

Accepted Manuscript

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PII: S1081-1206(19)30188-7

DOI: <https://doi.org/10.1016/j.anai.2019.03.009>

Reference: ANAI 2847

To appear in: *Annals of Allergy, Asthma and Immunology*

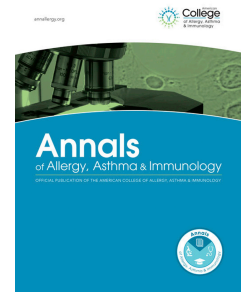
Received Date: 17 October 2018

Revised Date: 5 March 2019

Accepted Date: 7 March 2019

Please cite this article as: Stone B, Charap E, Black HL, Understanding Patient Experiences with Allergen Immunotherapy: “Living with Allergies Study”, *Annals of Allergy, Asthma and Immunology* (2019), doi: <https://doi.org/10.1016/j.anai.2019.03.009>.

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Understanding Patient Experiences with Allergen Immunotherapy: “Living with Allergies Study”

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Disclosures

B. Stone has served as a consultant and received research support from ALK-Abelló. E. Charap is a former employee of inVentiv Health, which provided contracting services for Merck & Co., Inc., Kenilworth, NJ, USA. H.L. Black is an employee of Merck & Co., Inc., Kenilworth, NJ, USA.

Funding

Funding for this study was provided by Merck & Co., Inc., Kenilworth, NJ, USA.

Role of Sponsor

The study sponsors participated in the design of the study, participated in the analysis and interpretation of the data, and participated in the writing of the report. The authors made the final decision to submit the article for publication.

Keywords: adherence; barriers; allergen immunotherapy; subcutaneous immunotherapy; sublingual immunotherapy; shared decision making

For patients with allergic rhinoconjunctivitis (AR) who are considering allergen immunotherapy (AIT), uncertainty over treatment choice due to whether the treatment fits with one's values and lifestyle may be common and problematic. Furthermore, a review of AIT adherence found that premature discontinuation occurred at rates ranging from 6% to 84% for subcutaneous immunotherapy (SCIT) and 21% to 93% for sublingual immunotherapy (SLIT).¹ Although shared decision making (SDM) between physicians and patients has been shown to impact adherence in other therapeutic areas,^{2,3} there is little insight into the role it may or may not play in patient decisions about AIT. The "Living With Allergies" study was conducted to better understand the barriers to AIT initiation and adherence by interviewing patients regarding their experience with AIT.

The study consisted of 30-minute semi-structured cognitive interviews by telephone of adult English-speaking patients with AR from a nation-wide allergy practice who had been recommended SCIT or SLIT within the past 3 years. The cognitive interviews⁴ were conducted to help patients recall their initial diagnostic and treatment decision conversations with their allergists. A stratified sample plan based on AIT use stage (never started, dose escalation, maintenance) and type (SCIT or SLIT) was created. A modified grounded theory approach was used in the development of the interview guide to elicit themes and formulate testable hypotheses for future research.⁵ Moderators were behavioral scientists trained and encouraged to probe on concepts, themes, metaphors, and other lexical data as they emerged de novo throughout interviews. As the study team generated hypotheses and questions about barriers and their interactive relationships, moderators adapted the interview guide to probe more deeply into these new questions. A constant comparison analysis approach was used, terminating recruitment on a

stratum-by-stratum basis as coders indicated that no new themes were emerging from the data (ie, saturation). Analytic comparisons within and between patients grouped into “adherent/mostly adherent” and “non-adherent/non-start” cohorts were conducted.

In all, 150 patients from across the US were recruited; 121 patients completed the interviews and 29 patients had partial interviews. The majority of respondents were white (78.7%) and female (70.6%; **Supplemental Table E1**).

We first compared responses of patients who reported adherence to AIT (n=70) to those categorized as non-adherent/non-start (n=80). Adherent patients more often than non-adherent/non-start patients used language indicating perceived very severe AR (61.8% vs 25.0%, respectively). Adherent patients also tended more often than non-adherent patients (43.2% vs 13.1%, respectively) to recount having been driven to see an allergist by a traumatic event (e.g., sinus surgery, embarrassment at work, etc). Additionally, adherent patients more often perceived their AR as a constant problem, whereas non-adherent/non-start patients more often perceived their AR as a seasonal and minor nuisance.

