ABSTRACT

Introduction Very preterm (VPT) infants may experience varying degrees of neurodevelopmental challenges. Lack of early markers for neurodevelopmental disorders may delay referral to early interventions. The detailed General Movements Assessment (GMA) could help us to identify early markers for VPT infants at risk of atypical neurodevelopmental clinical phenotype in the very early stage of life as soon as possible. Preterm infants with high risk of atypical neurodevelopmental outcomes will have the best possible start to life if early precise intervention in critical developmental windows is allowed.

Methods and analysis This is a nationwide, multicentric prospective cohort study that will recruit 577 infants born <32 weeks of age. This study will determine the diagnostic value of the developmental trajectory of general movements (GMs) at writhing and fidgety age with qualitative assessment for different atypical developmental outcomes at 2 years evaluated by the Griffiths Development Scales-Chinese. The difference in the General Movement Optimality Score (GMOS) will be used to distinguish normal GMs, poor repertoire (PR) and cramped synchronised (CS) GMs. We plan to build the percentile rank of GMOS (median, 10th, 25th, 75th and 90th percentile rank) in N, PR and CS of each global GM category and analyse the relationship between GMOS in writhing movements and Motor Optimality Score (MOS) in fidgety movements based on the detailed GMA. We explore the subcategories of the GMOS list, and MOS list that may identify specific early markers that help us to identify and predict different clinical phenotypes and functional outcomes in VPT infants.

Ethics and dissemination The central ethical approval has been confirmed from the Research Ethical Board of Children’s Hospital of Fudan University (ref approval no. 2022(029)) and the local ethical approval has been also obtained by the corresponding ethics committees of the recruitment sites. Critical analysis of the study results will contribute to providing a basis for hierarchical management and precise intervention for preterm infants in very early life.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first multicentre prospective cohort study presenting a nationwide scope with clinical setting in China.
⇒ The participants of the study are representatives who come from different regions in China.
⇒ Recruitment was done in specialised hospitals to ensure that all subjects receive the same developmental follow-up and/or early intervention.
⇒ The individual developmental trajectory of general movements can more accurately predict neurodevelopmental outcomes for preterm infants.
⇒ The time point for the neurodevelopmental outcome follow-up was limited in this study.

INTRODUCTION

Preterm birth has become a widely concerning global public health problem with the rapid rise in the survival rates of preterm infants with advances in obstetric and neonatal medicine. Preterm infants (<30 weeks’ gestation); 10%–15% will experience varying degrees of neurodevelopmental challenges in motor function, coordination, personal-social, communication, cognition, performance, attention, executive function and academic skills. The challenges are especially acute in very preterm (VPT) infants (<30 weeks’ gestation); 10%–15% will...
develop cerebral palsy (CP), which is the most common physical disability in childhood, 8 40% will develop mild motor disorder and 30%–60% will experience cognitive deficits. 9 The long-term adverse neurodevelopmental consequences of preterm infants may impose a heavy economic burden on families and society. 10 11

Quality early intervention programmes can help minimise the morbidities of neurodevelopmental disorders; however, for early intervention, early identification is essential. There is a strong interest in the early detection of predictive signs of developmental disorders in preterm infants, 12 13 as this provides a valuable opportunity for intervention at a young age, when the central nervous system is most plastic. 14 The Prechtl General Movements Assessment (GMA) is a diagnostic tool that is recommended for monitoring and evaluating preterm infants who are at risk of developmental motor problems. 15–18 The reliable and valuable GMA was used to predict infants’ brain function and effectively and accurately assess later neurodevelopmental outcomes, especially the possible diagnosis of CP. General movements (GMs) have age-specific characteristics, which were observed from birth to corrected age of 3–5 months, including the writhing movement stage (preterm GMs and writhing movements) and the fidgety movement stage (fidgety movements) according to the GM development process. The writhing movement stage includes three types of abnormal GMs: poor repertoire (PR) GMs, cramped synchronised (CS) GMs and chaotic (Ch) GMs. 19 The fidgety movements stage includes two types of abnormal GMs: abnormal fidgety (AF) movements and the absence of fidgety (F−) movements. 20 Most intensive studies have demonstrated persistent CS movements and F− as an early predictor of CP. 21 22 In recent years, many researchers have paid increasing attention to GMs for identifying infants at risk of other poor neurodevelopmental outcomes, particularly cognitive and speech development, in addition to motor disorders. Preterm infants with consistently abnormal GMs up to 8 weeks after term had lower IQs at school age than children with an early normalisation of GMs. 23 AF GMs in preterm infants were also found to be associated with a score on average 8 points lower than those with normal fidgety (NF) GMs. 24 These findings indicate that abnormal GMs in both the writhing and fidgety stages may presage later cognitive impairment. 25 Similar to studies in infants with very low birth weight, those with aberrant fidgety movements were also more likely to have worse motor, language and cognitive outcome. 24 26 Moreover, retrospective studies found that infants who were subsequently diagnosed with autism spectrum disorder had abnormal GMs in their early months of life. 27 28

