

# Predictive validity of the Hand Assessment for Infants in infants at risk of unilateral cerebral palsy

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## ABBREVIATIONS

AUC	Area under the curve
BoHM	Both hands measure
EaHS	Each hand sum score
HAI	Hand Assessment for Infants
GMA	Qualitative Assessment of General Movements
HINE	Hammersmith Infant Neurological Examination

**AIM** To evaluate the sensitivity, specificity, and predictive value of the Hand Assessment for Infants (HAI) in identifying infants at risk of being diagnosed with unilateral cerebral palsy (CP), and to determine cut-off values for this purpose.

**METHOD** A convenience sample of 203 infants (106 females, 97 males) was assessed by the HAI at 3, 6, 9, and 12 months. Sensitivity, specificity, predictive values, and likelihood ratios were calculated using receiver operating characteristic curve analysis. Cut-off values were derived for different ages. The clinical outcome (unilateral CP yes/no) at 24 months or more served as an external criterion to investigate the predictive validity of HAI.

**RESULTS** Half of the infants developed unilateral CP. The area under the curve ranged from 0.77 (95% CI [confidence interval] 0.63–0.91) to 0.95 (95% CI 0.90–1.00) across HAI scales and age intervals. Likewise, sensitivity ranged from 63% to 93%, specificity from 62% to 91%, and accuracy from 73% to 94%.

**INTERPRETATION** HAI scores demonstrated overall accuracy that ranged from very good to excellent in predicting unilateral CP in infants at risk aged between 3.5 and 12 months. This accuracy increased with age at assessment and the earliest possible prediction was at 3.5 months of age, when appropriate HAI cut-off values for different ages were applied.

Standardized motor assessments that have been thoroughly investigated are an essential component of early detection of cerebral palsy (CP), and are highly sought after by both professionals and parents.<sup>1,2</sup> Children in high-income countries are typically diagnosed with CP at an average age of 19 months or even later.<sup>3</sup> Early identification of infants that will develop CP is important for the accurate inclusion of infants in family support and early intervention programmes. For instance, constraint-induced movement therapy for infants that specifically targets the affected upper limb can be administered during the first year of life.<sup>4</sup> Concerning the identification of unilateral CP, hand asymmetry is a common early indicator.<sup>2</sup> Using the newly developed Hand Assessment for Infants (HAI) we can, for the first time, measure and describe hand function in terms of unilateral and bilateral hand use in infants with clinical signs of unilateral CP.<sup>5</sup> The HAI is a criterion- and norm-referenced test that quantifies the contribution of each hand separately, as well as the interplay between hands, and provides excellent validity and reliability of

scores in infants aged 3 to 12 months who are at risk of unilateral CP; results from a Rasch measurement model analysis have indicated a potential for measuring change over time.<sup>5</sup>

The question arises, how well can the HAI predict infants at risk that may be later diagnosed with unilateral CP? Previous studies have shown that the HAI can play a role in diagnosing unilateral CP at an early age in infants born at term as well as infants born preterm.<sup>6,7</sup> By combining the HAI with neonatal magnetic resonance imaging (MRI), gestational age, and sex it was possible to accurately identify the prognostic risk of unilateral CP as early as 3.5 to 4.5 months in infants with asymmetric perinatal brain injury.<sup>6</sup> This suggests that the HAI could also be used for predictive purposes and thereby complement existing methods in identifying and diagnosing unilateral CP. The aim of this research was to evaluate the sensitivity, specificity, and positive and negative predictive values of the HAI for identifying infants at risk of being diagnosed with unilateral CP, and to determine cut-off values for this purpose.

## METHOD

### Study design and setting

This longitudinal prospective study investigated the predictive validity of the HAI at various cut-off values for identifying infants aged 3 to 12 months who would go on to have a clinical diagnosis of unilateral CP (yes/no) at 24 months or more corrected age. The study was conducted in routine clinical care settings in Sweden, Italy, the Netherlands, and Australia.

