Evaluation of impact of continuous KMC initiated immediately after birth compared to KMC initiated after stabilization, in newborns with birth weight 1.0 to <1.8 kg on neurodevelopmental outcomes: protocol for a follow-up study

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Abstract

Background:

Preterm birth or low birth weight is the single largest cause of death in newborns, but the mortality can be reduced through newborn care interventions, including Kangaroo Mother Care (KMC). Previously, a multi-country randomized controlled trial, coordinated by the World Health Organization reported a significant survival advantage with initiation of continuous KMC immediately after birth compared with initiation of continuous KMC a few days after birth when the baby is considered clinically stable.

Whether the survival advantage would lead to higher rates of neurodevelopmental morbidity, or the immediate KMC will have a beneficial effect on cognitive development also, has not been investigated. We therefore propose to test the hypothesis that low-birth-weight infants exposed to immediate KMC will have lower rates of neurodevelopmental impairment in comparison to traditional KMC-treated infants, by prospectively following up infants already enrolled in the immediate KMC trial, for the first two years of life, and assessing their growth and neurodevelopment.

Methods:

This prospective cohort study will enroll surviving neonates from the main immediate KMC trial. The main trial as well as this follow-up study are being conducted in five low- and middle-income income countries in South Asia and sub-Saharan Africa. The sample size for comparison of risk of neurodevelopmental impairment is a total of about 2200 neonates. The primary outcomes will include rates of cerebral palsy, hearing impairment, vision impairment, mental and motor development, and epilepsy and will be assessed by the age of three years. The analysis will be by intention to treat.

Discussion

Immediate KMC can potentially reduce low-birth-weight associated complications such as respiratory disease, hypothermia, hypoglycemia and infection that can result in impaired neurocognitive development. Neuroprotection may also be mediated by improved physiological stabilization that may lead to better maturation of neural pathways, reduced risk of hypoxia, positive parental impact, improved sleep cycles and improved stress responses. The present study will, therefore, help in evaluating the overall impact of KMC by investigating the long-term effect on neurodevelopmental impairment in the survivors.

Trial registration

Clinical Trials Registry-India: CTRI/2019/11/021899 on 06 November 2019

Background
Nearly, 15.5 per cent of all births, or more than 20 million infants worldwide, are born with low birth weight (LBW) as a result of preterm birth or intrauterine growth restriction or a combination of the two [1, 2]. Preterm birth or LBW is the single largest cause of death in newborns, but the mortality can be reduced by effective newborn care interventions. However, for years it was demonstrated that although mortality was being improved by interventions for LBW newborns, the impact on morbidity including neurocognitive impairment and motor disabilities, was unchanged [3]. More recently there is evidence suggesting that infant survival with improved neurodevelopmental outcomes is increasing slightly and is associated with both improved medical interventions and maternal factors [4]. However, there is also concern of increased risk of neurodevelopmental impairment, and this enigma needs to be addressed by a systematic study. Therefore, while evaluating the impact of any intervention on mortality in this population, it is equally important to study the risk of neurodevelopment impairments, including cerebral palsy, hearing and vision impairment, cognitive impairment, and epilepsy.

World Health Organization (WHO) defines Kangaroo Mother Care (KMC) as a technique used in preterm and LBW infants of continuous skin-to-skin contact between mother and baby until the infant shows signs of intolerance. Exclusive breastfeeding is also encouraged as an essential component of KMC. Notably, however, it is currently recommended that continuous KMC should be initiated only once the baby is stable, meaning that the baby must be breathing spontaneously without additional oxygen [5].