Based on the above analysis, we found that both atypical writhing movements and fidgety movements at an early age were associated with worse motor outcomes and poor cognitive and language performance in preterm infants. Nevertheless, qualitative assessment of GMs cannot fully meet the needs of clinical practice and guide precise early intervention. First, very few studies have been published on the practicability and predictive value of prospective multicentre studies for a large sample of preterm infants in a general clinical setting. Second, the positive predictive value of F− for developmental outcomes of CP is low; that is, not all F− at an early age will develop CP. Therefore, how can F− be distinguished to predict different clinical phenotypes of neurodevelopmental outcomes (CP, cognitive and speech disorders, etc)? Such early phenotypical differentiation, including the dysfunction type, is clinically of utmost importance, as early intervention strategies can be specifically tailored to individual needs. Third, do abnormal GMs predict the severity of developmental outcomes? In addition to providing specific early support to the family, most caregivers or parents want to know about the severity of the child’s future physical disability. Fourth, how can we differentiate between infants whose PR GMs will deteriorate and those whose PR GMs will normalise? The longitudinal evolution trajectory from writhing movement to fidgety movement periods seems to be the best predictor for infants.

The contents discussed above are the interesting aspects of the present study. However, the detailed assessment of GMs can help us to fulfil the above ideals. The semiquantitative evaluation of GMA has been fulfilled by the detailed assessment of GM Optimality Score (GMOS) at the writhing movement period and the Motor Optimality Score (MOS) at the fidgety movement period based on the optimality concept. 20 29 30 The GMOS has a maximum score of 42, which indicates optimal performance, and a minimum score of 5, which indicates worst performance. 29 The ‘Motor Optimality List’ at the fidgety age consisted of the following five subcategories: fidgety movements, repertoire of coexistent movements, movement patterns, postural patterns and movement character. Adding up the scores for each subcategory implies that the MOS ranges from 5 (minimum) to 28 (maximum). The higher the MOS, the better the motor repertoire. 29 30

To the best of our knowledge, this is the first multicentre prospective cohort study presenting a nationwide scope with a clinical setting to identify early specific markers of the different clinical phenotypes and functional outcomes with the development based on the qualitative and the semiquantitative evaluation of GMA for preterm infants, which would allow a greater number of premature infants to receive effective and precise early interventions during the critical window of brain development.

Aims and hypothesis

Phase one: predictive value of GMA

The primary aim of phase one is to determine the diagnostic value of GMs for different atypical developmental outcomes at 2 years, to provide a reference for clinical medical decision-making of premature infants.

It is hypothesised that the developmental trajectory of GMs with qualitative assessment could be able to more accurately predict the long-term neurodevelopmental
outcome of preterm infants based on a prospective cohort study with a large sample in a multicentre clinical setting.

**Phase two: correlation between GMOS and MOS**

The primary aim of phase two is to differentiate between infants whose PR GMs will have deteriorated and those whose PR GMs will have normalised, to provide evidence for the referral and ultra-early intervention of preterm infants.

It is hypothesised that the GMOS at the writhing period can predict the results of the GMA with qualitative assessment and MOS at the fidgety period.

**Phase three: detailed GMA as markers**

The primary aim of phase three is to identify an early specific marker of different clinical phenotypes and functional outcomes with the development at 2 years, to provide a basis for personalised and accurate early intervention treatment for premature infants.

We explore the subcategories of the GMOS and MOS, which may be identified as early specific markers that help us to distinguish and predict different clinical phenotypes and functional outcomes in CP, cognitive and speech disorders, poor social skills, etc, for preterm infants.

