Assessing AIT Outcomes: How and why?

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Learning Objectives

- Understand the role of biomarkers in predicting and monitoring response to immunotherapy including specific IgE and IgG4 levels, and how they can be used to tailor and optimize treatment protocols.

- Evaluate the importance of outcome measurement in both clinical trials and clinical practice, understanding how these outcomes influence treatment strategies and patient management.

- Select appropriate tools for measuring treatment efficacy including symptom and medication scores, quality of life questionnaires, and objective clinical tools, to ensure comprehensive evaluation and patient-centered care.

Case:

50 year old female with asthma and allergic rhinitis

- AIT X 5 years
- Meds: albuterol PRN, fexofenadine 180mg PRN
- Should the patient stop AIT or continue?

Importance of Immunotherapy

- Effective for various allergies including rhinitis and asthma
- Modifies the underlying allergic disease process
- Provides long-term relief compared to temporary pharmacological treatments
- Beneficial for both adults and children
- Only treatment that potentially alters natural history of allergic diseases

Why Measure Outcomes?

- Essential for evaluating treatment effectiveness
- Helps in refining and validating treatment protocols
  - Ensures comparability across different studies and treatments
  - Helps in aggregating data for meta-analyses and systematic reviews
- Necessary for regulatory compliance and clinical trials
  - Allows for more precise and reliable interpretation of results
- Guides clinical decisions and patient management
  - Critical for developing guidelines and recommendations
- Supports personalized treatment approaches

Clinical Trials vs. Clinical Practice

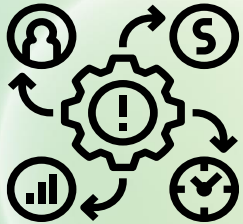
- Clinical trials require rigorous, standardized outcome measures.
- In clinical practice, outcomes guide treatment adjustments and patient care.
- Both settings aim to assess efficacy and safety of treatment.
- Outcomes measurement can vary in method but should be consistent in purpose.
- Clinical practice often focuses on real-world effectiveness and patient-reported outcomes.

Assessing Outcomes

Length of Treatment

Treatment Goals

Biomarkers/ Testing



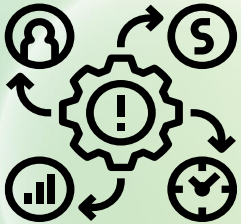
Patient Preference

Assessing Outcomes

Length of Treatment

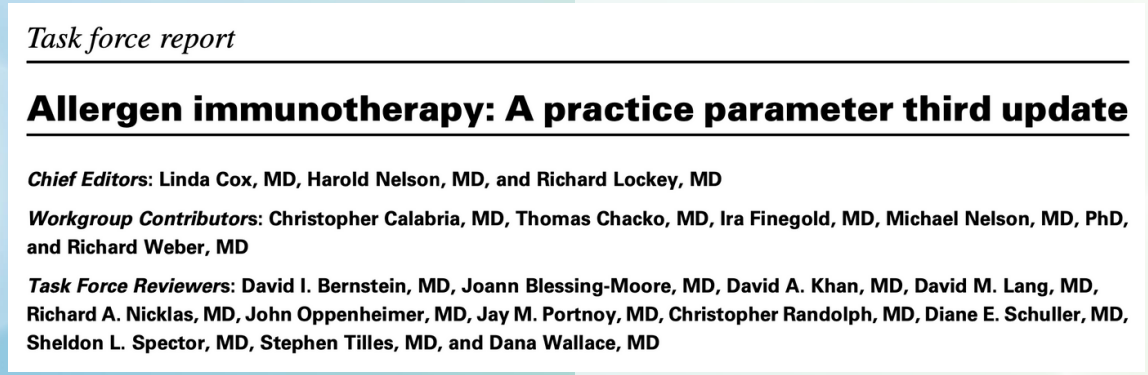
Treatment Goals

Biomarkers/ Testing



Patient Preference

Duration of Therapy: SCIT



Task force report

Allergen immunotherapy: A practice parameter third update

Chief Editors: Linda Cox, MD, Harold Nelson, MD, and Richard Lockey, MD

Workgroup Contributors: Christopher Calabria, MD, Thomas Chacko, MD, Ira Finegold, MD, Michael Nelson, MD, PhD, and Richard Weber, MD

Task Force Reviewers: David I. Bernstein, MD, Joann Blessing-Moore, MD, David A. Khan, MD, David M. Lang, MD, Richard A. Nicklas, MD, John Oppenheimer, MD, Jay M. Portnoy, MD, Christopher Randolph, MD, Diane E. Schuller, MD, Sheldon L. Spector, MD, Stephen Tilles, MD, and Dana Wallace, MD

- Both symptom and medication scores remained markedly reduced during the final 3 years
- No significant differences between participants who continued or discontinued immunotherapy during years 3–7
- No additional benefit could be obtained with the longer course of treatment.

