Neuroplasticity is fundamentally why we believe in early intervention. The aim of early intervention is to accelerate learning, or induce neuroplasticity.

In 2013, we wrote a paper summarizing effective interventions for cerebral palsy, and some readers we coded early intervention for cerebral palsy as a yellow traffic light for improving motor skills? The evidence we reviewed in 2013 I am going to call early intervention version 1.0. Using the GRADE system, the quality of the 1.0 evidence was low, meaning further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Early intervention 1.0 had a number of limitations, which I will now summarize.

1. **The TYPE of intervention.** In Morgan’s 2016 systematic review which extracted all of the early intervention studies that aimed to improve the motor skills of children with cerebral palsy, we notice a number of limitations:
   - First, there only 10 studies.
   - Second, only 2 of the 10 studies produced motor gains.
   - Third, only half the studies recruited more than 70% of the sample with CP, when 100% was the target, causing low statistical power.
   - Fourth, only 2 of 10 used a training approach which we now know form the green bubbles are the effective approaches with older children with CP and adult stroke.
   - Fifth, only half of the studies started early before the infants were 6 months old.

2. **TIMING.** Targeting the right infants at the right time has been a long standing problem. In early intervention version 1.0, we knew that the brain injury happened for 80% during pregnancy but because of the lack of biomarkers for cerebral palsy, the diagnosis came late after a historic silent period. Cerebral palsy is typically diagnosed between 12-24 months of age, and even later in some low income country settings e.g. 4yrs in Bangladesh.

3. **LATE LOW DOSE intervention.** Canadian data shows 50% of infants with cerebral palsy get no early intervention before one year of age, unless they are in NICU follow up.

4. **Historically EI has been GENERIC.** If we look at these 4 5-year olds with different disabilities: Autism Spectrum Disorder, Spina Bifida, Cerebral Palsy and Down Syndrome. I am sure we’d all agree at age 5, their rehabilitation programs would look very different, so we asked the question, should their rehabilitation be the same at 6-months of age? OR should it be diagnostic specific aiming to optimise neuroplasticity and minimise condition-specific maladaptive plasticity?
Our research aim was to design and test the effectiveness of Early Intervention 2.0. Early Intervention 2.0 includes a focus on

1. Early diagnosis to improve the timing of intervention & targeting of the right infants
2. Intensive training with environmental enrichment to introduce known effective interventions modified to be infant friendly at high dose to harness motor and cognitive plasticity

We published an international clinical practice guideline about how to accurately diagnose cerebral palsy early in JAMA Paediatrics.


To write the guideline, we conducted a systematic review. We found 6 Systematic Reviews & 2 Clinical Guidelines of very high quality.

We made 12 recommendations. Our recommendations are based on high quality published evidence (column 1). Plus we weighed up other factors such as the harm of not acting, or the cost and availability of tests (column 2), to determine the strength of the recommendations.

<table>
<thead>
<tr>
<th>RECOMMENDATIONS</th>
<th>STRENGTH OF RECOMMENDATIONS &amp; QUALITY OF EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Strong Recommendation based on moderate quality evidence for infant and parent outcomes</td>
</tr>
</tbody>
</table>

The clinical diagnosis of cerebral palsy can and should be made as early as possible, so that:
- The infant can receive diagnostic-specific early intervention and surveillance to optimize neuroplasticity and prevent complications
- The parent/s can receive psychological and financial support (when available)
1.1 When the clinical diagnosis is suspected but cannot be made with certainty, the interim clinical diagnosis of “high-risk of cerebral palsy” should be given, so that:
- The infant can receive diagnostic-specific early intervention and surveillance to optimize neuroplasticity and prevent complications
- The parent/s can receive psychological support and financial support (when available)
- Ongoing diagnostic monitoring can be provided

**Strong Recommendation** based on moderate quality evidence for infant and parent outcomes

2.0 Early standardized assessments and investigations for early detection of cerebral palsy should always be conducted in populations with newborn detectable risks, i.e. infants born preterm, infants with neonatal encephalopathy, infants with birth defects, infants admitted to NICU

**Strong Recommendation** based on high quality evidence of test psychometrics

### EARLY DETECTION OF CEREBRAL PALSY BEFORE 5-MONTHS CORRECTED AGE

3.0 **OPTION A:** The most accurate method for early detection of cerebral palsy in infants with “newborn detectable risks” and less than 5-months old (corrected age) is to use a combination of a standardized motor assessment and neuroimaging and history taking about risk factors

