

### Mobile health tool detects adherence rates in pediatric patients with eosinophilic esophagitis

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#### Clinical Implications

- Despite the intention to adhere to their swallowed topical steroids, adolescents with eosinophilic esophagitis have poor planning and low medication adherence rates. A digital sensor and mobile health tool may better assess adherence rates.

#### TO THE EDITOR:

Swallowed topical steroids are a mainstay of treatment for eosinophilic esophagitis (EoE) but have a wide range of reported effectiveness.<sup>1</sup> Several factors play a role including refractory EoE or medication nonadherence. Accurate assessment of adherence can prevent unnecessary escalation of care including the use of systemic steroids. This is particularly important in pediatric patients who may have long-term complications of steroids and who frequently undergo general anesthesia to assess disease control. We aimed to measure real-time adherence to swallowed steroids and explore factors related to adherence in adolescent patients with EoE. This study was approved by the Colorado Multiple Institutional Board.

We prospectively enrolled 7 adolescents (aged 13-18 years) with EoE treated with topical steroids (fluticasone) administered through a metered dose inhaler (MDI) and who had a smartphone capable of downloading applications (Apple iOS or Android). Subjects completed a questionnaire assessing self-reported adherence and known psychological predictors of adherence based on the theory of planned behavior (TPB). The TPB questionnaire was developed with the help of a social health psychologist (BMK) and was adapted from TPB questionnaires used in similar disease processes.<sup>2</sup> It assessed TPB constructs (attitudes, perceived norms, and perceived control) and planning regarding medication taking. Mean scores per construct were calculated (range, 1-7) with lower scores indicative of a more problematic factor. Subjects were provided with a Food and Drug Administration–cleared digital sensor by Propeller Health (Madison, Wis) for their inhaler and instructed to mail back the sensor after 2 months. This sensor linked via Bluetooth to the Propeller Health smartphone application (Propeller App) and monitored the date, time, and number of actuations used. Propeller Health also monitored the device's heartbeat—an automatically generated periodic signal indicating that the device is active and functioning properly. To our knowledge, no sensor malfunction occurred during the study. Subjects were also asked to complete the Pediatric Quality of Life Inventory Eosinophilic Esophagitis Module (PedsQL EoE) before sensor monitoring and 2 months later. The PedsQL EoE is a 33-item age-specific

validated quality of life instrument in pediatric patients with EoE, measuring 7 domains (eg, symptoms, feelings).<sup>3</sup> Symptom severity was approximated by using the Symptom Scale of the PedsQL EoE. Scores for the PedsQL EoE and Symptom Scale range from 0 to 100 with higher scores indicative of greater quality of life and less symptom severity. Adherence rate was calculated by dividing the number of actual doses of steroid as captured by the sensor by the prescribed number of doses. Descriptive statistics (means, standard deviations, range) were used to analyze survey measures. Pearson's correlations were computed to assess the relationship between self-reported adherence, sensor-based adherence, and questionnaire scores.

Adherence monitoring via a digital sensor occurred for a mean of 80 days (range, 24-115 days). Subject characteristics, self-reported adherence rates, sensor-detected adherence rate, and PedsQL measures are shown in Table I. Two subjects were prescribed once daily dosing, whereas the rest had twice daily dosing. The mean adherence rate was 36.6%. Adherence rates varied from 14% to 61% with the highest rates found among those who were prescribed once daily dosing. Of 7 subjects, 4 had stretches of greater than 2 weeks without using their steroid. Subject-reported adherence rate did not predict the true adherence rate measured via sensor monitoring ( $r = -0.35$ ). True adherence rate did not predict scores on the Symptom Scale and PedsQL EoE ( $r = -0.25$  and  $-0.12$ , respectively).

Figure 1 depicts baseline TPB constructs related to medication adherence. Planning and forgetfulness were the most problematic factors. Although subjects endorsed that they intended to take their swallowed steroids as prescribed, many reported forgetting. In addition, a minority of subjects reported engaging in planning (when and where they would take their medication), and most lacked confidence in taking their steroids during weekends and holidays, or taking their steroids when something unexpected happened (ie, disruptions to routine).

