Additional file 4: Tables for excluded and included studies

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| Table 4  *Key findings and characteristics of excluded studies for the GMA and the predictive ability for CP in late-preterm and term infants with NE* | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size (number of infants)** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for neurological examination** |
| Adde et al.32 | 2006 | Norway | Prospective cohort | 74 high and low-risk | Gender: 33 males (44.6%), 41 females (55.4%)  GA:   * 42 (57%) preterm * 32 term (43%)   Preterm: 24-36 wks, (median 30.5 wks)  Term: >36 - <42 wks  Late preterm: n.s.  BW: 540-3800 g (median 1367 g)  High-risk: preterm 40%, term 25%.  NE: 5 (all term GA)  CP diagnosis: 3  Therapeutic hypothermia: 0 | n.s. | Presence of major US abnormalities  or MRI findings or the clinical history | Prechtl | 10-18 wks post-term | 9-31 months (median age 23 months) | Method not stated but information retrieved from medical specialist notes of their evaluation &  parental report |
| Brogna et al.33 | 2013 | Italy | Cohort | 574 consecutive admissions | Gender: n.s.  GA: 34–36 completed wks  BW: 2299 ± 451  NE: n.s.  CP: 22 (4%)  Therapeutic hypothermia: 0 | Jan 2006- Dec 2010 | Admission to the Level II or III unit of the institution | Prechtl | 1-3 months post-term age | 24 months post-term age | Structured examination  in conformity with an extension of Touwen's criteria34, and Bayley scale35 |
| Cioni et al.36 | 1997 | Italy | Case series | 58 term | Gender: 34 males (58.6%), 24 females (41.4%)  GA: 37-41 wks (mean 39 (SD 1)) BW: 1870 - 4350g (mean 3166 (SD 540)  NE: 38 (16 severe and 22 mild)  CP: 14  Therapeutic hypothermia: 0 | 1985 | Serial US scans | Prechtl | Every 3–4 wks from “first days of life” up to 65 wks | 13–31 months (median age 23 months) | Amiel-Tison and Grenier37 examination, Touwen’s criteria34, Griffiths Scales38 |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GM A** | **Age at GMA** | **Age of CP diagnosis** | **Method used for neurological examinations** |
| Dimitrijević et al.39 | 2016 | Serbia | Prospective cohort | 79 | Gender: 41 males (51.9%),  38 females (48.1%)  GA: 25-36 weeks  Late-preterm: ?33 or 36 (different number quoted in table versus text)  BW: definitive numbers for range n.s. but divided into categories ELBW (4), VLBW (16), LBW (58), NBW (1).  NE: 18 (late-preterm % n.s.)  CP: in late-preterm 1  Therapeutic hypothermia: 0 | Jul 2011- Dec 2013 | History and physical examinations | Prechtl | 1-3 months corrected age | 24 months corrected age | Touwen's criteria34  and Surveillance of Cerebral  Palsy in Europe working group40 |
| Einspieler et al.41 | 2015 | China | Longitudinal study. Retrospective analysis of prospectively collected data | 61 | Gender: 46 males (75.4%), 15 females (24.6%)  GA:   * preterm: 29 (47.5%) * term: 32 (52.5%)   Late-preterm n.s.  BW: range n.s.  NE: 9 (GA n.s.)  CP: 10  Therapeutic hypothermia: 0 | Sep 2003 - Jun 2010 | Preterm birth or perinatal asphyxia at term, abnormal findings at pediatric examination or parental concerns | Prechtl | 9-16 weeks post term age | 2-3 years | n.s. but Classified by means of the GMFCS42 at 3-5 years |
| Einspieler et al.43 | 2019 | 24 sites worldwide (Europe, North America, South America, South Africa, Asia and Australia) | Retrospective | 468 | Gender: 58% male, 42% female  GA: (23- 42 weeks)   * preterm 56% * term 46%   Late preterm: n.s.  BW: 440-4500g  NE: yes, n.s. by GA  CP: yes, n.s. by GA  Therapeutic hypothermia: n.s. | 2012-2019 | Not detailed | Prechtl, including the MOS | 9-22 weeks post-term age | 2 years and 10 months - 5 years and 7 months | n.s. |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for neurological examinations** |
| Feng et al.44 | 2017 | China | Prospective case series | 110 high-risk | Gender: 71 males (64.5%), 39 females (35.5%)  GA:   * 28-37 wks: 65 * 37-40 wks: 35 * > 40 wks: 10   BW: n.s.  NE: 33  CP: 4  Therapeutic hypothermia: 0 | Jan 2012 - Jun 2013 | Unclear – possibly from clinical diagnosis | Prechtl | 1 month after delivery, done twice with a 1 wk interval | 1-year corrected age | Gesell developmental scale assessment45 |