**Strong Recommendation** based on high quality evidence of test psychometrics in “newborn detectable risk” populations

**Standardized Motor Assessment**

3.1 **TEST:** General Movements Assessment (GMs), to identify motor dysfunction [95-98% predictive of cerebral palsy]; combined with neuroimaging

**Strong Recommendation** based on high quality evidence of test psychometrics in “newborn detectable risk” populations

**Neuroimaging**

3.2 **TEST:** MRI (before sedation is required for neuroimaging) to detect abnormal neuroanatomy in the motor area/s of the brain [80-90% predictive of cerebral palsy]. Note: Normal neuroimaging does not automatically preclude the diagnosis of risk of cerebral palsy

**Strong Recommendation** based on high quality evidence of test psychometrics in “newborn detectable risk” populations

4.0 **OPTION B:** In contexts where the General Movements assessment is not available and/or MRI is not safe or affordable (e.g. in Low to Middle Income Countries), early detection of cerebral palsy in infants with “newborn detectable risks” and less than 5-months old (corrected age) is still possible and should be carried out to enable access to early intervention

**Strong Recommendation** based on moderate quality evidence of test psychometrics in “newborn detectable risk” populations
### Standardized Neurological Assessment

**4.1**

**TEST:** Hammersmith Infant Neurological Examination (HINE) [HINE<57 at 3-months is 96% predictive of cerebral palsy]

**Strong Recommendation**

Based on moderate quality evidence of test psychometrics in "newborn detectable risk" populations

---

### Standardized Motor Assessment

**4.2**

**TEST:** Test of Infant Motor Performance (TIMP)

**Conditional Recommendation**

Based on low quality evidence of test psychometrics in at-risk populations

---

### EARLY DETECTION OF CEREBRAL PALSY AFTER 5-MONTHS CORRECTED AGE

Accurate early detection of cerebral palsy in those with "infant discernable risks" and 5-24 months of age can and should still occur as soon as possible, but different diagnostic tools are required

**5.0**

Any infant with:
(a) inability to sit independently by 9 months of age; or
(b) hand function asymmetry; or
(c) inability to take weight through the plantar surface (heel and forefoot) of the feet should receive standardized investigations for cerebral palsy

**Strong Recommendation**

Based on high quality evidence of motor norms

---

**6.0**

**OPTION A:** The most accurate method for early detection of cerebral palsy in those with "infant detectable risks", older than 5-months of age (corrected for prematurity) but less than 2-years old, is to use a combination of a standardized neurological assessment, neuroimaging, and a standardized motor assessment with a history taking about risk factors

**Conditional Recommendation**

Based on moderate quality evidence of test psychometrics in "newborn detectable risk" populations

---

**Standardized Neurological Assessment**

**6.1**

**TEST:** Hammersmith Infant Neurological Examination (HINE) [90% predictive of cerebral palsy]. HINE scores lower than 73 (at 6, 9 or 12 months) should be considered at high-risk of cerebral palsy. HINE scores lower than 40 (at 6, 9 or 12 months) almost always indicate cerebral palsy; combined with neuroimaging and standardized motor assessments

**Conditional Recommendation**

Based on moderate quality evidence of test psychometrics in "newborn detectable risk" populations
### Neuroimaging

**6.2 TEST:** MRI to detect abnormal neuroanatomy in the motor area(s) of the brain (Sedation may be required >6-weeks up to 2-years of age). Well-defined lesions can be seen early but subtle white matter lesions may be difficult to detect due to rapid growth, myelination and activity-dependently plasticity. Repeat MRI scans are recommended at 2-years of age, for infants with initially normal MRI (at 12-18 months), but persistent motor and or neurological abnormality; combined with standardized motor assessments

| Conditional Recommendation | based on moderate quality evidence of test psychometrics in “newborn detectable risk” populations |

### Standardized Motor Assessments

**6.3 TEST:** Developmental Assessment of Young Children (DAYC) to quantify motor delay [89% predictive of cerebral palsy].

Additional assessments can improve congruency of findings.