When we discussed various hypothesized barriers to adherence, non-adherent/non-start patients stated that they had not just been less willing to pursue AIT, but also less able. Inconvenience relating to SCIT (87.9%), high cost of any AIT treatment (56.1%), and uncertainty about dosing schedule and/or duration of treatment (34.8%) were the most common barriers to AIT persistence (**Supplemental Table E2**). Adherent patients often were older, had no children or grown children, and were financially secure. The high cost of SLIT presented a significant

barrier to care, especially since it may not be covered by health insurance plans. The “hidden costs” of SCIT can also present an adherence problem, especially for those who may be in lower socioeconomic strata. Convenience, rather than cost, was more of a burden for late discontinuers and those who were irregular in their adherence.

Over half (61.3%) of adherent patients reported that during the initial visit and prior to doing a skin test, their allergist elicited their medical history, the physical and emotional experience of their allergies, and their treatment goals. Adherent patients highlighted the importance of healthcare provider empathy. In contrast, the majority (79.7%) of non-adherent/non-start patients reported that during the initial visit their allergist elicited only their medical history and their symptoms. Most non-adherent patients did not recall being asked about their treatment goals. Patients reported that they discontinued AIT because they initially believed that they could commit to AIT, but ultimately could not. We looked at differences in recalled decision making between those prescribed SCIT (n=80) and those prescribed SLIT (n=42), modes of administration which differ substantially in terms of time/convenience (in-office vs at-home dosing) and cost. Patients prescribed SLIT reported more conversational elements that are commonly aligned with SDM than those prescribed SCIT (**Table 1**). Patients who were adherent more commonly said that they felt they had been given adequate information about AIT, while patients prescribed SCIT more commonly said that they wished they had known more details about the treatment before starting:

INTERVIEWER: “What information do you wish that you knew back then that you know now?”

PATIENT: “That there would be so many build-up shots.”

Adherent patients more frequently reported having discussed barriers to different treatments with their allergists prior to making a final treatment decision and demonstrated greater certainty around dosing frequency and timing. When patients shared their treatment goals and limitations with their allergists, allergists were able to work with them to target AIT type to the patient's day-to-day life; when these topics went unaddressed, many patients could not fit AIT treatment logistics into their lives.

The findings of this study suggest that doctor-patient conversations play an important role in AIT use and adherence and that their structure likely interacts with cost and convenience barriers. Uncertainty about dosing schedule and duration of AIT was reported as a treatment barrier by one third of patients. We submit that education about AIT is a process, not an event, and reinforcing key educational points needs to be a focus at each visit, not just the initial consult. Eliciting information on the patients' treatment goals, values, and details of daily life during a SDM process can help allergists target to each patient the best treatment for them, potentially easing barriers to AIT before they ever lead to discontinuation. This can improve decisions regarding disease management, increase efficiency for allergists, and, most importantly, improve health outcomes.

Acknowledgments

Funding for this study was provided by Merck & Co., Inc., Kenilworth, NJ, USA. The authors would like to acknowledge Jeff Brodscholl and Kathleen Starr of Syneos Health (formerly inVentive Health) for their contributions to the study. Medical writing and editorial assistance were provided by Erin P. Scott, PhD, of Scott Medical Communications, LLC. This assistance was funded by ALK, Hørsholm, Denmark.

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Table 1. Frequency of conversational elements of SDM for patients prescribed SLIT vs SCIT.

Conversational element of SDM	SLIT, %	SCIT, %
Eliciting patient treatment goals	36.8	15.8
Describing all treatment options	42.1	21.0
Discussing dosing frequency and schedule for all treatment options	42.1	47.3
Eliciting potential barriers to adherence for each option	15.8	42.1
Helping the patient to choose the option that best fits into their life	15.8	36.8
SCIT, subcutaneous immunotherapy; SDM, shared decision making; SLIT, sublingual immunotherapy		

Supplemental Information

Methods

Ethics

Interview participants were identified through a clinic research staff review of patient treatment records. Interviews were conducted on a recorded, private conference line. Patients were informed in the consenting process that interviews were recorded to ensure specificity and accuracy in analysis and quotation. The study was approved in September of 2015 by the Copernicus Group/Western IRB (CGIRB-WIRB).

