

Allergen immunotherapy at university health services and allergist's reasons for guidelines nonadherence

Marilyn Karam, M.D.,^{1,2} Christine Holland, M.D.,² Zi Yang, B.S.,³ Kiela Samuels, Pharm.D.,^{2,4} and Georgiana Sanders, M.D., M.S.²

ABSTRACT

Background: Our previous pilot study conducted at the University of Michigan Health Services showed that fewer than 25% of the non-university allergen immunotherapy (AIT) prescribers adhered to AIT labeling guidelines which impacted both patients and healthcare personnel involved in AIT administration.

Objectives: We expand our study to characterize AIT labeling compliance and impact of practice variability at the "Big 10" University Health Services, and investigate prescribers motives for nonadherence to practice parameter guidelines.

Methods: Three online surveys were distributed: AIT Administrator and Manager surveys for healthcare personnel at the "Big 10"; University Health Services and Physician Survey for physician members of the AAAAI. Data were analyzed using frequency/bivariate analysis and logistic regression.

Results: 21 AIT administrators from 10 University Health Services responded. 90.4% (20/21) felt labels containing all recommended practice parameter guidelines, components would decrease error; and standardization of labels, buildup and missed dose schedules would increase workflow efficiency (76%; 16/21). 90% (17/19) felt standardized protocols for treatment of systemic reactions would increase patient safety, workflow efficiency and comfort level of administrators. Only 28.6% of AIT extract vial labels at University Health Services were in accordance with practice parameter guidelines. Despite familiarity with the guidelines (91.5%; 697/762), only 64% (488/762) of surveyed physicians had practice parameter adherent AIT extracts labels with higher odds of a complete label when physicians were in group practice (odds ratio 1.51; [95% confidence interval, 1.06–2.15]; $P=0.02$). Reasons for nonadherence included having personalized labeling systems (55.4%, 174/314), unfamiliarity (14%, 44/314) and disagreement (9%, 29/314) with practice parameter guidelines.

Conclusion: Poor adherence with AIT practice parameters labeling guidelines is an important concern in nonallergy offices. It is imperative that allergists comply with the highest recommended standards to provide the best clinical outcomes and ensure excellent and efficient care in both allergy and non-allergy offices.

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Providing the best possible allergen immunotherapy (AIT) clinical outcome requires the provision of high-quality and safe AIT extract preparation and labeling. Over the past 12 years, there have been three sets of published AIT guidelines,^{1–4} the most recent being the third AIT practice parameter (PP) update published in 2011 by the American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma and Immunology,

and the Joint Council on Allergy, Asthma and Immunology.⁴ Additional references are available for AIT extract prescribers or preparers, including allergen extract manufacturer preparation manuals,^{5–7} the United States Pharmacopeia's General Chapter 797⁸ and journal articles.^{5–7,9}

The AIT PPs recommends that all extract vial labels should contain two or more patient identifiers (PI), the expiration date or beyond-use date, abbreviations or names of allergen content or a link to a document that lists specific allergen content, and the concentration of each vial listed in a volume-to-volume (v/v) format of 1:1 that indicates the maintenance concentrate.^{1–4} During the buildup phase of immunotherapy, several dilutions of the patient's maintenance concentrate are needed. Guidelines recommend using a color-coding system with a red cap that indicates the 1:1 v/v concentrate, yellow for the 1:10 v/v, blue for the 1:100 v/v, green for 1:1,000 v/v, and silver for the 1:10,000 v/v dilution. An alphanumeric system beginning at "1" or "A" for the maintenance vials may be used instead of a color-coding system; however, these may be a source of confusion for health care personnel who administer

From the ¹Department of Internal Medicine, Division of Allergy and Clinical Immunology, American University of Beirut, Beirut, Lebanon, ²Department of Internal Medicine, Division of Allergy and Clinical Immunology, University of Michigan Health System, Ann Arbor, Michigan, ³Department of Statistics, University of Michigan, Ann Arbor, Michigan, and ⁴University of Michigan School of Pharmacy, Ann Arbor, Michigan

