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Can the Prechtl method for the qualitative assessment of general movements be used to predict neurodevelopmental outcome, at eighteen months to three years, of infants born preterm?
--Manuscript Draft--

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Abstract:	<p>Background: Preterm infants are more at risk of abnormal neurodevelopment and diagnosis of impairment often occurs later in life. The Prechtl method for the qualitative assessment of general movements has been found to predict neurodevelopmental outcome in full term infants. Despite this, it is not clear whether the Prechtl assessment is predictive of neurodevelopmental outcome when used for preterm infants.</p> <p>Objectives: To review the literature regarding the use of the Prechtl method for the qualitative assessment of general movements in predicting neurodevelopmental outcome, at eighteen months to three years, of infants born preterm.</p> <p>Methods: A systematic search of MEDLINE, CINAHL, Science Citation Index, PsycINFO, Science Direct, Scopus, Social Sciences Index, Education Source, ERIC, SPORTDiscus, SciELO and SocINDEX was conducted in November 2015. The methodological quality of the included studies was critically appraised using a modified version of the Downs and Black quality index.</p> <p>Results: Five articles met the inclusion criteria. The Prechtl method of assessment was found to be predictive of both neuromotor and cognitive impairments at eighteen months to three years. The writhing period was found to have higher sensitivity but lower specificity and correlation to neurodevelopmental outcomes compared to the fidgety period. Combining both periods of assessment led to higher predictive power. The assessment was also found to be more predictive of severe impairment as opposed to minor impairment.</p> <p>Conclusions: The results of this systematic review suggest that Prechtl method of assessment can be used to predict neurodevelopmental outcome in preterm infants.</p>

Title

Can the Prechtl method for the qualitative assessment of general movements be used to predict neurodevelopmental outcome, at eighteen months to three years, of infants born preterm?

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Introduction

In the UK one in thirteen babies are born preterm, defined as before thirty-seven weeks gestation.^{1,2} Babies born preterm are at risk of abnormal neurodevelopment as the incomplete development of the central nervous system at birth means they are more vulnerable to injury.³

A recent audit conducted by the Royal College of Paediatrics and Child Health (RCPCH)⁴ found that when assessed at two years of age, 20% of infants born preterm had a mild to moderate neurodevelopmental impairment and 20% had a severe impairment. Additionally, 23% had some degree of neurodevelopmental impairment however, at the time of assessment severity could not be determined.⁴ These figures are much higher in comparison to the estimated prevalence of 3-4% for neurodevelopmental disorders in all children in England.⁵

The Prechtl method for the qualitative assessment of general movements is considered to be a useful indicator for later diagnosis of neurodevelopmental disorders, such as cerebral palsy. It is a well held belief that these disorders are generally diagnosable within the first two years of life, with the average age of diagnosis at eighteen months.⁶ In the UK it is a standard of care that all infants admitted to neonatal units and born before thirty weeks gestational age are monitored and assessed up to two years of age.⁴

The Prechtl assessment is conducted during two periods, the writhing period and the fidgety period. General movements assessed at term equivalent age are known as writhing movements and can be classified as normal, cramped-synchronized, chaotic or poor repertoire (See Table 1).⁷ They are characterized by being of small to moderate amplitude and of slow to moderate speed.⁸ Between the ages of six and nine weeks corrected age, general movements gradually transition from writhing movements to fidgety movements.⁸ The fidgety movements are most distinct at three months corrected age and can be classified as absent, abnormal or normal.⁷ They can be identified as continuous movements involving the head, neck and limbs that are of small

amplitude, moderate speed and variable acceleration.⁹ Fidgety movements are present for the first six months of an infant's life at which point they begin to disappear and voluntary and anti-gravity movements become dominant.⁸

Recent systematic reviews have researched the predictive validity of the Prechtl assessment however they did not classify results in order to specifically come to a conclusion on the use of the assessment for preterm infants only.^{9,10} Therefore, the aim of this literature review is to identify whether the Prechtl method for the qualitative assessment of general movements can be used to predict neurodevelopmental outcome, between eighteen months and three years, in infants born preterm.

Methods

Search strategy

A systematic search of the electronic databases MEDLINE, CINAHL, Science Citation Index, PsycINFO, Science Direct, Scopus, Social Sciences Index, Education Source, ERIC, SPORTDiscus, SciELO and SocINDEX was conducted in November 2015. A full list of key terms and their search terms can be found in Table 2. Searches were conducted using Boolean logic. The search was limited to peer reviewed journals and restricted to articles published in the English language. A detailed breakdown of the search strategy used can be seen in Figure 1.