### Participants

A convenience sample of infants was recruited from different follow-up programmes and neurological clinics at Astrid Lindgren Children's Hospital, Stockholm, Sweden; the Wilhelmina Children's Hospital of the University Medical Center in Utrecht, the Netherlands; the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris Pisa, Italy; and the Cerebral Palsy Alliance, Sydney, Australia from 2006 to 2016. In Stockholm, infants with different types of perinatal stroke (included in the national stroke follow-up programme) and an asymmetric perinatal brain injury were identified, as well as infants from the child neurology department after referral to the hospital at 3 to 12 months. All infants were referred to the occupational therapy department for HAI assessments by a physician. In contrast, in Utrecht, Pisa, and Sydney, only infants at high risk of unilateral CP based on MRI findings were recruited and followed by HAI assessments. Several infants had participated in previous clinical trials or descriptive studies.<sup>4,6,8,9</sup>

Inclusion criteria were: (1) infants between 3 and 12 months corrected age, (2) with risk of unilateral CP due to either a history of a neonatal event such as a perinatal stroke ( $\geq 37$ wks' gestation), an asymmetric brain injury confirmed by brain imaging (MRI), or observed neurological signs of hand asymmetry, and (3) available information about the presence or absence of a diagnosis of unilateral CP at 24 months or more corrected age verified by medical records. Exclusion criteria were early signs of other subtypes of CP and infants with severe visual impairment that might affect testing.

### Ethical approval

All parents received oral and written information about the study before providing written informed consent. Ethical approval was granted from the regional ethics committee in Stockholm (2008/148-31, 2011/278-32, and 2018/1329-32) and in the other participating countries by the relevant institutional or regional review boards (Italy: IRCCS Fondazione Stella Maris; the Netherlands: Medical Ethical Committee Utrecht; and Australia: Sydney Children's Hospital Network, Cerebral Palsy Alliance, and the University of Notre Dame).

### Hand Assessment for Infants

The HAI test procedure comprises a video-recorded, semi-structured 10- to 15-minute play session with the infant

### What this paper adds

- The Hand Assessment for Infants (HAI) predicts unilateral cerebral palsy (CP) with high accuracy.
- HAI cut-off values can guide clinical practice for early identification and diagnosis of unilateral CP.

using carefully selected toys to elicit toy exploration, which makes a wide range of motor actions observable. The HAI measures 12 unimanual items for each hand individually and five bimanual items, scored on a 3-point rating scale, and their sum is transformed by Rasch measurement model analysis into an interval level logit-based both hands measure (BoHM) on a 0 to 100 HAI unit scale, where a higher score indicates better performance. The unimanual items are scored separately for each hand with a raw score ranging from 0 to 24 (each hand sum score [EaHS]). In addition, an asymmetry index (%) of the percent difference between hands based on the EaHS is provided ( $= [1 - \text{lesser functioning hand sum score} / \text{better functioning hand sum score}] \times 100$ ).<sup>5,10</sup> Interrater and test-retest reliability were excellent for the HAI BoHM and the EaHS for infants with neurological signs of hand asymmetry (intraclass correlation coefficient<sub>2,1</sub> = 0.96–0.99).<sup>11</sup>

### Data collection

HAI data were collected in the hospitals during regular follow-up mainly at about 3, 6, 9, and 12 months corrected age. Additional HAI assessments were performed for infants included in clinical trials. Infants that were not included in the national follow-up programme were assessed after later referral to the hospital, at various time points. As a result of the variation in age at inclusion, the numbers of HAI assessments per infant differed. All HAI assessments were analysed by the latest version of the HAI manual by a total of four certified and experienced therapists from Sweden, Italy, and the Netherlands.

The clinical diagnosis of unilateral CP (yes/no) that served as external criterion to investigate the predictive validity of HAI was collected from medical records of clinical routine care at 24 months or more corrected age. The diagnosis of unilateral CP was based on a clinical assessment in compliance with European guidelines.<sup>12</sup>

### Statistical analysis

The Shapiro–Wilk test was performed to test normality for continuous variables (including the scores of the contralesional EaHS, asymmetry index, and BoHM) and descriptive summary statistics were reported accordingly. Receiver operating characteristic curve analysis was performed and sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratios were calculated for the HAI contralesional EaHS, asymmetry index, and BoHM for each age interval. HAI assessments were grouped in six age intervals for analysis and, for infants with repeated HAI assessments, the earliest assessment was included per each corresponding age interval.

Stata/IC 15 (Statcorp, College station, TX, USA) was used to perform all analyses.