"WHO recommendations on interventions to improve preterm birth outcomes" recommends KMC for the routine care of newborns weighing 2.0 kg or less at birth, which should be initiated in health care facilities as soon as the newborns are clinically stable. [6] These babies should be provided as close to continuous KMC as possible. Intermittent KMC, rather than conventional care, is recommended for newborns weighing 2.0 kg or less at birth, if continuous KMC is not possible [6]. There is no current recommendation for KMC for unstable < 2.0 kg neonates. A recently updated Cochrane review reported 40% lower mortality in infants with birth weight < 2.0 kg given KMC compared to mortality in those who were given standard care in hospitals, at 40 to 41 weeks postmenstrual age. [7]. In almost all studies included in the Cochrane review, KMC was initiated after the baby was clinically stable, with the median age at initiation of KMC 3.2 to 24.5 days [7]. Two randomized controlled trials (RCTs) comparing immediate versus conventional KMC from South Africa and Vietnam [8–10] showed favourable results for immediate KMC initiation. This data led the World Health Organization to coordinate a multi-country randomized controlled trial to evaluate the effect of initiating continuous KMC immediately after birth on survival (compared with initiation of continuous KMC a few days after birth when the baby is considered clinically stable). This RCT assessed newborn survival outcomes over the acute hospital period up to a 28-day follow-up [11]. The study enrolled 3211 infant- mother dyads with 1609 dyads in intervention arm and 1602 in the control arm. The median daily duration of skin-to-skin contact was 16.9 hours (IQR 13.0–19.7) in the intervention and 1.5 hours (IQR 0.3–3.3) in control arm. Neonatal death occurred in 12.0% and 15.7% infants, respectively in the two arms (RR 0.75; 95% CI 0.64–0.89; p = 0.001). The study concluded that in infants with birthweight between 1.0 and < 1.8 kg, immediate KMC (versus conventional KMC care) resulted in a significant reduction in neonatal mortality [12]. However, in order to evaluate the overall impact of KMC, the long-term effect on neurodevelopment in the survivors should be assessed.
It has been observed that, KMC can reduce bradycardia and oxygen desaturation events in preterm infants, providing physiological stability and possible benefits for neurodevelopmental outcomes [13]. Few studies involving KMC initiated in stable infants show that KMC has a beneficial effect on both short-term [14] and long-term [15, 16] neurodevelopmental outcomes of preterm and LBW babies compared to no KMC. The long-lasting social and behavioural protective effects have been observed beyond 20 years after the KMC intervention [17].

Studies have suggested that there is a positive impact of KMC on parental interaction due to not only increased skin-to-skin contact but also increased opportunity for bonding through breastfeeding and as a result, impact on the child's behaviour, which can be long lasting. However, the degree of direct impact on cognition, language, motor, auditory, and vision impairment has not been consistent, although most studies do demonstrate a positive trend in these domains [17–21]. Furthermore, emerging evidence from smaller studies suggests that, in addition to the positive parental impact, the implementation of KMC may also be neuroprotective through both improved sleep cycles and brain maturation patterns seen on EEG [22, 23], as well as improved stress responses in general, which had lasting impact when reviewed over a 10-year period on both emotional and cognitive development [24].

Despite the evidence of benefit of KMC after stabilisation on neurodevelopmental outcomes, an evaluation of the long-term effects of the KMC initiated immediately after birth on the risk of neurodevelopmental impairment such as motor or sensory impairment or cognitive deficits is not well known.

We hypothesize that KMC initiated immediately after birth can improve physiological stabilization, and potentially lead to anatomical or functional changes in the brain in the neonatal period thus allowing for better maturation of brain and pathways leading to a possible decrease in neurocognitive morbidity as well as reduce the risk of hypoxia, thus decreasing long-term morbidity. In addition, given the positive impact of traditional KMC on parental bonding, it is argued that the earlier KMC is initiated (e.g., with immediate KMC), the stronger the bond, leading to better family motivation and stimulation and thus positively impacting on child development.

The main outcome of interest for the parent study on immediate KMC was the impact on neonatal mortality [11, 12]. Evidence of the longer-term effect of the intervention on risk of neurodevelopmental impairment, growth, and mortality beyond the neonatal period, on the other hand, will provide additional evidence and rationale for policy change as the intervention targets survival as well as helping babies to thrive.

We therefore propose to follow-up the newborns enrolled in the recently published immediate KMC study [11, 12], beyond the neonatal period up to three years of age to additionally study risk of neurodevelopmental impairments, specifically the risk on growth, feeding, caregiving practices, mortality and home environment. Our main hypothesis is that those newborns who were provided continuous KMC initiated immediately after birth will experience a reduced risk of neurodevelopmental impairment, including the risk of cerebral palsy, hearing impairment, vision impairment, mental and motor
impairments, and epilepsy, compared with a similar group in whom KMC was initiated only after stabilization.

Methods

Study design

This is a prospective cohort study of the children already enrolled in the immediate KMC randomized controlled trial to evaluate the impact of continuous Kangaroo Mother Care initiated immediately after birth (iKMC) on survival of newborns with birth weight between 1.0 to < 1.8kg [11, 12].