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Address correspondence to Marilyn Karam, M.D., Department of Internal Medicine, American University of Beirut, P.O. Box 11-0236 Riad El-Solh, Beirut 1107 2020, Lebanon

E-mail address: marilynkaram@gmail.com

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allergy injections, especially if one chooses to label in a reverse order with “5” being the concentrate.²⁻⁴

Differences in labeling of AIT extracts can be especially problematic in nonallergy health care settings (such as primary care offices or university health services [UHS]) where AIT is administered but not prescribed. Little is known about the effects of labeling variations on possible dosing errors and the confusion that results from such variation. In our previous study,¹⁰ we assessed the adherence rate to AIT extract labeling guidelines at the University of Michigan UHS, which provides the opportunity for patients to continue to receive AIT injections from non-University of Michigan, independent providers by using their originally prescribed and mixed serum extract. We showed that only 21% of AIT extract vials were in accordance with the PP guidelines and that the odds of adherence with a “complete label” decreased among this prescribing population in a linear fashion by 4% for each year in practice.¹⁰ A “complete label” was defined as a label that contains all elements recommended by the 2011 PP,⁴ including two PIs, v/v concentration, allergen content, expiration date, and either color or alphanumeric coding. In light of these results, we sought to expand our study to characterize AIT trends and the impact of variability at the “Big 10” UHS members of the Committee of Institutional Cooperation,¹¹ with the aim to contrast and compare with our previous findings. In addition, we also investigated potential reasons why AIT prescribers would be nonadherent to the guidelines.

METHODS

Three different surveys were designed for electronic distribution and data collection by using SurveyMonkey (Portland, OR). The “AIT Administrator Survey” was a 42-question survey that was sent *via* e-mail to all UHS health care personnel who administer AIT at UHS of the “Big 10” universities, which include the University of Chicago, University of Illinois, University of Iowa, Indiana University, University of Maryland, University of Michigan, Michigan State University, University of Minnesota, University of Nebraska—Lincoln, Northwestern University, Ohio State University, Pennsylvania State University, Purdue University, Rutgers University, and University of Wisconsin—Madison.¹¹ Survey questions inquired about the diversity of labeling on AIT extracts and variability in AIT administration, including variability in buildup or missed dose schedule and treatment of a local or systemic reaction. Questions also tackled the impact of this variability on nursing time spent clarifying directions, dosing errors that affected patient safety, and the level of comfort with the situation for personnel who administer AIT. A 17-question “UHS Manager Survey”

Table 1 Characteristics of respondents AIT administrators and physicians members of AAAAI

Characteristics of Respondents	Respondents, % (no.)
AIT administrators (N = 21)	
RN	90.5 (19)
LPN	9.5 (2)
Administering AIT is a significant part of job description	90.5 (19)
Average shots per day	
≥20 shots	61.9 (13)
<20 shots	38.1 (8)
Physicians (N = 586)	
Group practice	66.2 (388)
Solo practice	33.8 (198)
Time in practice	
<1 y	2.0 (12)
1–5 y	12.8 (75)
6–10 y	16.9 (99)
>10 y	68.3 (400)

AIT = Allergen immunotherapy; AAAAI = American Academy of Allergy, Asthma & Immunology; RN = registered nurse; LPN = licensed practical nurse.

was distributed to clinic managers and was targeted at understanding the flow of the clinic, the amount of time allocated for an AIT injection appointment, the load of patients per day and per AIT administrator, and systems in place to track systemic reactions.