The receiver operating characteristic curve plots sensitivity (vertical axis) against 1-specificity (horizontal axis) for all possible thresholds of a measure for the decision rule. The area under the curve (AUC) is an indicator of the accuracy of the measure over the range of thresholds and provides a means of comparing the overall strength between HAI scales. It shows how well the HAI can distinguish between infants that developed or did not develop unilateral CP; an AUC near 1.0 indicates excellent discrimination whereas an AUC of 0.5 is no better than chance. An AUC of 0.7 to 0.8 can be considered acceptable, 0.8 to 0.9 excellent, and over 0.9 outstanding.<sup>13</sup>

Values for the sensitivity and specificity of the HAI and their corresponding cut-off values were derived from the receiver operating characteristic curve analysis. For a given HAI scale (e.g. BoHM) we considered a cut-off value optimal if it maximized accuracy, where accuracy was defined as the total number of true test results (true positives plus true negatives) divided by the total number of test results (all positives and negatives). In cases of several cut-off values with equal accuracy, clinical reasoning as well as knowledge about hand development in infants and normative values of HAI were taken into account to reach consensus among authors (UCR, A-CE, and LK-S).<sup>9,10</sup> For a given HAI scale to be considered of clinical value for early prediction of unilateral CP, an a priori minimum threshold of 0.80 was required for the AUC as well as for sensitivity, specificity, accuracy, and predictive values.

**Table 1:** Demographic data of participants ( $n=203$ )

	Median (IQR)	<i>n</i>	Unilateral CP (yes/no)
Gestational age at birth (wks)	38.1 (32, 40.4)		
Term/preterm/very preterm <sup>a</sup>		130/ 37/ 36	
Female/male		106/ 97	
Country: Sweden/the Netherlands/ Italy/Australia		128/ 45/ 22/8	
Age at first HAI assessment: 3-5/6 -8/9-10mo CA		155/ 45/3	
Unilateral CP (yes/no) at $\geq 12$ mo CA		103/ 100	
Clinical diagnosis perinatal stroke, $n=102$			38/64
Asymmetric perinatal brain injury (other than perinatal stroke), $n=81$			53/28
Neurological signs of hand asymmetry, $n=20$			12/8

<sup>a</sup>Term:  $\geq 37$ wks gestational age (GA) at birth, preterm: 36-30wks GA, and very preterm:  $< 30$ wks GA. IQR, interquartile range; CP, cerebral palsy; HAI, Hand Assessment for Infants; CA, corrected age.

## RESULTS

### Participants

Demographic details of participants are summarized in Table 1. A total of 203 infants (106 females, 97 males) with a median gestational age of 38 weeks (interquartile range 32-40wks<sup>+4</sup>) participated and about one-half of them developed unilateral CP ( $n=103$ ). The majority of infants had a history of a neonatal event ( $n=183$ ) verified by brain imaging, except for 10 infants with perinatal stroke identified by other investigations like electroencephalogram and ultrasound (Table 1). MRI findings were mainly perinatal arterial ischaemic stroke in infants born at term and periventricular haemorrhagic infarction in infants born preterm. In addition, infants with other conditions such as white matter injuries or parenchymal haemorrhages were considered at high risk for unilateral CP. Twenty infants had no MRI information available and presented solely with neurological signs of hand asymmetry.

Each infant contributed one to five HAI assessments (mean 2.7, SD 1.01) to the analysis resulting in a total of 541 assessments between 13 and 53 weeks corrected age. The initial HAI assessment was performed before 6 months of age for the majority of infants (Table 1) and median HAI scores across the different age intervals are presented in Table 2. Variations in timing for the data collection of the HAI data resulted in different infants being included at different age intervals. Accordingly, the prevalence of unilateral CP varied across age intervals (40-62%) (Table 3).

### Predictive value of the HAI

The AUC provides a measure of the ability of a given HAI scale to correctly identify those infants who will go on to develop unilateral CP and those who will not. The AUC ranged from 0.77 to 0.95 across HAI scales and age intervals with excellent AUCs for the contralesional EaHS (0.81-0.94) and asymmetry index (0.81-0.95), and moderate AUCs for the BoHM (0.77-0.90) (Table 3 and Fig. 1).

The AUC for all HAI scales increased with age at assessment. At 3 months, the AUCs were moderate (0.77-0.81), but from about 3.5 to 4.5 months, the accuracy for all three scales was very good (AUC 0.81-0.88) with the highest level of accuracy for the contralesional EaHS. Then, from about 4.5 to 5.5 months, the contralesional EaHS and the asymmetry index showed excellent accuracy, and that of the BoHM was very good. Finally, excellent accuracy for all scales was found at about 5.5 to 6.5 months as well as between 7.5 and 12 months (Table 3).