Study setting:

As this study is a follow-up of the concluded and recently published iKMC trial [12], the study is being conducted at the same five LMIC study sites encompassing hospitals in Ghana, India, Malawi, Nigeria and Tanzania. The selected facilities are tertiary care hospitals that care for small and sick newborns with a high proportion of LBW babies and follow-up high risk newborns. As part of standardization across the involved study sites, prior to the study, trainings and standardization assessments were done to ensure all participating sites could offer the WHO minimum package of care for small and sick newborns [11].

Study population:

All infants born with birth weight between 1.0 to < 1.8 kg, enrolled in the main trial, who survive the neonatal period, and whose parents consent for their participation in the follow-up study, are eligible to be enrolled.

All infants who die within the first month of life or whose parents refuse consent for follow-up will be excluded from the study.

Sample size calculation

The initial sample size for the main iKMC trial was a total of 4200 neonates. Early completion in January 2020 led to a total of 3211 neonates being enrolled in the main iKMC trial. Preliminary review of literature of neurodevelopment in infants between 1 to < 1.8 kg shows the prevalence of any of the conditions of cerebral palsy, hearing impairment, vision impairment, and mean development scores to vary from 5 to 25% [25–27]. Any neurodevelopmental impairment (e.g., cerebral palsy, Bayley score < 85, hearing or vision impairment) in the study population is estimated to be approximately at 15–25%. We estimated the sample size for comparison of risk of neurodevelopmental impairment in control and intervention groups (20% compared with 15% or 25% (25% lower or higher) with 80% power and a significance level of 5% to be 1100 per group, requiring a total of about 2200 neonates.

We thus propose to enroll 2200 babies from the main trial to reach the above-mentioned sample size.
The intervention

The proposed study is a follow-up of the already concluded randomized controlled trial for evaluating the effect of immediate KMC on infant survival. The intervention and control groups were assigned during the main iKMC trial where KMC is defined as continuous skin-to-skin contact with mother or her surrogate aiming for at least 20 hours per day, support for exclusive breastfeeding, and required medical care without separation from the mother as much as possible.

In the intervention group, the mother and baby remained in skin-to-skin contact from the time of randomization whereas the newborns randomized to the control group received conventional care, and the mother and baby were separated until the baby was clinically stable. The details of intervention and control arms and care of the newborns in both the arms are described in the already published protocol paper [1].

Care of newborns in both intervention and control groups for the follow-up study

For the on-going follow-up study, care of the children continues to be as per each site’s routine policy and standard of care, including routine health monitoring visits, care for acute illnesses and management of morbidities including neurodevelopmental impairments. This includes appropriate early diagnosis and management of the neurodevelopmental outcomes of interest. Children with suspicion of epilepsy are referred to appropriate neurologic or child health services for confirmation and management according to national protocols. Those with motor impairments are referred to local rehabilitation specialists for available physical therapy resources as per local availability. For any child with signs of developmental impairment (motor, cognitive, or social-behavioural), referral to appropriate early stimulation programs is provided. Early monitoring for vision and hearing impairment is performed routinely and in case of any suspicion, the infants are referred to appropriate ophthalmologic and audiology or otolaryngology specialists for appropriate management and to adapt to environment. For every child that has been identified as having neurodevelopmental impairment, each site in line with their standard protocol for the identification, assessment, management, and follow-up care, develops an individual care plan (incl. rehabilitation, psychosocial support etc) in consultation with the child’s parents.

Primary and secondary outcomes

The primary outcome of the follow-up study is presence of neurodevelopmental impairments assessed by the age of three years in all enrolled children. The window for the outcome assessments was extended from two years to three years after ethics approval due to the COVID-19 pandemic. Specifically, this includes rates of motor impairment and risk of cerebral palsy, hearing impairment, vision impairment, cognitive, language, motor, socio-emotional or adaptive behaviour, and epilepsy. Secondary outcomes include growth and feeding practices, mortality and home environment (maternal depression and parent-child interactions), and rates of overnight hospital admissions.
Outcomes are assessed via standardized tools and questionnaires (Table 1). Motor impairment and risk of cerebral palsy is measured by standardized neurologic evaluation, using a validated tool, Hammersmith Infant Neurological examination (HINE) at 6-month, one year and two years of age. Cognitive, language, motor, socio-emotional or adaptive behaviour is assessed using Bayley Scales of Infant and Toddler Development (BSID III) at 2 to 3 years of age. Epilepsy is diagnosed using a standardized questionnaire, with operationalization of International League against Epilepsy (ILAE) definition. Hearing is evaluated at discharge from hospital or as soon as possible after enrolment in the follow-up study. First an assessment by screening auditory brainstem responses (ABR) is performed at the facility. If the infant clears this assessment no further assessment for hearing is required. In case the infant fails this initial screening, he/ she is referred to the audiologist or specialist for re-screening including a diagnostic ABR if required. Visual acuity is measured using Teller Acuity Cards, at or any time after one year of age at the facility.