**METHODS**

**Study design**

This is a nationwide, multicentric prospective cohort study of 577 babies. The results of this cohort study will be reported in accordance with the ‘Strengthening the Reporting of Observational Studies in Epidemiology’ and the ‘Standard for Reporting of Diagnostic Accuracy Studies’ Statement.

**Setting**

The present study will be carried out in a nationwide, multicentric clinical setting in China. To ensure that the cohort study sample is representative and the high quality of GM assessment, participating units must meet the following requirements: (a) member unit of GM Trust China Training Site (Children’s Hospital of Fudan University); (b) children’s specialised hospital or maternal and child healthcare hospital; (c) equipped with GM paediatric diagnosis and treatment application system. Eventually, eight hospitals participated in the study.

**Participant recruitment**

This study will recruit a total of 577 preterm infants from high-risk infant follow-up management outpatients in different provinces of China between October 2022 and September 2024. The parents/guardians of the prospective participants will be invited to meet with the research coordinator to discuss the study and provide detailed information about the eligibility criteria. If preterm infants are eligible and their parents/guardians are interested in participating, they will be invited for a series of GMAs after physical examination by specialist physicians. When informed consent was obtained, infants born preterm were asked to join the developmental follow-up cohort. The guardians of participants will be informed about the GMA results through interviews, emails and phone calls. Premature infants with abnormal GMA results will receive early rehabilitation intervention.

**Sample size calculation**

The present study is a diagnostic accuracy of prospective cohort study. The primary aim was to determine the diagnostic value of abnormal GMs for atypical neurodevelopmental outcomes of language delay at correction for 24 months in preterm infants. Based on published research, the specificity of GMA during the fidgety movement period for predicting cognitive delay was 85% in infants born VPT. The present study sample size will be calculated to establish 90% expectation specificity of clinical value for predicting atypical neurodevelopmental outcomes. This calculation assumes that 26% of participants have at least mild language delay according to our previous preliminary study and published research. At an alpha level of 0.05, 461 preterm infants will be required for the cohort to ensure a statistical power of 0.8. Considering a 20% dropout rate, a total of 577 premature infants will be needed.

**Inclusion criteria**

Participants meeting the following inclusion criteria will be included:

1. Born <32 weeks' gestational age between 2022 and 2024.
2. The vital signs are stable.
3. Voluntary participation and signed informed consent.

**Exclusion criteria**

Participants with any of the following exclusion criteria will be excluded:

1. Infants with known congenital or chromosomal abnormalities.
2. Parents of infants who do not want to sign informed consent.
3. Participation in another early intervention clinical trial.

**Bias**

As a prospective cohort study, selection bias is minimised because participants will be enrolled very soon after birth. Subjects with early screening abnormalities in present cohort studies will receive early intervention; exposure to early interventions will be explored as potential biases.

**Predictive variables**

**Basic characteristic variables**

All of the participants’ general demographic information (neonatal variables), such as birth and maternal data, acquired medical factors and cerebral ultrasonogram and/or MRI characteristics, will be collected from medical records during hospitalisation. Demographic and neonatal data details of the included cohort are summarised in table 1.
GM assessment

Video recordings

All infant GM videos were recorded lying in the supine position with minimal clothing and in an adequate behavioural state by the GM paediatric application diagnosis and treatment system. Sequences that included fussing and crying were discarded. Video recordings of the infants were taken during the writhing movement and fidgety movement period and lasted between 3 and 5 min. The video recording time was specified as follows: time period 1 ‘writhing movements’—videos collected at <32, 32+0 to 36+6, 37+0 to 40+6 weeks’ postmenstrual age and 1+0 to 4+6 weeks’ post-term age; time period 2 ‘fidgety movements’—videos collected at 10+0 to 14+6 and 15+0 to 19+6 weeks’ post-term age.

