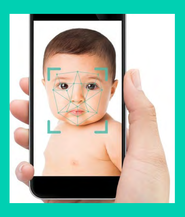

PainChek® Infant: Clinical Feasibility for Assessing Procedural Pain

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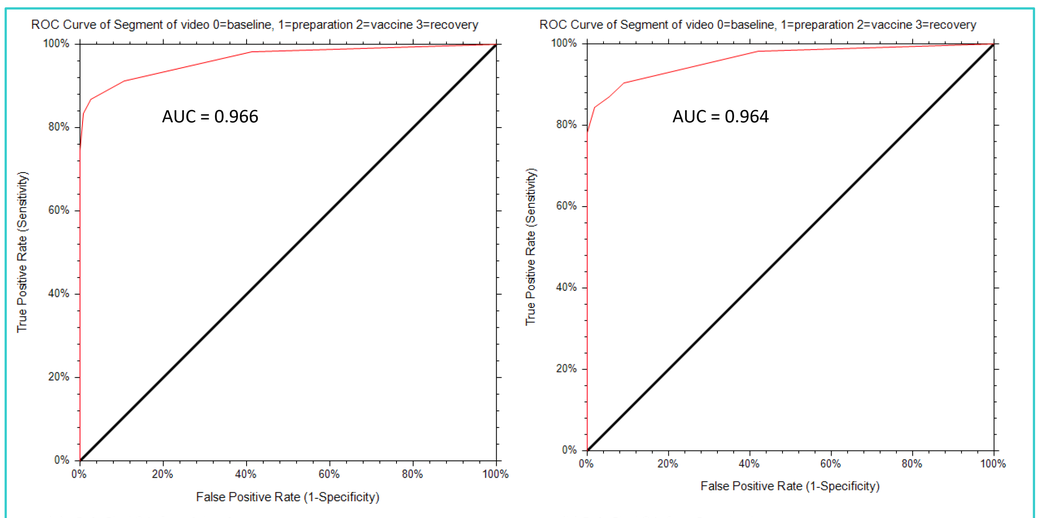
Background: Procedural pain is acute pain associated with investigations, treatments, or procedures done in the course of delivering health care.[1,2] As such, pain can arise from any procedure causing actual or potential tissue damage.[1] Such interventions include simple procedures such as intravenous cannulation, venepuncture, finger and heel pricks, immunisations, and dressing changes, to more invasive procedures such as lumbar punctures or bone marrow biopsies.[1,2] Procedures occur in a variety of settings, from hospitals or day surgery centres to ambulatory care clinics, general practice, dental clinics, and the home care environment.[1] Despite procedural pain being common amongst infants, its management remains suboptimal, in part, compounded by the scarcity of simple, accurate, and reliable methods of assessing such pain.

Aim: In this study, we aimed to evaluate the clinical feasibility of PainChek® Infant, a point-of-care mobile app that uses artificial intelligence to assess procedural pain in infants.

Methods: PainChek® Infant is a unidimensional, observational pain assessment tool, in the form of a smart device application. It uses automated facial detection and analysis to detect six facial features (facial action units or AUs) indicative of pain in infants aged 1 to 12 months. Four trained assessors completed pain assessments on a total of 160 videos segments of infants undergoing immunisation, using PainChek® Infant standard (3 second video) mode, PainChek® Infant adaptive (1 frame minimum) mode, the Neonatal Facial Coding System-Revised (NFCS-R) single observation, the NFCS-R multiple observations, and the observer administered Visual Analogue Scale (VASObs), on two separate occasions. The video segments showed the infants at different phases of the immunisation process, namely (1) Baseline, (2) During Preparation, (3) Immediately post-vaccination and (4) Recovery (30-40 seconds post-injection). Accuracy and precision of the tool were evaluated, together with the cut-off score (defined as the score where sensitivity = specificity)[3] using Receiver Operator Characteristic (ROC) analysis. Clinician comprehensibility was evaluated using a standardized questionnaire using a 5 point Likert scale to evaluate assessors' level of agreement. Other feasibility aspects where evaluated based on COSMIN Guidelines for selecting Outcome Measurement Instruments (OMIs).[4]