| Guzetta et al.46 | 2007 | Italy | Prospective case series | 115 | Gender: 56 males (49%), 59 females (51%)  GA: 103 preterm and 12 term infants  Preterm: (wks), mean (SD)   * GA: 32.3 (2.8) range: 23–35 * late-preterm: n.s. * BW (g): mean 1776.3 (SD: 563.9), range: 500–3100 * CP: 4   Term: (wks): mean (SD)   * GA 39.6 (1.5), range: 37–41 * BW (g): mean 3471.1 (SD: 401.1) range: 2550–4100   - CP: 3  NE: n.s.  Therapeutic hypothermia: 0 | Jan 2002 - Apr 2003 | History of NE | Prechtl | 0-20 weeks GA (used one closest to term age for the writhing period and to 12 weeks post-term age for the fidgety | At least at 18 months | Expanded version of the Amiel-Tison and Grenier37 and  Touwen34 |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for neurological examinations** |
| Hadders-Algra et al. 47 | 1997 | Not stated | Caseseries | 16 | Gender: distribution n.s.  GA:   * 26-36 wks: 10 with 1 late-preterm * 38-43 wks: 6   BW:   * preterm: 850- 2750g * term: 2500- 3525g   NE: 7 (6 term and 1 late-preterm)  CP: 7  Therapeutic hypothermia: 0 | Not stated | History of HIE and an abnormal GM | Prechtl | 1 wk - 4 months post-term | 18-31  months corrected age (median 19 months) | Hempel**48** |
| Morgan et al.49 | 2016 | Australia | Prospective longitudinal and  cross-sectional study | 187 | Gender: distribution n.s. to maintain anonymity in a small hospital site  GA:   * term: 134 * late-preterm: n.s.   BW: n.s.  Late-preterm: n.s.  NE: 19  CP: 40  Therapeutic hypothermia: 0 | 2011 - 2013 | Medical history  and/or neuroimaging | Prechtl | 10 - 20 weeks post term age | 12–24 months post term age - mean age 8.5 months (SD  = 4 months) | Neurological examination, clinical history and developmental  motor assessment |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for**  **neurological examinations** |
| Morgan et al.50 | 2019 | Italy | Retrospective case controlled | 441 | Gender: Female (%)   * Normal: 52 * Mild disability: 1 * CP: 48   GA: < 32 weeks  Normal: 44  Mild disability: 42  CP: 44  32-36 weeks  Normal: 63  Mild disability: 65  CP: 63  >37 weeks:  Normal: 40  Mild disability: 40  CP: 40  Late preterm: n.s.  BW: n.s.  NE: HIE and perinatal asphyxia included but n.s. by GA  CP: yes, but n.s. by GA  Therapeutic hypothermia: n.s. | 2003-2014 | Exam and neuroimaging | Combined 3 month GMA by Prechtl, HINE | Described as writhing and fidgety period up to 12 weeks post term | By 2 years of age | HINE51, Clinical Developmental Assessment |
| Øberg et al.52 | 2015 | Norway | Prospective cohort | 87 participants and 86 non-participants | Gender: 41 males (47%), 46 females (53%)  GA:   * preterm: 28.1-36.9 wks 46% (40) * ≥ 37 wks: 16% (14) * late preterm n.s. separately   BW: 1,528 g, (SD 1,045)  NE: 25  CP: 10 (12%)  Therapeutic hypothermia: 0 | Nov 3,  2002 - Oct 11, 2010 | Medical history | Prechtl | 3  months of age | 24 months | History and examination, definition by Rosenbaum et al.**53** |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for**  **neurological examinations** |
| Seme-Ciglenecki54 | 2003 | Slovenia | Prospective cohort | 132 high-risk preterms divided into 2 arms for assessment (high-risk and control) | Gender: 111 males (47.8%), 121 females (52.1%)  Boys/girls:   * high-risk: 56/64 * control: 55/57   112 age-matched low-risk controls  GA: <37wks median(range)  -high-risk: 33 (26-37)  -control:34 (24-37)  -late-preterm: n.s. separately  BW (g) median (range):  -high-risk: 1.975 (660-3.820)  -control: 1.930 (600-3.680)  NE: n.s. separately  CP:   * high-risk: 31 * control: 33   Therapeutic hypothermia: 0 | Oct 1, 1994 - Dec 31, 2000 | Random number table for selection amongst high-risk admissions | Prechtl | 3 months corrected age | 24 months corrected age | Amiel-Tison and Grenier**37** and Illingworth examinations**55** |