RECOMMENDATION: 3-5 years at maintenance

Duration of Therapy: SLIT

Rhinitis, sinusitis, and upper airway disease

SQ-standardized sublingual grass immunotherapy: Confirmation of disease modification 2 years after 3 years of treatment in a randomized trial

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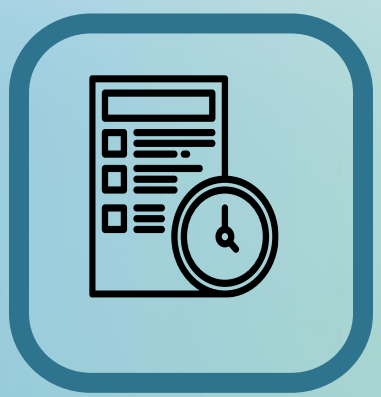
J Allergy Clin Immunol 2012;129:717–25.

- Dose-dependent efficacy and that a minimum of 1–2 months treatment is needed for immunological changes
- 3–6 months therapy is optimal for development of IgE-blocking antibodies and onset of clinical efficacy

RECOMMENDATION: 3-5 years at maintenance

Assessing Outcomes

Length of Treatment



Treatment Goals

Biomarkers/ Testing

Patient Preference

Patient symptom diaries

- Daily symptom score
- Daily log of medication use
- Tips for success
  - Clear and easy to understand instructions
  - Small and handy size to be carried around easily
  - Only one page for each day
  - Large print for elderly patients
  - Waterproofed bindings
  - Multiple-choice questions as well as some space for free text

PROS: Reliable data without recall bias

CONS: Compliant and motivated patient needed

Rhinoconjunctivitis Total Symptom Score (RTSS)