The schedule of outcome assessments is shown in Table 2. As this is a follow-up study of the main iKMC trial participants, infants are enrolled on a rolling basis. Assessments for outcome measurements are performed at the earliest age-appropriate time point feasible for the individual child upon enrolment for this follow-up study. Due to challenge posed by COVID-19 pandemic with ensuing lockdowns and permanent movement of many of the children of migrant labourers to distant areas, the age window for enrolment was extended from 24 months up to 36 months after due approval from the institutional review boards (IRBs) or ethics committees.

Blinding

While the main iKMC trial evaluating the impact on newborn survival did not incorporate blinding due to the nature of the intervention, during the follow-up assessments, evaluators conducting the standardized assessments are blinded to whether the child received the intervention or not to decrease the bias.

Study implementation strategy

The iKMC follow-up study is being conducted in a standardized manner across all the sites in the five countries. Each site has constituted multidisciplinary teams to perform the different activities- study conduct, internal quality control, project management and data management. Each team member is trained in the protocol, Good Clinical Practice (GCP) and study specific standard operating procedures specific to their role and responsibility. A site coordinator is responsible for coordinating the implementation of the follow-up study at each site. A central team led by WHO coordinates the conduct across all sites, ensures harmonization of processes and monitors quality and study progress.

Infrastructure

An important fallout of the study has been- infrastructure development. Each site has developed a designated child development assessment unit. The unit has separate designated areas for registration and screening, consent, anthropometry, structured neurological assessment using HINE, developmental
assessments using BSID III, visual acuity using Teller Acuity Cards, hearing assessment using auditory brainstem responses and data entry and management.

**Enrolment and outcome measurements**

The study conduct research staff is responsible for consent as well as follow-up of the enrolled infants for outcome measurements.

They are blinded to the intervention or control group allocation of enrolled infants as they were not involved with intervention delivery during the main trial conduct. The staff performing outcome assessments had an initial intensive training on the standardized and validated tools being used for assessing primary and secondary outcomes of the follow-up study described in Table 1. For any identified neurodevelopmental impairment, appropriate standard of care management is provided to the child.

**Quality assurance and quality control**

The study has a well-structured quality assurance plan that is being implemented at all sites. The site coordinators ensure adherence to the manual of operations. The study has employed several checks to ensure quality of all aspects of the follow-up study including the consent process, and the outcome measure assessments. Internal quality checks are conducted by the site coordinators and study Principal Investigators (PIs) at each site. The data acquisition for the outcome measurements is verified by the site coordinator. Ten percent of the data acquisition is reviewed by the expert investigator/designee for completeness and consistency. The investigators monitor at least 10% of processes being performed for different outcome measurements by the study conduct team. The observations are documented in specifically designed forms. Appropriate corrective and preventive action are taken based on expert observations. External oversight and support are provided by WHO staff to ensure quality of study implementation. This is done through site visits by WHO staff or consultants using a standardized monitoring checklist. Additionally, sites transfer data to WHO every month and this data is reviewed by the central team at WHO for quality, and feedback for improvement is provided to the PIs at respective sites.

**Training and standardization**

The research staff including the conduct team, project management team, data management and internal quality control team underwent an intensive training before the start of the study. All were oriented to the protocol and GCP guidelines. Orientation and sensitization of regular health care staff of the Departments of Pediatrics, Physical Medicine and Rehabilitation, Ophthalmology and Nose and Throat regarding the study and its processes was done to ensure smooth functioning. The research staff has been provided role specific intensive training and standardization. The research assistants and coordinators from the conduct team were trained on screening for eligibility, administering written informed consent from the parents, enrolment, outcome measure assessments and scheduling and tracking for the 3-year follow-up of the infants to minimize deviations and non-compliance to the follow-
up time points. All research staff were trained in rapport building and communication with the mother and the families. Training for specific outcome measurements like visual acuity using Teller Acuity Cards, hearing using screening ABR, maternal depression using the 9-question patient health questionnaire (PHQ-9) was provided to the designated staff. There was a two-week intensive training for Bayley’s assessment by experts. A training of trainers (TOT) workshop for standardization of anthropometry measurements of length, head circumference and weight was conducted by experts and the Safdarjung hospital, India investigators for all the five study sites. Each site was trained in implementation of each tool, counselling of families if neurodevelopmental impairment is identified with appropriate referral system in place, and to train local providers at each site.