| Soleimani et al.56 | 2015 | Iran | Case series | 15 late-preterm ≥ 35 wks and term | Gender: 8 males (53.3%), 7 females (46.7%)  GA: mean 37.3 ± SD 1.1  BW: mean 2800 ± SD 234  NE: 15 (12 Sarnat II, 3 Sarnat III)**8**  Abnormal neurological outcome (not definitely designated as CP): 10  Therapeutic hypothermia: 0 | 2012-2013 | Medical history | Prechtl | 3-5 months | 12-18 months age | Infant Neurological International Battery test (Infanib)**57** |
| Stoen et al.58 | Oct 2019 | Norway | Observational study | 405 | Gender: 54.3% male, 45.7% female  GA:  Late preterm: n.s.  BW: n.s.  NE: 57 (13.8%), n.s. by GA  CP: 42 (10.4%), but n.s. by GA  Therapeutic hypothermia: n.s | 2009-2014 | Undefined | Prechtl | 10 – 15 weeks post-term age | By mean age 3 years and 1 month | Surveillance of cerebral palsy in Europe (SCPE)40 |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for neurological examinations** |
| Sustersic et al.59 | 2008 | Slovenia | Prospective cohort | 45 | Gender: 23 males (51.1%), 22 females (48.9%)  GA:  - 23-36 wks (mean,  31.6 weeks; SD, 3.3 wks)  - late-preterm: n.s.  BW: 525-3240 g (mean,  1788 g; SD, 718 g)  NE: 12 (27%)  CP: 6  Therapeutic hypothermia: 0 | Jan 2002 – Mar 2004 | Consecutive referrals and medical history | Prechtl | Term - 20 weeks of post-term  age | 24 months | Amiel-Tison and Gosselin37 |
| van Iersel et al.60 | 2010 | The Netherlands | Prospective cohort | 51  (17 preterm high-risk and 34 low-risk) | Gender: matched for gender but gender distribution n.s.  34 matched preterm controls  GA:   * <35 wks PMA * late-preterm 34 to 35 wks: n.s.   Median (range, wks):   * study group 32 (28–34) * control group 32 (28–34)   BW, g (± SD):   * study group 1817 (±611) * control group 1886 (±385)   NE: 17  CP:   * study group 2 (11%) * control group 2 (11%)   Therapeutic hypothermia: 0 | Jun 1999 - Jun 2007 | Medical history | Hadders-Algra | “preterm” (around 34 weeks  PMA), “writhing” (around term age) and “fidgety” GM age (around 3 months post term). | 18 months corrected age | Touwen**34** |
| Table 4 continued | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of study** | **Population size** | **Population**  **(general characteristics)** | **Period of study** | **High risk identification** | **GMA** | **Age at GMA** | **Age of CP diagnosis** | **Method used for examinations** |
| Yang et al.61 | 2012 | China | Longitudinal study | 79 | Gender: 60 males (75.9%), 19 females (24.1%)  Total: term: 47 (59.5%)  Male: female ratios:   * preterm 23:9 (72%:28%) * term 37:10 (79%:21%) n.s.   GA, wks (median):   * preterm: 32 (P25–P75=30–34) * term: 39 (P25–P75=38–40)   BW, g (mean):   * preterm: 1548 (SD=549) * term: 3200 (SD=423)   NE:   * preterm: 1 (3%) * term: 11 (23%)   CP: Total 65   * preterm: 29 (45%) * term: 36 (55%)   Therapeutic hypothermia: 0 | Sep 2003 - May 2009 | History and examination | Prechtl | 9 -20 weeks post-term age | 2-5 years | History and examination, definition of Rosenbaum et al.**53** |
| *Note*. BW = birth weight, CP = cerebral palsy, ELBW = extremely low birth weight), g = grams, GA = gestational age, GMA = general movements assessment, LBW = low birth weight, NE = neonatal encephalopathy, n.s = not stated, SD = standard deviation, VLBW (very low birth weight), MOS = motor optimality score, NBW = normal birth weight, wks = weeks | | | | | | | | | | | |

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| Table 5  *Key findings and limitations of excluded studies for the GMA and the predictive ability for CP in late-preterm and term infants with NE* | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** |
| Adde et al.32 | GMs can strongly predict the development of CP in a clinical setting in both high-risk infants and identified infants that did not develop CP | 100%  (95% CI 73-100%) | 98%  (95% CI 91-99%) |  |  |  | Health professionals that followed up the low-risk group may not have been trained to detect subtle neurological changes and so a lower detection rate for CP may have occurred | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes |
| Brogna et al.33 | GMs done in the fidgety period have a high sensitivity and specificity for CP prediction.  Trajectories of GM are also important predictors of outcomes, in that, consistently normal  GM trajectories lead into normal outcomes (95%). Transient GM abnormalities  (Abnormal–Normal trajectory) can either progress to a normal outcome (72%) or to a motor deficit (28%) | For CP: In the writhing period | | | | | Not stated | NE was not clearly identified as a diagnosis in this study although it was stated that patients were from a high-risk population |
| 100% | 86% |  |  | Spearman rank correlation  rs 0.68  (p < 0.001) |
| For CP: In the fidgety period | | | | |
| 100% | 97% |  |  | Spearman rank correlation  rs 0.78  (p < 0.001) |
| For CP: For the trajectories of GM | | | | |
| 100% | 97% |  |  | Spearman rank correlation  rs 0.69  (p < 0.001) |
| Table 5 continued | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** |
| Cioni et al.36 | For all ages assessed GM observation highly correlated with neurological outcome and sensitivity and specificity was slightly higher than neurological observation.  Consistent poor repertoire pattern has more than 50% correlation with CP.  False positives and negatives were higher with neurological examination | Consistent GM abnormalities (PR or CS) as a strong predictor of an unfavorable outcome:  Sensitivity 88.9% | Consistently normal or transiently abnormal GMs generally predict normal  Development:  Specificity 95% |  |  | Range of agreement: 78-83%, between neurological and GM assessment was between | None stated | Term infants not separated by diagnosis so unsure of the outcomes related to NE |
| Dimitrijević et al.39 | GMs that are CS are highly predictive of CP, but not the same for the PR pattern | 100% | 72.1% |  |  |  | External validity is limited by a small population size with PR movements. Neuroimaging data not available for all patients | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes. |
| Einspieler et al.43 | Sporadic FMs indicate adverse neurodevelopmental outcome but not necessarily CP | 15% of infants who later developed CP had sporadic FMs which was linked to a slightly better (although not normal) concurrent movement repertoire |  |  |  |  | There was a small sample of only 9, for those with sporadic FMs.  Only high-risk groups were used and so no comparator for sporadic fidgety movements available from general population | Term and late-preterm infants were included in this study but not delineated as a group for their specific diagnosis of NE nor for their specific outcomes.  Computer based analysis was used for coding of temporal organization of FM |

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| Table 5 continued | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** | **Limitations identified by authors** | **Summarized reasons for exclusion** |
| Einspieler et al.43 | In children with CP:   * 95% did not have fidgety movements * 100% had a non-optimal MOS * GMFCS level was strongly correlated to MOS * An MOS > 14 was most likely associated with GMFCS outcomes I or II, whereas GMFCS outcomes IV or V were hardly ever associated with an MOS > 8.   A number of different movement patterns were associated with more severe functional impairment (GMFCS III–V. | - | - | - | - | - | Variable:  - access to prenatal care  - neonatal intensive care managements  - environmental factors such as socio-economic status, teratogens,  etc.  - varied ethnic backgrounds.  The number of individuals varied compared to the usual occurrence rate:  - dyskinesia overrepresented  -ataxia and hypotonia  underrepresented.  Heterogeneous local settings for assessment of GM videos. | Sensitivity, specificity, PPV and NPV not calculated specifically.  Term GA not differentiated from preterm for outcome. |

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| Table 5 continued | | | | | | | | | | | | | |
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| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | **Specificity** | | **PPV** | | | **NPV** | | **Other correlations** | |
| Feng et al.44 | Both the qualitative assessment of GMs and EEG examination can be used to predict high-risk neonatal adverse neurodevelopmental outcome with the combination having higher sensitivity, specificity, PPV and NPV | Prediction of CP of PR movements | | | | | | | | | | Not stated | Term and late-preterm infants were included in this study but not delineated as a group for their specific diagnosis of NE nor for their specific outcomes |