Inclusion and exclusion criteria

Studies assessing neurodevelopmental outcome between eighteen months and three years were included in this review. Studies were considered for inclusion if they used the Prechtl method for qualitative assessment of general movements to assess both writhing and fidgety movements and included participants born before thirty-seven weeks gestational age.

Studies were excluded if they did not differentiate their results between term and preterm participants, if they did not look at the relationship between the Prechtl assessment and neurodevelopmental outcome between eighteen months and three years, or if they did not include assessment of both the writhing and fidgety periods.

Quality assessment

The methodological quality of the included studies was appraised using a modified version of the Downs and Black quality index¹¹ (see Table 3). A modification to the final question was made where scoring mirrored that of the rest of the questions where 1 was awarded if power was adequate and 0 if not to avoid the excessive weighting to this question. The tool was selected as it has been found to be a robust tool to for appraisal of quantitative literature and is suitable to assess the quality of non-randomized studies.^{11,12} Elements of each study were scored using the appraisal criteria and then an overall score out of twenty-three was given.

Results

A total of five studies were eligible for this review. Data extracted is summarized in Table 4.

Of these five studies, three assessed neurological outcomes at two years.¹³⁻¹⁵ The remaining two studies assessed neurological outcome at various points between eighteen months and three years.^{16,17} The studies used various methods of assessment to assess neurological outcome. Three studies used versions of the Bayley scales of infant and toddler development^{14,15,17} where as two used the Amiel-Tison neurological assessment.^{13,16}

All studies assessed neurological outcome in terms of neuromotor development. One study assessed neurological outcome only in terms of whether a diagnosis of cerebral palsy was given.¹⁶ Two of the five studies also assessed cognitive developmental outcome.^{15,17}

Four studies found that the Prechtl method of assessment had 62-100% sensitivity (true positive rate) during the writhing period and 50-100% sensitivity for the fidgety period.¹⁴⁻¹⁷ These studies also found that the assessment had 23-86% specificity (true negative rate) during the writhing period and 46-97% specificity during the fidgety period.¹⁴⁻¹⁷ Additionally, both Brogna et al.¹⁴ and Sustersic and Paro-Panjan¹³ found a positive correlation between general movements in both the writhing period ($r=0.51-0.68$) and the fidgety period ($r=0.62-0.78$), however assessment during the fidgety period showed a stronger correlation to neuromotor outcome.

There was 80-100% sensitivity and 25-41% specificity during the writhing period for prediction of cognitive development.^{15,17} During the fidgety period there was 70-83% sensitivity and 55-85% specificity.^{15,17}

Quality index

All studies were scored out of a possible twenty-three points. Scores ranged between twelve and fifteen. All studies demonstrated similar threats to bias and scored zero for justification of sample size, external validity and blinding of participants.

Overall, despite methodological limitation there is moderate evidence to suggest that the Prechtl method for the qualitative assessment of general movements can be used to predict neurodevelopmental outcomes in the motor domain, at eighteen months to three years, in infants born preterm.¹⁸ There was also moderate to limited evidence to suggest that the Prechtl method of assessment can be used to predict neurodevelopmental outcomes in the cognitive domain in preterm infants.¹⁸

Discussion

Methodological analysis

All studies only partially described principle confounders. The studies all reported birth weight of participants however other confounders such as gestational age, gender, APGAR score and incidence of additional conditions, such as infection or intraventricular hemorrhage, were only reported in some of the studies. As each study described a different selection of confounders, it is difficult to determine how these impacted on results.

Only Constantinou et al.¹⁶ made adjustment for principle confounders to the analyses from which main findings were drawn. All other studies did not make any adjustment and therefore it is not clear whether the influence of these factors was considered when investigating neurological outcome.^{13-15,17}

All studies failed to blind participants however it could be argued that this would not cause any bias as the population being studied were young infants and were unlikely to understand the purpose of the assessments conducted.

Assessors were blinded to prior assessments and information when assessing general movements in all studies during both the writhing and fidgety period, reducing the risk of investigator or recall bias. However, three studies did not blind assessors at the final neurodevelopmental

assessment, thus previous results may have had an influence on the conclusion of this assessment.^{13,14,16}

All studies did not illustrate how representative participants were of the general population of preterm infants or whether the care they received between assessments was representative of standard care protocols. This could limit the generalizability of the results of these studies to the wider population of preterm infants.

