul H. Brookes Publishing Co, 2009:256.
21 Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry* 1997;38:581–6.
22 Goodman R. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry* 2001;40:1337–45.
23 Mullick MSI, Goodman R. Questionnaire screening for mental health problems in Bangladeshi children: a preliminary study. *Soc Psychiatry Psychiatr Epidemiol* 2001;36:94–9.
24 Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* 2001;39:800–12.
25 StataCorp. Stata statistical software: release 18. College Station, TX: StataCorp LLC, 2023.
26 Sotiriadis A, Tsiami A, Papatheodorou S, *et al*. Neurodevelopmental Outcome After a Single Course of Antenatal Steroids in Children Born Preterm. *Obstet Gynecol* 2015;125:1385–96.
27 Alam MI, Mansur M, Barman P. Early childhood development in Bangladesh and its socio-demographic determinants of importance. *Early Child Dev Care* 2022;192:1901–20.
28 Hasan MN, Babu MR, Chowdhury MAB, *et al*. Early childhood developmental status and its associated factors in Bangladesh: a comparison of two consecutive nationally representative surveys. *BMC Public Health* 2023;23:687.
29 Gil JD, Ewerling F, Ferreira LZ, *et al*. Early childhood suspected developmental delay in 63 low- and middle-income countries: Large within- and between-country inequalities documented using national health surveys. *J Glob Health* 2020;10:010427.
30 Hee Chung E, Chou J, Brown KA. Neurodevelopmental outcomes of preterm infants: a recent literature review. *Transl Pediatr* 2020;9:S3–8.
31 Hsiao C, Richter L, Makusha T, *et al*. Use of the ages and stages questionnaire adapted for South Africa and Zambia. *Child Care Health Dev* 2017;43:59–66.
32 van Heerden A, Hsiao C, Matafwali B, *et al*. Support for the feasibility of the ages and stages questionnaire as a developmental screening tool: a cross-sectional study of South African and Zambian children aged 2-60 months. *BMC Pediatr* 2017;17:55.
33 Barros AJD, Matijasevich A, Santos IS, *et al*. Child development in a birth cohort: effect of child stimulation is stronger in less educated mothers. *Int J Epidemiol* 2010;39:285–94.
34 Forns J, Julvez J, García-Esteban R, *et al*. Maternal intelligence-mental health and child neuropsychological development at age 14 months. *Gac Sanit* 2012;26:397–404.
35 Draper CE, Yousafzai AK, McCoy DC, *et al*. The next 1000 days: building on early investments for the health and development of young children. *The Lancet* 2024;404:2094–116.
36 Runge RA, Soellner R. Cultural Bias in Parent Reports: The Role of Socialization Goals When Parents Report on Their Child's Problem Behavior. *Child Psychiatry Hum Dev* 2024;55:1020–30.
37 Adhikari S, Ma J, Shakya S, *et al*. Parents' perception of adolescents' difficulties and impact of problems in different castes and ethnic groups in Nepal. Do they converge with the frequencies of symptoms reported on the child behavior checklist (CBCL)? *Soc Psychiatry Psychiatr Epidemiol* 2025;60:1695–705.
38 Laugesen K, Skajaa N, Petersen I, *et al*. Mental Disorders Among Offspring Prenatally Exposed to Systemic Glucocorticoids. *JAMA Netw Open* 2025;8:e2453245.
39 Gyamfi-Bannerman C, Clifton RG, Tita ATN, *et al*. Neurodevelopmental Outcomes After Late Preterm Antenatal Corticosteroids: The ALPS Follow-Up Study. *JAMA* 2024;331:1629–37.