| 25% | | 68.9% | | 2.9% | 96% | |  | | |
| Prediction of CP of CS movements | | | | | | | | | |
| 50% | | 98.1% | | 50% | 98.1% | |  | | |
| Prediction of CP of absent fidgety movements | | | | | | | | | |
| 75% | | 99% | | 75% | 99% | |  | | |
| Prediction of CP of combined GM and EEG | | | | | | | | | |
| 90.48% | | 95.45% | | 86.36% | 96.92% | |  | | |
| For predicting high-risk neonatal neurodevelopmental outcome | | | | | | | | | |
| 83.87% | | 84.81% | | 68.42% | 93.06% | |  | | |
|  |  |  | | | | | | | | | |  |  |
| Guzetta et al.46 | Confirms the high sensitivity and specificity, both during writhing and during fidgety period, of the Prechtl’s method of assessment of GMs based on video  observation. The results also support the use of GMs by direct assessment when the full application of the standard video observation is not routinely possible | Writhing period GM assessment | | | | | | | | | | The level of expertise of the examiners may have been higher than average, therefore making the findings not  replicable in other contexts | Term and late-preterm infants were included in this study but not delineated as a group for their specific diagnosis of NE. Late-preterms were also not separated from other preterms for their outcomes |
| 100% | | 84% | | 43% | 100% | |  | | |
| Fidgety period GM assessment | | | | | | | | | |
| 100% | | 95% | | 58% | 100% | |  | | |
| Table 5 continued | | | | | | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | **Specificity** | | **PPV** | | | **NPV** | | **Other correlations** | |
| Hadders-Algra et al.47 | GM quality after 47 weeks PMA was  strongly related to neurodevelopmental outcome at l 1/2 years of age, suggesting that the absence of the age-specific ‘fidgety’ character of GMs could be a herald of disability | Neurological outcome of CP and mental retardation | | | | | | | | | | Not stated | Outcomes not delineated into neuromotor outcomes of CP but given as a combined outcome with mental retardation |
| 88% | | 88% | | 88% | 88% | |  | | |
|  | |  | |  |  | |  | | |
| Morgan et al.49 | GMA had excellent sensitivity and specificity to predict infants who would later be diagnosed with CP as well as those with  normal outcomes. One benefit of early detection  using GMA was that diagnosis occurred earlier, on average  at 8.5 months in the study compared to 17 months in their CP registry | 98%  (95% CI 86.79–99.58) | | 94%  (95% CI 88.69–97.16) | |  |  | |  | | | Sampling bias was possible, as all infants in the study were already considered at high-risk of adverse neurodevelopmental outcome. Outcome data were mostly only at 12 months but milder forms of CP may be first diagnosed later in  childhood when the motor impairment was deemed as definitely permanent. There was practice variation between sites in terms of number of blinded GMs scorers although they stated that there was no scoring accuracy differences | Term infants were included in this study but not delineated as a group for their specific diagnosis of NE as it related to their specific outcomes |
| Table 5 continued   |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** | | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** | | | | | | | | | | | | | | |
| Morgan et al.50 | In a routine clinical setting, the GMA strongly predicts  neurodevelopmental impairments at 2 years in high-risk infants.  FM assessment proves to be a valuable tool for detecting subsequent motor problems early in life when performed in a routine hospital  clinical practice. The risk of developing motor problems by the age of 2 years increases linearly with the extent of abnormal FM findings. This risk is also 10 times higher if FMs are absent by 3 months of age than if FMs are normal. | When absent FMs were considered to be a positive test result (and normal, abnormal, or sporadic FMs were considered to be a negative test result) | | | | | | | | | | Relatively small study sample.  Study sample  did not include all infants hospitalized  during the study period, only the high-risk which could introduce sampling bias | Term and late-preterm infants were included in this study but not delineated as a group for their specific diagnosis of NE nor for their specific outcomes |