The third “Physician Survey” was electronically distributed, with permission, to the physician members of the AAAAI. Physicians who did not formulate and label their own extracts were excluded. This 10-question survey inquired about demographics, including age, type of practice, and time in practice. The physicians were also asked about their familiarity with the PP guidelines and whether they thought that their extracts were adherent to the guidelines. Reasons and barriers for guideline nonadherence were also queried. Questions of all three surveys included multiple-choice questions and rating questions that used a Likert scale. At the end of each survey, respondents had the opportunity to add subjective comments that they thought were pertinent issues. Electronic informed consent was obtained for all three surveys, and this study was approved by the University of Michigan Medical School Institutional Review Board. Collected data were pooled within the survey software and downloaded to an Microsoft Excel (2010, Redmond, WA) spreadsheet then uploaded into a statistical program for analysis. Data were analyzed by using R environment for descriptive statistics, including frequency analysis as well

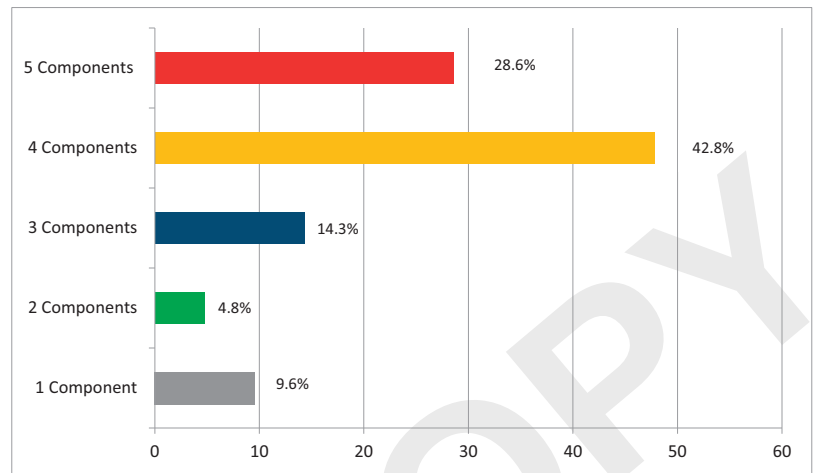


Figure 1. The number of recommended label components on allergen immunotherapy (AIT) vial labels at the different university health services (UHS).

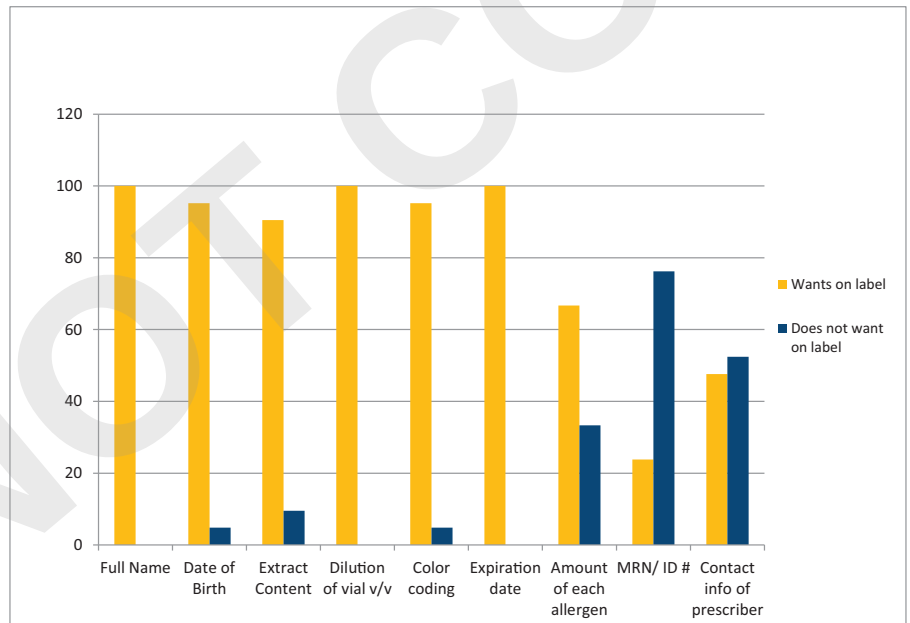


Figure 2. Different components that allergen immunotherapy (AIT) administrators would like to have on an AIT extract vial label.

as bivariate and/or proportional inferential analysis and logistic regression for associative trends. “AIT Administrator” and “UHS Manager” surveys were analyzed separately from the “Physician Survey”.