Values for sensitivity and specificity were reported for specific cut-off values of the HAI scales that were derived from the receiver operating characteristic curve analysis (Table S1, online supporting information). Sensitivity ranged from 63% to 97% and specificity from 62% to 91% across HAI scales and age intervals, while accuracy for the related cut-off values ranged from 69% to 94%. At about

**Table 2:** Median values (interquartile ranges) for Hand Assessment for Infants scales of infants with and without unilateral cerebral palsy (CP)

	Unilateral CP	No unilateral CP
Wk 13–14 (3mo), <i>n</i> =45	<i>n</i> =19	<i>n</i> =26
Contralesional EaHS	9 (5, 12)	14 (11, 17)
Asymmetry index	22 (9, 59)	0 (0, 8)
BoHM	37 (30, 44)	47 (42, 54)
Wk 15–19 (3.5–4.5mo), <i>n</i> =89	<i>n</i> =39	<i>n</i> =50
Contralesional EaHS	6 (4, 10)	16 (12, 18)
Asymmetry index	60 (41, 74)	11 (5, 19)
BoHM	40 (35, 49)	56 (50, 59)
Wk 20–24 (4.5–5.5mo), <i>n</i> =82	<i>n</i> =32	<i>n</i> =50
Contralesional EaHS	7 (4, 13)	19 (17, 21)
Asymmetry index	68 (38, 81)	7 (0, 14)
BoHM	46 (43, 55)	63 (59, 69)
Wk 25–29 (5.5–6.5mo), <i>n</i> =100	<i>n</i> =54	<i>n</i> =46
Contralesional EaHS	8 (3, 14)	21 (19, 22)
Asymmetry index	63 (33, 82)	5 (4, 9)
BoHM	50 (43, 60)	74 (66, 79)
Wk 30–34 (6.5–7.5mo), <i>n</i> =74	<i>n</i> =45	<i>n</i> =29
Contralesional EaHS	7 (4, 14)	21 (19, 23)
Asymmetry index	70 (39, 83)	13 (4, 14)
BoHM	50 (44, 61)	77 (68, 84)
Wk 35–53 (7.5–12mo), <i>n</i> =151	<i>n</i> =93	<i>n</i> =58
Contralesional EaHS	11 (3, 15)	23 (22, 24)
Asymmetry index	54 (38, 86)	4 (0, 5)
BoHM	57 (45, 66)	84 (77, 93)

EaHS, each hand sum score; BoHM, both hands measure.

3 months, the sensitivity (63–79%) and specificity (62–81%), as well as accuracy (69–78%), at corresponding thresholds of HAI scales ranged from low to moderate. The predictive ability became better with increasing age. At about 3.5 to 4.5 months, the contralesional EaHS and the asymmetry index showed the same predictive ability with all values (sensitivity, specificity, accuracy, and predictive values), exceeding the a priori specified threshold of 80% except sensitivity (79%) (Table S1). Finally, at about 4.5 to 5.5 months, all performance values for the contralesional EaHS and the asymmetry index exceed the a priori threshold of 80%. In contrast, the BoHM yielded very good predictive ability from 5.5 to 6.5 months at the earliest (Table S1). Moderate positive likelihood ratios were found for the contralesional EaHS from 3.5 to 6.5 months, and excellent positive likelihood ratios for the asymmetry index from 4.5 to 6.5 months indicating a moderate to large change towards diagnosing unilateral CP when performing a HAI within these age ranges. The BoHM again yielded moderate positive likelihood ratios only at later age. A positive likelihood ratio greater than 10 indicates strong evidence for the presence of unilateral CP, while a negative likelihood ratio less than 0.1 indicates strong evidence for the absence of unilateral CP.<sup>14</sup>

## DISCUSSION

This study provides evidence of very good to excellent overall accuracy of HAI scores in predicting unilateral CP in infants at various age intervals between 3.5 and 12 months of age. The predictive performance increased with age at assessment and use of the HAI contralesional