Assessment method

Qualitative assessment

Writhing movement period: normal GMs are characterised by complexity, variability, and fluency of the movement sequence, amplitude, speed and intensity. Abnormal GMs in the writhing period can be divided into three types, namely, PR GMs, CS GMs and Ch GMs.19 36

Fidgety movements period: the typical characteristics of NF movements are small movements of moderate speed and variable acceleration of the neck, trunk and limbs, in all directions, continual in the awake infant, except during crying and fussing. The atypical GMs in the fidgety movement period can be divided into two types, namely, the F− movements and AF movements. If the typical characteristics of NF movements are not observed between 3 and 5 months post-term, we call this abnormality the ‘absence of fidgety movement’. However, other movements can also be commonly observed. AF movements resemble NF movements, but their amplitude, speed and jerkiness are exaggerated.19 36

Semiquantitative assessment

GM Optimality Score

The GMOS was assessed with reference to Prechtl’s optimality concept in the preterm and writhing GM periods.30 The optimality score is a detailed analysis of the quality of GMs based on the optimality concept. Detailed scores focus on the neck and trunk and the upper and lower extremities. For each item, a description of the optimal performance is given and corresponds to a score of ‘2’. A suboptimal performance is given a score of ‘1’, and a non-optimal performance is given a score of ‘0’. The following three items were given a score of ‘2’ or ‘1’: (1) involvement of the neck; (2) the amplitude of upper and lower limb movements; and (3) the speed of upper and lower limb movements. Summing the scores for each item in a category (‘neck and trunk’, ‘upper extremity’ and ‘lower extremity’) and the general score for each ‘sequence’ gives the GMOS a maximum score of 42, indicating optimal performance. The minimum score (worst performance) is ‘5’.29

Motor Optimality Score

The ‘Assessment of Motor Repertoire-3 to 5 Months’ is an observational instrument designed to meticulously assess movements and postures in non-manipulated infants.30 The assessment focuses on movement patterns (25 items), postural patterns (13 items) and movement character (8 items). The scoring of these 44 items is taken as a basis for the ‘Motor Optimality List’, which comprises the following five subcategories: (1) temporal organisation and quality of fidgety movements: NF movements scored 12, AF movements scored 4 or F− movements scored 1; (2) quality of movement patterns other than fidgety movements: predominantly normal scored 4, equal number of normal and atypical patterns scored 2, or predominantly atypical scored 1; (3) age-adequate movement repertoire: present scored 4, reduced scored 2
or absent scored 1; (4) postural patterns: predominantly normal scored 4, equal number of normal and atypical patterns scored 2, or predominantly atypical scored 1; and (5) movement character: smooth and fluent scored 4, monotonous and/or jerky, stiff, tremulous, slow/fast scored 2 or CS scored 1. Finally, adding up the scores of the five subcategories together means that the MOS has a maximum of 28 and a minimum of 5.20,31,36

Scorers and assessment procedure
All multicentre GM recordings will be submitted to the study sponsor of Children’s Hospital, Fudan University, for evaluation. Before starting this study, all three GM Trust-certified scorers (JW, XZ and HG) had completed advanced level training on detailed GMA.20 The three scorers conduct their assessments in accordance with the scoring criteria of the GMA.22 Throughout the study process, JW, XZ and HG do not know the medical history of the infants to be scored; they only receive the recording age. All three scorers assessed each of the video recordings separately in a prearranged order.24 They are also not allowed to communicate with each other but could view the video sequences repeatedly. In case of a disagreement, the scorers re-evaluate the recordings until a consensus is reached on a final score.

Neurodevelopmental assessment
The Griffiths Development Scales–Chinese
The Griffiths Mental Development Scale (GMDS) consists of six separate subscales and is used to assess the development of children aged 0–8 years. The subscales range from subscale A to subscale F: subscale A evaluates ‘motor function’; subscale B measures ‘personal-social’ abilities; subscale C assesses ‘hearing and language’; subscale D appraises ‘eye and hand coordination’; subscale E covers ‘performance’ and subscale F corresponds to ‘practical reasoning’.37,38 In 2016, the Chinese version of the GMDS was revised based on the Chinese child population.39 The cross-cultural comparative study of the GMDS confirmed that it can adapt well to the Chinese environment and can be reliably used to assess the development of Chinese children.37 According to a large number of clinical studies, the Griffiths Development Scales–Chinese (GDS-C) effectively evaluates motor function, congenital mental development status and developmental disorder, learning difficulties, vision problems, degree of premature birth, autism and social/emotional development skills in Chinese children.40