All participating hospitals are supported to make quality-of-care improvement and provide standard of care with breast milk feeding support, complementary feeding support and attention to hygiene for all infants.

**Data collection**

The data for the study is being collected on paper-based case report forms which are transcribed into an electronic database. The electronic database has been developed on a clinical data management platform ‘REDCap’ with all the data quality checks. The questions, response options, variable names and data structure are identical for all sites. Double data entry is done at each site by trained entry personnel. The data manager at each site is responsible for data quality checks, query management, and for ensuring completeness of data. Any discrepancies are addressed within 24 hours of data collection. All data collected is password protected and stored in a local server in each site. No personal identifiers are entered in the database. All paper forms will be stored in locked filing cabinets at the respective sites.

**Data management and analysis**

The data management is coordinated centrally by a team from WHO, but each site is responsible for site data management and data security. A central data repository has been created at the WHO. Sites share cleaned data every month to WHO where additional checks are run and a list of queries sent to the sites for clarification. All data sent to WHO does not have any personal identifiers.

The data from this multicentre study will be accessible to all the participating research teams to jointly answer the study questions. After publication of the manuscript reporting the results on primary and secondary outcomes, the data will be made publicly accessible.

**General principles for analysis**

The analysis will be by intention to treat. There will be no post randomization exclusions except those who die before 29 days of age.

The primary and secondary outcomes will be compared between the intervention and control groups. All planned analysis will use 5% significance level. Risk Ratios and their confidence intervals will be calculated and will be the primary analysis if the loss of follow is 2.5% or lower. In case the loss to follow-
up for the primary outcome is greater than 2.5%, we will additionally calculate Hazards Ratios and their confidence intervals. Additionally, we will adjust the results for confounding using multiple logistic regression and Cox proportional hazards models if there are any important differences in baseline characteristics between immediate KMC and control groups.

Subgroup analysis will be conducted by i) birth weight categories (<1.2 kg, 1.2–1.5 kg and 1.5–1.8 kg), ii) gestation (<34, 34–36, >37 weeks) and iii) singleton/multiple birth. Secondary analysis will be limited to an analysis by compliance. This secondary analysis will present the efficacy of the intervention by average duration of skin-to-skin contact over the first three days of life, categorized as: >20 hours/day; 10–19 hours/day; and <10 hours/day. In this secondary analysis, reverse causality will be carefully assessed, because newborns who are about to die may be provided less or no skin-to-skin contact for a variety of reasons

**Study oversight**

The study Steering Committee comprises of all PIs from study sites, BMGF representatives and WHO technical staff functioning as its secretariat. This committee is responsible for designing and implementing the study in a harmonized way. Study PIs are responsible for contributing to the development of the research proposal, study manual, data management system, outcome measurement and data collection, data analysis and interpretation and dissemination of results. All activities are facilitated and supported by WHO. On a fortnightly basis, the sites submit a brief status report to WHO. A formal progress report is submitted by each site every year.

The study is coordinated by a technical team from WHO, ensuring arrangements are in place to support teams in any challenges being faced to implement this study. WHO technical staff conducted intensive training at the beginning of the study. The technical team performs monitoring visits to each site every year. Monitoring visits have the dual function of identifying problems and supporting the sites in improving data collection, follow-up, and monitoring.

A Technical Advisory Group (TAG) has been setup in the field. The TAG members serve in their individual capacity and reviewed the final research protocol for any major concern prior to trial implementation. TAG members’ terms of reference also include revision of manual of operations, study forms and consent forms and advise on practical issues in implementing the trial in the field.