RESULTS

Nine UHS managers and 21 AIT administrators who treated ~1300 patients from 10 different UHS responded. Ninety percent ($n = 19$) of the AIT administrators were registered nurses and 10% ($n = 2$) were licensed practical nurses. Almost all AIT administrators (90.5% [$n = 19$]) believed that giving AIT injections was a significant part of their job, with an average of ≥ 20 AIT shots per day (62% [$n = 13$]) (Table 1). Most UHS (7/11) did not have an affiliated group of allergists directly involved in patient care, which meant that 75% of the patients at UHS received AIT prescribed at a distance by physicians not associated with the UHS. The process that led to AIT administration

varied among UHS. Although all UHS required that the patients provided a complete checklist of information before initiating AIT, the administrators still thought the need, 57% of the time, to clarify and obtain additional information from nonaffiliated prescribing physicians regarding AIT content, buildup dosing, reaction treatment, and dosing adjustment after systemic reactions. Before initiation of AIT, the prescriptions were reviewed by UHS physicians in 30% of the cases (3/11) and, rarely, by an allergist, in 10% of the cases (1/11). Onsite supervision for AIT administration was provided at almost all UHS (94% [10/11]); however, the supervisor was physically present in the suite when the AIT was being administered only 58% of the time. Only 7 of 11 UHS tracked systemic reactions, with an estimate of 0–1 reactions per month.

Times allotted for AIT injections varied from 5 minutes (one UHS) to 30 minutes (one UHS), with an average time of 15 minutes. The main reason given for

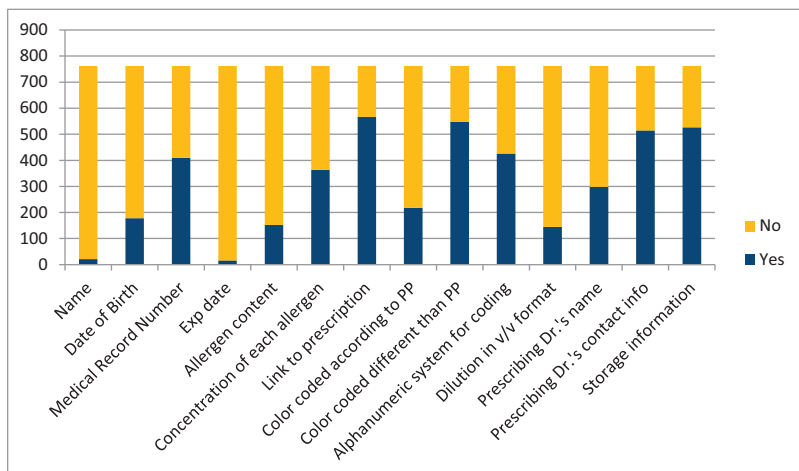


Figure 3. Different components on prescribing physicians' allergen immunotherapy (AIT) extract vial label. Exp = Expiration date or beyond-use date; PP = practice parameter.

the extended time allocated was the tedious work required before giving the AIT injection, including checking the vials and assessing the patients. All the patients were routinely asked about any recent illnesses or any reactions during their last AIT shot, but fewer patients were asked about asthma flares, changes in medications, or an increase in allergy symptoms. The patients were required to stay in the clinic for 20–30 minutes, although there was no actual method to keep time (90% [19/21]). Also, 76% of the patients (16/21) were not required to carry their self-injectable epinephrine with them despite the fact that they were receiving immunotherapy at a distance from the prescribing physician.

When looking at the AIT extract vial labels, 70% of them were missing one or more of the following recommended components: two PIs, dilutions of the extract in volume/volume (v/v) format with its corresponding color coding, vial allergen content, and expiration date (Fig. 1). Twenty of 21 respondents (90.4%) believed that the labels that contained all the latter components would decrease error when administering AIT, with two PIs specifically referring to the patient's name and date of birth (Fig. 2). In contrast, most respondents ($n = 16$ [76%]) did not think that registration or college number (identification numbers), contact information of the prescribing physician, or the amount of each allergen in the extract were necessary to decrease error. The respondents also indicated that standardizing AIT extract labels, buildup, and missed dose schedules would increase workflow efficiency (76% [16/21]). Of the AIT administrators, 89.5% (17/19) thought that standardizing the protocol for treatment of systemic reactions would also increase patient safety, workflow efficiency, and their comfort level as AIT administrators (Fig. 3).

