Eosinophilic Esophagitis
Patient Reported Outcome (PRO)
Instrument Development

James P. Franciosi, M.D., M.S., M.S.C.E., F.A.A.P.
Associate Chief, Division of Gastroenterology, Hepatology and Nutrition
Nemours Children’s Hospital
Cincinnati Children’s Hospital Medical Center and Dr. James Franciosi may receive financial compensation from the Mapi Research Trust, a nonprofit research institute that charges distribution fees to for-profit companies that use the PEESS© v2.0.
Guidance for Industry
Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2009
Clinical/Medical
Remission Endpoint Model: Treatment of Disease (EoE)

Figure 1. Endpoint Model: Treatment of Disease X

Concept

**Indication**
Treatment of Disease X

**Supportive Concepts**
Improvement in symptoms/signs of Disease X

Endpoints

**Primary**
Physiologic effect
(non-PRO assessment)

**Secondary**
- Symptoms diary
  (PRO assessment)
- Signs diary
  (PRO assessment)
- Physical exam
  (non-PRO assessment)
- Physical performance
  (PRO or non-PRO assessment)

Guidance for Industry
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Current Eosinophilic Esophagitis

A focus on esophageal mucosal eosinophil counts as the primary outcome variable

> 15 eos/HPF  <= 5 eos/HPF

Success?
World Health Organization: World Health Organization:
Definition of Health

A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity
### Endpoint Model: Treatment of Symptoms

#### Concept

**Indication**
- Treatment of symptoms of Disease Y

**Supportive Concepts**
- Other treatment benefit

#### Endpoints

**Primary**
- Total Disease Y symptoms score (PRO assessment)

**Secondary**
- Physical performance (PRO or non-PRO assessment)
- Disease Y-related physical limitations (PRO assessment)

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**Guidance for Industry**

Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims
2008 CDHNF Grant
EoE PRO Instrument Development
PEESS© v2.0 &
PedsQL™ EoE Module

Phase I  Phase II  Phase III  Phase IV

Construct Validation & Reliability

Responsiveness

© v2.0 & PedsQL™ EoE Module

Phase I  Phase II  Phase III  Phase IV

Construct Validation & Reliability

Responsiveness

Nemours, Children's Hospital
**Qualitative Methods**

**Focus Interviews** — 1 hour semi-structured open-ended individual interviews were conducted. All sessions were audio-recorded, transcribed verbatim, and analyzed by the research team.

**Cognitive Interviews** — Additional individual interviews were conducted to review the PRO instruments in a different cohort.
Qualitative Peer-Reviewed Publications: EoE PROs


PRO Instrument Development

- 75 individual interviews were conducted for both PEESS©v2.0 & PedSQL™ Symptom Scales
- External expert opinion was solicited between the focus and cognitive interview steps
Development of a validated patient-reported symptom metric for pediatric Eosinophilic Esophagitis: qualitative methods


Abstract

Background: Previous attempts to measure symptoms in pediatric Eosinophilic Esophagitis (EoE) have not fully included self-report and self-administered questionnaires.

Methods: Following the aims of a previously published qualitative study, individual focus interviews, followed by cognitive interviews for face and content validation. Initial domains of symptom frequency and severity were developed, and open-ended questions were used to generate specific items during the focus interviews. Once developed, the instrument construct, instructions, timeframe, scoring, and specific items were systematically reviewed with a separate group of patients and their parents during the cognitive interviews.
PEESS
Pediatric Eosinophilic Esophagitis (EoE) Symptom Severity Module
Version 2.0
CHILDREN AND TEENS REPORT (Ages 8 - 18)

DIRECTIONS
Tell us about your problems with EoE in the past MONTH.
There are no right or wrong answers. Please circle the best number.

Please answer the question in the **Frequency** section and then the related question in the **Severity** section.

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<tr>
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<td></td>
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How often do you get sick?

0 1 2 3 4

How bad is it when you get sick?