**6.4 TESTS:** Alberta Infant Motor Scale (AIMS) [86% predictive of an abnormal motor outcome]; the Neuro Sensory Motor Development Assessment (NSMDA) [82% predictive of an abnormal motor outcome]

| Conditional Recommendation | based on low-moderate quality evidence of test psychometrics in “newborn detectable risk” populations |

### Standardized Neurological Assessment

**7.0 OPTION B:** In contexts where MRI is not safe or affordable, early detection of cerebral palsy is still possible in those with “infant detectable risks” between 5-24 months corrected age and should be carried out to enable access to early intervention

### Standardized Motor Assessment

**7.1 TEST:** Hammersmith Infant Neurological Evaluation (HINE) [90% predictive of cerebral palsy at 2-24 months of age] HINE scores at 6, 9 or 12 months: <73 indicates high-risk of cerebral palsy <40 indicates abnormal outcome, usually cerebral palsy

| Strong Recommendation | based on moderate quality evidence of test psychometrics in “newborn detectable risk” populations |

### EARLY DETECTION OF MOTOR SEVERITY OF CEREBRAL PALSY

**7.2 TEST:** Developmental Assessment of Young Children (DAYC) to quantify motor delay [89% predictive of cerebral palsy].

**7.3 TEST:** Motor Assessment of Infants (MAI) to quantify motor delay [73% predictive of cerebral palsy]

| Conditional Recommendation | based on low-moderate quality evidence of test psychometrics in “newborn detectable risk” populations |

### EARLY DETECTION OF MOTOR SEVERITY OF CEREBRAL PALSY

Prognosis of long-term motor severity is most accurate in children over 2-years of age using the Gross Motor Function Classification System (GMFCS)

**8.0** In infants less than 2-years old, prognosis of motor severity predictions should be made cautiously and always involve the...
use of standardized tools, since incomplete development of voluntary motor skills and/or abnormal tone might confound clinical observations. Motor severity of cerebral palsy under 2-years of age is most accurately predicted using the:

**Standardized Neurological Assessment**

#### 8.1 TEST: Hammersmith Infant Neurological Evaluation (HINE)
Cut-off scores predict the probable severity

- **HINE scores at 3, 6, 9 or 12 months:**
  - 50-73 indicates likely unilateral CP (i.e. 95-99% will walk)
  - <50 indicates likely bilateral CP

- **HINE scores at 3-6 months:**
  - 40-60 indicates likely GMFCS I-II
  - <40 indicates likely GMFCS III-V

**Neuroimaging**

#### 8.2 TEST: MRI
Non-ambulant cerebral palsy is more likely following:

- Bilateral parenchymal haemorrhages (Grade IV)
- Bilateral cystic periventricular leukomalacia (cPVL) (Grade III)
- Brain maldevelopment
- Basal ganglia injury

Ambulant cerebral palsy is more likely following:

- Unilateral lesions (Grade IV haemorrhage, Perinatal Arterial Ischemic Stroke)
- Periventricular leukomalacia (PVL) (non-cystic)
- Moderate/Severe white matter injury

Normal imaging does not preclude cerebral palsy, and abnormal imaging does not automatically lead to cerebral palsy.

### EARLY DETECTION OF MOTOR SUB-TYPE AND TOPOGRAPHY OF CEREBRAL PALSY

#### 9.0
Early detection of motor sub-type and topography can be difficult in under 2-year olds, but wherever possible it is very important to identify unilateral versus bilateral cerebral palsy early, as the early interventions (e.g. Constraint Induced Movement Therapy) and long-term musculoskeletal outcomes and surveillance needs differ (e.g. hip surveillance).

**Conditional Recommendation** based on low-high quality evidence

### EARLY INTERVENTION

---

Clinical diagnosis of cerebral palsy or the interim diagnosis “high-risk of cerebral palsy” should always include standard medical investigations for associated impairments and functional limitations (e.g. vision impairment, hearing impairment, epilepsy).

**Strong Recommendation** based on high quality population register evidence of rates of associated impairments.

Parents experience grief and loss at the time of diagnosis or “high-risk” notification, and therefore communication with a family should be a series of well-planned and compassionate conversations. Communication should be: face-to-face, with both parents or caregivers present (where appropriate), private, honest, jargon-free, with empathic communication tailored to the family, followed by: written information, identification of strengths, invitation to ask questions, discussion of feelings, recommendations to use parent-to-parent support and arrangement of early intervention.

**Strong Recommendation** based on high quality qualitative parent interviews.

### In Conclusion

1. EARLY diagnosis guidelines now exist = GO implement
2. PASSIVE interventions don’t work = STOP using these interventions and redirect our efforts
3. EARLY training + enrichment probably = better motor & cognitive skills & less complications

---