**Table 3:** AUC with 95% CI for HAI scales at different ages

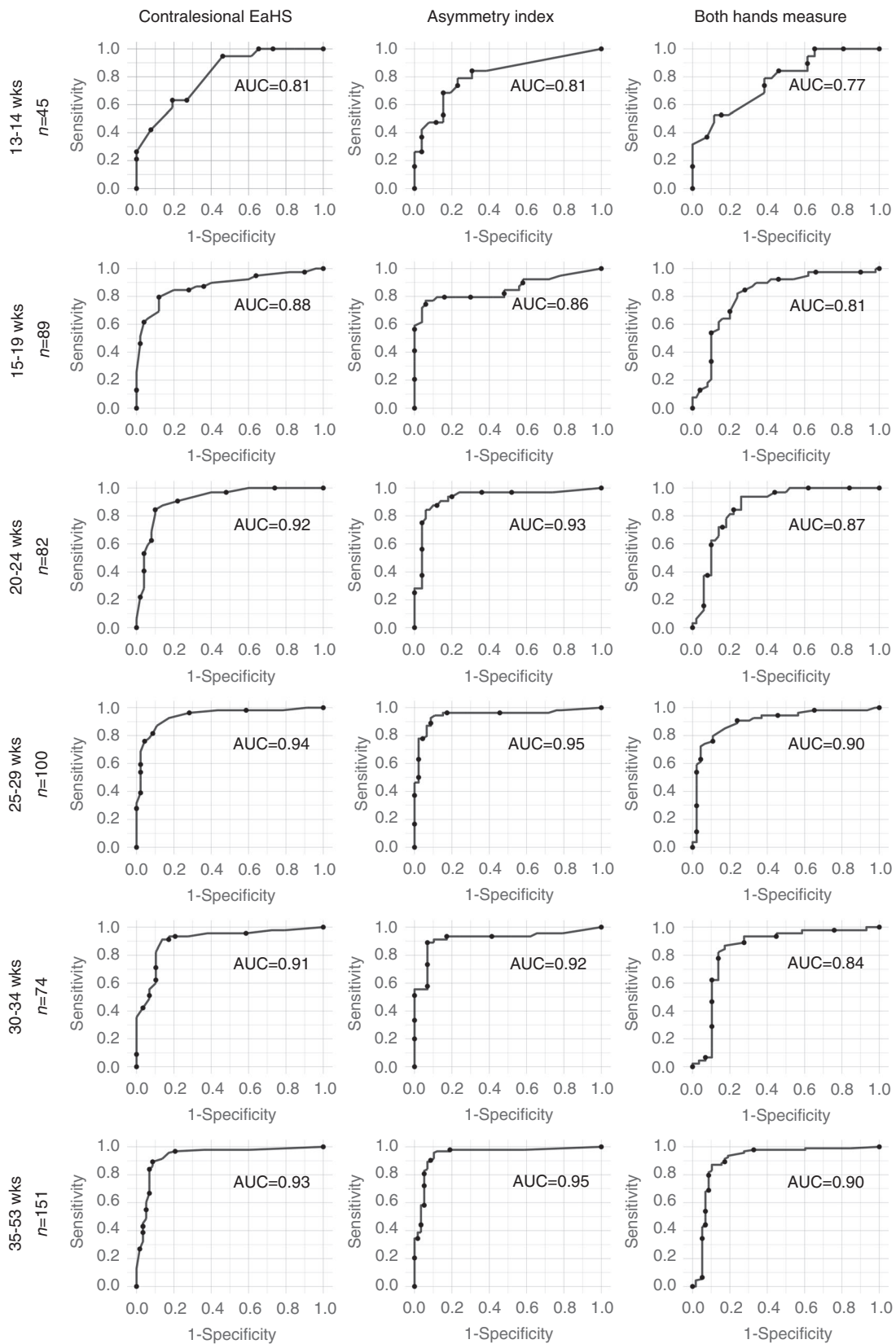
	AUC	95% CI
Wk 13–14 (3mo), <i>n</i> =45		
Unilateral CP prevalence 42%		
Contralesional EaHS	0.81	0.69–0.93
Asymmetry index	0.81	0.68–0.94
BoHM	0.77	0.64–0.91
Wk 15–19 (3.5–4.5mo), <i>n</i> =89		
Unilateral CP prevalence 44%		
Contralesional EaHS	0.88	0.80–0.96
Asymmetry index	0.86	0.77–0.95
BoHM	0.81	0.72–0.91
Wk 20–24 (4.5–5.5mo), <i>n</i> =82		
Unilateral CP prevalence 40%		
Contralesional EaHS	0.92	0.85–0.98
Asymmetry index	0.93	0.86–1.00
BoHM	0.87	0.79–0.95
Wk 25–29 (5.5–6.5mo), <i>n</i> =100		
Unilateral CP prevalence 54%		
Contralesional EaHS	0.94	0.90–0.99
Asymmetry index	0.95	0.90–1.00
BoHM	0.90	0.84–0.97
Wk 30–34 (6.5–7.5mo), <i>n</i> =74		
Unilateral CP prevalence 61%		
Contralesional EaHS	0.91	0.83–0.98
Asymmetry index	0.92	0.85–0.99
BoHM	0.84	0.73–0.96
Wk 35–53 (7.5–12mo), <i>n</i> =151		
Unilateral CP prevalence 62%		
Contralesional EaHS	0.93	0.89–0.98
Asymmetry index	0.95	0.91–0.99
BoHM	0.90	0.84–0.97

