

Accepted Manuscript

“A Reliability Study Using Network-Oriented Research Assistant (NORA[®]) to Evaluate the Use of Digital Photographs in the Assessment of Atopic Dermatitis”

Meagan E. Hughes, MD, Hilary Aralis, PhD, Kevin W. Bruhn, PhD, Jonathan Cotliar, MD, Noah Craft, MD PhD, Ilana J. DeLuca, MD PhD, Reyhaneh Hamidi, MD, Kathy Nguyen, PA-C, Mayha Patel, DO, Vishal A. Patel, MD, Howard Sofen, MD, Belinda H. Tan, MD PhD, Consuelo V. David, MD, MSc

PII: S0190-9622(19)30150-1

DOI: <https://doi.org/10.1016/j.jaad.2019.01.043>

Reference: YMJD 13123

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 28 August 2018

Revised Date: 20 December 2018

Accepted Date: 22 January 2019

Please cite this article as: Hughes ME, Aralis H, Bruhn KW, Cotliar J, Craft N, DeLuca IJ, Hamidi R, Nguyen K, Patel M, Patel VA, Sofen H, Tan BH, David CV, “A Reliability Study Using Network-Oriented Research Assistant (NORA[®]) to Evaluate the Use of Digital Photographs in the Assessment of Atopic Dermatitis”, *Journal of the American Academy of Dermatology* (2019), doi: <https://doi.org/10.1016/j.jaad.2019.01.043>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



“A Reliability Study Using Network-Oriented Research Assistant (NORA[®]) to Evaluate the Use of Digital Photographs in the Assessment of Atopic Dermatitis”

¹Meagan E. Hughes MD, ²Hilary Aralis PhD, ³Kevin W. Bruhn PhD, ^{3,4}Jonathan Cotliar MD, ³Noah Craft MD PhD, ⁷Ilana J. DeLuca MD PhD, ³Reyhaneh Hamidi MD, ³Kathy Nguyen PA-C, ³Mayha Patel DO, ³Vishal A. Patel MD, ^{3,5,6}Howard Sofen MD, ^{3,4}Belinda H. Tan MD PhD, ³Consuelo V. David MD, MSc

¹Children’s Hospital of Los Angeles, Los Angeles CA 90027; ²University of California Los Angeles, Department of Biostatistics Los Angeles, CA, 90095; ³Science 37 Inc, Los Angeles, CA 90094; ⁴Harbor-UCLA Medical Center, Division of Dermatology, Torrance, CA 90502; ⁵David Geffen School of Medicine at UCLA, Division of Dermatology, Los Angeles CA, 90095, ⁶Dermatology Research Associates, Los Angeles, CA 90045, ⁷George Washington University, School of Medicine and Health Sciences, Department of Dermatology, Washington DC 20052

Correspondence:

Consuelo V. David, MD
Science 37, Inc
12121 Bluff Creek Drive #100, Los Angeles, CA 90094
Mobile: (301) 655-8058
Email: vera.david@directderm.com | vera@science37.com

Word Count: 497

Tables: 1

References: 4

Statement on Prior presentation: This work has not been previously presented or published

Reprint requests: Contact Vera David, MD (vera.david@directderm.com, vera@science37.com)

Financial disclosures:

Dr Hughes has no conflict of interest.
Drs Aralis, M. Patel and Sofen are consultants for Science 37, Inc
Drs Bruhn, Cotliar, Craft, David, DeLuca, Tan, Hamidi, Patel and Kathy Nguyen PA-C are employees of Science 37, Inc with option grants.
This study was funded by Science 37, Inc.

To the editor: Atopic dermatitis (AD) profoundly impacts quality of life due to unrelenting pruritus, sleep disturbance, infections, and stigma.^{1,2} Treatment options are limited. Telemedicine-enabled, decentralized clinical trials (DCTs) may accelerate clinical trials and bring new treatments to market faster.³ To use these tools with confidence, it is important to ensure that telemedicine-based clinical outcome assessments (COAs) are scientifically reliable in comparison to conventional in-person assessments.

This reliability study evaluated levels of agreement between assessment of AD in-person and via digital photographs. Enrollment was open to participants age 13 and older. Patients presented to one of two dermatology clinics in Los Angeles. AD severity was scored using body surface area (BSA), eczema area and severity index (EASI), investigator global assessment (IGA) and scoring atopic dermatitis (SCORAD) scales. During their in-person visit, patients completed pruritus and sleeplessness visual analog scales (VAS) on paper and on a mobile application in a teledermatology platform called NORA[®] (Network-Oriented Research Assistant). Immediately following the in-person assessment, a clinical research coordinator captured a standardized set of full-body digital photographs using the NORA[®] mobile application on an iPhone SE. After a minimum of 14 days, the dermatology rater who scored the patient in-person reviewed and scored the photographs stored in NORA[®]. A total of six different raters were used in the study. Given the 0-100 scale range of BSA, the complexity of EASI and SCORAD systems, and the number of patients typically scored per day, the 2-week intervening period was deemed sufficient to minimize recall bias.