Scorers and assessment procedure
In this study, developmental assessment was performed using the GDSC at 2 years of corrected age. The physiotherapists who assessed the children using the GDS-C were registered users of the Griffiths scale and had rich experience with psychological testing in the present study. Each of the six subscales was scored according to a standardised procedure. The raw scores of the six subscales were converted to the corresponding percentiles and functional age standard by the Chinese norm. The functional age recorded in each subscale was obtained through ascribed computations. Developmental quotients (DQs) were determined for each subscale by dividing the functional age of the child by his chronological age at the time of testing. The results are reported as DQs with a mean of 100 and an SD of 15.40 Z scores were calculated for all neurodevelopmental scores based on five subscales to compare neurodevelopmental outcomes at 2 years of corrected age. Neurodevelopmental outcomes were classified as normal (Z score ≥−1), mildly delayed (−2≤Z score <−1) and severely delayed (Z score <−2).41,42

Outcome data were obtained from high-risk infant follow-up clinic visits when available until October 2026. Criteria for development outcomes of motor, personal-social, language, hand-eye coordination, performance: the results of GDS-C evaluation and clinical neurological examination after correcting for 24 months of age were the basis for determining development outcomes. Neurological examination and the diagnosis of CP were performed by the paediatrician, GDS-C measurement was performed by the therapist and the results of the last follow-up assessment were used to determine the developmental outcomes of the subjects. The development outcomes were determined according to the following criteria:
1. CP was confirmed according to the 2006 international definition of CP.
2. Motor retardation: the Z score of the locomotor A and/or the hand–eye coordination D subscales was <−1, and CP was excluded clinically.
3. Personal-social disorder: the Z score of the subscale personal–social B was <−1.
4. Language disorder: the Z score of the subscale language C was <−1.
5. Performance disorder: the Z score of the subscale performance E was <−1.

Figure 1 presents the general logistics for the nationwide multicentre collection of data and specimens, and the flow diagram of study assessment timeline.

Study procedure
Phase one: predictive value of GMA
In this part of the present study, we mainly focused on which types of GM trajectories were more associated with typical neurodevelopmental outcomes, CP and other atypical neurodevelopmental outcomes in preterm infants and further analysed the predictive value of GMA for different developmental outcomes (table 2). Moreover, longitudinal neonatal GM trajectories in the writhing movement period were described for predicting the short-term neurodevelopmental outcome, which was defined by the presence of the fidgety movements (NF, F and AF) evaluated at 3 months’ corrected age in the fidgety movement period (table 3).

GM trajectories were defined by dividing the observational period into two stages: the first part referred to the period from birth to term age, and the second part
corresponded to fidgety age. Serial GMs were recorded to define neonatal GM trajectories at three different time points: time one at <32 or 32+0 to 36+6 weeks in the preterm period; time two at 37+0 to 40+6 weeks’ post-menstrual age or 1+0 to 4+6 weeks’ post-term age; and time three at 10+0 to 14+6 or 15+0 to 19+6 weeks’ post-term age. GMs in personal developmental trajectory were classified as normal (N), PR or CS, whereas at 3 months’ corrected age, GMs were scored as NF and AF or F−. The Ch GMs of writhing movements is a very rare subtype in

Figure 1  The general logistics for the nationwide multicentre collection of data and specimens, and the flow diagram of study assessment timeline. GDS-C, Griffiths Development Scales-Chinese; GMA, General Movements Assessment; GMOS, General Movement Optimality Score; MOS, Motor Optimality Score.
clinical setting practice, so this subtype was not included in this study. When there were multiple records within the same period, the optimal performance of GM recording was used for the study. In the writhing movement period, the following five GM trajectories were identified:\textsuperscript{43}

1. Normal trajectory, when normal GMs were present at both preterm and term age (N–N).
2. Transient PR trajectory, when PR GMs were present at either preterm or term age (PR–N or N–PR).
3. Persistent PR trajectory, when PR was present at both preterm and term age (PR–PR).
4. Transient CS trajectory, when CS was present at either preterm or term age (CS–PR or PR–CS).
5. Persistent CS trajectory, when CS was present at both preterm and term age (CS–CS).

At the fidgety movement period, three of these GMAs were classified according to the presence or absence or abnormal fidgety movements, resulting in 13 final trajectories (table 2).