| 90%  (95% CI 56%, 100%) | | 90%  (95% CI 81%, 95%) | | 53% | 99% | | LR for a positive test result:  8.7 (95% CI 4.4, 17.2)  LR for a negative test result:  0.1 (95% CI 0, 0.7) | | |
| When any finding but normal (normal FMs) was considered to be a positive test result | | | | | | | | | |
| 100%  (95% CI69%, 100%) | | 70%  (95% CI59%, 80%) | | 30% | 100% | | LR for positive test result:  3.3 (95% CI 2.4, 4.7)  LR for a negative test result: 0 (95% CI 0, 1.1) | | |
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| Table 5 continued | | | | | | | | | | | | | |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** | | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** | | | | | | | | | | | | | | |
| Morgan et al. cont’d | Pooled predictive power of early GMA, neuroimaging, plus HINE was higher than the 3 tools in isolation. | Using GMA only | | | | | | | | | Retrospective data: impacts accuracy and generalizability of results.  Selection bias: Recruitment is exclusively from hospitals.  The individuals selected as controls may under-represent the population.  Generalisability affected: Highly skilled assessors used.  Imperfect interrater reliability of tests: lack of 1000% agreement on the scoring of each of the 3 tests. | | GA and NE not differentiated into categories the results |
| 95% | 97% | |  | | |  | |  |
| Combined predictive  power (GMA, HINE and neuroimaging) | | | | | | | |  |
| 97.86% | 99.22% | | 98.56% | | | 98.84% | |  |
|  |  | |  | | |  | |  |
| Table 5 continued | | | | | | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | **Specificity** | | **PPV** | | | **NPV** | | **Other correlations** | |
| Seme-Ciglenecki et al.54 | GM assessments have better validity, sensitivity, specificity, PPV,  and NPV when compared to the classical neurological examination of preterm infants that are high-risk | For GM assessment | | | | | | | | | | In Slovenia GMs are not routinely used limiting the comparison of  results of the study and the results of other investigators, that is limiting control of interscorer agreement | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes |
| 94% | | 92% | | 81% | 98% | | Validity  92% | | |
| For classical neurological assessment | | | | | | | | | |
| 60% | | 97% | | 43% | 44% | | 97% | | |
| Soleimani et al.56 | In children born at term GA  with neonatal HIE, FMs assessment improves the ability to predict later neurodevelopmental outcomes | The predictive values of FMs: Neurodevelopmental outcomes of abnormal FM (mild to moderate and moderate to severe HIE) | | | | | | | | | | Recurrent assessments and long-term follow-ups may have been a limitation for families. Neuroimaging was limited to limited resources | The outcomes were described in the terms “neurodevelopmental outcomes” as the authors considered it not possible to diagnose CP definitively at 12 - 18 months |
| 80  (95% CI, 44 - 96) | 100  (95% CI, 47 -100) | |  | | |  | | Accuracy  87 (95% CI, 57 to 100)  Cramer's V 0.661 | |
| The predictive values of FMs: Neurodevelopmental outcomes of abnormal FM (meaning moderate to severe HIE only) | | | | | | | | | |
| 83.3  (95% CI, 35.9 - 99.6) | 66.7  (95% CI, 29.9 - 92.5) | |  | | |  | | Accuracy 73.3 (95% CI, 42.8 to 94.4)  Cramer's V 0.491 | |
| Stoen et al.58 | Predictive accuracy of GMA increased when sporadic FM not categorized as a marker for later CP.  Absence of FM correctly predicted CP in about 50% of cases.  Neonatal cerebral imaging in combination with GMA increased the predictive accuracy. | Absent/sporadic FM | | | | | | | | | | Longer follow-up might have resulted in more children presenting  with a mild CP phenotype  being diagnosed with CP and, consequently, poorer performance  of GMA. | Assessed CP diagnosis done past 2 years of age. |