Our findings showed that self-reported past adherence did not predict future objectively measured adherence. Much evidence in medication adherence supports that self-reported adherence can be unreliable.<sup>4</sup> In pediatric patients with asthma, numerous studies have shown not only low adherence rates, but also inaccurate assessments when using self-report or physician-reported measures. On the contrary, electronic monitoring devices can capture more detailed and precise adherence trends.<sup>5</sup> With respect to eosinophilic gastrointestinal diseases, only 1 study has measured adherence using MDIs. Subjects with EoE or eosinophilic gastroenteritis aged 2.5 to 18 years were studied using parent-proxy adherence questionnaires and objective monitoring of MDI data. Adherence ranged from 0% to 100% via maternal report, 79% to 100% via paternal report, and 0% to 194% via objective monitoring.<sup>6</sup> The wide range of objective adherence rates in this study suggest that patients may both under and overdose. Moreover, given that a different sensor was used without the ability to track each actuation, subjects may also have intentionally wasted actuations with the knowledge that their adherence was being measured. This study in conjunction with our results indicates that there is wide variability in reported adherence rates depending on the method of adherence assessment.

**TABLE I.** Subject characteristics, adherence rates, symptoms severity, and quality of life (QoL)

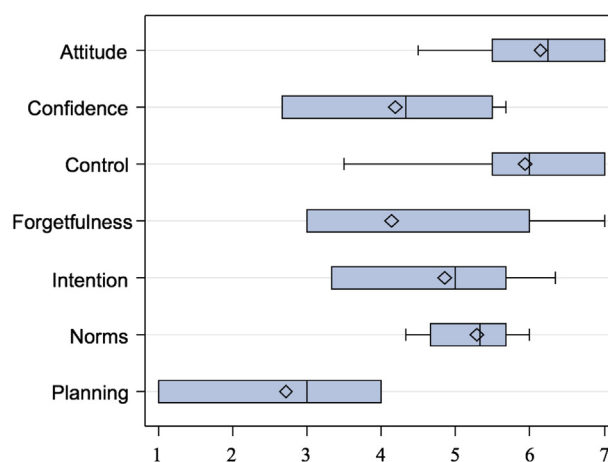
| Age (y) | Sex    | Disease duration (y) | Presenting symptoms           | Structuring disease | Comorbidities                                                                                 | Self-reported adherence rate (%) | Adherence rate by sensor (%) | Symptom severity: pre | PedsQL: pre | Symptom severity: post | PedsQL: post |
|---------|--------|----------------------|-------------------------------|---------------------|-----------------------------------------------------------------------------------------------|----------------------------------|------------------------------|-----------------------|-------------|------------------------|--------------|
| 14      | Female | 1                    | Dysphagia                     | No                  | Allergic rhinitis                                                                             | 64                               | 44                           | 50                    | 61.5        | 30                     | 45           |
| 17      | Male   | 1                    | Dysphagia                     | No                  | Allergic rhinitis, asthma, atopic dermatitis                                                  | 67.5                             | 37                           | 67.5                  | 84.6        | 50                     | 58.6         |
| 18      | Female | 2                    | Pain with eating, nausea      | Yes                 | Asthma, atopic dermatitis as a child (resolved), IgE-mediated food allergies                  | 71                               | 54                           | 90                    | 91          | 77.5                   | 79.5         |
| 16      | Male   | 14                   | Chronic cough, abdominal pain | No                  | Allergic rhinitis, attention deficit disorder, atopic dermatitis, IgE-mediated food allergies | 57                               | 23                           | 90                    | 75.7        | 82.5                   | 78           |
| 13      | Male   | 12                   | Dysphagia                     | No                  | Allergic rhinitis, asthma, atopic dermatitis                                                  | 86                               | 23.5                         | 77.5                  | 78.9        | 97.5                   | 96.2         |
| 14      | Female | 3                    | Dysphagia                     | Yes                 | Allergic rhinitis                                                                             | 86                               | 13.6                         | 77.5                  | 49.2        | 67.5                   | 56.1         |
| 15      | Male   | 4                    | Dysphagia                     | Yes                 | Allergic rhinitis, asthma                                                                     | 71                               | 60.8                         | 65                    | 65.9        | 72.5                   | 67.4         |

Possible scores range from 0 to 100 with higher scores indicative of better adherence, lower symptoms severity, and greater quality of life.