Results: A total of 4,303 pain assessments were completed. The study involved 40 videoed infants aged 2.2–6·9 months (median age 3.4 months). ROC analysis demonstrated **high accuracy** (defined as Area Under the Curve [AUC] >0.900) for PainChek® Infant Adaptive and Standard modes (AUC = 0.966 and 0.964, respectively) [**Figure 1**]. Sensitivity and specificity at the chosen **cut-off score of ≥ 2** were 0.912 and 0.897 for the Adaptive mode and 0.904 and 0.911, for the Standard mode, respectively [**Table 1**]. The Feasibility and Usability Survey demonstrated **high levels of agreement** across all items for PainChek® Infant [**Figure 2**]. Evaluation of the feasibility aspects of PainChek® Infant demonstrated **positive results** [**Table 2**].



(a) PainChek® Infant Adaptive (b) PainChek® Infant Standard

Figure 1. ROC curves for PainChek Infant Adaptive (a) and Standard (b) modes

Table 1. Sensitivity, Specificity calculated for different cut-off scores for PainChek® Infant assessment methods

Cut-off Score	PainChek® Adaptive						PainChek® Standard					
	Sensitivity	L CI	U CI	Specificity	L CI	U CI	Sensitivity	L CI	U CI	Specificity	L CI	U CI
≥ 0.0	1.000	0.968	1.000	0.000	0.000	0.032	1.000	0.968	1.000	0.000	0.000	0.032
≥ 1.0	0.983	0.938	0.998	0.588	0.492	0.679	0.983	0.939	0.998	0.580	0.483	0.673
≥ 2.0	0.912	0.845	0.957	0.895	0.823	0.944	0.904	0.835	0.951	0.911	0.842	0.956
≥ 3.0	0.868	0.792	0.924	0.974	0.925	0.995	0.870	0.794	0.925	0.946	0.887	0.980
≥ 4.0	0.833	0.752	0.897	0.991	0.952	1.000	0.844	0.764	0.905	0.982	0.937	0.998
≥ 5.0	0.746	0.656	0.823	1.000	0.968	1.000	0.783	0.696	0.854	1.000	0.968	1.000
≥ 6.0	0.658	0.563	0.744	1.000	0.968	1.000	0.704	0.612	0.786	1.000	0.968	1.000

Note. Pain was categorized as segment 1 (baseline) no pain, segment 3 (vaccination) pain. L CI lower 95% confidence interval, U CI upper 95% confidence interval