Interview process

A modified grounded theory approach was used in the development of the interview guide to elicit themes and formulate testable hypotheses for future research.¹ The modifications made allowed for formulation of some a priori assumptions about possible barriers and motivators to AIT use based on the general medical adherence literature; these a priori assumptions provided a structure and flow to the discussion and coding guides. Moderators were trained and encouraged to probe on concepts, themes, metaphors, and other lexical data as they emerged de novo throughout interviews.

Full and partial interviews were conducted. Partial interviews were due to interrupted cell phone reception on the part of respondents and other technical difficulties. Partial interviews were only included for analysis when they included enough relevant data to systematically compare to other complete interviews.

Coding process

Stepwise comparative analysis of identified codes was conducted for each interview.

Moderators/coders were trained in the therapeutic area by a clinical expert and in specifics of qualitative interviewing and coding by the primary investigators of the study. Moderators met weekly by phone to discuss and negotiate codes; two other larger study team-level coding meetings were held for the purposes of data interpretation and hypothesis generation. As the study team generated hypotheses and questions about barriers and their interactive relationships, moderators adapted the interview guide to probe more deeply into these new questions.

All recordings of interviews were coded with NVivo 11; moderators downloaded mp3 files from a secured, protected server and uploaded coded data sets back to that server. The study director merged coding sets into the NVivo client on the secured server for inter-rater reliability checks. NVivo is a qualitative data analysis computer software package produced by QSR International designed for qualitative researchers working with very rich text-based and/or multimedia information. Inter-rater reliability was good (Cohen's Kappa = .896).

Analysis

Each stratum quota was set at 50 patients, for a potential 400 total interviews. Response patterns were analyzed within and between the “adherent/mostly adherent” and “non-adherent/non-start” cohorts. Analytic frameworks included content analysis through constant comparison (CITE)² and linguistic analysis. No statistical comparisons between cohorts were conducted as this was a qualitative study.

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1 **Supplemental Table E1.** Patient demographics.

Demographic Variable	Total, N=150
Age	
Mean, y	48.1
Range, y	21-81
Male, n (%)	44 (29.3)
Race, n (%)	
American Indian/Alaskan Native	2 (1.3)
Asian	6 (4.0)
Black	18 (12.0)
White	118 (78.7)
Other	2 (2.7)
Unreported	3 (2.0)
Ethnicity, n (%)	
Hispanic	15 (10.0)
Non-Hispanic	129 (86.0)
Unreported	7 (4.7)
Insurance status, n (%)	
Private insurance	115 (76.7)
Public insurance (ie, Medicaid)	32 (21.3)
Unreported	4 (2.7)
State, n (%)	
California	17 (11.3)
Georgia	2 (1.3)
Missouri	2 (1.3)
North Carolina	62 (41.3)
New Mexico	27 (18)
Nevada	8 (5.3)
Oregon	1 (0.7)
South Carolina	16 (10.7)
Tennessee	2 (1.3)
Texas	1 (0.7)
Virginia	12 (8.0)
AIT recommended, n (%)	
SCIT	97 (64.7)
SLIT-tablets	20 (13.3)
SLIT-drops	24 (16.0)
Unreported	15 (10.0)
Treated seasonally, n (%)	7 (4.7)

Presence of asthma, n (%) 58 (38.6)

Presence of atopic dermatitis, n (%) 18 (12.0)

SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy

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23 **Supplemental Table E2.** Barriers to AIT use and adherence in patients who dropped or didn't
 24 start AIT and provided responses.

	n (%)
AIT Barriers	(n=66)
Inconvenience (SCIT)	58 (87.9)
Cost	37 (56.1)
Uncertainty about dosing schedule or treatment duration	23 (34.8)
Adverse events	21 (31.8)
Perceived lack of efficacy	16 (24.2)
Insurance coverage (either lack of insurance or insurance does not cover SCIT/SLIT)	14 (21.2)
Poor follow through/relationship with clinic (either patient or clinic follow through)	13 (19.7)
Perceived success	6 (9.1)
Perceived plateau	3 (4.5)
Taste (SLIT drops only)	1 (1.5)

25 AEs, adverse events; AIT, allergen immunotherapy; SCIT, subcutaneous immunotherapy; SLIT,
 26 sublingual immunotherapy.

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