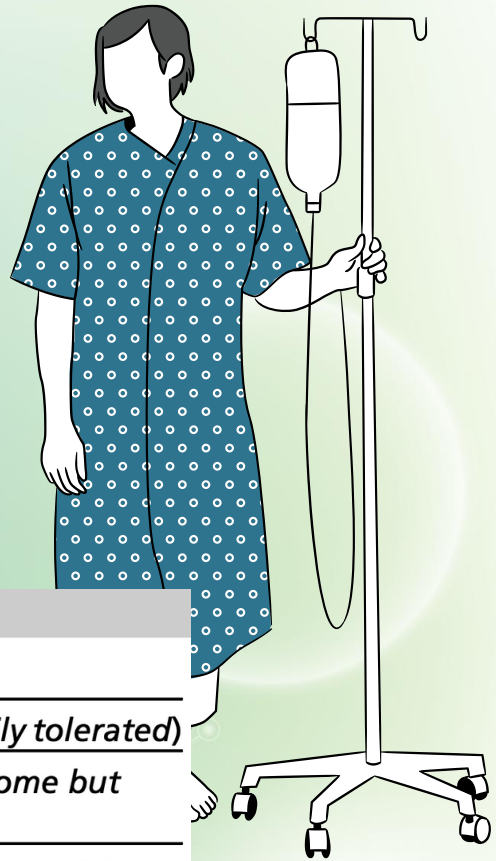
NASAL

- Congestion
- Sneezing
- Itching
- Secretions

OCULAR

- Itching
- Secretions

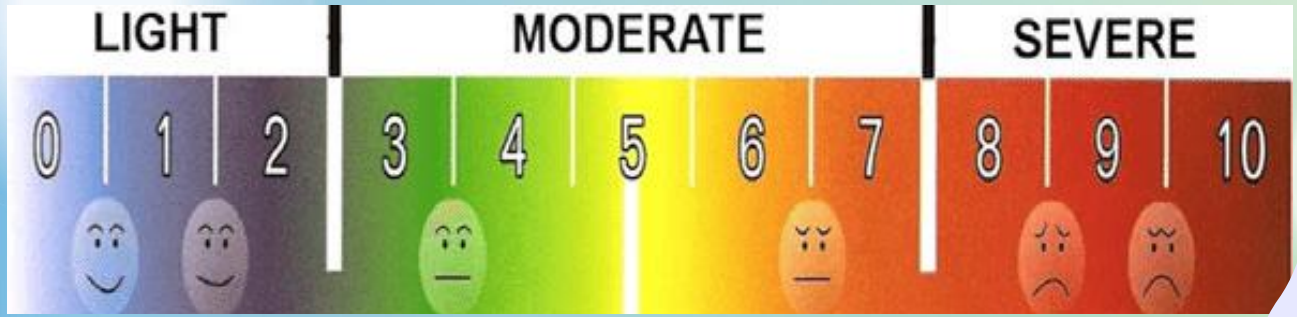
TOTAL SCORE=0–18



Evaluation of nasal symptoms using a 4-digit score

0	*No sign/symptom evident*
1	Mild symptoms (*sign/symptom clearly present, but minimal awareness; easily tolerated*)
2	Moderate symptoms (*definite awareness of sign/symptom that is bothersome but tolerable*)
3	Severe symptoms (*sign/symptom that is hard to tolerate; causes interference with activities of daily living and/or sleeping*)

Visual analog scale (VAS) or Visual rating scale (VRS)



PROS: Quick and easy

CONS: Recall bias; small improvements won't be detected

Objective Clinical Tools

- Does the patient have pulmonary data?
  - Asthma Control Test (ACT)
  - Peak expiratory flow
  - Forced expiratory volume in 1 second (FEV1)
  - Methacholine bronchial provocation test has not been shown to be helpful

- Has the patient's medication usage decreased?
  - Decreased dosage or frequency of antihistamines?
  - Decreased repertoire of medication needed?
  - Decreased prescription refills?

Quality of Life Questionnaires

GENERIC QoL QUESTIONNAIRES	VALIDATING STUDIES
Medical Outcome Study Short Form-36	Stewart et al, Ware and Sherbourne
Medical Outcome Study Short From-20	Carver et al
Munich Life Dimension List (MLDL)	Kremer et al
Work Productivity and Activity Impairment Questionnaire (WPAI)	Prasad et al
DISEASE-SPECIFIC QoL QUESTIONNAIRES	**VALIDATING STUDIES**
Asthma Quality of Life Questionnaire	Juniper et al
Mini Asthma Quality of Life Questionnaire	Juniper et al
Asthma Questionnaire 30	Barley et al
Asthma Questionnaire 20	Barley et al
Rinoconjunctivitis Quality of Life Questionnaire	Juniper and Guyatt
Mini-Rhinoconjunctivitis Quality of Life Questionnaire	Juniper et al
Pediatric Rhinoconjunctivitis Quality of Life Questionnaire	Juniper et al
Rhinasthma	Baiardini et al

Generic and Disease-specific QoL questionnaires

PRO

GENERIC QoL
- globally assessed independently from the specific, underlying disease

DISEASE-SPECIFIC QoL
- valuable tools in finding small, but clinically relevant changes

CON

GENERIC QoL
- very little depth of assessment
- insensitive and often unresponsive to changes that might be small
- the effect on QoL may be different in children and adolescents

DISEASE-SPECIFIC QoL
- only evaluates QoL as related to AR symptoms but not to allergic asthma
- the effect on QoL may be different in children and adolescents

Technology to Enhance Patient Engagement

Use of Mobile Apps: To track symptoms and medication use
Benefits: Real-time data collection, improved patient adherence
Challenges: Requires continuous engagement and tech-savviness of patients
Examples: Apps that allow symptom logging and medication reminders
Outcome Impact: Potential for more personalized and responsive treatment adjustments

Assessing Outcomes

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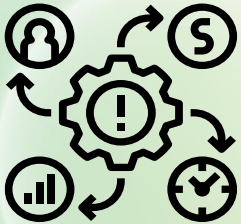


Patient Preference

Biomarkers

- IgE levels and specific IgE
  - Initial rise and then decrease in specific IgE
  - Not recommended: Does not correlate to clinical symptoms
- Allergen-specific IgG4 levels
  - Controversial
- Ratios
  - sIgG4/sIgE
  - sIgE/total IgE
  - Conflicting efficacy
- Nasal smears and biopsy for tissue inflammatory cells
  - Decreased accumulation of eosinophils and CD41 cells as well as a significant increase in cells expressing mRNA for IFN-gamma
- Eosinophil count and other inflammatory markers
  - Decreased eosinophil count and reduced inflammatory markers indicate a positive response to immunotherapy