The number of participants in the five studies ranged from five hundred and seventy-four to twenty-six. There was a lack of justification of sample sizes in all studies analysed meaning the power of the studies to detect a clinically important effect cannot be determined.

Themes

The evidence suggests that neurodevelopmental outcome can be predicted using the Prechtl method of assessment. However, the predictive validity of the Prechtl assessment varies depending on the period assessed, the combination of both assessment periods and whether the neurodevelopmental outcome is severe or minor.

In general, there were conflicting results as to whether the writhing period or the fidgety period was more predictive of neurodevelopmental outcome. There was found to be a stronger correlation and higher specificity for assessment during the fidgety period compared to assessment in the writhing period.¹³⁻¹⁷ In contrast, sensitivity was found to either be lower or equivocal.¹⁴⁻¹⁷ Similar differences were also identified in systematic reviews studying the predictive validity of Prechtl assessment when used for both preterm and term infants.^{9,10}

The greater extent of correlation and differences in specificity between the two periods could be explained by the normalising of general movements. Four of the studies had participants that were found to have abnormal general movements in the writhing period however when assessed in the fidgety period were considered normal.¹⁴⁻¹⁷ One explanation of why normalising may occur is that general movements in each period are thought to have different neural mechanisms. Prechtl¹⁹ stated that it can be assumed that general movements are generated by different central pattern generators as there is an overlap between the emergence of fidgety movement patterns and the loss of the writhing movement patterns. Furthermore, early abnormalities can be transient and therefore may not affect movement during the fidgety period.¹⁹ Prechtl¹⁹

hypothesized that although general movements are produced by central pattern generators, the quality of the movement is likely to be modulated by more cranial structures. Therefore, any disruption in these structures could produce either transient or consistent abnormalities in the quality of general movements.¹⁹ Due to the transient nature of some abnormalities and the assumed difference in neural mechanisms, it is important to take into account both periods of assessment when using the Prechtl method due to the potential of normalising movements between the two periods.

The differences in sensitivity could be explained by the impact of intervention programmes on general movements. In one study, all participants were also taking part in a preventative care at home programme.¹⁵ All other studies did not report whether participants were undergoing additional care or treatment.^{13,14,16,17} Additional treatment may have impacted on infants' neurodevelopmental outcome as neuroplasticity is most enhanced during the first few years of childhood.²⁰ This can be explained by the initial overproduction of neurons and synapses in early childhood.²¹ Moreover, the Hebbian learning rule highlights that the strengthening and preservation of connections in the brain is also dependent on activity.²² Both of these factors have led to the belief that early stimulation can have an impact on synaptogenesis, neuronal connectivity and myelination and can therefore determine the connections that are made and maintained into later childhood and adulthood.²⁰ Based on this, if additional treatment is given following abnormal results in the writhing period, it is possible the infant may have learnt movement considered to be more normal, potentially masking signs that would otherwise be noticeable and used to predict neurodevelopmental outcome. This is not only important as it may have affected the outcomes of the infants in the studies analysed but it also suggests that early intervention may have a role in enhancing neurodevelopmental outcome in infants.

Some of the studies also demonstrated that the trajectories of abnormal movements are also important when using the Prechtl assessment as a predictive tool. Two studies found that those that were diagnosed with a severe neurodevelopmental impairment had all consistently scored abnormal when assessed in both the writhing and fidgety period.^{13,14} Additionally, it was found that the majority of those who had a moderate to severe neurodevelopmental impairment had consistently abnormal general movements.¹³ However, despite assessing in both periods three

studies did not provide information on general movement trajectories in relation to neurodevelopmental outcome.¹⁵⁻¹⁷

The importance of trajectories can be explained by the combination of a number of developmental factors already discussed. Firstly, as explained above, general movements have the potential to normalise between the writhing period and the fidgety period due to either transient brain abnormalities or the difference in neural mechanisms.¹⁹ If the infant scored consistently abnormal, then based on this theory, it is more likely that any brain abnormality is global or permanent and is therefore likely to present as a neurodevelopmental impairment in a later assessment. Secondly, if early intervention has the potential to affect general movements and decrease signs of impairment, it may also affect long term neurodevelopmental outcome. Additional research would however need to be conducted to determine if this does have an impact on long term neurodevelopmental outcome. By examining the trajectories of an infant's general movements, there is the potential to further determine the likelihood of an infant having a neurodevelopmental impairment. However, due to the limited amount of evidence in this review, this hypothesis should be exercised with caution.