| 69.1  (95% CI 52.9–82.4) | 91.5  (95% CI 88.1–94.1) | | 48.3  (95% CI 38.7–58.1) | | | 96.2  (95% CI 94.2–97.6) | | Accuracy % (CI 95%)  89.1  (85.7–92.0) | |
| Abnormal neonatal imaging | | | | | | | | | |
| 81.0  (95% CI 65.9–91.4) | 85.3  95% CI 81.2–88.8) | | 39.1  (95% CI 32.5–46.1) | | | 97.5  (95% CI 95.4–98.6) | | Accuracy %  (CI 95%)  84.9  (81.0–88.2) | |
| Absent/sporadic FM and/or abnormal imaging | | | | | | | | | |
| 88.1  (95% CI 74.4–96.0) | 70.3  (95% CI 65.3–75.0) | | 25.7  (95% CI 22.3–29.6) | | | 98.1  (95% CI 95.7–99.1) | | Accuracy %  (CI 95%)  72.1 (67.5–76.5) | |
| Absent/sporadic FM and abnormal imaging | | | | | | | | | |
| 61.9  (95% CI 45.6–76.4) | 94.2  (95% CI 91.3–96.4) | | 55.3  (95% CI 43.4–66.6) | | | 95.5  (95% CI 93.5–96.9) | | Accuracy %  (CI 95%)  90.8 (87.6–93.5) | |
| Absent FM and/or abnormal imaging | | | | | | | | | |
| 88.1  (95% CI 74.4–96.0) | 77.6  (95% CI 72.9–81.8) | | 31.4  (95% CI 26.8–36.3) | | | 98.3  (95% CI 96.1–99.2) | | Accuracy %  (CI 95%)  78.7 (74.3–82.6) | |
| Absent FM and abnormal imaging | | | | | | | | | |
| 61.9  (95% CI 45.6–76.4) | 99.2  (95% CI 97.6–99.8) | | 89.7  (95% CI 73.3–96.5) | | | 95.7  (95% CI 93.8–97.1) | | Accuracy %  (CI 95%)  95.3 (92.7–97.1) | |
| Sustersic et al.59 | Confirmed the importance of abnormal  general movements at ages 2-4 months in predicting  CP | Correlation between general movements and neurologic outcome at term age | | | | | | | | | | The study group was relatively small and heterogenous in terms of risk factors for brain damage. Compared with previous studies, the group were much younger at  time of evaluation of neurologic state. | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes |
|  | |  | |  |  | | Pearson’s R  0.51 | | |
| Correlation between neurologic outcome and assessment during the fidgety period | | | | | | | | | |
|  | |  | |  |  | | Pearson’s R  0.50  (in the group of children with minimal CP) | | |
| Table 5 continued | | | | | | | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | | | | | | **Limitations identified by the authors** | **Summarized reasons for exclusion** |
| **Sensitivity** | | **Specificity** | | **PPV** | **NPV** | | **Other correlations** | | |
| van Iersel et al.60 | Perinatal asphyxia in preterm infants is not associated with an increased risk for neurodevelopmental  problems including CP. Respiratory problems during the neonatal period are associated with PVL and  adverse neurological outcome |  | |  | |  |  | | Chi square for  Trend, p=0.001  Quality of GMs at “preterm” and “writhing” GM age were not related to the development of CP. The quality of GMs at “fidgety” GM age was related to the development of CP | | | Limited access to neuro-imaging.  Inherent to the limitations of the setting, only information on the ultrasound scans were available. A small sample size was obtained as the institution was not a referral center for neonates with asphyxia | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes |
| Yang et al.61 | Later functional limitations in children with CP can be predicted with the aid of the assessment of the quality of motor performance at 9 - 20 wks post-term age (irrespective of the GA) | The association between the quality of movements at 9 - 20 weeks post-term age and the GMFCS levels | | | | | | | | | | Participants are a sample of convenience:  inclusion criteria were that their motor performance was videoed  around their 4th month post-term age and that they had developed  CP | Late-preterm infants were included in this study but not delineated as a group for their specific outcomes |
|  | |  | |  |  | | Spearman correlation coefficient −0.52 (p<0.001). | | |
| The association between the postural patterns found at 9 to 20 weeks post-term age and the children's later GMFCS levels | | | | | | | | | |
|  | |  | |  |  | | Kendall-Tau-c −0.19  (p<0.05) | | |
| The association between a cramped-synchronized movement character and the later GMFCS levels | | | | | | | | | |
|  | |  | |  |  | | Kendall-Tau-c 0.41  (p<0.001) | | |