Although most patients respond to topical steroids, a subset of patients may be refractory.<sup>7</sup> In these patients, clinical practice suggests that adherence should be assessed before initiating dietary treatment that may be more difficult, incur larger impact on quality of life, and be costlier. Use of an electronic adherence monitor may be a useful clinical adjunct before escalating therapy. As smartphones allow collection of real-time data including timing and location information, and with the addition of “Just-In-Time” interventions that respond to daily behavior, smartphones represent a state-of-the-art method of studying and intervening on adherence. This may be particularly useful for the pediatric population with nearly 3 quarters of teenagers now having access to smartphones.<sup>8</sup>

Planning on when, where, and how to take medications as well as planning on how to overcome disruptions to routine is associated with increased adherence.<sup>9</sup> Current interventions to improve medication adherence focus on reminders, which are necessary but insufficient. Future interventions to improve adherence to medication therapy in patients with EoE should focus on planning. For instance, guiding patients to establish “implementation intentions” can be effective.<sup>10</sup> This entails having patients write down “if-then” statements indicating when they will take their medications, such as “If I have just eaten breakfast in the morning, then I will use my inhaler.” Encouraging patients to keep their inhaler in a location visible to where they eat breakfast will cognitively activate this plan at the appropriate time.

This study highlights several important points: (1) adolescents with EoE are often nonadherent to their swallowed steroids, despite having positive attitudes and intentions to adhere, (2) real-time monitoring using a digital sensor is a modern-day method of capturing adherence and may serve as a useful clinical tool, and (3) interventions to improve adherence should

**FIGURE 1.** Responses to our psychological factors questionnaire were categorized by psychological constructs. Mean scores per construct were calculated. Possible scores ranged from 1 to 7 with higher scores indicative of a less problematic factor.

focus on enhancing planning, especially for situations interrupting normal routine—rather than emphasizing education.

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## REFERENCES

1. Chuang MY, Chinnaratha MA, Hancock DG, Woodman R, Wong GR, Cock C, et al. Topical steroid therapy for the treatment of eosinophilic esophagitis (EoE): a systematic review and meta-analysis. *Clin Transl Gastroenterol* 2015;6:e82.
2. Ajzen I. The theory of planned behaviour: reactions and reflections. *Psychol Health* 2011;26:1113-27.
3. Franciosi JP, Hommel KA, Bendo CB, King EC, Collins MH, Eby MD, et al. PedsQL eosinophilic esophagitis module: feasibility, reliability, and validity. *J Pediatr Gastroenterol Nutr* 2013;57:57-66.
4. Garber MC, Nau DP, Erickson SR, Aikens JE, Lawrence JB. The concordance of self-report with other measures of medication adherence: a summary of the literature. *Med Care* 2004;42:649-52.
5. Chan AH, Reddel HK, Apter A, Eakin M, Riekert K, Foster JM. Adherence monitoring and e-health: how clinicians and researchers can use technology to promote inhaler adherence for asthma. *J Allergy Clin Immunol Pract* 2013;1:446-54.
6. Hommel KA, Franciosi JP, Hente EA, Ahrens A, Rothenberg ME. Treatment adherence in pediatric eosinophilic gastrointestinal disorders. *J Pediatr Psychol* 2012;37:533-42.
7. Leung J, Mehrzad R, Hundal NV, Alejos A, Hesterberg PE, Katz AJ, et al. Longitudinal perspective on managing refractory eosinophilic esophagitis. *J Allergy Clin Immunol Pract* 2015;3:951-6.
8. Lenhart A. *Teens, Smartphones & Texting*. Washington, DC: Pew Research Center; 2012.
9. Pakpour AH, Gellert P, Asefzadeh S, Updegraff JA, Molloy GJ, Sniehotta FF. Intention and planning predicting medication adherence following coronary artery bypass graft surgery. *J Psychosom Res* 2014;77:287-95.
10. Neter E, Stein N, Barnett-Griness O, Rennert G, Hagoel L. From the bench to public health: population-level implementation intentions in colorectal cancer screening. *Am J Prev Med* 2014;46:273-80.

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