The results of the studies reviewed suggest that the Prechtl method of assessment is more predictive of severe neurodevelopmental impairments, such as cerebral palsy, compared to minor neurodevelopmental impairments. Two studies found that sensitivity in the fidgety period was higher for the prediction of cerebral palsy compared to other neuromotor impairments.^{15,17} Additionally, Kodric et al.¹⁷ also found that sensitivity was higher in the writhing period for the prediction of cerebral palsy. Moreover, one study found greater correlation between abnormal general movement patterns and severe neurodevelopmental outcome, therefore suggesting that the Prechtl assessment is more indicative of severe impairment.¹³ Brogna et al.¹⁴ found the Prechtl assessment to have very high predictive validity for the prediction of cerebral palsy. On the other hand, Constantinou et al.¹⁶ found lower levels of sensitivity compared to the other studies despite only assessing the presence of cerebral palsy as an outcome. They did however assess neurological outcome at eighteen months, an age when the process of diagnosis may still be ongoing, resulting in the levels of sensitivity being lower.^{6,16}

The age of assessment for neurological impairment may also be a factor contributing to the Prechtl method of assessment being found to be less predictive of mild impairments. The

prevalence for minor neurological impairments in children has been found to rise with increasing age.^{23,24} This is thought to be a result of maturation of the central nervous system, as dysfunction can only be assessed once all structures of the brain involved are functionally active.²⁴ This suggests that if the neurological assessment is conducted at an early age, minor neurological impairments may not be detectable as they are not fully expressed at that stage. As a consequence, the prevalence of minor impairments may be underestimated when using the Prechtl method of assessment.

Based upon this, the Prechtl method of assessment should be used with caution if being used as a predictive tool for minor neurological impairments due to its decreased sensitivity for this level of impairment.

Overall, the evidence reviewed suggests that the predictive power of the Prechtl method of assessment is dependent on many factors. The period of assessment can lead to differences in predictive validity. The writhing period has higher sensitivity but lower specificity and correlation to neurodevelopmental outcome compared to the fidgety period.¹³⁻¹⁷ In addition, there is limited evidence to suggest that using the trajectories between assessment periods increases the predictive power of the Prechtl method of assessment.^{13,14} Furthermore, this review has found evidence to suggest that the Prechtl method of assessment is more predictive of severe neurodevelopmental outcomes as opposed to minor impairments.^{13-15,17}

Limitations

There are a number of limitations of this review. Firstly, no grey literature or studies published in languages other than English were included, leading to the possibility of publication bias. Only a small number of studies were reviewed therefore the generalisability of the findings may be limited. Furthermore, eligible papers in this review shared a number of the same authors, leading to another potential risk of bias.

Conclusion

In conclusion, evidence suggests that the Prechtl method for the qualitative assessment of general movements, during the writhing and fidgety period, can be used to predict the

neurodevelopmental outcome in the motor domain, at eighteen months to three years, in infants born preterm. The Prechtl assessment was found to be more predictive of severe neurological impairments compared to minor neurological impairments. There was limited evidence to suggest that the Prechtl method of assessment can be used to predict neurodevelopmental outcome in the cognitive domain therefore further research needs to be conducted in order to confirm this. Further research also needs to be conducted to investigate the impact on neurodevelopmental outcome when an early intervention programme, for preterm infants showing abnormal general movements, is implemented.

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Figure 1. PRISMA flow-diagram of the search