| *Note*. CI = confidence interval, CP = cerebral palsy, CS = cramped-synchronized, EEG = electroencephalogram, FM = fidgety movements, GA = gestational age, GM = general movements, GMA = general movements assessment, GMFCS = gross motor function classification system, LR = likelihood ratio, NE = neonatal encephalopathy, NPV = negative predictive value, PR = poor repertoire, PPV = positive predictive value | | | | | | | | | | | | | |

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| Table 6  *General characteristics of identified studies for the GMA and the predictive ability for CP in late-preterm and term infants with NE* | | | | | | | | | | | |
| Article | **Date of publication** | **Country** | **Type of studies included** | **Population size** | **Population (general characteristics)** | **Period of study** | **Method of high-risk identification** | **GM assessment** | **Age at GM assessment** | **Age of CP diagnosis** | **Method used for neurological examinations** |
| Ferrari et al.62 | 2011 | Italy | Case series | 34 term | Gender: 20 males (58.8%), 14 females (41.2%)  GA: mean 40.4 ± 1.2 wks  BW: mean 3536 9 (SD ± 457g)  NE: 34  CP: 16  Therapeutic hypothermia: 0 | 2003 -  2006 | History of HIE | Prechtl | At 1-3 postnatal months | 24 months | Amiel-Tison and Grenier37  and an extension of Touwen’s criteria34 |
| Prechtl et al.63 | 1993 | Italy | Case series | 26 term | Gender: 8 males (30.7%), 18 females (69.2%)  GA: 37 – 41 wks (mean and SD not done)  BW: 2250 – 4150g (mean and SD not done)  NE: mild to moderate: 13  severe: 13  CP: 10  Therapeutic hypothermia: 0 | Jan 1985 -1989 | Medical history | Prechtl | 0-22 wks | 17-24 months of age | Griffiths Scales35 |
| *Note.* BW = birth weight, CP = cerebral palsy, GA = gestational age, GMA general movements assessment, HIE = hypoxic ischemic encephalopathy, NE = neonatal encephalopathy, n.s. = not stated, SD = standard deviation, US = ultrasound, wks = weeks | | | | | | | | | | | |

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| Table 7  *Key findings and limitations of included studies for the GMA and the predictive ability for CP in late-preterm and term infants with NE* | | | | | | | |
| **Article** | **Key findings with respect to GM and CP** | **Predictive value of GM** | | | | | **Limitations identified by the authors** |
| **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Other correlations** |
| Ferrari et al.62 | With HIE in term neonates, the site and severity of brain lesions seen on early MRI are highly correlated  with GMs  Central gray matter damage leads to CS GMs and poor motor outcome.  For the prediction of motor outcomes, both early MRI scans and GMs are complementary | For cramped-synchronized movements | | | | | Fewer grade 1 HIE infants may be present in the sample as not all HIE infants are referred to that tertiary center (not representative of the population).  MRI performed over first 6 postnatal wks (relatively wide period)  Very early MRI scans are not as reliable in predicting motor outcome versus when performed later. Transient abnormalities, such as cerebral edema, can lead to either overestimation or underestimation of the severity of damage |
| 100% | 68.7% | 100% | 78.3% |  |
| Prechtl et al.63 | Changes in spontaneous motility and especially GM developmental trajectories  are good predictors of the neurological outcome  The predictive value of GM assessment is similar to that of EEG and neuro-imaging, and better than neurological  examination | Early observation (first 2 wks) | | | | | None stated |
| 100% | 46.2% | 65% | 100%. | GM quality and outcome correlation:  r = 0.61, (P < 0.001)  Neurological findings and outcome correlation:  r = 0.34, (P > 0.1) |
| Late observation (15-22 wks) | | | | |
| 84.6% | 84.6% | 84.6% | 84.6% | Both observation and neurological assessment are highly correlated with the  outcome and for both:  r = 0.88  (P < 0.001) |
| *Note.* CP = cerebral palsy, CS = cramped synchronized, EEG = electroencephalogram, GM = general movements, GMA = general movements assessment, HIE = hypoxic ischemic encephalopathy, MRI = magnetic resonance imaging, NE = neonatal encephalopathy, NPV = negative predictive value, PPV = positive predictive value, wks = weeks. | | | | | | | |