Given that only 28.6% of AIT extract vial labels were in accordance with PP guidelines, we surveyed physician members of the AAAAI to inquire about their

experiences and opinions pertaining to AIT extract vial labeling. With permission from the AAAAI, we sent the survey to 3578 practicing members and received 952 responses, which equated to a 26.6% response rate (Table 1). Eighty-five percent of the responding physicians (586/692) formulated their own AIT at their offices. Of these physicians, most had been in practice for >10 years (68.3% [400/586]) and were in a group practice (66.2% [388/586]), whereas only 2% of them (12/586) were practicing for <1 year. A good proportion of the physicians (36% [211/586]) had at least 10% of their patients receiving AIT injections at remote locations, such as a UHS or primary care physician's office. Yet, only 64% (375/586) always provided the recommended information required for the safe administration of AIT when their patient's care was transferred to a different provider or location, whether temporarily or permanently.

The majority of physicians were familiar with the PPs (91.8% [538/586]); however, only 64% (375/586) had AIT extract labels that were actually adherent with the guidelines (Fig. 3). Overall, the odds of having a "complete label" were higher when the prescribing physician was in a group practice (odds ratio [OR] 1.51 [95% confidence interval {CI}, 1.06–2.15]; $p = 0.02$). Labels with two PIs had 2.22 times higher odds of having both a v/v concentration listed and its corresponding color coding (OR 2.22 [95% CI, 1.36–3.61]; $p = 0.001$). Labels that specified the extracts' content were more likely to have the v/v concentration listed (OR 6.29 [95% CI, 3.61–10.94]; $p < 0.0001$) or both the v/v concentration and the corresponding color coding (OR 5.36 [95% CI, 3.10–9.27]; $p < 0.0001$) (Table 2). Among the physicians who were familiar with the PPs and who identified their AIT extract labels as being adherent to guidelines, only 77% (283/367) had a "complete label." The time in practice overall had negative effects on the individual entities of a complete label, but only the negative effect on having two PIs

Table 2 Trends of AIT extract vial labeling

Trend	OR (95% CI)	<i>p</i>
If two PIs were present		
v/v listed	2.29 (1.39–3.77)	0.001
Color-coding present	2.94 (1.06–8.16)	0.038
Had both v/v and color coding	2.22 (1.36–3.61)	0.001
If content present		
v/v listed	6.29 (3.61–10.94)	<0.001
Color-coding present	1.13 (0.25–5.07)	0.84
Had either v/v or color coding	5.36 (3.10–9.27)	<0.001

AIT = Allergen immunotherapy; OR = odds ratio; CI = confidence interval; PI = patient identifier; v/v = volume to volume.

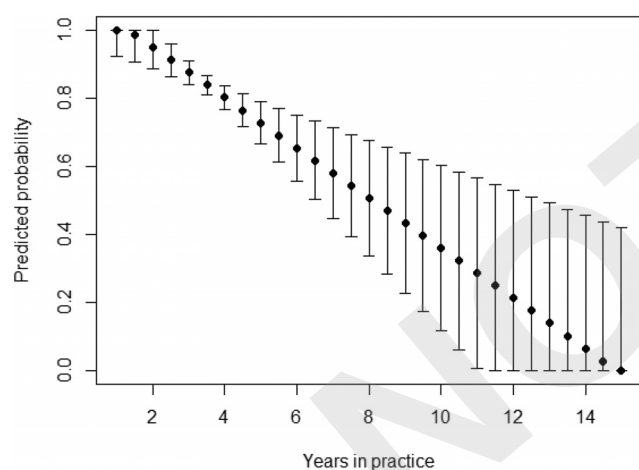


Figure 4. Predicted probability of two patient identifiers (PI) labeling compliance. The relationship between compliance with allergen extract labels that contain two PIs as a function of the number of years of practice. Error bars represent 95% confidence intervals.