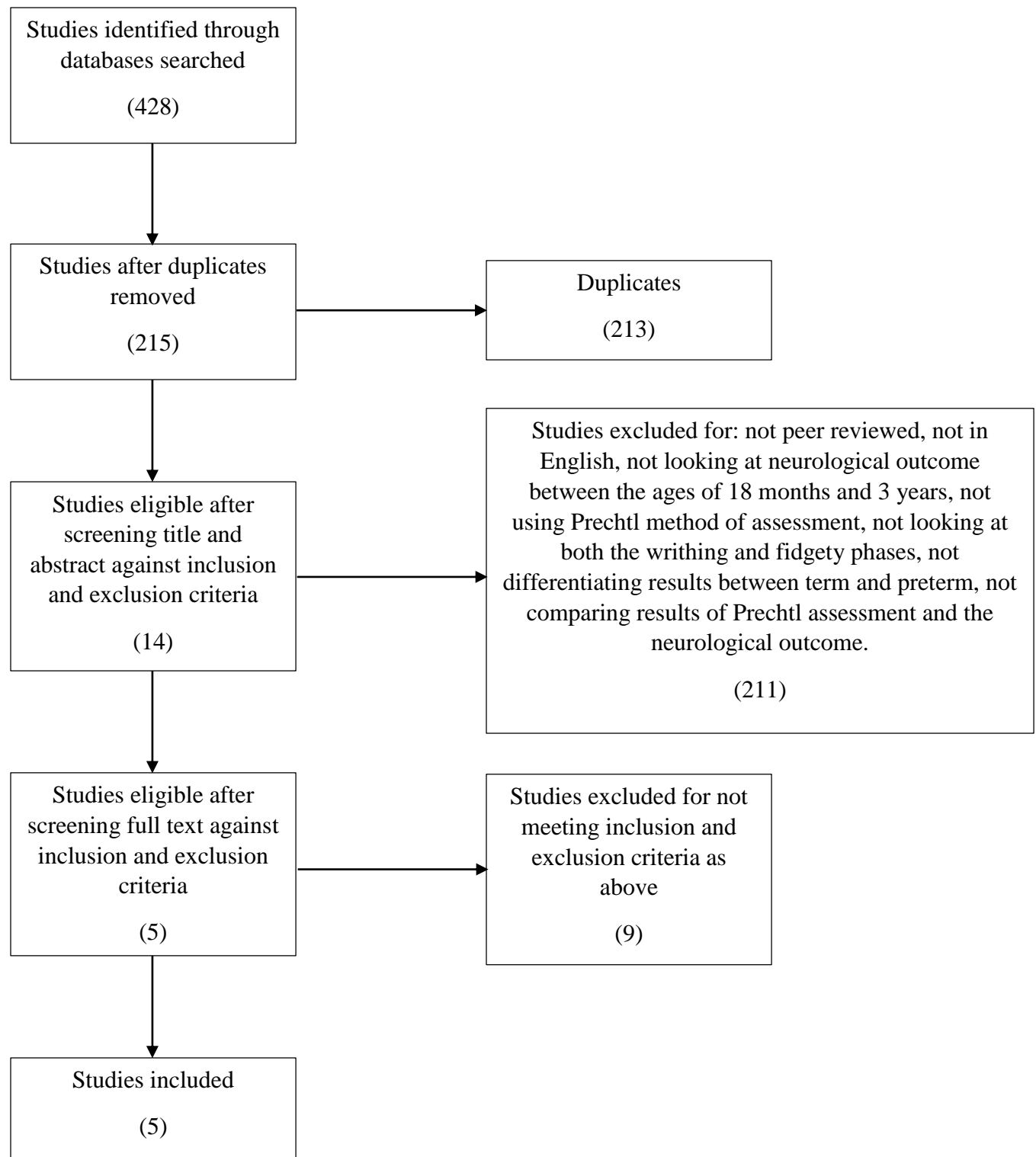


Table 1. Classification of general movements (amended from Einspieler et al.⁷).

Period	Classification	Description
Writhing	Normal	Ellipsoid in form, small amplitude and slow speed. Present even in sleep.
	Cramped-synchronized	Movements are rigid and lack fluidity. Limb and trunk muscles relax and contract almost simultaneously.
	Chaotic	Large in amplitude movement of all limbs that occur in a chaotic order. They lack fluidity and smoothness.
	Poor repertoire	Monotonous sequence of movement that is less complex than movement seen normally in the writhing period.
Fidgety	Normal	Small movements, moderate speed with variable acceleration of the neck, trunk and limbs in all directions. Continual in the awake infant unless crying. Absent when asleep.
	Abnormal	Appear similar to normal fidgety movements however their amplitude, speed and jerkiness are moderately or greatly exaggerated.