**Discussion**

This international multi-site study is the first of its kind aiming to assess the effect of immediate KMC on long term outcomes. The literature has demonstrated immediate benefit of KMC in stable neonates and is part of WHO guidelines for newborn care [5, 6]. More recently, the main iKMC trial showed that the benefits of KMC can be extended to unstable low birth weight babies, beginning right at birth and iKMC had 25% lower risk of death at 28 days than those who received conventional care with kangaroo mother care initiated after stabilization [12]. With the parent trial successfully conducted across these sites, there
is no better opportunity to study the effect of this intervention on long term outcomes. The follow-up study has the objective of elaborate and precise assessment of all the domains of neurodevelopment, including cerebral palsy (HINE), developmental delay (BSID III), hearing, vision and epilepsy screening which would be evaluated by trained personnel ensuring optimal standardization on the large sample size in the five LMIC countries. The training and standardization conducted as part of this study has already strengthened the infrastructure and supported capacity building in the participating sites. This can be scaled up in future at various tertiary centers in LMICs, in order to ensure quality, follow-up care for each and every mother-NICU/ NICU graduate.

In addition, the final results will provide crucial insights and higher level of evidence for the much-awaited long term outcome of immediate KMC in the vulnerable sick low-birth-weight neonates. If proven effective, this intervention would be a value addition to the set of cost-effective strategies in reducing neurological impairment in resource limited countries.

**Trial status**

The trial is ongoing in all five sites – Ghana, India, Malawi, Nigeria and Tanzania. The first participant was recruited on 11 January 2019. Participant recruitment is expected to be completed by 20 July 2022. The current protocol is version 3.2 dated 7th April 2021.

**Abbreviations**

KMC  
Kangaroo mother care  
iKMC  
Immediate kangaroo mother care  
LIMC  
Low- and middle-income income countries  
LBW  
Low birth weight  
WHO  
World Health Organization  
RCT  
Randomized Controlled Trials  
HINE  
Hammersmith Infant Neurological examination  
BSID III  
Bayley Scales of Infant and Toddler Development  
ILAE  
International League against Epilepsy  
ABR
Auditory brainstem responses
IRB
Institutional Review Board
GCP
Good Clinical Practice
PI
Principal Investigator
PHQ-9
Patient Health Questionnaire-9
TOT
Training of trainers
TAG
Technical Advisory Group

**Declarations**

**Acknowledgements**

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**Authors’ contributions**

All named authors contributed to protocol development, drafting the manuscript, review of the manuscript for intellectual content, approved the final version of the manuscript and have agreed to publication. All authors agree to adhere to the authorship guidelines of *Trials*.

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**Availability of data and materials**

The datasets generated during the current study will be available from the corresponding author on reasonable request.
**Ethics approval and consent to participate**

Since this is a multi-country, multicentre study with a single protocol, approvals on the same protocol has been obtained from the WHO Ethics Review Committee (reference no. EC0002910 approved on 23 Nov 2017) as well as the local Institutional Review Boards (IRBs) of the five participating hospital sites: Ghana's School of Medical Sciences/ Komfo Anokye Teaching Hospital Committee on Human Research, Publication and Ethics (reference number CHRPE/AP/170/19, initial approval on 11 April, 2019), Tanzania’s National Institute for Medical Research (reference number NIMR/HQ/R.8c/Vol. I/708, initial approval on 17 June, 2019), Malawi’s College of Medicine Research and Ethics Committee (COMREC) (reference number P:08/17/2235, initial approval on 21 April, 2020), Nigeria’s OAUTHC Ethics and Research Committee (reference number IRB/IEC/0004553, approval on 30 May, 2019), New Delhi-India’s Vardhman Mahavir Medical College and Safdarjung Hospital Institutional Ethics Committee (reference number IEC/VMMC/SJH/Project/2019-06/52, initial approval on 21 October, 2019). Each updated version of the protocol was approved by the each of the above-mentioned ethics committees.

A verbal consent was taken from the parents during the 29-day follow-up visit in the main iKMC trial and a written informed consent for participation in the follow-up study is obtained at the time of initiation of the three-year follow-up.

**Consent for publication**

Not relevant

**Competing interests**

The authors declare that they have no competing interests.

**Trial Registration**

The iKMC neurodevelopment follow-up study is registered with the Clinical Trial Registry-India with number CTRI/2019/11/021899 on 06 November 2019.

**References**


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44. Committee on practice and ambulatory medicine, section on ophthalmology, American Association of Certified Orthoptists, American Association for Pediatric Ophthalmology and strabismus,


Tables

Table 1 and 2 are available in the Supplementary Files section.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1and2.pdf
- SPIRITFillablechecklist.pdf