reached statistical significance (OR 0.46 [95% CI, 0.31–0.70]; $p < 0.001$) (Fig. 4). Reasons for current nonadherence varied and included having personalized labeling systems (26.1% [55/211]), having joined practices that have their own labeling systems (11.4% [24/211]), being unfamiliar with the guidelines (9.5% [20/211]), and disagreeing with these later (6.6% [14/211]). Some respondents also pointed out that they were transitioning to the newer labeling guideline; however, 15% (31/211) noted that they had been trying to do so for >3 years.

DISCUSSION

In the >100 years since the successful introduction by Noon¹² in 1911, AIT has been an essential feature of the clinical allergy practice. Much effort has been channeled toward reducing and preventing systemic reac-

tions,^{5,13,14} standardizing dosing regimens for selected antigens, establishing more efficient compounding processes, and standardizing labeling guidelines to enhance communication and improve safety. However, to our knowledge, our previous article was the first to assess the variability in labeling AIT extract vials and potential safety concerns when these extracts are administered in offices remote to the prescribing allergist.¹⁰ UHS accommodate students from varied geographic locations to continue already established AITs as evidenced in our study, in which 75% of patients cared for at the “Big 10” UHS received AITs prescribed elsewhere. Results of our previous study at University of Michigan UHS showed that only 21% of the AIT prescribers were adherent to AIT PP labeling guidelines.¹⁰

Similarly, this study indicated that this was a generalizable concern because only 28% of AIT extract vial labels in the responding “Big 10” UHS were in accordance with labeling guidelines. A detailed documentation of the patient’s schedule and allergen extract content must be provided when a patient transfers responsibility for immunotherapy care from one physician to another,⁴ yet only 64% of physicians readily provide this information. Poor guideline adherence raises concerns at many levels, including patient safety, workflow efficiency, and AIT administrators’ comfort level when administering AIT injections, as clearly reflected in our results. Although AIT reactions were estimated at only one to two reactions per month, 4 of 11 UHS did not formally track their AIT reactions, and, 90% of the time, there was no system in place to monitor whether patients stay the recommended 30 minutes after the injection, which potentially caused an underestimate of the actual reaction rate. The low estimate of reactions might also be attributed to the experienced administrators and the lengthy time allotted to the visits. In fact, some respondents noted that policies were put in place that extended the time of an AIT injection appointment to 30 minutes to avoid errors. Evidently, this led to workflow inefficiency because AIT administrators spent more than half of their time calling AIT prescribing physicians to clarify or obtain additional information pertaining to AIT content, dosing, and treatment of reactions; a situation that could certainly be avoided by adhering to a unified labeling and AIT administration protocol.

Despite widespread knowledge about AIT PPs, a significant proportion of the physicians still did not comply with the recommended guidelines and noted that they had personalized labeling systems. Although physicians may argue that personalized systems do not pose concerns for patient safety in their offices, this may not translate to external practices. PPs indicate that transition to the recommended labeling system should be done gradually to reduce potential error, but

analysis of our data raised concerns that practices were lingering and that transition may not be occurring because more than half of the respondents noted that they had been transitioning for >3 years. There were several limitations to this study. Surveys are subjected to participation bias, and some physicians noted that colleagues in the same practices who did not have “complete labels” willingly declined participation in the survey. This study explored differences in adherence to AIT extract vial labeling recommendations at the “Big 10” UHS, it did not investigate if nonadherence actually led to a higher rate of adverse reactions. Although further studies are needed to generalize our findings, we propose that similar results would occur because we sampled a geographically diverse population.

CONCLUSION

To our knowledge, this was the first study that explored adherence to AIT extract labeling guidelines at the “Big 10” UHS and was the first to address providers’ personal views and reasons for nonadherence to these guidelines. It is imperative as AIT prescribing and compounding practices come under more scrutiny that allergists comply with the highest recommended standards to provide the best clinical outcomes.

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