Table 2. Search terms

Key term	Search terms
Prechtl	Prechtl OR general movement OR fidget* OR writhing
Neurodevelopment	neurodevelopment* OR neurolog* OR development*
Preterm	Preterm OR premature
Predictive validity	predict* OR sensitivity OR specificity OR correlation*

Table 3. Quality appraisal using modified version of Downs and Black appraisal tool¹¹ (1=Yes 0=No; question 5, 2=Yes 1=partially 0=No)

Question	Spittle et al. ¹⁵	Brojna et al. ¹⁴	Kodric et al. ¹⁷	Sustersic and Paro-Panjan ¹³	Constantinou et al. ¹⁶
1	1	1	1	1	1
2	1	1	1	1	1
3	1	1	1	1	1
4	1	1	1	1	1
5	1	1	1	1	1
6	1	1	1	1	1
7	1	0	1	0	0
8	1	1	1	1	0
9	1	1	0	0	0
10	0	0	0	0	0
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	1	1	1	1	1
15	1	1	1	1	1
16	1	1	0	1	1
17	1	1	1	1	0
18	0	0	0	0	0
19	1	1	1	1	1
20	0	0	0	0	1
21	1	1	1	1	1
22	0	0	0	0	0
Total score (/23)	15	14	13	13	12

Table 4. Data extraction

Study	Sample	Method	Outcome measured	Results	Comments
Spittle et al. ¹⁵	99 infants born <33 weeks preterm.	20-30 minute video recordings of GMs obtained at 1 and 3 months corrected.	Outcome measured at 2 years and 4 years. At 2 years: Motor and cognitive outcomes assessed using the Bayley-III (local reference group used). At 2 years a diagnosis of CP was made by the child's paediatrician, confirmed by an assessing physiotherapist.	<u>Motor:</u> 1 month - 100% sensitivity for moderate to severe impairment or CP and 43% specificity (42% CP). 3 months – 70/100% sensitivity for moderate to severe impairment/CP, specificity 85/84% for moderate to severe impairment /CP. <u>Cognitive:</u> 1 month 80% sensitivity, 41 % specificity. 3 months- 70% sensitivity, 85% specificity.	Participants were also taking part in a randomized controlled trial of a preventative care programme . Assessors for all assessment were blinded.
Brognia et al. ¹⁴	574 born at 34-36 weeks.	Video recording at 1 month and 3 months.	Neuromotor outcome and presence of CP was assessed at 2 years. Used a structured examination in conformity with an extension of Touwen's criteria and the Bayley scale.	Neuromotor outcome: Correlation between GMs and outcome for the writhing period (rs 0.68; p=<0.001) and the fidgety period (rs0.78; p=<0.001). Development of CP: Writhing period- 100% sensitivity, 86% specificity. Fidgety period- 100% sensitivity, 97% specificity.	Assessors of GMs blinded to the infant's medical history. Assessors not blinded at 3 year assessment. Consistently abnormal GMs were more predictive of severe impairment .
Kodric et al. ¹⁷	26 infants born at	15 minute video recordings	Developmental assessment at 2-3 years-	Mental domain	Assessors for all

	23-36 weeks.	from term to 20 weeks post-term at 2-4 week intervals. Quality of GMs assessed at term and 3 months corrected.	standardized Slovenian version of the Bayley scales of infant development (2 nd edition). Mental development index (MDI) and psychomotor developmental index (PDI) used in the analysis.	Writhing period-sensitivity 100%, specificity 25%. Fidgety period-sensitivity 83%, specificity 55%. Motor domain Writhing period-sensitivity 85%, specificity 23%. CP excluded- 80% sensitivity, 23% specificity. Fidgety period-sensitivity 54%, specificity 46%. CP excluded- 40% sensitivity, 46% specificity.	assessment s blinded. Children with higher gestational age and birth weight scored higher on mental and motor scales. Pilot study.
Sustersic and Paro-Panjan ¹³	45 infants born at 23-36 weeks.	Assessed from term to 20 weeks post term age.	Neurological assessment from term to 2 years as described by Amiel-Tison and Gosselin.	Correlation between GMs at term age and neurological outcome. (Pearson's R= 0.51) Correlation between fidgety GMs and neurological outcome (Pearson's R= 0.62 / 0.50 for children with CP / minimal CP).	GMs assessed by a blind assessor. Decreased correlation of GMs and minor neurological signs.
Constantinou et al. ¹⁶	130 infants born at <32 weeks and birth weight <1500g.	15 minute videos of GMs at 36 and 52 weeks post conceptual age.	At 18 months corrected age assessed using the Amiel-Tison neurological assessment. Bayley scales of infant development was also administered.	GMs 36 weeks- 62% sensitivity, 69% specificity. GMs 52 weeks- 50% sensitivity, 86% specificity.	Assessors of GMs blinded. Assessed for CP only.