AUC, area under the curve; CI, confidence interval; HAI, Hand Assessment for Infants; CP, cerebral palsy; EaHS, each hand sum score; BoHM, both hands measure.

EaHS and asymmetry index is suggested alongside existing methods for the identification of infants at risk of diagnosis of unilateral CP from 3.5 months of age. Earlier prediction (3–3.5mo) remains difficult, indicated by moderate accuracy in discriminating between infants with and without unilateral CP.

In addition to overall predictive performance, cut-off values for different ages were established in order to facilitate clinical application and comparison with existing methods suggested for prediction. Here, we aimed for the best trade-off between sensitivity and specificity for maximum accuracy being aware of the importance of both characteristics in this context. On the one hand, high sensitivity is required so that infants that will develop unilateral CP are not missed (false negatives are minimized) in order to offer the best possible support to them and their families. On the other hand, specificity is important to the same extent because one does not want to cause unnecessary concern in parents. The predictive values are of interest as the positive predictive value informs about the proportion of infants that will be diagnosed with unilateral CP given a HAI score indicating hand asymmetry, and similarly the negative predictive value gives information about the infants that will not be diagnosed with unilateral CP based on a HAI score indicating no hand asymmetry. However, predictive values as well as likelihood ratios





**Figure 1:** Receiver operating characteristic curves for the Hand Assessment for Infants (HAI). EaHS, each hand sum score; AUC, area under the curve.

depend on the prevalence of unilateral CP in the population of interest. In our study, a convenience sample of infants from four hospitals that were at risk of unilateral CP was assessed. Accordingly, the predictive values can be expected to be similar only in a population with a comparable prevalence.

We suggest that the contralesional EaHS should primarily be used for the prediction of unilateral CP, although the predictive ability of the asymmetry index was very similar, as it is based on the EaHS. Thus, the asymmetry index is the percentage difference between the EaHS of both hands in relation to the ipsilesional hand (non-affected hand), and thus is highly influenced by the natural development of the non-affected hand. Although the affected hand may also develop with time, the asymmetry index could increase just because the non-affected hand develops at a faster pace. This may be one explanation for the unsystematic increase and decrease of the asymmetry index across ages, unlike the other HAI scales. The BoHM was shown to be less suitable for the prediction of unilateral CP until later age because bimanual actions develop later in infancy.<sup>10</sup>

For diagnostic purposes, MRI is widely used to detect asymmetric perinatal brain lesions. Visual analysis of the corticospinal tract on MRI has been shown to be predictive for unilateral CP, especially when performed near term age, but the risk of overestimating the number of infants that will develop unilateral CP is large because of its limited specificity.<sup>6,15</sup> Better predictive performance was found for diffusion tensor imaging compared with the separate use of either conventional MRI or the HAI, particularly for infants born preterm.<sup>7</sup> Unfortunately, the cut-off values for the HAI asymmetry index reported by Wagenaar et al. cannot be compared with our thresholds as they used a different calculation method for the asymmetry index than the score form in the final manual.<sup>5,7</sup> The advantage of brain imaging techniques is they give information at term age; however, when MRI was combined with the HAI and other risk factors like gestational age and sex, the prediction of unilateral CP became excellent being both sensitive and specific, as early as at 3.5 months of age.<sup>6</sup>