### Table 2 GM trajectories’ predictive neurodevelopmental outcomes at 24 months

<table>
<thead>
<tr>
<th>Trajectory</th>
<th>Typical neurodevelopmental outcomes (n)</th>
<th>Atypical neurodevelopmental outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24-month follow up—Griffiths assessment</td>
<td>Motor disorder (n)</td>
</tr>
<tr>
<td>PRp–Nt–F\textsuperscript{+} or Np–Prt–F\textsuperscript{+}</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>PRp–Prt–F\textsuperscript{+}</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>CSp–Prt–F\textsuperscript{+} or PRp–Cst–F\textsuperscript{+}</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>CSp–Cst–F\textsuperscript{+}</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

AF, abnormal fidgety; CS, cramped synchronised; F\textsuperscript{+}, absent and sporadic fidgety; GMs, general movements; N, normal general movements; n, number of infants; NF, normal fidgety; p, preterm; PR, poor repertoire; t, term.

### Table 3 GM trajectories of the writhing movements predictive of the short-term neurodevelopmental outcome at 3 months

<table>
<thead>
<tr>
<th>Trajectory</th>
<th>3-month follow up—GMA (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal fidgety</td>
</tr>
<tr>
<td>Np–Nt</td>
<td>?</td>
</tr>
<tr>
<td>PRp–Nt or Np–Prt</td>
<td>?</td>
</tr>
<tr>
<td>PRp–Prt</td>
<td>?</td>
</tr>
<tr>
<td>CSp–Prt or PRp–Cst</td>
<td>?</td>
</tr>
<tr>
<td>CSp–Cst</td>
<td>?</td>
</tr>
</tbody>
</table>

CS, cramped synchronised; GMA, General Movements Assessment; GMs, general movements; n, number of infants; N, normal general movements; p, preterm; PR, poor repertoire; t, term.

### Phase two: correlation between GMOS and MOS

In this part of the study, we pay attention to the following three aspects:

1. The GMOS can be used to differentiate between N, PR and CS GMs. We plan to build the GMOS (median, 10th, 25th, 75th and 90th percentile rank, minimum and maximum) in N, PR and CS of each global GM category. It will help us to differentiate between infants whose PR GMs will have normalised (PR–N) and those whose PR GMs will have deteriorated (PR–CS), etc.
2. To explore the different CIs of GMOS in the preterm and post-term periods for NF, AF and F at 3–5 months’ corrected age.
3. To analyse the relationship between GMOS in the writhing movement period and MOS in the fidgety movement period.

**Phase three: detailed GMA as markers**
In this part of the study, we want to address two main issues:
1. To identify the unique items in the GMOS list and MOS list as specific predictors of different neurodevelopmental outcomes in preterm infants at 24 months.
2. To set up the different CIs of GMOS in the writhing movement period and MOS in the fidgety movement period for the different severity functional impairments of the different atypical neurodevelopmental outcomes.

**STATISTICAL ANALYSIS**
The data will be analysed by statisticians in the Clinical Trial Unit (CTU) of Children’s Hospital, Fudan University. Summary statistics will be described using either percentiles or the mean (SD) for continuous variables according to the frequency (percentage) or distribution of the categorical variables. The GMOS, MOS and their subcategories are ordinal data. The number of normal or atypical movements or postural patterns in the MOS list, gestational age at birth and assessment age are interval data. All different atypical neurodevelopmental outcome data (motor retardation, personal-social disorder, language disorder and performance disorder) and CP outcome data (activity limitation in two categories, topography, motor form) were analysed as categorical variables. Differences with p<0.05 were assumed to be statistically significant.

For phase one, a univariate logistic regression analysis was performed to evaluate the association between each of the 13 GM trajectories and the different neurodevelopmental outcomes at 24 months’ corrected age. We identified high-risk and low-risk GM trajectories in preterm infants based on the results of univariate analysis. Furthermore, the extent to which any trajectory increased the diagnostic accuracy of GM trajectories in predicting CP was estimated by sensitivity and specificity. In addition, the relationship between the GM trajectories in the writhing movement period and the 3 months’ corrected age GMA was studied using logistic regression analysis, focusing on differences between normal versus non-normal (F or AF). Meanwhile, sensitivity, specificity, positive and negative predictive values, as well as accuracy (number correctly identified) and their 95% CIs were calculated for GM at both writhing movement and fidgety movement periods for predicting neurodevelopmental impairment at 24 months’ corrected age.

For phase two, the GMOS and MOS (median, 10th, 25th, 75th and 90th centile rank, minimum and maximum) for each global GM category were described first. We then used the Spearman rank correlation coefficient (r) to study the correlations between GMOS and MOS. After confirming the correlation between GMOS and MOS, we performed univariate regression analysis using the GM-associated variables.