Seventy patients, 56 [80%] female and 14 [20%] male with a mean [SD] age of 37 [15] years were enrolled. To evaluate agreement between in-person and photographic AD assessments, intraclass correlation coefficients (ICC) and corresponding 95% confidence intervals were calculated (Table 1). An ICC of 0.9 or greater indicates excellent agreement; 0.75 to 0.90 indicates good agreement; 0.5 to 0.75 indicates moderate agreement; less than 0.5 indicates poor agreement.⁴ The ICC for EASI (0.95),

SCORAD (0.92), and BSA (0.94) indicated excellent agreement. The ICC for IGA (0.82) indicated good agreement. Excellent agreement was found between paper and electronic VAS pruritus and sleeplessness scores reported by patients (ICC = 0.94). Because IGA is a discrete variable ranging from 0-4, we also evaluated IGA via percent perfect agreement. Perfect agreement was observed between photograph and in-person assessments for 73% of patients (weighted Kappa = 0.70 [0.58, 0.83]. The absolute difference in score between the photograph and in-person assessment was never greater than 1; 16% of patients scored higher by photograph assessment and 11% of patients scored higher in-person.

This study demonstrates that AD, a chronic condition with high physical and psychosocial burden, can be reliably assessed via digital photographs using commonly administered scoring systems. Future studies will address any inter- and intra-rater variabilities associated with photograph-based assessments. The results herein support the continued development of COAs that leverage telemedicine-based methodologies, which will facilitate DCTs that accelerate trial completion, reduce barriers to enrollment, and help bring new treatments to market faster.⁹

Acknowledgment Section/Author Contributions:

Dr Consuelo V. David had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Aralis, Bruhn, Craft, David, Tan.

Acquisition, analysis, and interpretation of data: Aralis, Cotliar, Bruhn, David, DeLuca, Nguyen, (V) Patel, (M) Patel, Sofen

Drafting of the manuscript: Hughes, David

Critical revision of the manuscript for important intellectual content: Hughes, Bruhn, David, Hamidi, Tan

Statistical analysis: Aralis

Obtained funding: David, Bruhn

Administrative, technical, or material support: Patel, Craft, Hamidi, Nguyen

Study supervision: David

Conflicts of Interest and Financial disclosures:

Dr Hughes has no conflict of interest.

Drs Aralis, M. Patel and Sofen are consultants for Science 37, Inc

Drs Bruhn, Cotliar, Craft, David, DeLuca, Hamidi, Tan, Patel and Kathy Nguyen PA-C are/were employees of Science 37, Inc with option grants.

This study was funded by Science 37, Inc

Abbreviation and Acronym List

AD – Atopic Dermatitis

DCTs – Decentralized Clinical Trials

COAs – Clinical Outcome Assessments

BSA – Body Surface Area

EASI – Eczema Area and Severity Index

IGA – Investigator Global Assessment

SCORAD – SCORing Atopic Dermatitis

VAS – Visual Analog Scale

NORA – Network Oriented Research Assistant

ICC – Intraclass Correlation Coefficient

References

1. Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Ann Nutr Metab.* 2015;66 Suppl 1(1):8-16. doi:10.1159/000370220.
2. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: Results from an international survey. *Allergy.* 2018;130:1344. doi:10.1111/all.13401.
3. Hirsch IB, Martinez J, Dorsey ER, et al. Incorporating Site-less Clinical Trials Into Drug Development: A Framework for Action. *Clin Ther.* 2017;39(5):1064-1076. doi:10.1016/j.clinthera.2017.03.018.
4. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine.* 2016;15(2):155-163. doi:10.1016/j.jcm.2016.02.012.

Table 1

In-person versus photograph-based atopic dermatitis severity scores

	N	Mean	SD	Min	Max	ICC [95% CI]
EASI						
In-person	70	10.78	12.58	0.3	57.0	0.95 [0.91, 0.98]
Photo	70	10.34	11.05	0.1	44.9	
SCORAD						
In-person	69	41.49	17.56	9.1	91.2	0.92 [0.84, 0.97]
Photo	69	41.11	17.38	9.1	83.4	
IGA						
In-person	70	2.51	0.88	1	4	0.82 [0.72, 0.90]
Photo	70	2.56	0.85	1	4	
BSA						
In-person	70	22.67	25.16	1.0	98.0	0.94 [0.89, 0.97]
Photo	70	20.86	23.39	1.0	98.0	