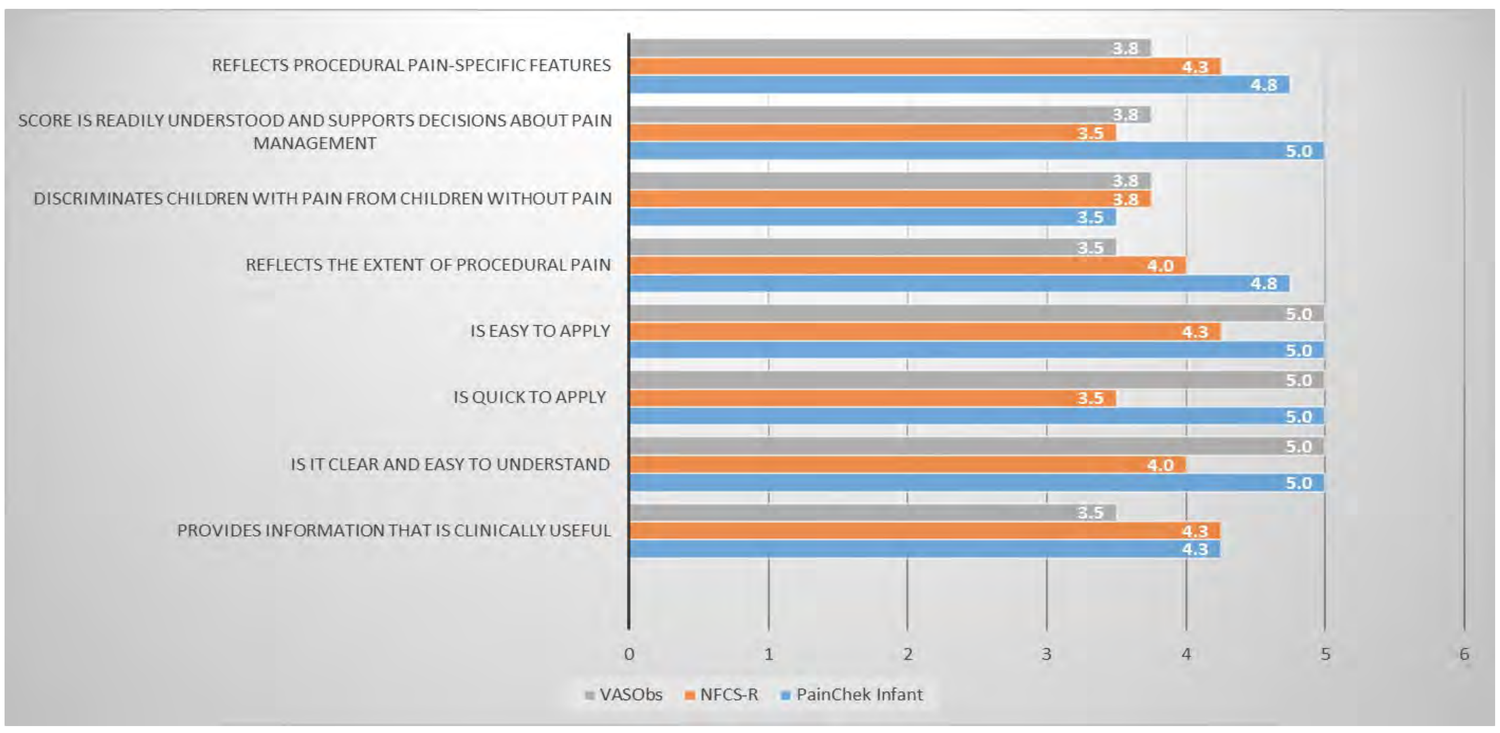


Figure 2. Assessors' Evaluations of the Feasibility and Clinical Usability of PainChek® Infant, NFCS-R and VASObs

Note: Responses rated on a 5-point Likert scale when 0 = strongly disagree and 5 = strongly agreed; Results presented as mean scores

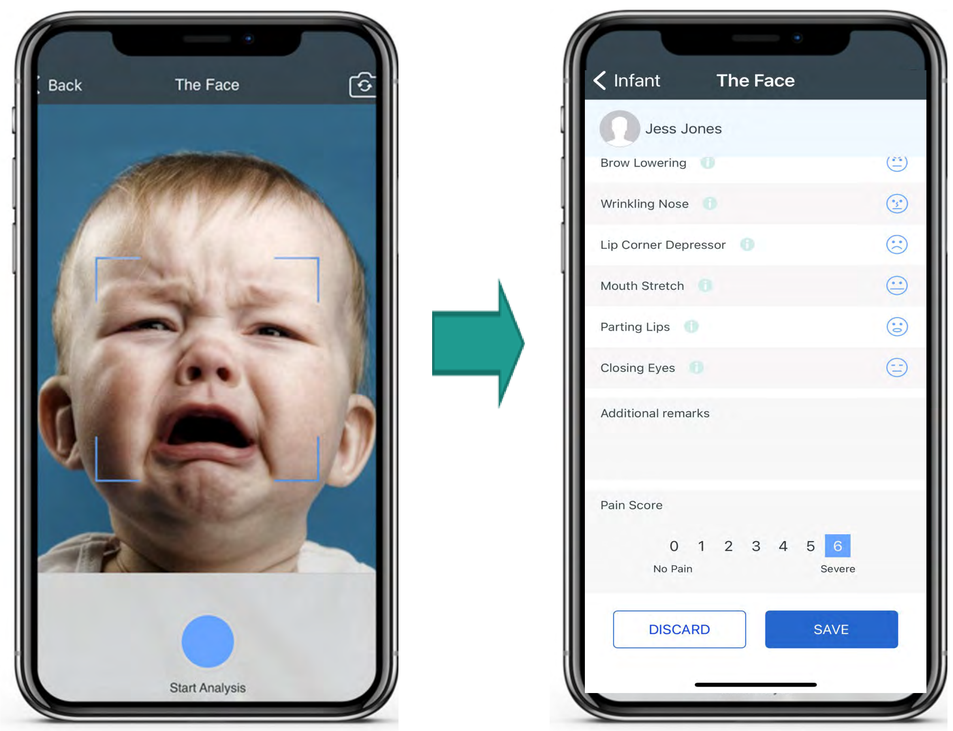


Figure 3. PainChek® Infant Pain Assessment

Table 2. Evaluation of Feasibility Aspects of PainChek® Infant as an Outcome Measure Instrument as per the COSMIN Guidelines[1]