Integration of Immunologic Markers

Why Use Immunologic Markers: To assess the underlying changes in immune response due to AIT
Examples of Markers: Specific IgE and IgG4 levels, eosinophil count, cytokines
Utility in Clinical Practice: Helps in understanding the mechanistic effects of AIT and tailoring therapy
Limitations: Not always correlated directly with clinical symptoms and outcomes
Future Direction: Potential markers for predicting response to therapy

Testing

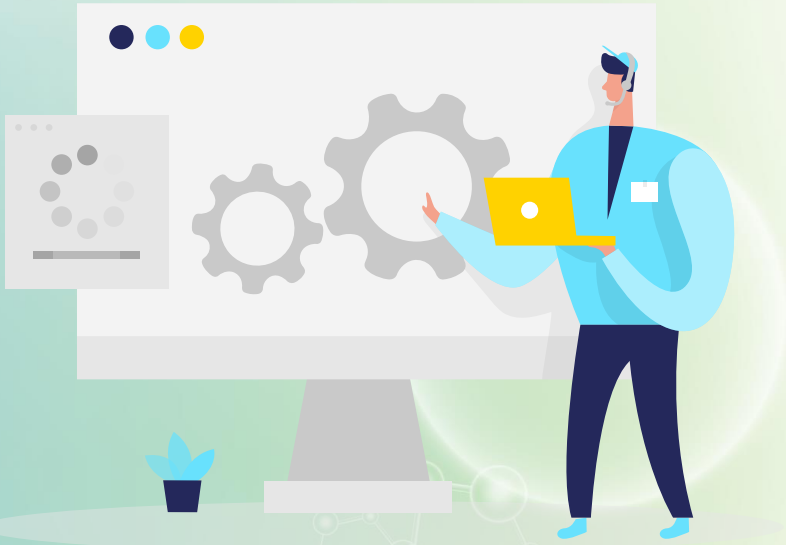
- Skin Prick Testing (SPT)
  - Possible surrogate to biomarkers such as mast cells and specific IgE
  - Further research is needed for use in clinical decision making
  - Not recommended- does not correlate to clinical symptoms
- Nasal Provocation Testing
  - Reproduces response of the upper airways to allergen exposure under controlled and reproducible conditions
  - Time consuming and laborious
- Conjunctival Provocation Testing
  - Very sensitive test
- Allergen Challenge Chambers
  - Reproduce conditions with sensitivity and specificity
  - Lacks the extended exposure seen in “real life”
- Sting challenge
- Food challenge

Food AIT Outcomes

TABLE 1 | Immunological markers and their potential predictive value in food AIT.

Biomarker	Predictor for successful AIT*	Marker during/ at the end of AIT	Marker for SU
Functional tests			
SPT	+ (↓)	+++ (↓)	+(↓)
CD63 (BAT)	+ (↓)	+++ (↓)	+ (↓)
Humoral responses			
sIgE	+ (↓)	+++ (↑→↓) Early increase followed by decrease	+ (↓)
sIgE/total IgE ratio	+ (↓)	(+)(↓)	++ (↓)
Specific IgG4	+ (↑)	+++ (↑)	++ (↑)
IgG4/IgE ratio	(+)(↑)	+++ (↑)	++ (↑)
IgA	+/- (↑ and ↓)	+++ (↑)	(+) (↑)

**The smaller (↓) or higher (↑) the better chance of success.*
+indicates the biomarker changes during AIT or differs between responders vs. no-responders.
-indicates the biomarker does not change during AIT or does not differ between responders vs. no-responders
+, one study/weak evidence.
++, two studies/medium level of evidence.
+++, at least three studies showing the same thing/strong evidence.
This table only lists immunological markers that were reported to have predictive value for desensitization (successful AIT), sustained unresponsiveness (SU), or that showed significant changers during AIT in at least two studies.