For phase three, the same procedure was used to determine the association between the individual detailed GMA scores and the degree of atypical neurodevelopmental outcomes. General linear models were used to analyse the association between GMOS, MOS and DQs of the GDS-C. Moreover, a univariate logistic regression analysis was performed to evaluate the association between the GMOS, MOS (and its subcategories) and the different atypical neurodevelopmental outcomes at 24 months’ corrected age, regardless of the qualitative results of GMA. The OR was used as a measure of association and was reported along with its 95% CIs. In the case of sparse data, ORs were estimated using exact logistic regression. The identification of a set of GMOS and MOS (and its subcategories) associated with different atypical neurodevelopmental outcomes was executed using a forward stepwise regression.

**QUALITY CONTROL**
At the beginning of the study, all researchers from multiple centres were required to attend a series of training courses. These sessions will ensure that the staff members involved fully understand the study protocol and standard operating procedures. During the course of the study, the research sponsor organises a research quality control meeting monthly to analyse the research progress and problems that need to be improved. Meanwhile, the CTU of Children’s Hospital of Fudan University will monitor the study documents, case report forms, informed consent forms and data records regularly. After the study, all data analyses and results reporting for this study were performed by a third party (CTU).

**ETHICS AND DISSEMINATION**
The central ethical approval has been confirmed from the Research Ethical Board of Children’s Hospital of Fudan University (ref approval no. 2022(029)) and the local ethical approval has been also obtained by the corresponding ethics committees of the recruitment sites. The purpose of the study will be explained in detail to the participants, and full written and informed consent will be obtained from all participants.

The preliminary findings of the study will be published in peer-reviewed scientific papers and presented by oral presentations at conferences. The datasets analysed in the process of the current research are available from the corresponding author upon reasonable request.
PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not directly involved in the design and recruitment of the study.

DISCUSSION

Early detection of atypical neurodevelopmental outcomes is critical to identify infants who do not need special attention and those who may need close individualised follow-up for paediatric specialists and preterm infants’ families.44 The GMA is a very useful diagnostic tool that is strongly recommended worldwide for assessing and monitoring preterm infants who are at risk of developmental problems.16 The GMA tool was introduced in China in 2003 and the GM Trust of China Training Base was established in 2007 by Children’s Hospital of Fudan University.

The present study has a number of strengths. First, this is a prospective, clinical setting design with a large sample. Second, the participants are representative in the study and come from different regions in China. With the combined characteristics of study design and subject recruitment scope, the present study results will be more objective and reliable, which will have the vital practical significance for evaluating or predicting neurodevelopmental outcomes for VPT infants. Third, the participating units of the multicentre are all member units in the GM Trust of China, which ensures the research can be carried out with high quality. In this study, we paid more attention to atypical developmental disorders, including speech and cognitive disorders, and social skills problems except motor dysfunction. Last, the individual developmental trajectory of GMs based on qualitative GMA combined with the movement and postural patterns of detailed GMA based on quantitative GMA can more accurately predict neurodevelopmental outcomes for preterm infants in this study. The highlights of this study will fill the gap of previous research, especially based on the Chinese population.

Of course, this study also has many potential limitations. On the one hand, the time point of neurodevelopmental outcome follow-up was only 2 years of age. We will continue to observe the social behaviour and performance of these preterm infants at school age and even in adolescence in the future. On the other hand, we also sincerely feel that premature infants need to come to the outpatient department for GMA several times from birth to 3–5 months, which is a challenge for fragile preterm infants and a great burden for families. Therefore, we are constantly optimising and developing new models of GM recordings at home, and GMAs were implemented through the internet, which should also be the future development trend of GMA for high-risk infants in China.

In conclusion, we hope to provide a basis for hierarchical management and precise intervention for preterm infants based on the results of this study. On the one hand, premature infants at high risk of atypical neurodevelopment can be detected at an ultra-early stage, and early precise intervention will be provided as soon as possible to reduce or avoid the risk of severe neurodevelopmental disorders. On the other hand, premature infants with normal neurobehavioural performance can be identified early to avoid overdiagnosis and intervention and to relieve the anxiety of parents of preterm infants. We also anticipate that such a management model for premature infants can be further promoted and applied in China, which will certainly provide more convenient and economical services for preterm infants.

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