Feasibility aspect	Evidence	Evaluation
1. Patient's comprehensibility	PainChek Infant is to be used by healthcare professional/carer	Not applicable
2. Interpretability	Cut-off score of 2 out of 6 indicate presence of pain **(See Figure 1 and Table 1)** , higher score more intense pain Assessors reported (**See Figure 2**): a) Score readily understood and supports decisions about pain management b) Discriminates children with pain from children without pain c) Reflects the extent of procedural pain d) It is clear and easy to understand e) Provides information which is clinically useful	Demonstrates clinical utility
3. Ease of administration	Automated facial analysis using smart device at point-of-care Assessors reported (**See Figure 2**): a) Is easy to apply b) Is quick to apply	Quick and easy to use
4. Length of the outcome measurement instrument	Consists of a single domain [face] with 6 items (comparable to NFCS-R, i.e. 1 domain [face] and 5 items) Shorter than other tools used for assessing procedural pain such as the FLACC# and MBPS* scales	Short and simple
5. Completion time	3 seconds Assessors reported it was quicker to administer than NFCS-R and comparable to VASObs (**See Figure 2**)	Quick
6. Patient's mental ability level	PainChek Infant is to be used by healthcare professional/carer	Not applicable
7. Ease of standardization	Automated facial analysis using artificial intelligence (**See Figure 3**) Objective with no user bias	Ensures reproducible and repeatable results
8. Clinician's comprehensibility	Clear and easily understood (**See Figure 2**)	Clear and simple
9. Type of outcome measurement instrument	Objective, unidimensional, observational pain assessment tool	Desirable
10. Cost of an outcome measurement instrument	To be established	Could not be assessed
11. Required equipment	iOS or Android Smart Device No requirement of specialised equipment	Positive, smart devices increasingly being used in clinical practice
12. Type of administration	Point-of-care	Essential for pain assessment
13. Availability in different settings	All setting where a smart device can be used	Broad usability
14. Copyright	Yes (also covered by patent)	Intellectual property protected
15. Patient's physical ability level	PainChek Infant is to be used by healthcare professional/carer	Not applicable
16. Regulatory agency's requirement for approval	Yes	Yes
17. Ease of score calculation	App automatically calculates a pain score out of six and displays the facial features detected (**See Figure 3**)	Simple and automated

FLACC = Faces, Legs, Arms, Cries and Consolability scale; * MBPS = Modified Behavioural Pain Scale

Discussion: The available evidence supports the feasibility (accurate, rapid, and easy to use and interpret) of using PainChek® Infant in clinical practice for its intended use, i.e. assessment and monitoring of procedural pain in infants. Given its comparative performance against the NFCS-R which is indicated for the assessment of post-surgical pain, PainChek® Infant could potentially also be used in that setting. The latter requires further investigation.

References: 1 Czarnecki ML, et al. Procedural pain management: a position statement with clinical practice recommendations. Pain Manag Nurs 2011;12: 95–111; 2. Wilson-Smith EM. Procedural pain management in neonates, infants and children. Rev Pain 2011; 5: 4–12.1;
3. Habibzadeh F et al. On determining the most appropriate test cut-off value: the case of tests with continuous results. Biochem Med (Zagreb) 2016; 26: 297-307; 4. Prinsen CAC et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" – a practical guide. Trials 2016; 17:449

Declaration of Conflict of Interest: KH and JH are shareholders in PainChek (formerly known as EPAT Technologies), which is commercialising the PainChek Infant. They are also named as co-inventors with Mustafa Atee on the patent entitled a pain assessment method and system. KH is employed as a consultant by PainChek, while also serving as a Professor at the University of Prishtina, Kosovo and university associate at the Curtin Medical School, Curtin University, WA, Australia. JDH is employed as the Chief Scientific Officer of PainChek and holds an Emeritus Professor appointment in the Curtin Medical School, Curtin University, WA, Australia. PC has no conflict of interests to declare.