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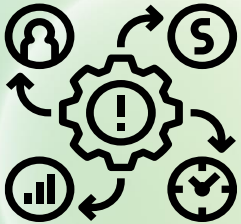


Patient Preference

Longitudinal Assessment

Purpose: To maintain consistency in outcome assessment over long treatment periods

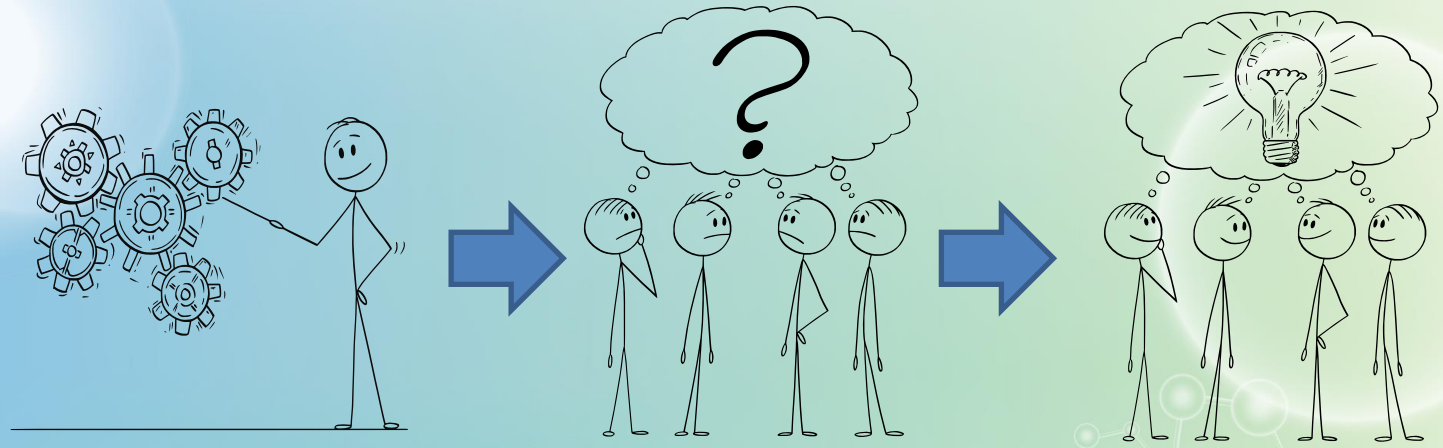
Components: Regular intervals for testing, standardized scoring systems

Impact on Research and Practice: More reliable data, better comparisons across studies and practices

Challenges: Requires commitment from patients and resources from practices

Examples: Use of Rhinoconjunctivitis Quality of Life Questionnaire at 6-month intervals

Shared Decision Making



Information Sharing

Deliberation

Plan

The Future: Using AI

Purpose: Using historical data to predict outcomes and refine treatment protocols

Data Inputs: Symptom scores, medication use, quality of life assessments

Technology Utilized: Machine learning models to analyze patterns

Potential Benefits: Personalized treatment plans, predictive adjustments before clinical symptoms exacerbate

Challenges and Considerations: Data privacy, need for extensive data collection

Eastern Allergy Conference – Takeaways

1. Personalized Approach: Tailoring the length of treatment to individual patient responses ensures optimal outcomes, with a focus on achieving long-term tolerance to allergens, but typically 3-5 years of therapy.

2. Comprehensive Evaluation: Monitor progress and adjust treatment strategies, aiming for a significant reduction in symptom severity and medication use.

3. Patient-Centric Goals: Prioritize understanding and incorporating patient preferences in treatment plans to enhance satisfaction and adherence, fostering a collaborative and informed decision-making process.

35-year-old female has been undergoing allergen immunotherapy for the past 2 years to manage their severe pollen allergy. She reports a significant reduction in symptom severity but expresses a desire to shorten the treatment duration due to personal reasons. How should the healthcare provider proceed?

a. Discontinue the treatment immediately without further evaluation.
b. Adjust the treatment plan without considering the potential implications on the patient's health.
c. Discuss the potential risks and benefits of modifying the treatment duration and make a collaborative decision with the patient.
d. Ignore the patient's preference and continue with the current treatment plan.
e. Increase the intensity of the treatment to speed up the process without assessing the patient's tolerance level.

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60-year-old individual, is about to start allergen immunotherapy. They are interested in understanding the potential outcomes of the therapy. What should be highlighted as a potential positive outcome?

a. Temporary relief from symptoms
b. Development of new allergies
c. Long-term tolerance to specific allergens
d. Increased use of allergy medications
e. Frequent need for emergency interventions

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Question Or Comment ?

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