This study demonstrated that HAI can offer additional information to existing diagnostic methods for infants at risk of unilateral CP during the first year of life.<sup>1,6</sup> Other widely used standardized tools to identify infants at risk of CP early on include Precht's Qualitative Assessment of General Movements (GMA) and the Hammersmith Infant Neurological Examination (HINE).<sup>16,17</sup> Precht's GMA is considered the most predictive tool for the identification of CP based on a lack of fidgety movements at 3 months corrected age, but cannot be used at later ages.<sup>18,19</sup> Targeting unilateral CP in infants with neonatal cerebral infarction, Precht's GMA showed moderate sensitivity of 75% (95% CI 36–96) and excellent specificity of 100% (95% CI 46–100) in a small study; however, wide CIs around both estimates limit the precision of prediction.<sup>20</sup> The HINE, a neurological examination used in infants up to 24 months

of age, is reported to predict atypical motor outcomes and developmental disorders from 3 months corrected age.<sup>18,21,22</sup> Regarding the possible prediction of unilateral CP, the HINE asymmetry score has been recommended in combination with a higher cut-off for the HINE total score compared with CP in general; however, its predictive validity requires further evaluation in a prospective setting.<sup>23,24</sup> Both Precht's GMA and HINE primarily focus on identifying atypical motor development and CP in general, while the HAI has been especially developed for unilateral CP. This underlines the importance of using several complementary assessments for early accurate diagnosis, which is essential for counselling and supporting of families as well as for treatment guidance.<sup>1,6</sup> Additional validation research will be an interesting next step to learn more about the relationship between the HAI, Precht's GMA, and HINE.

### Methodological considerations

Decisions about whether infants are at risk of unilateral CP can be a complicated issue, since there are many risk factors that can be considered.<sup>25</sup> For this validity study, we aimed for a wide inclusion range of a population at risk of unilateral CP; therefore, we based our inclusion criteria on various types of asymmetric brain lesions as well as judgements and concerns of child neurologists that indicated possible development of unilateral CP. We intentionally omitted some medical information because the aim of the study was to indicate whether HAI assessment, performed at different ages, could add information to the existing clinical risk factors during diagnostic decision-making. Variations in age at data collection may be another limitation. In each interval, some infants were assessed for the first time while others were assessed for the *n*th time, which may have introduced selection bias because some infants were more often represented across age intervals than others. Such relatedness of data across time points may have resulted in an overestimation of predictive values. At the same time, the prevalence of unilateral CP across age intervals was similar. In addition, differences in recruitment might have had an impact on predictive values, yet subgroup analyses could not be performed owing to the limited number of participants in possible subgroups. However, the number of infants that were included at a later age based on observed neurological signs of hand asymmetry was small, presumably limiting the influence on the predictive values. Exclusion of infants that did not have HAI assessments at the same age intervals would have resulted in a limited sample size. Data collection over such a long period may be seen as a limitation since the assessment in question actually was not finalized and published in the beginning of this period, but the advantage regarding the HAI was that earlier videos could be reassessed using the final manual by experienced raters.<sup>5</sup> Furthermore, different time points for inclusion are typical for clinical samples of infants at risk of unilateral CP. The clinical diagnosis of unilateral CP may be considered a less

optimal external criterion for investigating the predictive validity of the HAI because it is a symptomatic diagnosis; nonetheless, it is based on international classification.<sup>12</sup> The diagnosis of unilateral CP was collected from medical records at about 2 years of age and was not verified by an additional clinical examination at later age, which could have contributed to extremely mild cases being missed.<sup>26,27</sup> As for any other study investigating the sensitivity and specificity of a method, the retrieved estimates may to some extent have been overestimated because estimation and evaluation of the cut-off values was performed in the same study sample, and need to be externally validated in another similar sample.<sup>28</sup>

### Clinical implications and relationship with other assessments

Specific cut-off values for the HAI can assist in predicting unilateral CP at different age intervals between 3.5 and 12 months corrected age. This can help to identify infants for early intervention and health care programmes, and can also be used for follow-up investigations in order to confirm or refute an initial risk for unilateral CP. The HAI may also be of special interest in situations where MRI is not readily accessible.

In conclusion, HAI scores demonstrated very good to excellent overall accuracy for the range of scores as well as

for specific thresholds to predict unilateral CP in infants at risk at different ages within the first year of life. For all of the HAI scales, this accuracy increased with age at assessment and the earliest possible prediction was at 3.5 months of age.

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### DATA AVAILABILITY STATEMENT

Author elects to not share data.

### SUPPORTING INFORMATION

The following additional material may be found online:

**Table S1:** Sensitivity, specificity, positive and negative predictive values, accuracy, and positive and negative likelihood ratios for HAI cut-off values

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