0 1 2 3 4

Office Use Only

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<th>Study ID:</th>
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<tbody>
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<td></td>
<td>Month / Day / Year</td>
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In the past 7 days, how much of a problem has this been for you …

### About My Symptoms I (problems with…)

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<tr>
<th>About My Symptoms</th>
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<td>4. I throw up (vomit)</td>
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<td>5. I feel like I am going to throw up, but don’t (nausea)</td>
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<td>3</td>
<td>4</td>
</tr>
<tr>
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### About My Symptoms II (problems with…)

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<thead>
<tr>
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<th>Almost Never</th>
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PEESS™ v2.0 & PedsQL™ EoE Module

Phase I
Phase II
Phase III
Phase IV

Focus Interviews
Cognitive Interviews
Responsiveness
Quantitative Peer-Reviewed Publications: EoE PROs

- Over 200 child participants as self-report for both PEESS®v2.0 and PedsQL™ Symptoms Scales
- Feasibility
- Internal-consistency reliability
- Construct validity
- Item scaling tests
- Test-retest reliability
- Active vs. inactive histologic disease
# Journal of Pediatric Gastroenterology & Nutrition

**PedsQL Eosinophilic Esophagitis Module: Feasibility, Reliability and Validity**

---Manuscript Draft---

<table>
<thead>
<tr>
<th>Manuscript Number:</th>
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</thead>
<tbody>
<tr>
<td>Full Title:</td>
<td>PedsQL™ Eosinophilic Esophagitis Symptoms Scales</td>
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<tr>
<td>Article Type:</td>
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<tr>
<td>Section/Category:</td>
<td></td>
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<tr>
<td>Keywords:</td>
<td>health-related quality of life;</td>
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</table>
| Corresponding Author: | James P Francosi, MD, MS, MSCE  
Nemours Children's Hospital  
Orlando, FL UNITED STATES |
Pediatric PRO Self-report

- Poor internal-consistency reliability for children ages 5-7 years of age
- Excellent for children 8-18 years of age
1. Franciosi JP et al. Pediatric Eosinophilic Esophagitis (EoE) health-related quality of life: Feasibility, reliability and validity of the PedsQL™ EoE module. (Includes PedsQL™ Symptoms Scales)

PEESS™ v2.0 & PedsQL™ EoE Module

Phase I
Phase II
Phase III
Phase IV

Focus Interviews
Cognitive Interviews
Construct Validation & Reliability
Choice of recall period for patient-reported outcome (PRO) measures: criteria for consideration

Josephine M. Norquist · Cynthia Girman · Sheri Fehnel · Carla DeMuro-Mercon · Nancy Santanello

• Event driven or daily diary recall
• Weekly recall
• > Weekly recall (monthly)
Adult MDQ (not validated in EoE)

30 day vs 14 day recall
### Recall Period

**Table 4: PedsQL™ Eosinophilic Esophagitis Module Scales Interclass Correlation Coefficients (ICC) for Test-Retest Reliability for Child Self-Report and Parent Proxy-Report**

<table>
<thead>
<tr>
<th>PedsQL™ EoE Symptoms Scales</th>
<th>Test-Retest Agreement Parent ICCs n = 102</th>
</tr>
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<tbody>
<tr>
<td>EoE Module Total Scale Score</td>
<td>0.82</td>
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<tr>
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<tr>
<td>Symptoms I</td>
<td>0.83</td>
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<td>Symptoms II</td>
<td>0.75</td>
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<tr>
<td>Treatment</td>
<td>0.62</td>
</tr>
<tr>
<td>Worry</td>
<td>0.60</td>
</tr>
<tr>
<td>Communication</td>
<td>0.67</td>
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<tr>
<td></td>
<td><strong>0.77</strong>b</td>
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<tr>
<td>Food and Eating</td>
<td>0.84</td>
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<td>Food Feelings</td>
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Note: *n = 40; b n = 69 (smaller sample sizes as a result of age differences across forms). ICCs = Intraclass Correlation Coefficients. ICCs are designated as ≤0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.81–1.00 excellent agreement.
Daily Dairies

- Every day for a 60-90 days
- If 1 day is missed - invalidates entire subject
- Mandating a daily diary limits discovery
- Compromise proposed - 1 week recall period
Sign in to the Questionnaires:

Instructions. Please enter your User Name and Password below to sign in.

User Name: 
Password: 
Login
Clinical Trials = Responsiveness

- Electronic weekly diary
- Ages 8-18 for child PRO self-report
- PEESS©v2.0 & PedsQL™ EoE Symptoms Scales

w0, w1, w2, w3, w4, w5, w6, w7, w8
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PEESS 2.0 (8-18) Not to be reproduced without permission  Copyright © 2010 CCHMC  All rights reserved  Developed by James P. Francosi, M.D.
**PedsQL™**
Eosinophilic Esophagitis Symptoms Scales

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